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Quantitative Risk and Exposure Assessment for Carbon Monoxide - Amended

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Quantitative Risk and Exposure Assessment for Carbon Monoxide - Amended

U.S. Environmental Protection Agency
Office of Air Quality Planning and Standards
Health and Environmental Impacts Division
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PREFACE

This amended *Quantitative Risk and Exposure Assessment for Carbon Monoxide* (CO REA) contains revised results reflecting corrections to one of the input variables used in the dose model to generate estimates of carboxyhemoglobin (COHb). Modeling results presented in the May 2010 CO REA were generated with erroneous values for altitude for both the Los Angeles and Denver study areas. This error has been corrected and the model simulations repeated resulting in increases to the COHb estimates in both study areas. These increases, in terms of the ambient contribution to COHb levels, were small for the Denver study area and negligible for the Los Angeles study area, with somewhat larger increases to the total COHb estimates. Because altitude was not used in calculating exposure estimates, none of the exposure results previously presented were affected by this error. The sections of the REA revised to reflect the corrected dose estimates include several tables and associated text in chapters 5, 6, 7 and 8 and Appendix B. The specific areas of the report containing revisions to address this error include section 5.10.4 (Table 5-27), section 6.2 (Tables 6-15 through 6-23, Figures 6-5 and 6-6), section 6.3 (Tables 6-24 and 6-25), section 7.2.1.2 (Table 7-4), section 7.2.2 (Tables 7-5 through 7-8, 7-10, 7-11, and 7-14), chapter 8 and Appendix B.6 (Tables B-4 through B-6, Figures B-2 through B-5). In addition, the presentation of exposure estimates has been modified to reflect a correction to the rounding convention for percentages of the population less than 0.1%. Previously, values between 0.05 and 0.09% were rounded upwards to 0.1%. This correction is reflected in the presentation of exposure estimates in Tables 6-4, 6-7, 6-10, 6-13, and 6-14.

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1 INTRODUCTION

This document, *Quantitative Risk and Exposure Assessment for Carbon Monoxide,* describes the quantitative human exposure assessment and risk characterization being conducted to inform the U.S. Environmental Protection Agency's (EPA's) current review of the National Ambient Air Quality Standards (NAAQS) for carbon monoxide (CO). Given the significant time constraints of this review,[1] results of the analyses are provided in this document without substantial interpretation. Rather, interpretative discussion of these results is provided in the Policy Assessment document for the review (US EPA, 2010a).

1.1 BACKGROUND

The EPA is presently conducting a review of the national ambient air quality standards for CO. Sections 108 and 109 of the Clean Air Act (Act) govern the establishment and periodic review of the NAAQS. These standards are established for certain pollutants that may reasonably be anticipated to endanger public health and welfare, and whose presence in the ambient air results from numerous or diverse mobile or stationary sources. The NAAQS are to be based on air quality criteria, which are to accurately reflect the latest scientific knowledge useful in indicating the kind and extent of identifiable effects on public health or welfare that may be expected from the presence of the pollutant in ambient air. Based on periodic reviews of the air quality criteria and standards, the Administrator is to make revisions in the criteria and standards, and promulgate any new standards, as may be appropriate. The Act also requires that an independent scientific review committee advise the Administrator as part of this NAAQS review process, a function performed by the Clean Air Scientific Advisory Committee (CASAC).

The current NAAQS for CO includes two primary standards to provide protection for exposures to carbon monoxide. In 1994, EPA retained the primary standards at 9 parts per million (ppm), 8-hour average and 35 ppm, 1-hour average, neither to be exceeded more than once per year (59 FR 38906). These standards were based primarily on the clinical evidence relating carboxyhemoglobin (COHb) levels to various adverse health endpoints and exposure modeling relating CO exposures to COHb levels. With the 1994 decision, EPA also reaffirmed an earlier decision that the evidence did not support the need for a secondary standard for CO (59 FR 38906).

A subsequent review of the CO NAAQS was initiated in 1997, which led to the completion of the 2000 *Air Quality Criteria Document for Carbon Monoxide* (US EPA, 2000;

[1] As noted below, the schedule for this review is governed by the terms of a court order.

henceforth referred to as the 2000 AQCD) and a draft exposure analysis methodology document (US EPA, 1999). EPA put on hold the NAAQS review when Congress requested that the National Research Council (NRC) review the impact of meteorology and topography on ambient CO concentrations in high altitude and extreme cold regions of the U.S. In response, the NRC convened the Committee on Carbon Monoxide Episodes in Meteorological and Topographical Problem Areas, which focused on Fairbanks, Alaska as a case-study. A final report, "Managing Carbon Monoxide Pollution in Meteorological and Topographical Problem Areas" (NRC, 2003), offered a wide range of recommendations regarding management of CO air pollution, cold start emissions standards, oxygenated fuels, and CO monitoring. Following completion of this NRC report, EPA did not conduct rulemaking to complete the review.

EPA initiated the current review of the NAAQS for CO on September 13, 2007, with a call for information from the public (72 FR 52369) requesting the submission of recent scientific information on specified topics. A workshop was held on January 28–29, 2008 (73 FR 2490) to discuss policy-relevant scientific and technical information to inform EPA's planning for the CO NAAQS review. Following the workshop, EPA outlined the science-policy questions that would frame this review, outlined the process and schedule that the review would follow, and provided more complete descriptions of the purpose, contents, and approach for developing the key documents for the review in a draft Plan for Review of the National Ambient Air Quality Standards for Carbon Monoxide (US EPA, 2008a). After CASAC and public input on the draft plan, EPA made the final plan available in August 2008 (US EPA, 2008b). In January, 2010, EPA completed the process of assessing the latest available policy-relevant scientific information to inform the review of the CO standards. This assessment, the Integrated Science Assessment for Carbon Monoxide (hereafter, "ISA") (US EPA, 2010b), includes an evaluation of the scientific evidence on the health effects of CO, including information on exposure, physiological mechanisms by which CO might adversely impact human health, an evaluation of the clinical evidence for CO-related morbidity, and an evaluation of the epidemiological evidence for CO-related morbidity and mortality associations.[2]

EPA's Office of Air Quality Planning and Standards (OAQPS) has developed this Risk and Exposure Assessment (REA) describing the quantitative assessment conducted by the Agency to support the review of the primary CO standards. This document is a concise presentation of the methods, key results, observations, and related uncertainties associated with the quantitative analyses performed. The REA builds upon the health effects evidence presented in the ISA, as well as CASAC advice (Brain, 2009; Brain and Samet, 2009; Brain and Samet,

[2] The ISA also evaluates scientific evidence for the effects of CO on public welfare which EPA will consider in its review of the need for a secondary standard. EPA has not developed a quantitative risk assessment for the secondary standard review.

2010a; Brain and Samet, 2010b) and public comments on a scope and methods planning document for the REA (hereafter, "Scope and Methods Plan") (US EPA, 2009a) and on the first and second draft REA documents (US EPA, 2009b; US EPA, 2010c). This final REA was completed by May 28, 2010, consistent with the court order governing the schedule for completion of this review. The court order also specified that EPA sign for publication notices of proposed and final rulemaking concerning its review of the CO NAAQS no later than October 28, 2010 and May 13, 2011, respectively.

The ISA and REA are used to inform the policy assessment and rulemaking steps that lead to final decisions on the CO NAAQS. The policy assessment is described in a Policy Assessment (hereafter, "PA") document, which include staff analyses of the scientific basis for alternative policy options for consideration by the Administrator prior to rulemaking (US EPA, 2010a). The PA integrates and interprets information from the ISA and the REA to frame policy options for consideration by the Administrator. The PA is intended to link the Agency's scientific and technical assessments, presented in the ISA and REA, to judgments required of the Administrator in determining whether it is appropriate to retain or revise the existing standards. Development of the PA is also intended to facilitate elicitation of CASAC's advice to the Administrator on the adequacy of existing standards, and any new standards or revisions to existing standards as may be appropriate.

1.2 PREVIOUS REVIEWS AND ASSESSMENTS

Reviews of the CO NAAQS completed in 1985 and 1994 included analyses of exposure to ambient CO and associated internal dose, in terms of COHb levels, which were used to characterize risks for populations of interest (50 FR 37484; 59 FR 38906). These prior risk characterizations compared the numbers and percent of the modeled population that exceeded several potential health effect benchmarks, expressed in terms of COHb levels. The COHb levels of interest in these reviews were drawn from the evidence of COHb levels associated with reduction in time to exercise-induced angina and other indicators of myocardial ischemia in controlled human exposure studies involving short-term (shorter than 8 hours) exposures of patients with diagnosed ischemic heart disease (IHD)[3] to elevated CO concentrations (US EPA, 1979; US EPA, 1984; US EPA, 1991).

[3] Ischemic heart disease is a category of cardiovascular disease associated with narrowed heart arteries; it is often also called coronary artery disease (CAD) and coronary heart disease (CHD). Individuals with CHD have myocardial ischemia, which occurs when the heart muscle receives insufficient oxygen delivered by the blood. Exercise-induced angina pectoris (chest pain) occurs in many of them. Among all patients with diagnosed CAD, the predominant type of ischemia, such as that indicated by ST segment depression, is asymptomatic (i.e., silent). Also, patients who experience angina typically have additional ischemic episodes that are asymptomatic (2000 AQCD, section 7.7.2.1).

In the review completed in 1994, this characterization was performed for the population of interest in the city of Denver, Colorado (US EPA, 1992; Johnson et al., 1992). That analysis indicated that if the current 8-hour standard were just met, the proportion of the nonsmoking population with cardiovascular disease[4] experiencing exposures to ambient CO at or above 9 ppm for 8 hours decreased by an order of magnitude or more as compared to the proportion under then-existing ambient CO levels, down to less than 1 percent of the total person-days in that population. Likewise, just meeting the current 8-hour standard reduced the proportion of the nonsmoking cardiovascular-disease population person days at or above COHb levels of concern by an order of magnitude or more relative to then-existing ambient CO levels. More specifically, upon just meeting the 8-hour standard, EPA estimated that less than 0.1% of the nonsmoking cardiovascular-disease population would experience a COHb level of about 2.1% as a result of exposure to ambient CO.[5] A smaller percentage of the at-risk population was estimated to exceed higher COHb levels. The analysis also considered additional exposure scenarios that included certain indoor sources (e.g., passive smoking, gas stove usage). However, the indoor sources were shown to contribute to total CO exposure to a much greater extent than ambient air CO sources, leading to a conclusion that inclusion of indoor sources was of limited utility in considering risk related to CO in ambient air. Further, it was noted that these indoor source emissions would not be effectively mitigated by setting more stringent ambient air quality standards (59 FR 38914).

In the review initiated in 1997, EPA consulted with CASAC (Mauderly, 1999) on a draft exposure analysis methodology document, *Estimation of Carbon Monoxide Exposures and Associated Carboxyhemoglobin Levels in Denver Residents* (Johnson et al., 1999), using the Probabilistic NAAQS Exposure Model (pNEM/CO, Version 2.0). Although the EPA did not complete the review initiated in 1997, OAQPS continued work on the CO exposure assessment to further develop the exposure assessment modeling component of EPA's Total Risk Integrated Methodology (TRIM). A subsequent draft technical report (Johnson et al., 2000) was produced documenting the application of the CO exposure and dose modeling methodology for two study

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[4] In characterizing the population of interest with regard to demographics (age and sex), the assessment for the review completed in 1994 drew from estimates of the prevalence of ischemic heart disease (IHD) provided by the National Health Interview Survey and corresponding estimates of undiagnosed ischemia developed by EPA. Estimates of undiagnosed IHD were based on two assumptions: (1) there are 3.5 million persons in U.S. with undiagnosed IHD (drawn from estimate by American Heart Association) and (2) persons with undiagnosed IHD are distributed within the population in the same manner as persons with diagnosed IHD (US EPA, 1992).

[5] In the 1992 assessment, the person-days (number of persons multiplied by the number of days per year exposed) and person-hours (number of persons multiplied by the number of hours per year exposed) were the reported exposure metrics. Upon meeting the 8-hour standard, it was estimated that less than 0.1% of the total person-days simulated for the nonsmoking cardiovascular-disease population were associated with a maximum COHb level greater than or equal to 2.1% (US EPA, 1992; Johnson et al., 1992).

areas (Denver and Los Angeles). The exposure and dose estimates were obtained by applying pNEM/CO version 2.1, a predecessor to the currently used Air Pollutants Exposure Model (APEX), to adults with IHD residing within each urban area.[6] This report was subjected to an external peer review by three exposure modeling experts and convened by Science Applications International Corporation (SAIC, 2001).

In the 2000 pNEM/CO assessment, the Denver study area was defined as all census tracts located within 10 km of each of six fixed-site monitors within the Denver metropolitan area. Air quality data for 1995 reported by these monitors were used to represent existing conditions in the study area. Because the second highest non-overlapping 8-hour average CO concentration equaled 9.5 ppm, the existing conditions in Denver for 1995 were considered to approximate just meeting the 8-hour average CO standard.[7] In a similar manner, the Los Angeles study area was defined as all census tracts within 10 km of ten fixed-site monitors in the Los Angeles area, though air quality data for 1997 were adjusted downwards so that the concentrations associated with the design monitor just met the 8-hour NAAQS. A total of 15 distinct microenvironments were modeled using a mass balance model accounting for the infiltration of outdoor (ambient) CO, air exchange rates, as well as CO emissions from two indoor sources (residential gas stoves and passive cigarette smoke).

In the 2000 pNEM/CO assessment, approximately 0.5% of the non-smoking IHD population in both urban areas was estimated to experience a maximum end-of-hour COHb level of about 2.0% as a result of exposure to ambient CO under air quality conditions just meeting the current 8-hour standard.[8] A smaller percentage of the at-risk population was estimated to exceed higher COHb levels (e.g., <0.1% of persons were estimated to have COHb levels at or above 3.0% in either location). Indoor CO sources were a much greater contributor to COHb levels, with their inclusion impacting a much larger portion of the simulated population at the higher COHb levels (i.e., those persons with >1% COHb). For example, in Denver with indoor sources included, nearly 20% of persons with IHD were estimated to have a maximum end-of-hour COHb level of about 2.0%. In Los Angeles with indoor sources included, the estimated percent of persons having a COHb level at or above 2.0% was lower (i.e., about 17%), though still a

[6] This is consistent with the demographic group modeled in the 1992 assessment described above (Johnson et al., 1992; US EPA, 1992), and drew from updated information with regard to prevalence demographics (Johnson et al., 2000, section 2.5.2).

[7] A rounding convention allows the second highest 8-hour average CO concentration (i.e., the design value (DV)) to be as high as 9.4 ppm for the 8-hour CO NAAQS of 9 ppm (Laxton, 1990).

[8] Note that the contemporaneous design value for Denver was 0.1 ppm above just meeting the current 8-hour standard (9.5 versus 9.4 ppm).

much greater percentage than that estimated in the absence of indoor sources (i.e., <1% of the simulated at-risk population).

1.3 CURRENT REVIEW, CASAC ADVICE AND PUBLIC COMMENT

In preparing the draft Scope and Methods Plan for the REA (US EPA, 2009a), we considered the scientific evidence presented in the ISA and the key science policy issues raised in the IRP (US EPA, 2008b). EPA held a consultation with CASAC to solicit comments on the draft Scope and Methods Plan during a May 2009 CASAC meeting. Public comments were also requested (74 FR 15265). Those CASAC and public comments were considered in developing the first draft REA (US EPA, 2009b) which implemented a simplified, screening-level approach to assess population exposure and dose in two urban study areas, Denver and Los Angeles. The current version of EPA's exposure model for CO (APEX/CO) was used to estimate exposure and dose for a simulated at-risk population within 20 km of a single fixed-site monitor[9] in each location. Only two microenviroments were simulated; one in-vehicle and the second comprising all other locations persons might visit.[10] In using this simplified approach, the results were considered by staff as likely more representative of upper level exposure and doses experienced by a portion of the simulated at-risk population rather than the simulated at-risk population as a whole.

Following the review of the first draft REA by CASAC (Brain and Samet, 2010a) and by public commenters, we made a number of modifications to our initial approach and developed the second draft REA (US EPA, 2010c) to better estimate population exposure and dose distributions in each location modeled.[11] Specifically in the second draft assessment, we 1) expanded each of the two original modeling domains to include a greater number of ambient monitors used as input to APEX, 2) increased the number of microenvironments modeled from two to eight, 3) improved the representation of variability in estimated microenvironmental concentrations, including in-vehicles, 4) included an algorithm that adjusts for spatial heterogeneity in estimated outdoor concentrations across each model domain, 5) implemented the mass-balance model for estimating concentrations in all indoor microenvironments, 6) implemented the algorithm that allows commuters to experience home-tract and work-tract

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[9] The single monitor used in each location was the design monitor, that is, the monitor used to evaluate concordance with the NAAQS. This monitor would measure the highest CO concentrations pertaining to the NAAQS (i.e, the greatest 2nd highest 8-hour (or 1-hour) average CO concentration).

[10] In the first draft REA, in-vehicle concentrations were estimated by applying a factor of 2.0 to ambient CO concentrations. All other microenvironmental concentrations (i.e., both outdoor and indoor) were assumed to be the same as measured at the single ambient monitor.

[11] Public Comments on the first draft REA were submitted to the docket for this review and also presented in March, 2010 at the CASAC second draft review meeting.

ambient concentrations, and 7) expanded the at-risk population to also include undiagnosed persons with CHD.

This final REA was produced in consideration of comments received on the second draft REA from CASAC (Brain and Samet, 2010b) and the public. The approach used to estimate population CO exposure and COHb levels in this final REA has remained largely the same as that used in the second draft REA, with the following adjustments or additions:

- Inclusion of a further expanded simulated at-risk population based on prevalence rates for all types of heart disease (as well as including the previous estimates of persons with undiagnosed CHD);
- Evaluation of endogenous CO production and ambient CO exposure separately and their contributions to individual and population COHb levels in a larger and more representative population subset;
- Identification of the specific microenvironments that contribute to low- and high-level exposures;
- Inclusion of estimates of persons experiencing multiple occurrences per year at or above selected COHb levels;
- Evaluation of the distribution of microenvironmental factors used to estimate exposure concentrations in response to concerns regarding the application of the microenvironmental algorithm; and
- Performance of additional sensitivity analyses including
    - An evaluation of the impact additional monitors had on estimated COHb dose levels experienced by the at-risk populations;
    - An evaluation of the potential impact to estimated COHb dose levels experienced by the at-risk populations by varying undiagnosed prevalence rates by gender; and
    - An evaluation of the potential impact to estimated COHb dose levels experienced by a hypothetical anemic CHD population by using alternative hemoglobin content distributions.

The chapters and appendices that follow describe the technical details in the exposure and dose modeling approach used for this assessment, as well as the data analysis results. More specifically,

- Chapter 2 provides a conceptual overview of the assessment of CO exposure and risk with particular focus on aspects pertinent to this REA;

- Chapter 3 summarizes some of the general trends in CO ambient monitoring across the U.S. and presents additional air quality analyses relevant to the two urban areas of focus in this REA;
- Chapter 4 provides a technical overview of EPA's APEX model including model algorithms and databases common to most pollutant applications as well as the description of approaches used specifically for estimating CO exposure and dose;
- Chapter 5 details the site- and pollutant-specific data used for the application of APEX to the two study areas assessed in this REA;
- Chapter 6 provides the exposure and dose results;
- Chapter 7 presents an analysis of how variability was addressed in this assessment and qualitatively characterizes how uncertainties in input data and model algorithms might affect exposure and dose results; and
- Chapter 8 summarizes the key observations associated with each chapter.

1.4 REFERENCES

Brain JD. (2009). Letter from Dr. Joseph Brain to Administrator Lisa Jackson. Re: Consultation on EPA's *Carbon Monoxide National Ambient Air Quality Standards: Scope and Methods Plan for Health Risk and Exposure Assessment.* CASAC-09-012. July 14, 2009.

Brain JD and Samet JM. (2009). Letter from Drs. J.D. Brain and J.M. Samet to Administrator Lisa Jackson. Re: Review of the EPA's *Integrated Science Assessment for Carbon Monoxide (First External Review Draft).* EPA-CASAC-09-011. June 24, 2009.

Brain JD and Samet JM. (2010a). Letter from Drs. J.D. Brain and J.M. Samet to Administrator Lisa Jackson. Re: Review of the *Risk and Exposure Assessment to Support the Review of the Carbon Monoxide (CO) Primary National Ambient Air Quality Standards: First External Review Draft.* EPA-CASAC-10-006. February 12, 2010.

Brain JD and Samet JM. (2010b). Letter from Drs. J.D. Brain and J.M. Samet to Administrator Lisa Jackson. Re: Review of the *Risk and Exposure Assessment to Support the Review of the Carbon Monoxide (CO) Primary National Ambient Air Quality Standards: Second External Review Draft.* EPA-CASAC-10-012. May 19, 2010.

Johnson T, Capel J, Paul R, Wijnberg L. (1992). Estimation of Carbon Monoxide Exposure and Associated Carboxyhemoglobin Levels in Denver Residents Using a Probabilistic version of NEM. Report prepared by International Technology for U.S. EPA, Office of Air Quality Planning and Standards, Durham, NC, Contract No. 68-D0-0062.

Johnson T, Mihlan G, LaPointe J, Fletcher K, Capel J. (1999). Estimation of Carbon Monoxide Exposures and Associated Carboxyhemoglobin Levels in Denver Residents Using pNEM/CO (Version 2.0). Report prepared by ICF Kaiser Consulting Group for U.S. EPA, Office of Air Quality Planning and Standards, under Contract No. 68-D6-0064, WA Nos. 1-19 and 2-24. Available at: http://www.epa.gov/ttn/fera/human_related.html.

Johnson T, Mihlan G, LaPointe J, Fletcher K, Capel J. (2000). Estimation of Carbon Monoxide Exposures and Associated Carboxyhemoglobin Levels for Residents of Denver and Los Angeles Using pNEM/CO (Version 2.1). Report prepared by ICF Consulting and TRJ Environmental, Inc., under EPA Contract No. 68-D6-0064. U.S. Environmental Protection Agency, Research Triangle Park, NC. Available at: http://www.epa.gov/ttn/fera/human_related.html.

Laxton, WG. (1990). Memorandum on "Ozone and Carbon Monoxide Design Value Calculations". June 18, 1990. Available at: http://www.epa.gov/ttn/naaqs/ozone/ozonetech/laxton.htm.

Mauderly J. (1999). Letter from Dr. Joe Mauderly, Chair, Clean Air Scientific Advisory Committee, to Administrator Carole M. Browner. Re: Notification of a Consultation on the *Estimation of Carbon Monoxide Exposures and Associated Carboxyhemoglobin Levels in Denver Residents using pNEM/CO (Ver. 2.0).* July 12, 1999.

National Research Council. (2003). Managing Carbon Monoxide Pollution in Meteorological and Topographical Problem Areas. Washington, DC, The National Academies Press.

SAIC. (2001). Memo to Harvey Richmmond, EPA, Technical Peer Review (including reviewers comments) of "Estimation of Carbon Monoxide Exposures and Associated Carboxyhemoglobin Levels for Residents of Denver and Los Angeles Using pNEM/CO (version 2.1)", Docket EPA-HQ-OAR-2008-0015. Available at: http://www.epa.gov/ttn/fera/human_related.html.

US EPA. (1979). Air Quality Criteria for Carbon Monoxide. Research Triangle Park, NC: Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, report no. EPA/600/8-79-022.

US EPA. (1984). Review of the NAAQS for Carbon Monoxide: Reassessment of Scientific and Technical Information. Office of Air Quality Planning and Standards, report no. EPA-450/584-904. Research Triangle Park, NC.

US EPA. (1991). Air Quality Criteria for Carbon Monoxide. Research Triangle Park, NC: Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, report no. EPA/600/8-90/045F.

US EPA. (1992). Review of the National Ambient Air Quality Standards for Carbon Monoxide: Assessment of Scientific and Technical Information. Office of Air Quality Planning and Standards Staff Paper, report no. EPA/452/R-92-004.

US EPA. (1999). Total Risk Integrated Methodology - TRIM.Expo Technical Support Document, External Review Draft, November 1999. Office of Air Quality Planning and Standards, U.S. Environmental Protection Agency, Research Triangle Park, NC, report no. EPA-453/D-99-001. Available at: http://www.epa.gov/ttn/fera/trim_fate.html#1999historical.

US EPA. (2000). Air Quality Criteria for Carbon Monoxide. National Center for Environmental Assessment, Office of Research and Development, U.S. Environmental Protection Agency, Research Triangle Park, NC, report no. EPA/600/P-99/001F. June 2000. Available at: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=18163.

US EPA. (2008a). Draft Plan for Review of the National Ambient Air Quality Standards for Carbon Monoxide. U.S. Environmental Protection Agency, Research Triangle Park, NC, report no. EPA/452D-08-001. Also known as *Draft Integrated Review Plan*. Available at: http://www.epa.gov/ttn/naaqs/standards/co/s_co_cr_pd.html.

US EPA. (2008b). Plan for Review of the National Ambient Air Quality Standards for Carbon Monoxide. U.S. Environmental Protection Agency, Research Triangle Park, NC, report no. EPA/452R-08-005. Also known as *Integrated Review Plan.* Available at: http://www.epa.gov/ttn/naaqs/standards/co/s_co_cr_pd.html.

US EPA. (2009a). Carbon Monoxide National Ambient Air Quality Standards: Scope and Methods Plan for Health Risk and Exposure Assessment. U.S. Environmental Protection Agency, Research Triangle Park, NC, report no. EPA-452/R-09-004. Available at: http://www.epa.gov/ttn/naaqs/standards/co/s_co_cr_pd.html.

US EPA. (2009b). Risk and Exposure Assessment to Support the Review of the Carbon Monoxide Primary National Ambient Air Quality Standards: First External Review Draft. U.S. Environmental Protection Agency, Research Triangle Park, NC, report no. EPA-452/P-09-008. Available at: http://www.epa.gov/ttn/naaqs/standards/co/s_co_cr_rea.html.

US EPA. (2010a). Policy Assessment to Support the Review of the Carbon Monoxide Primary National Ambient Air Quality Standards. U.S. Environmental Protection Agency, Research Triangle Park, NC, report no. EPA-452/R-10-007. Available at: http://www.epa.gov/ttn/naaqs/standards/co/s_co_cr_pa.html.

US EPA. (2010b). Integrated Science Assessment for Carbon Monoxide. U.S. Environmental Protection Agency, Washington, DC, report no. EPA/600/R-09/019F. Available at: http://www.epa.gov/ttn/naaqs/standards/co/s_co_cr_isa.html.

US EPA. (2010c). Risk and Exposure Assessment to Support the Review of the Carbon Monoxide Primary National Ambient Air Quality Standards: Second External Review Draft. U.S. Environmental Protection Agency, Research Triangle Park, NC, report no. EPA-452/P-19-004. Available at: http://www.epa.gov/ttn/naaqs/standards/co/s_co_cr_rea.html.

2 CONCEPTUAL OVERVIEW: ASSESSING AMBIENT CARBON MONOXIDE EXPOSURE AND RISK

In this chapter, we have summarized the conceptual model for assessing exposure to ambient CO and associated health risk. Subsections focus on different components of the model including identification of the key emission sources to ambient concentrations (section 2.1), exposure pathways and key microenvironments (section 2.2), exposure and dose metrics (section 2.3), at-risk populations (section 2.4), health endpoints (section 2.5), and the risk characterization approach (section 2.6). Section 2.7 presents the key observations for this chapter.

2.1 SOURCES OF CARBON MONOXIDE

Carbon monoxide in ambient air is formed primarily by the incomplete combustion of carbon-containing fuels and photochemical reactions in the atmosphere. The amount of CO emitted from these reactions, relative to the amount of carbon dioxide (CO_2) generated, is sensitive to conditions in the combustion zone. CO production relative to CO_2 generally decreases with any increase in fuel oxygen (O_2) content, burn temperature, or mixing time in the combustion zone (ISA, section 3.2). As a result, CO emissions from large fossil-fueled power plants are typically very low because optimized fuel consumption conditions make boiler combustion highly efficient. In contrast, internal combustion engines commonly used to power mobile sources have widely varying operating conditions. Therefore, higher and more variable CO emission levels result from the operation of these mobile sources (ISA, section 3.2). In 2002, CO emissions from on-road vehicles accounted for a substantial majority of total emissions by individual source sectors in the U.S. (ISA, Figure 3-1).[1] As in previous NAAQS reviews, mobile sources continue to be a significant emission source of CO to ambient air, although in some areas, local stationary sources may be important contributors to ambient CO concentrations.

Sources of CO inside buildings include infiltration of ambient air indoors, as well as, where present, indoor (nonambient) sources such as gas stoves and tobacco smoke (ISA, section 3.6.5.2). In addition to infiltration of ambient air, CO inside motor vehicles may also receive contributions from nonambient sources in the cabin, which can be substantial under air ventilation modes that limit inflow from outside the vehicle (ISA, p. 3-89). In past CO assessments, nonambient sources were estimated to have a substantially greater impact on the highest total exposures experienced by the simulated population than have ambient sources (as

[1] The 2002 National Emissions Inventory (NEI; US EPA, 2006) was the most recently available NEI meeting data quality objectives for the ISA (US EPA, 2010a). The NEI includes data from various sources such as industries and state, tribal, and local air agencies (ISA, p. 3-1).

summarized in section 6.3 below). However, the focus of this REA, conducted to inform the current review of the CO NAAQS, is on sources of ambient CO. We provide quantitative estimates of population exposure and dose originating from ambient CO in two urban areas (details on site selection are provided in chapter 3 below). The exposure modeling in this assessment does not quantitatively estimate the contribution of indoor sources to estimated population exposure and dose. In section 2.2 below, however, we qualitatively draw upon available information regarding potential indoor source contributions to estimated population exposure and dose.

2.2 EXPOSURE PATHWAYS AND IMPORTANT MICROENVIRONMENTS

Human exposure to CO involves the contact (via inhalation) between a person and the pollutant in the various locations (or microenvironments) in which people spend their time. Studies of personal exposure have generally found that the largest portion of the day is generally spent indoors and the largest percentage of the time in which an individual is exposed to ambient CO occurs indoors (ISA, sections 2.3 and 3.6). As a result, CO concentrations in indoor microenvironments are an important determinant of an individual's total CO exposure. Recent population exposure studies conducted in Milan, Italy support this conclusion (Bruinen de Bruin et al., 2004), indicating that over 80% of the population exposure to CO can occur in indoor microenvironments (ISA, Table 3-13). Taking into account the infiltration of ambient CO indoors, indoor CO concentrations are similarly an important determinant in an individual's exposure to ambient CO.

Microenvironments that may influence CO exposures typically include residential indoor environments and other indoor locations, near-traffic outdoor microenvironments and other outdoor locations, and inside vehicles. Consideration of microenvironmental exposures illustrates the variability in the relationship between personal exposure and ambient concentrations. For example, one study summarized the relationship between personal CO exposure concentrations in five broadly defined microenvironments (i.e., indoor residence, indoor other, outdoor near road, outdoor other, and in-vehicle) and ambient CO concentrations[2] in Baltimore, MD (ISA, section 3.6.5.2; Chang et al., 2000). For most of the microenvironments, the mean indoor-to-ambient and outdoor-to-ambient concentration ratios were about one, though most of the individual ratios observed across this set of indoor and outdoor microenvironments were less than one. With the exception of ratios for the in-vehicle microenvironments, which as a group had most of the ratio distribution (as well as the mean ratio) above one, few ratios were

[2] The ambient CO concentrations were those measured at a fixed site monitor (winter) or reflected average concentrations across three fixed-site monitors (summer) (Chang et al., 2000).

above unity (ISA, p. 3-85, Figure 3-46). Given the expected stability of CO as it infiltrates indoor microenvironments from outdoor air and the lack of significant removal mechanisms of CO in outdoor microenvironments, it is likely that the variability in personal- or microenvironmental-to-ambient monitor and outdoor-to-ambient monitor concentration ratios is the result of variability in outdoor concentrations that are not correlated with simultaneously measured ambient concentrations at fixed-site monitors. This lack of correlation is a function of the presence of local ambient and nonambient source emissions as well as local meteorology

Typically the highest CO exposure concentrations are experienced while inside vehicles. Because motor vehicle emissions continue to be important contributors to ambient CO concentrations, both the time spent in motor vehicles and the elevated CO concentrations occurring on and near heavily trafficked roads continue to be important contributors to personal exposures. For example, in the study summarized above on personal exposures occurring within particular microenvironments (i.e., Chang et al., 2000), most in-vehicle CO exposure-to-ambient concentration ratios were greater than one, with the median being approximately 2.5. The average ratio was approximately 2.5 in summer, but a few somewhat higher in-vehicle measurements in the winter period, contributed to a winter average of approximately 4 (ISA, section 3.6.5.2, Figure 3-46; Chang et al., 2000 Figure 5).[3] Given this relationship, it should not be surprising that while about 8% of a person's time per day is spent in transit, approximately 13-17% of their total daily exposure occurs within an in-vehicle microenvironment (e.g., Bruinen de Bruin et al., 2004; Scotto di Marco et al., 2005).

Similarly, the influence of mobile sources to microenvironmental concentrations and personal exposurs was observed in the CO population exposure studies conducted in Denver CO and Washington, DC during the winter of 1982 and 1983 (Akland et al., 1985).[4] In both cities, when comparing the distribution of measured CO concentrations from the monitoring network to measured personal exposures, two common phenomena were observed. At the lowest percentiles of each distribution, ambient CO concentrations were consistently greater than the personal exposures. At the highest percentiles of each distribution, ambient concentrations were consistently lower than the personal exposures (US EPA, 2000). These studies determined that the highest average CO concentrations occurred when subjects were in a mobile source-influenced microenvironment (e.g., inside parking garages, in-vehicles). Commute time was also a factor; those who commuted 6 hours or more per week had higher average exposures than

[3] Information on the distance of the ambient monitors from highly trafficked roadways or potential for in-vehicle (nonambient) sources was not provided.

[4] Both studies collected measurements and activity pattern diaries from a random sample of the population, defined as including non-institutionalized, non-smoking residents, 18 to 70 years of age, who lived in each respective city's metropolitan area (Akland et al., 1985).

those who commuted fewer hours per week. Furthermore, mean CO concentrations within in-vehicle microenvironments (ranging from 7.0 to 9.8 ppm) were greater than common outdoor locations (ranging from 1.4 to 3.2 ppm) (US EPA, 2000). In considering the results from the Denver and Washington personal exposure studies it is important to recognize that CO emissions from motor vehicle sources have declined dramatically since the early 1980's when these studies were conducted. Consequently, both ambient fixed-site CO concentrations and in-vehicle CO concentrations have also been reduced significantly since that time period.

Given their influence on ambient exposures, exposures to CO near roadways and in vehicle microenvironments are of particular importance in this assessment. Data from several studies that have compared concentrations inside vehicles to concentrations immediately outside vehicles indicate that indoor/outdoor concentration (I/O) ratios on average range from just above to just below unity (Chan et al., 1991; Rodes et al., 1998; Boulter and McCrae, 2005; Sharp and Tight, 1997). These studies are supported by a review by Flachsbart (1999) regarding other studies published between 1982 and 1992 that measured interior and exterior CO concentrations simultaneously during motor vehicle trips and reported I/O ratios just below unity (Petersen and Allen, 1982; Koushi et al., 1992). Some studies reported no effect of ventilation setting on I/O ratios, while others reported an effect. For example, one study described in the ISA indicated I/O ratios could exceed unity with the ventilation set to re-circulate vehicle air (Abi Esber and El-Fadel, 2008). However, the study authors attributed this finding to unaccounted sources of CO that caused increases in CO concentrations within the vehicle cabin under those conditions (ISA, section 3.6.6.2; Abi Esber and El-Fadel, 2008).

In general, the above results suggest that the I/O ratio tends toward unity when there are no interior sources of CO, the automobile engine does not contribute directly to its own interior concentrations, and the measurement probes are properly installed on the vehicle. This conclusion is consistent with theoretical expectations for a non-reactive pollutant. For example, CO concentrations inside vehicles can be estimated as a function of outside CO concentration, air exchange rate, a penetration factor, and the emission rates of indoor sources (e.g., exhaust leaks, smoking). If one assumes that (1) steady-state ventilation conditions exist, (2) the indoor removal rate (k) is zero (i.e., no loss of CO as it moves from outside to inside the vehicle), and (3) there are zero emissions from interior sources, then the CO concentration inside a vehicle can be simplified to a function of outside CO concentrations and the penetration rate (i.e., infiltration is generally equivalent to penetration).[5] Under these stated conditions, the I/O ratio would ultimately converge to unity.

[5] See section 3.6.2 of the ISA.

There are a few studies that have measured both in-vehicle and fixed-site monitoring concentrations. The data from these studies can also inform the development of microenvironmental factors used for estimating in-vehicle CO exposures. The ISA notes that studies summarized in the 2000 CO AQCD found that in-vehicle CO concentrations were generally two to five times higher than ambient CO concentrations obtained at fixed-site monitors within the cities studied. For example, Shikiya et al. (1989) reported such concentrations measured as part of a southern California study. When using the reported in-vehicle CO measurements, one could estimate concentration ratios ranging from 1.8 to 2.7, a range of ratios dependent on the time-of-year measurements were collected. Note however that there are several factors that could contribute to variability in reported or calculated concentration ratios. For example, often times in these measurement studies, the averaging time associated with the companion measurements differ, that is there may be a much shorter sampling interval for the in-vehicle measurement when compared with that of the ambient monitor. More specifically, Shikiya et al. (1989) measured in-vehicle CO concentrations during commutes lasting, on average, 33 minutes, while fixed site monitoring values averaged over 4 hours. It is possible that the time-averaged concentrations are less than that of the true fixed-site concentrations that occurred during the 33 minute commute, perhaps resulting in an overestimation of the concentration ratios when using this data. Furthermore, Shikiya et al. (1989) reported seasonal differences for the in-vehicle CO concentrations (winter averaged 10.1 ppm; summer averaged 6.5 ppm), but not for the fixed-site monitor (average for both seasons was 3.7 ppm). Typically ambient concentrations are greater in winter (e.g., ISA Figure 3-22 for Los Angeles). Therefore, when using the fixed-site seasonal average and in-vehicle seasonally stratified measurements from Shikiya et al. (1989) to calculate the ratios as was done above, the winter I/O ratio may be overestimated while the summer value could be underestimated. In addition to the factors mentioned above, this relationship can vary based on several other factors that may influence the fixed-site monitor concentration, such as the nearby roadway traffic density, the monitor siting characteristics (e.g., proximity to the roadway), and local scale meteorology (e.g., downwind), with each described in greater detail in chapter 3. Of the few studies reporting in-vehicle and companion fixed-site measurements, most do not measure all of the potentially influential factors or provide the data stratified by such factors. Thus, a general range of two to five may be adequate to represent the total variability for this particular relationship, recognizing that there are limitations in the available measurement data to better define this relationship.

Although not the focus of this review, indoor sources such as gas stoves and environmental tobacco smoke can, where present, be important contributors to total CO exposure and may, consequently, be of particular concern for such at-risk populations as individuals with

cardiovascular disease, among others (see section 2.4 below). For example, some assessments performed for previous reviews have included modeling simulations both without and with indoor sources (gas stoves and tobacco smoke) to provide context for the assessment of ambient CO exposure and dose (e.g., US EPA, 1992; Johnson et al., 2000). The 2000 pNEM/CO simulations with indoor sources indicated that the impact of such sources on the proportion of the population experiencing higher exposures and COHb levels can be substantial (Johnson et al., 2000), as summarized in section 1.2 above and in section 6.3 below.[6]

2.3 EXPOSURE AND DOSE METRICS

Exposure concentration over a time period of interest (e.g., one hour or eight hours) is a common exposure metric which reflects the integration of exposures to pollutant concentrations that occur in each microenvironment in which time is spent (see section 4.4.6 below). In the case of CO, for which the common mechanism underlying biological response is binding to heme proteins, COHb level in blood is well recognized as an important internal dose metric used in evaluating CO exposure and the potential for health effects (ISA, p. 2-4, sections 4.1, 4.2, 5.1.1). Accordingly, COHb levels are used in this assessment.

Carboxyhemoglobin occurs in the blood due to endogenous CO production from biochemical reactions associated with normal breakdown of heme proteins, as well as in response to inhaled (exogenous) CO exposures (ISA, section 4.5).[7] Levels of COHb associated with endogenous CO production in healthy individuals have been described to range down to 0.3% and generally be less than 1% (ISA, pp. 4-9, 4-23, 2-6). However, the production of endogenous CO and levels of endogenous COHb vary with several physiological characteristics (e.g., slower COHb elimination with increasing age), as well as some disease states, which can lead to higher endogenous levels in some individuals (ISA, section 4.5). Other factors affecting CO uptake and elimination include physical activity and altitude (ISA, section 4.4).

The amount of COHb formed in response to exogenous CO is dependent on the CO concentration and duration of exposure, exercise (which increases the amount of air removed and replaced per unit of time for gas exchange), the pulmonary diffusing capacity for CO, ambient pressure, health status, and the specific metabolism of the exposed individual (ISA, chapter 4; 2000 AQCD, chapter 5). The formation of COHb is a reversible process, but the high affinity of CO for Hb, which affects the elimination half-time for COHb, can lead to increased COHb levels

[6] As has been recognized in previous CO NAAQS reviews, such sources cannot be effectively mitigated by setting more stringent ambient air quality standards (59 FR 38914), and are therefore not a focus of this assessment.

[7] The dosimetry and pharmacokinetics of CO are discussed in detail in chapter 4 of the ISA.

in some circumstances.[8] Exogenous CO, ambient and nonambient[9], can contribute to CO uptake and increased levels of COHb. As recognized in sections 2.1 and 2.2 above, nonambient (indoor) sources of CO (ISA, section 3.6.5.2) can result in much greater CO exposures and associated COHb levels than those associated with ambient sources.[10] Further, baseline COHb levels in active smokers have been estimated to range from 3 to 8% for one- to two-pack-per-day smokers. As a result of their higher baseline COHb levels, smokers may exhale more CO into the air than they inhale from the ambient environment when not smoking. Tobacco smoking can also contribute to increased CO exposures and associated COHb levels in nonsmokers (2000 AQCD, p. 7-4). In order to focus on the impact of ambient CO sources on population COHb levels, exposure modeling for this REA does not include indoor CO sources; the impact of indoor sources has been evaluated in previous assessments (see section 6.3 below).

As described in section 4.4.7 and Appendix B, blood levels of COHb have been estimated in this REA using a nonlinear solution of the Coburn-Forster-Kane (CFK) model (Coburn et al., 1965), which remains "the most extensively validated and applied model for COHb prediction (ISA, section 4.2.3).

2.4 AT-RISK POPULATIONS

The term 'susceptibility' (and the term "at-risk") has been used to recognize populations that have a greater likelihood of experiencing effects related to ambient CO exposure (ISA, section 5.7). This increased likelihood of response to CO can potentially result from many factors, including pre-existing medical disorders or disease states, age, gender, lifestyle or increased exposures (ISA, section 5.7). For example, medical disorders that limit the flow of oxygenated blood to the tissues have the potential to make an individual more susceptible to the potential adverse effects of low levels of CO, especially during exercise. Based on the available evidence in the current review, coronary artery disease (CAD), also known as coronary heart disease (CHD) is the "most important susceptibility characteristic for increased risk due to CO exposure" (ISA, p. 2-11). While persons with a normal cardiovascular system can tolerate

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[8] Fortunately, mechanisms exist in normal, healthy individuals to compensate for the reduction in tissue oxygen caused by increasing levels of COHb. Cardiac output increases and blood vessels dilate to carry more blood so that the tissue can extract adequate amounts of oxygen from the blood (ISA, chapter 4). As discussed in sections 2.4 and 2.5 below, however, there are several medical disorders that can make an individual more susceptible to the potential adverse effects of low levels of CO, especially during exercise.

[9] A significant source of nonambient CO long recognized as contributing to elevated COHb levels is tobacco smoking (e.g., ISA, Figure 4-12).

[10] For example, in addition to COHb estimates from previous assessments discussed in sections 2.1 and 2.2, indoor source-related exposures, such as faulty furnaces or other combustion appliances, have been estimated in the past to lead to COHb levels on the order of twice as high as those short-term exposures to ambient CO considered more likely to be encountered by the general public (2000 AQCD, p. 7-4).

substantial concentrations of CO if they vasodilate or increase cardiac output in response to the hypoxia produced by CO, those that are unable to vasodilate in response to CO exposure may show evidence of ischemia at low concentrations of COHb (ISA, p. 2-10). There is strong evidence for this in controlled human exposure studies of exercising individuals with CAD, which is supported by results from recent epidemiologic studies reporting associations between short-term CO exposure and increased risk of emergency department visits and hospital admissions for individuals affected with ischemic heart disease (IHD)[11] and related outcomes (ISA, section 5.7). This combined evidence, briefly summarized in section 2.5.1 below and described in more detail in the ISA, supports the conclusion that individuals with CAD represent the population most susceptible to increased risk of CO-induced health effects (ISA, sections 5.7.1.1 and 5.7.8). The 2007 estimate of the size of the U.S. population with coronary heart disease, inclusive of those with angina pectoris (cardiac chest pain) and those who have experienced a heart attack (ISA, Table 5-26) is 13.7 million people, some fraction of whom have IHD (ISA, pp.5-117). Further, there are estimated to be several million additional people with silent ischemia or undiagnosed IHD (AHA, 2003). In combination this represents a large population that is more susceptible to ambient CO exposure when compared to the general population (ISA, section 5.7).

Other types of cardiovascular disease[12] may also potentially contribute to increased susceptibility to the adverse effects of low levels of CO, especially during exercise (ISA, section 5.7.1.1). For example, some evidence with regard to other types of cardiovascular disease such as congestive heart failure, arrhythmia, and non-specific cardiovascular disease, although more limited for peripheral vascular and cerebrovascular disease, indicates that "the continuous nature of the progression of CAD and its close relationship with other forms of cardiovascular disease suggest that a larger population than just those individuals with a prior diagnosis of CAD may be susceptible to health effects from CO exposure" (ISA, p. 5-117).

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[11] Ischemic heart disease is a category of cardiovascular disease associated with narrowed heart arteries, which is often also called CAD (coronary artery disease) and CHD (coronary heart disease). Individuals with CHD have myocardial ischemia, which occurs when the heart muscle receives insufficient oxygen delivered by the blood. Exercise-induced angina pectoris (chest pain) occurs in many of them. Among all patients with diagnosed CAD, the predominant type of ischemia, as identified by ST-segment depression, is asymptomatic (i.e., silent). Also, patients who experience angina typically have additional ischemic episodes that are asymptomatic (2000 AQCD, section 7.7.2.1). In addition to such chronic conditions, CHD can include myocardial infarction (ISA, p. 5-24).

[12] Cardiovascular disease comprises many types of medical disorders, including heart disease, cerebrovascular disease (e.g., stroke), hypertension (high blood pressure), and peripheral vascular diseases. Heart disease, in turn, comprises several types of disorders, including ischemic heart disease (i.e., CHD, CAD, myocardial infarction, and angina), congestive heart failure, and disturbances of cardiac rhythm (dysrhythmias and arryhthmias) (2000 AQCD, p. 7-7).

Beyond persons with cardiovascular diseases, other populations may be potentially susceptible to CO-related health effects. These populations are listed in the paragraphs below. However, little empirical evidence is available by which to specify health effects associated with ambient or near-ambient CO exposures in these potentially at-risk groups.

Populations with other preexisting diseases, such as chronic obstructive pulmonary disease, diabetes or anemia have been identified as potentially susceptible to CO-induced health effects (ISA, p. 5-123). For example, although there are no controlled human exposure or epidemiological studies examining potential CO-induced effects in people suffering from hematologic diseases, such as anemia, that affect oxygen-carrying capacity or transport in the blood, it is reasonable to assume that the potential combination of hypoxic effects of CO together with reduced oxygen availability and/or elevated baseline COHb levels in people suffering with anemia[13] may make those with anemia susceptible to CO-induced effects (ISA, section 5.7.1.4). Included in this category of anemia diseases is sickle cell anemia, which is documented at a higher incidence in African-American populations (ISA, section 5.7.1.4). Asthma and COPD are other oxygen-limiting diseases which may be exacerbated by CO-related oxygen limitation. Another population that may be potentially susceptible to CO includes those persons that may have increased endogenous production of CO and potentially higher endogenous COHb levels such as diabetics, for which a few epidemiological studies provide suggestive evidence of increased risk for cardiovascular emergency department visits and hospital admissions compared to non-diabetics in response to short-term CO concentrations (ISA, section 5.7.1.3). Additionally, older adults, especially those with compromised cardiovascular function, represent a potentially susceptible population (ISA, section 5.7.2.1).

The developing young (e.g., gestational development and newborns) may also represent a population potentially susceptible to CO-induced health effects (ISA section 5.7.2.2; 2000 AQCD, section 7.7.1). For example, although the effects of CO on maternal-fetal relationships are not well understood, fetal circulation is likely to have a higher COHb level than the maternal circulation because of differences in uptake and elimination of CO from fetal Hb, which may contribute to an enhanced sensitivity to CO exposure during gestation (ISA, section 5.7.2.2). The comparatively higher rate of oxygen consumption and lower oxygen-transport capacity for Hb in newborn infants as compared to adults may make them susceptible to CO-induced hypoxic effects (2000 AQCD, section 7.7.1). Data from laboratory animal studies on CO developmental toxicity suggest that prolonged exposure to high CO levels (>60 ppm) during gestation may produce reduction in birth weight, transient cardiomegaly and delayed behavioral development,

[13] Individuals affected with anemias of different etiologies may have low hematocrit, reduced capacity of the blood to carry oxygen, or increased COHb levels due to increased endogenous CO production, all of which would decrease the oxygen available for organs and tissues (ISA, pp. 118-119).

or may disrupt the normal physiological roles of endogenous CO in the body (ISA, section 5.4.2.2); multiple-day prenatal animal exposures to exposures at or above 12 ppm indicated effects on the developing auditory system (ISA, pp. 5-75 to 5-76). Limited epidemiological evidence suggests some association of short-term ambient CO exposure with pre-term birth and birth defects, and weak evidence suggests an association with reduction in birth weight and fetal growth, and infant mortality (ISA, section 5.7.2.2; 2000 AQCD, section 7.7.1), although a clear understanding of the mechanisms by which CO may induce those effects and at what exposure levels is lacking (ISA, section 5.4.3).

Other populations that may be potentially susceptible due to impacts on endogenous CO production, uptake and elimination of CO, or increased exposure concentrations include visitors to high-altitude locations, persons using medicinal or recreational drugs with central nervous system depressant properties or that that increase endogenous formation of CO, and people that spend a substantial amount of time on or near heavily traveled roads which may contribute to higher CO exposures (ISA, section 5.7).

As discussed in section 2.5 below, the sensitive endpoint which is the focus of this quantitative assessment is exacerbation of myocardial ischemia. Based on the current evidence for this endpoint, two target populations have been identified for this REA: (1) adults with CHD (also known as ischemic heart disease IHD or CAD), both diagnosed and undiagnosed;[14] and (2) adults with diagnosed heart disease (HD) which includes CHD as well as other conditions (e.g., arrhythmias), along with undiagnosed CHD.

As mentioned above, there is little empirical evidence currently available by which to specify health effects associated with relevant CO exposures in the other, potentially at-risk groups identified above. Such evidence characterizing the nature of specific health effects of CO in these populations is extremely limited and does not include COHb levels related to a particular health effect identified in these potentially susceptible populations. Quantitative evidence relating exposure or an applied dose to an adverse health outcome is requisite to the conduct of a quantitative exposure and risk assessment. As a result, while we continue to recognize the potential susceptibility of the larger cardiovascular disease population to health effects of CO, as has been recognized in past reviews, as well as the potential susceptibility of several other populations identified above (ISA, section 5.7), the at-risk populations simulated in this assessment are individuals with CAD (diagnosed and undiagnosed and inclusive of individuals with angina pectoris and heart attacks), as well as the larger HD population. We additionally note that the still broader cardiovascular disease population and the potential susceptibility of

[14] As described in section 1.2 above, this is the same population group that was the focus of the exposure/dose assessments conducted previously (e.g., US EPA, 1992; Johnson et al., 2000).

other populations is further considered with regard to the review of the CO NAAQS in the Policy Assessment document (US EPA, 2010b).

2.5 HEALTH ENDPOINTS

Carbon monoxide elicits various health effects by binding to heme proteins and altering the function of a number of heme proteins (ISA, section 2.4.2). The level of CO bound to hemoglobin as carboxyhemoglobin (COHb) in the blood is the best characterized dose metric for evaluating CO exposure and the potential for associated health effects, as described in section 2.3 above.

The best characterized health effect associated with CO levels of concern is hypoxia (reduced oxygen availability) induced by increased COHb levels in blood (ISA, section 5.1.2). The formation of COHb reduces the oxygen carrying capacity of the blood and impairs the release of oxygen from oxy-hemoglobin complexes to the tissues. Accordingly, CO is especially harmful in individuals with impaired cardiovascular systems (as discussed in section 2.4 above) and the clearest evidence of causal relationships with CO exists for cardiovascular effects. In characterizing the combined evidence, the ISA concluded that cardiovascular effects are likely causally related to short-term exposures to CO at relevant concentrations, with "relevant CO concentrations" defined in the ISA as "generally within one or two orders of magnitude of ambient CO concentrations" (ISA, p. 2-5). The "most compelling evidence of CO-induced effects on the cardiovascular system comes from a series of controlled human exposure studies among individuals with coronary heart disease (CHD) (ISA, sections 5.2.4 and 5.2.6).

Other potential effects of CO which are less well characterized at relevant exposure concentrations are those on the central nervous system, reproduction and prenatal development, and the respiratory system (ISA, section 2.5). These additional health endpoints, for which the limited available evidence is suggestive of causal relationships (ISA, sections 5.3, 5.4 and 5.5), are also considered in this review and are discussed in detail in the ISA and summarized briefly in section 2.5.2 below. Across the health endpoints identified here, however, the focus of the quantitative analysis described in this document is on cardiovascular disease-related effects that have been observed in adults with CHD, most specifically decreased time to exercise-induced angina and changes to the ST-segment of an electrocardiogram that are indicative of myocardial ischemia. This focus is based on the strength of the evidence and availability of quantitative information from human studies of controlled CO exposures in which the resulting COHb levels were associated with these effects (as discussed in sections 2.5.1 and 2.6 below).

2.5.1 Cardiovascular Disease-related Effects

The best characterized cardiovascular disease-related effects associated with CO are markers of myocardial ischemia observed in studies of controlled CO exposures of CHD patients[15] and effects on exercise duration and maximal aerobic capacity observed in controlled exposure studies of healthy adults.[16] As noted in the ISA, the decreases in exercise duration among healthy adults (associated with COHb levels from 3 up to 20%) were relatively small and only likely to be noticed by competing athletes, although they are considered to provide coherence with the exercise-induced cardiovascular effects of greater concern that have been demonstrated in CHD patients. The controlled human exposure studies involving individuals with preexisting CHD provide strong evidence for an association between short-term exposure to CO and measures of ischemia (US EPA, 2000, section 6.2.2; ISA, section 5.2.4). Multiple controlled human exposure studies have shown that short-term exposure to CO and subsequent elevation of COHb to levels of approximately 2-6% reduces time to onset of exercise-induced myocardial ischemia in individuals with preexisting CAD, with no evidence of a threshold at the lowest levels tested (ISA, section 5.2.4).

The controlled exposure study of principal importance is a large multi-laboratory study designed to evaluate myocardial ischemia, as documented by reductions in time to change in the ST-segment of an electrocardiogram[17] and in time to onset of angina, during a standard treadmill test, at CO exposures targeted to result in mean subject COHb levels of 2% and 4%, as measured by gas chromatographic technique[18] (ISA, section 5.2.4, from Allred et al., 1989a, 1989b, 1991). In this study, subjects on three separate occasions underwent an initial graded exercise treadmill test, followed by 50- to 70-minute exposures under resting conditions to average CO concentrations of 0.7 ppm (room air concentration range 0-2 ppm), 117 ppm (range 42-202 ppm)

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[15] Epidemiological studies have consistently shown associations between ambient CO measurements and emergency department visits and hospital admissions for IHD, which is coherent with the effects observed in controlled human exposure studies of CAD patients (ISA, p. 2-14, section 5.2.6.1). Additional studies have shown associations between ambient CO and hospital admissions for congestive heart failure and cardiovascular disease as a whole (which includes IHD), although this evidence is not as consistent among studies as the IHD evidence (ISA, sections 5.2.3 and 5.2.6.1).

[16] Human clinical studies of individuals without diagnosed heart disease that were conducted since the 2000 CO AQCD did not report an association between CO and ST-segment changes or arrhythmia (ISA, section 2.5.1).

[17] The ST-segment is a portion of the electrocardiogram, depression of which is an indication of insufficient oxygen supply to the heart muscle tissue

[18] As stated in the ISA, the gas chromatographic technique for measuring COHb levels "is known to be more accurate than spectrophotometric measurements, particularly for samples containing COHb concentrations < 5%" (ISA, p. 5-41). CO-oximetry is a spectrophotometric method commonly used to rapidly provide approximate concentrations of COHb during controlled exposures (ISA, p. 5-41). At the low concentrations of COHb (<5%) more relevant to exposures to ambient CO, co-oximeters are reported to overestimate COHb levels compared to GC measurements, while at higher concentrations, this method is reported to produce underestimates (ISA, p.4-18).

and 253 ppm (range 143-357 ppm). After the 50- to 70-minute exposures, subjects underwent a second graded exercise treadmill test, and the percent change in time to onset of angina and time to ST endpoint between the first and second exercise tests was determined. Relative to clean-air exposure that resulted in a mean COHb level of 0.6% (post-exercise), exposures to CO resulting in post-exercise mean COHb concentrations of 2.0% and 3.9%[19] were shown to decrease the time required to induce ST-segment changes by 5.1% ($p=0.01$) and 12.1% ($p<0.001$), respectively. These changes were well correlated with the onset of exercise-induced angina the time to which was shortened by 4.2% ($p=0.027$) and 7.1% ($p=0.002$), respectively, for the two CO exposures (ISA, section 5.2.4; Allred et al., 1989a, 1989b, 1991).

No human clinical studies have been specifically designed to evaluate the effect of controlled exposures to CO resulting in study mean COHb levels lower than 2% (ISA, section 5.2.6). However, an important finding of the multi-laboratory study was the dose-response relationship observed between COHb and ischemia without evidence of a measurable threshold effect (Allred et al., 1989b, 1991). As reported by the authors, the results comparing "the effects of increasing COHb from baseline levels (0.6%) to 2 and 3.9% COHb showed that each produced further changes in objective ECG measures of ischemia" implying that "small increments in COHb could adversely affect myocardial function and produce ischemia" (Allred et al., 1989b, 1991). For each 1% increase in COHb resulting from the experimentally increased CO exposure concentrations the dose-response analysis performed by the authors indicated decreases of 1.9% in time to exercise-induced angina and 3.9% in time to exercised-induced ST-segment change in persons with pre-existing CAD (ISA, section 5.2.4, from Allred et al., 1989a, 1989b, 1991).

Other controlled human exposure studies (Adams et al., 1988; Anderson et al., 1973; Kleinman et al., 1989, 1998) involving individuals with stable angina have confirmed the Allred et al. findings at COHb concentrations between 3 and 6% (as measured by CO-oximeter) (ISA, section 5.2.4). Among the evidence is also a study of a small group of patients with CAD which reported no change in time to onset of angina or maximal exercise time following a 1 hour exposure targeted to result in 4% COHb. A subsequent study conducted by the same laboratory reported a significant increase in number of ventricular arrhythmias during exercise relative to room air among individuals with CAD following a 1-hr CO exposure targeted to yield 6% COHb, but not following a 1-hr exposure targeted to yield a COHb level of 4% (ISA, p. 5-42; Sheps et al., 1987, 1990). Although there was no clear pattern across the different studies with respect to the magnitude of the decreased time to onset of angina versus dose level, differences

[19] The corresponding co-oximeter measured post-exercise levels were 2.7% and 4.7%. The post-exposure, pre-exercise COHb levels for the two CO exposures were 2.4% and 4.7% by GC and 3.2% and 5.6% by co-oximetry (ISA, p. 5-41).

in study protocols and analytical methods do not allow for an informative pooled or quantitative meta-analysis of the dose-response relationship across studies (ISA, section 5.2.4). Although the subjects evaluated in the controlled human exposure studies described above are not necessarily representative of the most sensitive population, the level of disease in these individuals ranged from moderate to severe, with the majority either having a history of myocardial infarction or having ≥ 70% occlusion of one or more of the coronary arteries (ISA, p. 5-43).

We also note that, in the current review, a number of epidemiological studies are now available that investigate associations of cardiovascular morbidity with ambient measurements of CO (ISA, sections 5.2.4 and 5.2.5). These studies have observed associations between ambient monitor CO concentrations and increases in emergency department visits and hospital admissions for cardiovascular disease (ISA, sections 5.2.1.9). In considering the epidemiological evidence in the case of CO, we recognize that there is coherence between the available clinical and much expanded epidemiological evidence since the prior review, with regard to the health effects of CO in the cardiovascular system (primarily for ischemia-related events). As discussed in the ISA, the epidemiological studies reported associations of CO concentrations at ambient monitors with emergency department visits and/or hospital admissions for IHD and other cardiovascular disease-related outcomes that are plausibly related to the effects on physiological indicators of myocardial ischemia (e.g., ST-segment changes) demonstrated in the controlled human exposure studies, providing coherence between the two sets of findings. Furthermore, in consideration of the epidemiological studies for cardiovascular outcomes in light of the larger body of evidence, the ISA notes that the "known role of CO in limiting O_2 availability lends biological plausibility to ischemia related health outcomes following CO exposure", providing coherence between the two sets of findings.

2.5.2 Other Effects

Other health effects for which the evidence is suggestive of causal relationships with CO exposures include some effects on the central nervous system, reproduction and prenatal development, and the respiratory system (ISA, section 2.5).

High CO exposures have "long been known to adversely affect central nervous system (CNS) function", although the evidence does not include such effects associated with exposures close to ambient CO concentrations (ISA, p. 5-49). Further, the evidence indicates that healthy adults may be protected against such CNS effects at ambient levels through compensatory responses such as increased cardiac output and cerebral blood flow, although these compensatory mechanisms may be impaired among certain groups, such as those with reduced cardiovascular function (ISA, section 5.3.3).

Epidemiological and toxicological studies provide limited evidence of CO effects on the developing fetus and newborn infants, as summarized in section 2.4 above. For example, some epidemiological studies have reported associations of CO exposure during early pregnancy with pre-term births and cardiac birth defects, with animal toxicological studies providing some support and coherence for these effects at prolonged exposure concentrations ranging from 60-500 ppm (ISA, section 5.4.3, pp. 5-80 and 5-120). The ISA notes that overall, there is limited though positive evidence for CO-induced effects on pre-term birth and birth defects, and weak evidence for a decrease in birth weight and fetal growth, and infant mortality; with animal toxicological studies providing support and coherence for those effects. A clear understanding of the mechanisms by which CO may induce those effects is still lacking (ISA, section 2.5.3).

New epidemiologic studies report positive associations for CO-induced lung-related health outcomes, although interpretation is affected by uncertainties including with regard to the biological mechanism that could explain CO-induced respiratory outcomes (ISA, section 5.5.5).

While only briefly summarized here, the evidence for the health effects identified here is further discussed and considered with regard to the review of the CO NAAQS in the Policy Assessment.

2.6 RISK CHARACTERIZATION APPROACH

In identifying an approach to characterize the risk of cardiovascular effects of exposures to ambient CO, we considered 1) approaches employed in previous assessments, 2) the currently available evidence regarding associations between CO concentrations and cardiovascular outcomes, and 3) advice from CASAC (Brain, 2009; Brain and Samet, 2009, 2010a, 2010b). As summarized in section 1.2, the last CO NAAQS review included analyses of exposure to ambient CO and associated internal dose, in terms of COHb levels, which were used to characterize risks for the population of interest (US EPA, 1992). The prior risk characterization considered the percent of the modeled population that exceeded COHb levels of interest which were drawn from the evidence of COHb levels associated with a decrease in time to exercise-induced angina in controlled human exposure studies involving short-term (shorter than 8 hours) exposures of patients with diagnosed CAD[20] to elevated CO concentrations (US EPA, 1991).

In the current review, the controlled human exposure studies among individuals with CAD continue to provide the clearest evidence of CO-induced effects on the cardiovascular system as the most sensitive endpoint. In contrast to epidemiological studies, human exposure studies also provide quantitative information linking CO exposures through COHb levels with

[20] Study subjects met certain criteria with respect to evidence of coronary artery disease, often also called CHD or IHD.

these effects. Among these studies, the multilaboratory study of Allred et al. (1989a, 1989b, 1991) continues to be the principal study informing our understanding of the effects of CO on individuals with pre-existing CAD at the low end of the range of COHb levels studied (US EPA, 1991, 2000, 2010a). The strength of the evidence more broadly continues to support the use of COHb level as the internal dose metric for assessing exposure to ambient levels of CO and characterizing associated potential for cardiovascular disease-related health risk. Thus, based on the strength of the evidence and the availability of quantitative information from controlled human exposure studies, this REA also focuses on estimates of the percent of the simulated at-risk population expected to experience maximum end-of-hour COHb levels of interest based on findings of those studies.

As noted in section 2.5.1 above, a number of epidemiological studies are now available in the current review that have observed associations between ambient monitor CO concentrations and increases in emergency department visits and hospital admissions for cardiovascular disease (ISA, sections 5.2.1.9). These studies are coherent with the controlled human exposure studies (ISA, section 5.2.6), however, a number of uncertainties complicate their use for our purposes in a quantitative risk assessment (ISA, pp. 2-14 to 2-17, section 5.2.3). These uncertainties are discussed and considered in greater detail in the Policy Assessment. Accordingly, in light of the longstanding body of evidence that links exposures to effects through the internal dose metric, COHb, we have characterized health risk of ambient CO exposures in this assessment using estimates of associated COHb levels and a benchmark level approach, with benchmarks identified in consideration of the controlled human exposure literature.[21]

In drawing from the results of the controlled human exposure studies to inform the characterization of potential CO risk in this assessment, staff considered a number of factors, listed below.

- Myocardial ischemic effects, as documented by reductions in times to exercise-induced change in the ST-segment of an electrocardiogram and to exercise-induced onset of angina, were observed in response to CO exposures involving subjects with pre-existing CAD. Staff gives primary focus here to the multi-laboratory study in which COHb was analyzed by the more accurate GC method (Allred et al., 1989a, 1989b, 1991).
- Relative to clean-air exposure that resulted in a mean level of 0.6% COHb (post-exercise), exposures to CO resulting in post-exercise mean COHb levels of 2.0% and

[21] While not used for the purposes of this quantitative assessment, EPA is considering all of the current health evidence, including the epidemiological studies, in the Policy Assessment, along with considerations based on the risk and exposure assessment findings.

3.9%[22] were shown to decrease the time required to induce ST-segment changes by 5.1% ($p=0.01$) and 12.1% ($p<0.001$), respectively. These changes were well correlated with the onset of exercise-induced angina, the time to which was shortened by 4.2% ($p=0.027$) and 7.1% ($p=0.002$), respectively, for the two CO exposures (Allred et al., 1989a, 1989b, 1991).

- There is no evidence of a threshold for the measures assessed at the lowest levels tested, with incremental additions of COHb from baseline mean levels of 0.6% to 2 and 3.9% COHb showing changes in the monitored measures of ischemia (Allred et al., 1989b, 1991). The average of the regressions of the individual study subject data for these measures at baseline COHb and the two COHb levels resulting from the two controlled CO exposures was summarized by the authors as indicating decreases of roughly 1.9% in time to exercise-induced angina and 3.9% in time to exercise-induced ST-segment change per 1% increase in COHb concentration in persons with pre-existing CAD (ISA, section 5.2.4; Allred et al., 1989a, 1989b, 1991).
- Studies have not been designed to evaluate similar effects of exposures to increased CO concentrations eliciting average COHb levels below the 2% target level of Allred et al. (1989a, 1989b, 1991). In addition, these studies do not address the fraction of the population experiencing a specified health effect at various dose levels. These aspects of the evidence contributed to EPA's conclusion that at this time there are insufficient controlled human exposure data to support the development of quantitative dose-response relationships which would be required in order to conduct a quantitative risk assessment for this health endpoint, rather than the benchmark level approach.

In drawing on this information, staff recognize the uncertainty associated with interpretation of COHb levels estimated to result from CO exposure concentrations in this assessment that are much lower than the CO exposure concentrations used in the clinical studies to elicit increases in participant's COHb levels to target levels for the study.

We have reviewed the daily maximum end-of-hour COHb estimates developed in this REA with attention to both the total COHb levels, which represent the combined influence of ambient CO exposures and endogenous CO production, and the ambient CO contribution to COHb levels, derived by subtracting the COHb produced in the absence of any CO exposure from the total COHb level (see section 6.2 below). Results from the model simulations are reported in terms of percent of population expected to experience daily maximum end-of-hour COHb levels (or ambient CO contribution to daily maximum end-of-hour COHb levels) at or above a series of levels that range as low as 1%. These results are interpreted in the Policy Assessment document in light of potential health effects benchmarks.

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[22] Subjects were exposed to two levels of CO exposure, resulting in COHb levels in the range of 2.0 to 2.4% and 3.9 to 4.7%, respectively. The upper end of each range is the average COHb level obtained post-exposure and the lower end is the average COHb level obtained after the subsequent exercise test (Allred et al., 1989a, 1989b, 1991).

With regard to total COHb, staff identified benchmark levels of 1.5%, 2.0%, 2.5% and 3% COHb based on consideration of the evidence from controlled human studies of CHD patients discussed above, and is inclusive of the range of levels considered in the review completed in 1994 (US EPA, 1992). This range extends below the lowest mean COHb level (e.g., 2.0% post-exercise in Allred et al., 1989b) resulting from controlled exposure to increased CO concentration in the clinical evidence. This extension reflects comments from the CASAC CO panel on the draft Analysis Plan (Brain and Samet, 2009) and consideration of the uncertainties regarding the actual COHb levels experienced in the controlled human exposure studies; that these studies did not include individuals with most severe cardiovascular disease; the lack of studies evaluating effects of controlled short-term CO exposures resulting in COHb levels below study mean 2.0-2.4% and the lack of evidence of an effect threshold at these levels. We note that CASAC comments on the first draft REA recommended the addition of a benchmark at 1% COHb and staff has presented results for this COHb level in this REA. In considering this advice, we recognize, however, that a level of 1% COHb overlaps with the upper part of the range of endogenous levels in health individuals as characterized in the ISA (ISA, p. 2-6) and with the upper part of the range of baseline COHb levels in the study by Allred et al. (1989b, Appendix B). As a result, while noting population dose estimates in relation to this level, we have not placed weight on this level as a potential health effects benchmark in discussions of the results below and in the Policy Assessment document.

We additionally consider the assessment results in light of the multi-laboratory clinical study conclusions regarding response to specific increases in COHb level over the subjects' pre-exposure or air exposure, with the increased COHb resulting from short-term controlled CO exposure exposures of persons with pre-existing CAD (ISA, section 5.2.4; Allred et al., 1989a, 1989b, 1991).[23] For this, we present the percentage of the simulated populations estimated to experience ambient CO contribution or increment to daily maximum end-of hour COHb levels greater than a series of levels that range as low as 1%. These results are interpreted in the Policy Assessment document in light of potential health effects benchmarks, which for this ambient contribution (or increment) to daily maximum end-of-hour COHb levels include the range from

[23] Relative to clean-air exposure that resulted in a mean COHb level of 0.6% (post-exercise), exposures to CO resulting in post-exercise mean COHb concentrations of 2.0% and 3.9% were shown to decrease the time required to induce ST-segment changes by 5.1% ($p=0.01$) and 12.1% ($p<0.001$), respectively. These changes were well correlated with the onset of exercise-induced angina the time to which was shortened by 4.2% ($p=0.027$) and 7.1% ($p=0.002$), respectively, for the two CO exposures. A dose-response analysis in which the individual regressions of study subject responses at baseline COHb and at the two increased COHb levels were averaged was summarized as indicating decreases of roughly 1.9% in time to exercise-induced angina and 3.9% in time to exercised-induced ST-segment change per 1% increase in COHb concentration in persons with pre-existing CAD (ISA, section 5.2.4; Allred et al., 1989a, 1989b, 1991).

1.4% up to 2.4%, COHb increments associated with reduced time to exercise-induced angina and ST-segment change in those studies.

The benchmark levels identified are used to interpret COHb levels estimated to occur in the modeled population in response to exposures to ambient CO in different air quality scenarios in light of the evidence discussed above for cardiovascular effects observed in individuals with CHD when exposed to CO. More specifically, we have estimated the number of persons and percent of the simulated at-risk population expected to experience COHb levels below each of these potential health effect benchmark levels as a result of ambient CO exposures associated with a set of air quality scenarios employed to inform the current review of the CO NAAQS (see chapter 5 below). As noted in chapter 1 above, given the significant time constraints of this review, results are provided in this document without substantial interpretation. Rather, discussion of health risk and public health implications of these results in the context of the NAAQS review is provided in the Policy Assessment.

2.7 KEY OBSERVATIONS

Presented below are key observations for this conceptual overview of the assessment of ambient CO exposure and health risk.

- Carbon monoxide in ambient air is formed primarily by the incomplete combustion of carbon-containing fuels and photochemical reactions in the atmosphere, with on-road mobile sources representing significant sources of CO to ambient air.
- Microenvironments influenced by on-road mobile sources are important contributors to ambient CO exposures, particularly in urban areas. Where present, other (nonambient) CO sources can also be important influences on total CO exposure and on the impact of ambient CO exposure on COHb levels.
- The formation of COHb is a key step in the elicitation of various health effects by CO. Further, COHb level is commonly used in exposure assessment and is considered the best biomarker for evaluating CO exposure and potential for health effects of concern.
- An individual's COHb levels reflect their endogenous CO production, as well as CO taken into the body during exposure to ambient and nonambient CO sources. CO uptake into the bloodstream during exposure is influenced by a number of variables including internal levels of CO and COHb, such that net uptake may be lower or negligible in instances where a preceding exposure has been substantially higher than the current one. Thus, the magnitude of the change in COHb level in response to ambient CO exposure may decrease with the presence of concurrent or preceding nonambient CO exposure.
- Individuals with CHD are the population with greatest susceptibility to short-term exposure to CO, and the population for which the current evidence indicates health effects occurring at the lowest exposures. The evidence further indicates a potential for other underlying cardiovascular conditions, particularly other types of heart disease, to

contribute susceptibility to CO effects. Other populations potentially at risk include those with diseases such as chronic obstructive pulmonary disease (COPD), anemia, or diabetes, and those in prenatal or elderly life stages.

- Cardiovascular effects are the category of health effects for which the evidence is strongest and indicative of a likely causal relationship with relevant short-term CO exposures, particularly for people with CHD. Other endpoints for which the evidence is suggestive of causal relationships include effects on the central nervous system, reproduction and prenatal development, and the respiratory system.
- The specific cardiovascular effects occurring at the lowest COHb levels studied in CHD patients are reduced time to exercise-induced angina and other markers of myocardial ischemia, in particular, specific changes to the ST-segment of an electrocardiogram.
- Risk is characterized in this REA through evaluation of COHb estimated in simulations involving ambient CO exposures experienced by two target populations: (1) individuals with CHD (including undiagnosed CHD persons) and (2) individuals with HD, including CHD (diagnosed and undiagnosed).
- Two types of COHb estimates are considered for the two target populations: (1) daily maximum end-of-hour COHb levels and (2) ambient contribution to daily maximum end-of-hour COHb levels (i.e., the change in COHb associated with ambient CO exposure alone).
- Results from simulations are reported in terms of percent of the simulated at-risk population expected to experience daily maximum end-of-hour COHb levels (or ambient CO contribution to daily maximum end-of-hour COHb levels) at or above a series of levels that range as low as 1%. These results are interpreted in the Policy Assessment document in light of potential health effects benchmarks.
    - For daily maximum end-of-hour COHb levels (absolute), these benchmarks range from 1.5%, which is below the lowest study mean COHb level resulting from experimental CO exposure in controlled human exposures of subjects with CAD, up to 3.0%, a level within the range associated with effects in those studies. For ambient contribution to daily maximum end-of-hour COHb levels, the comparison benchmarks include the range from 1.4% up to 2.4%, which are the COHb increments associated with effects in those studies.
- Beyond the at-risk populations and myocardial ischemia-related effects that are the focus of this quantitative REA, the current evidence regarding other potentially susceptible populations and other health effects associated with CO exposures is discussed and considered with regard to the review of the CO NAAQS in the Policy Assessment.

2.8 REFERENCES

Abi-Esber L and El-Fadel M. (2008). In-vehicle CO ingression: validation through field measurements and mass balance simulations. *Sci Total Environ*. 394:75-89.

Adams KF, Koch G, Chatterjee B, Goldstein GM, O'Neil JJ, Bromberg PA, Sheps DS, McAllister S, Price CJ, Bissette J. (1988). Acute elevation of blood carboxyhemoglobin to 6% impairs exercise performance and aggravates symptoms in patients with ischemic heart disease. *J Am Coll Cardiol*. 12:900-909

Akland GG, Hartwell TD, Johnson TR, Whitmore RW. (1985). Measuring human exposure to carbon monoxide in Washington, DC, and Denver, Colorado, during the winter of 1982-1983. *Environ Sci Technol*. 19:911-918.

Allred EN, Bleecker ER, Chaitman BR, Dahms TE, Gottlieb SO, Hackney JD, Pagano M, Selvester RH, Walden SM, Warren J. (1989a). Short-term effects of carbon monoxide exposure on the exercise performance of subjects with coronary artery disease. *N Engl J Med*. 321:1426-1432.

Allred EN, Bleecker ER, Chaitman BR, Dahms TE, Gottlieb SO, Hackney JD, Hayes D, Pagano M, Selvester RH, Walden SM, Warren J. (1989b). Acute effects of carbon monoxide exposure on individuals with coronary artery disease. Cambridge, MA: Health Effects Institute; research report no. 25.

Allred EN, Bleecker ER, Chaitman BR, Dahms TE, Gottlieb SO, Hackney JD, Pagano M, Selvester RH, Walden SM, Warren J. (1991). Effects of carbon monoxide on myocardial ischemia. *Environ Health Perspect*. 91:89-132.

AHA. (2003). Heart and Stroke Facts. American Heart Association, Dallas, TX. Available at: http://www.americanheart.org/downloadable/heart/1056719919740HSFacts2003text.pdf.

Anderson EW, Andelman RJ, Strauch JM, Fortuin NJ, Knelson JH. (1973). Effect of low level carbon monoxide exposure on onset and duration of angina pectoris. *Annals of Internal Medicine*. 79:46-50.

Boulter P and McCrae I. (2005). Carbon Monoxide Inside Vehicles: Implications for Road Tunnel Ventilation. In: Annual Research Review 2005. TRL Academy.

Brain JD. (2009). Letter from Dr. Joseph Brain to Administrator Lisa Jackson. Re: Consultation on EPA's Carbon Monoxide National Ambient Air Quality Standards: Scope and Methods Plan for Health Risk and Exposure Assessment. CASAC-09-012. July 14, 2009.

Brain JD and Samet JM. (2009). Letter to EPA Administrator Lisa Jackson: Clean Air Scientific Advisory Committee's (CASAC) Peer Review of the Agency's 1st Draft Carbon Monoxide Integrated Science Assessment. EPA-CASAC-09-011. June 24, 2009.

Brain JD and Samet JM. (2010a). Letter from Drs. J.D. Brain and J.M. Samet to Administrator Lisa Jackson. Re: Review of the Risk and Exposure Assessment to Support the Review of the Carbon Monoxide (CO) Primary National Ambient Air Quality Standards: First External Review Draft. CASAC-10-006. February 12, 2010.

Brain JD and Samet JM. (2010b). Letter from Drs. J.D. Brain and J.M. Samet to Administrator Lisa Jackson. Re: Review of the Risk and Exposure Assessment to Support the Review of the Carbon Monoxide (CO) Primary National Ambient Air Quality Standards: Second External Review Draft. EPA-CASAC-10-012. May 19, 2010.

Bruinen de BruinY, Hanninen O, Carter P, Maroni M, Kephalopoulos S, Scotto De Marco G, Jantunen M. (2004). Personal carbon monoxide exposure levels: contribution of local sources to exposures and microenvironmental concentrations in Milan. *J Expo Anal Environ Epidemiol*. 14:312-322.

Chan C, Ozkaynak H, Spengler J, Sheldon L. (1991). Driver exposure to volatile organic compounds, CO, ozone, and NO_2 under different driving conditions. *Environ Sci Technol*. 25(5):964-972.

Chang LT, Koutrakis P, Catalano PJ, Suh HH. (2000). Hourly personal exposures to fine particles and gaseous pollutants - results from Baltimore, Maryland. *J Air Waste Manage Assoc*. 50:1223-1235.

Coburn R, Forster R, Kane P. (1965). Consideration of the physiological variables that determine the blood carboxyhemoglobin concentrations in man. *J Clin Invest*. 44:1899-1910.

Flachsbart P. (1999). Human exposure to carbon monoxide from mobile sources. *Chemosphere – Global Change Science*. 1:301-329.

Petersen WB and Allen RA. (1982) Carbon monoxide exposures to Los Angeles area commuters. *J Air Pollution Control Assoc*. 32:826-833.

Johnson T, Mihlan G, LaPointe J, Fletcher K, Capel J. (2000). Estimation of Carbon Monoxide Exposures and Associated Carboxyhemoglobin Levels in Denver Residents Using pNEM/CO (Version 2.1), prepared by ICF Kaiser Consulting Group for U.S. EPA, Office of Air Quality Planning and Standards, under Contract No. 68-D6-0064, WA Nos. 1-19, 2-24, 2-30, and 3-3, Docket EPA-HQ-OAR-2008-0015-0010.

Kleinman MT, Davidson DM, Vandagriff RB, Caiozzo VJ, Whittenberger JL. (1989). Effects of short-term exposure to carbon monoxide in subjects with coronary artery disease. *Arch Environ Health*. 44:361-369.

Kleinman MT, Leaf DA, Kelly E, Caiozzo V, Osann K, O'Niell T. (1998). Urban angina in the mountains: effects of carbon monoxide and mild hypoxemia on subjects with chronic stable angina. *Arch Environ.Health*. 53:388-397.

Koushi P, Al-Dhowalis K, Niazi S. (1992). Vehicle occupant exposure to carbon monoxide. *J Air Waste Manag*. 42:1603-1608.

Rodes C, Sheldon L, Whitaker D, Clayton A, Fitzgerald K, Flanagan J, DiGenova F, Hering S, Frazier C. (1998). Measuring Concentrations of Selected Air Pollutants Inside California Vehicles. Final Report. Prepared by Research Triangle Institute under Contract No. 95-339. California Air Resources Board. Sacramento, California.

Scotto di Marco G, Kephalopoulos S, Ruuskanene J, Jantunene M. (2005). Personal carbon monoxide exposure in Helsinki, Finland. *Atmos Environ*. 39Z:2697–2707.

Sharp D and Tight M. (1997). Vehicle occupant exposure to air pollution. In: Policy, Planning, and Sustainability: Proceedings of Seminars C and D Held at PTRC European Transport Forum, Brunel University. Pages 481-492.

Sheps DS, Adams KF Jr, Bromberg PA, Goldstein GM, O'Neil JJ, Horstman D, Koch G. (1987). Lack of effect of low levels of carboxyhemoglobin on cardiovascular function in patients with ischemic heart disease. *Arch Environ Health*. 42:108-116.

Sheps DS, Herbst MC, Hinderliter AL, Adams KF, Ekelund LG, O'Neil JJ, Goldstein GM, Bromberg PA, Dalton JL, Ballenger MN, Davis SM, Koch GG. (1990). Production of arrythmias by elevated carboxyhemoglobin in patients with coronary artery disease. *Ann Intern Med*. 113:343-351.

Shikiya D, Liu C, Kahn M, Juarros J, Barcikowski W. (1989). In-Vehicle Air Toxics Characterization Study in the South Coast Air Basin. Office of Planning and Rules, South Coast Air Quality Management District.

US EPA. (1991). Air Quality Criteria For Carbon Monoxide. Research Triangle Park, NC: Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office; report no. EPA/600/8-90/045F.

US EPA. (1992). Review of the National Ambient Air Quality Standards for Carbon Monoxide: Assessment of Scientific and Technical Information. Office of Air Quality Planning and Standards Staff Paper, report no. EPA/452/R-92-004.

US EPA. (2000). Air Quality Criteria for Carbon Monoxide. National Center for Environmental Assessment, Office of Research and Development, U.S. Environmental Protection Agency, Research Triangle Park, NC 27711; report no. EPA/600/P-99/001F. June 2000. Available at: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=18163.

US EPA. (2006). 2002 National Emissions Inventory Data and Documentation. U.S. Environmental Protection Agency, Office of Air and Radiation, Office of Air Quality Planning and Standards, Research Triangle Park, NC. Available at: http://www.epa.gov/ttn/chief/net/2002inventory.html.

US EPA. (2010a). Integrated Science Assessment for Carbon Monoxide. U.S. Environmental Protection Agency, Washington, DC, report no. EPA/600/R-09/019F. Available at: http://www.epa.gov/ttn/naaqs/standards/co/s_co_cr_isa.html.

US EPA. (2010b). Policy Assessment for the Review of the Carbon Monoxide National Ambient Air Quality Standards, External Review Draft. Office of Air Quality Planning and Standards Staff Paper, report no. EPA-452/P-10-005.

3 AIR QUALITY CONSIDERATIONS

Ambient air quality data can be used as an indicator of exposure or used in conjunction with other information to estimate exposure concentrations. How well the ambient air quality is represented in a particular location is dependent on a number of factors including the ambient monitoring network design relative to the spatial and temporal characteristics of the pollutant as well understanding the concentration contribution from important local source emissions. This chapter summarizes findings about the current air quality conditions and their temporal and spatial distribution, with particular focus on aspects informative to the design and conduct of this assessment and including descriptions of CO measurement methods, monitor siting requirements, and monitor locations (section 3.1). Section 3.2 then draws upon the information presented in sections 3.1, among other data, to select ambient air quality/study locations most useful in meeting the objectives of the REA. Finally, key observations of the chapter are presented in section 3.3.

3.1 AMBIENT CO MONITORING

In this section, a broad overview of the monitoring network is provided (section 3.1.1) and is followed by a summary of analytical detection issues (section 3.1.2). Ambient CO concentrations and their spatial and temporal variability are characterized in section 3.1.3. Estimates of policy-relevant background (PRB) concentrations which are defined as those ambient concentrations that would occur in the US in the absence of anthropogenic emissions in continental North America are presented in section 3.1.4. And finally, section 3.1.5 presents an analysis of the specific CO concentration trends observed in individual monitors.

3.1.1 Monitoring Network

Ambient CO concentrations are measured by monitoring networks that are operated by state and local monitoring agencies in the US, and are funded in part by the EPA. The main network providing ambient data for use in comparison to the NAAQS is the State and Local Air Monitoring Stations (SLAMS) network. The subsections below provide specific information regarding the methods used for obtaining ambient CO measurements and the requirements that apply to states in the design of the CO network.

Minimum monitoring requirements for CO were revoked in the 2006 revisions to ambient monitoring requirements (see 71 FR 61236, October 17, 2006). This action was made to allow for reductions in measurements of some criteria pollutants (CO, SO_2, NO_2, and Pb) where the current measured levels were all well below the applicable NAAQS. CO monitoring activities

have been maintained at some SLAMS and these measurements of CO at these monitoring sites are required to continue until discontinuation is approved by the EPA Regional Administrator.

CO monitors are typically sited to represent one of the following spatial scales.[1]

- **Microscale:** Data represent concentrations within a 100 meter (m) radius of the monitor. For CO, microscale monitors are sited 2 – 10 m from a roadway. Measurements are intended to represent the near-road or street canyon environment.
- **Middle scale:** Data represent concentrations averaged over areas defined by 100 – 500 m radii. Measurements are intended to represent several city blocks.
- **Neighborhood scale:** Data represent concentrations averaged over areas defined by 0.5 – 4.0 km radii. Measurements are intended to represent extended portions of a city.

In addition to monitoring required for determining compliance with the NAAQS, the EPA is currently in the process of implementing plans for a new network of multi-pollutant stations, called NCore, that is intended to meet multiple monitoring objectives. A subset of the SLAMS network, these NCore stations are intended to address integrated air quality management needs to support long-term trends analysis, model evaluation, health and ecosystem studies, as well as the more traditional objectives of NAAQS compliance and Air Quality Index reporting.[2] The complete NCore network, required to be fully implemented by January 1, 2011, will consist of approximately 63 urban and 20 rural stations and will include some existing SLAMS sites that have been modified to include additional pollutant and meteorological measurements. Each state will contain at least one NCore station, and 46 of the states plus Washington, D.C. will have at least one urban station. CO will be measured using high sensitivity monitors (see section 3.1.2 below), as will SO_2, NO, and NO_Y.[3] The majority of NCore stations will be sited to represent neighborhood, urban, and regional scales, consistent with the NCore network design objective of representing exposure expected across urban and rural areas in locations that are not dominated by local sources.

3.1.2 Analytical Sensitivity

To promote uniform enforcement of the air quality standards set forth under the CAA, EPA has established provisions in the Code of Federal Regulations (CFR) under which analytical methods can be designated as federal reference methods (FRMs) or federal equivalent methods (FEMs). Measurements for determinations of NAAQS compliance must be made with FRMs or

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[1] A complete description of spatial scales is listed in 40 CFR Part 58 Appendix D, section 1.2. Ambient monitoring of other NAAQS pollutants such as NO_2 and SO_2 follow the same general spatial scales.

[2] (http://www.epa.gov/ttn/amtic/ncore/index.html).

[3] NCore sites must measure, at a minimum, $PM_{2.5}$ particle mass using continuous and integrated/filter-based samplers, speciated $PM_{2.5}$, $PM_{10\text{-}2.5}$ particle mass, speciated $PM_{10\text{–}2.5}$, O_3, SO_2, CO, NO/NO_Y, wind speed, wind direction, relative humidity, and ambient temperature (http://www.epa.gov/ttn/amtic/ncore/index.html).

FEMs.[4] Specifications for CO monitoring are designed to help states utilize equipment that has met performance criteria utilized in the FRM or FEM approval process; operational parameters are documented in 40 CFR Part 53, Table B-1. Given the levels of the current CO NAAQS (35 ppm, 1-hour; 9 ppm, 8-hour average), the required 1.0 ppm lower detectable limit (LDL)[5] is well below the NAAQS levels and is therefore determined sufficient for demonstration of compliance. However, with ambient CO levels now routinely near or below 1 ppm, there is greater uncertainty in a larger portion of the distribution of monitoring data because a large percentage of these measurements are below the LDL of conventional monitors. For this reason, a new generation of ambient CO monitors has been designed that provides measurements with improved sensitivity at or below the typical ambient CO levels measured in most urban and all rural locations. Additionally, the higher sensitivity CO measurements are needed to support additional objectives such as validating the inputs to chemical transport models and assessing the role of transport between urban and rural areas because policy relevant background CO concentrations on the order of 0.1 ppm are well below the LDL of conventional monitors. Newer GFC instruments have been designed for automatic zeroing to minimize drift (US EPA, 2000).

Currently, a total of 13 approved FRMs are in use in the SLAMS network, based on a retrieval of data reported between 2005 and 2009. Among these methods, nine are "legacy" monitors with a federal method detection limit (MDL)[6] given as 0.5 ppm according to records in EPA's Air Quality System (AQS).[7] As discussed in the ISA (US EPA, 2010), many of the reported concentrations in recent years are near or below these MDLs (ISA, section 3.5.1.2). Four of these new methods are high sensitivity methods with a federal MDL of 0.02 ppm and there is a growing body of ambient data from high sensitivity CO instruments becoming available. Among newer gas filter correlation (GFC) high sensitivity instruments, manufacturer-declared LDLs range from 0.02 – 0.04 ppm, with 24-hour zero drift varying between 0.5%

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[4] As of August 2009, twenty automated FRMs had been approved for CO measurement. All EPA FRMs for CO operate on the principle of non-dispersive infrared (NDIR) detection and can include the gas filter correlation (GFC) methodology. An extensive and comprehensive review of NDIR, GFC, and alternative, non-FRM techniques for CO detection was included in the 2000 CO AQCD (US EPA, 2000).

[5] Defined in 40 CFR Part 53.23 as the minimum pollutant concentration which produces a signal of twice the noise level.

[6] Defined in 40 CFR Part 136 as the minimum concentration of a substance that can be measured and reported with 99% confidence that the analyte concentration is greater than zero and is determined from analysis of a sample in a given matrix containing the analyte.

[7] Among several of the older instruments (Federal Reference Method codes 008, 012, 018, 033, 041, 050, 051, and 054), performance testing has shown LDLs of 0.62 – 1.05 ppm, with 24-hour drift ranging from 0.044 – 0.25 ppm and precision ranging from 0.022 – 0.067 ppm at 20% of the upper range limit of the instrument (Michie et al., 1983).

within 1 ppm and 0.1 ppm, and precision varying from 0.5% to 0.1 ppm. EPA performed MDL testing on several high sensitivity CO monitors in 2005 and 2006 following the 40 CFR Part 136 procedures. Those tests demonstrated MDLs of approximately 0.017 – 0.018 ppm, slightly below the stated LDL of 0.02 – 0.04 ppm.

Based on a retrieval of data reported to AQS for the time period between 2005 and 2009, a total of 36 high sensitivity CO monitors have reported data with the majority of these monitors currently active. Most of these active monitors are associated with the implementation of the NCore network. The extent to which high sensitivity monitors become integrated into non-NCore SLAMS stations, however, will depend on the availability of funding for states to replace operating legacy CO monitors as well as the possibility that monitoring requirements for CO might either encourage or require increased sensitivity.

3.1.3 General Patterns of CO Concentrations

As discussed in the ISA, the spatial and temporal patterns of ambient CO concentrations are heavily influenced by the patterns associated with mobile source emissions (ISA, section 3.2.1). Based on the 2002 National Emissions Inventory (NEI; US EPA, 2006), on-road mobile sources comprise about half of the total anthropogenic CO emissions, though in metropolitan areas of the US the contribution is as high as 75% of all CO emissions due to greater motor vehicle density. For example, emissions in Denver county originating from on-road mobile sources is about 71% of total CO emissions (ISA, section 3.2). When considering all mobile sources (non-road and on-road combined), the contribution to total CO emissions is roughly 80% nationwide and can be higher in some metropolitan areas. Again using Denver County as an example, all mobile sources combined contribute to about 98% of the total CO emissions in the county. Temporally, the national-scale anthropogenic CO emissions have decreased 35% between 1990 and 2002. Nearly all the national-level CO reductions since 1990 are the result of emission reductions in on-road vehicles (ISA, Figure 3-2).

Nearly 400 ambient monitoring stations report continuous hourly averages of CO concentrations across the US. Over the period 2005-2007, 291 out of 376 monitors met a 75% completeness requirement, spread among 243 counties, cities, or municipalities (ISA, section 3.4.2.2). No violations of the NAAQS were reported at these monitoring sites during this time period. For example, in 2007, none of the monitors reported a second-highest 1-hour CO concentration above 35 ppm, the level of the current 1-hour NAAQS, while only two sites reported 2nd highest 1-hour CO concentrations between 15.1 and 35.0 ppm (ISA section 3.5.1.1). Only five counties reported a 2nd highest 8-hour CO concentration of 5.0 ppm or higher.

The current levels of ambient CO across the US reflect the steady declines in ambient concentrations that have occurred over the past several years. On average across the US the

decline has been on the order of 50% since the early 1990s (ISA, Figure 3-34). As an example, Figures 3-1 illustrate the trends observed in Denver and Los Angeles ambient concentrations, for several selected monitors within the urban core of each area during 1993 through 2008. Note that there is a significant decrease in the 2nd highest 1-hour and 8-hour average CO concentrations since the last review.

Ambient monitor siting characteristics can influence ambient CO concentrations. Microscale and middle scale monitors are commonly used to measure significant local source impacts, while neighborhood and urban scale monitors are designated for population-oriented monitoring (40 CFR Part 58 Appendix D). As CO concentrations primarily originate from vehicle emissions, the microscale and middle scale data can be a useful indicator of near-road air quality. Such data analyzed in the ISA were concluded to be consistent with hourly concentrations reported in the literature for the near-road environment in the US (ISA, p. 3-57). Further, when considering monitoring scale across ambient monitors in the US, the median hourly CO concentration measured at microscale monitors was about 25% higher than at middle scale monitors and 67% higher than at neighborhood scale monitors (ISA, Table 3-12). In general, similar patterns were present in the 1-hour daily max, 1-hour daily average, and 8-hour daily max distributions (ISA, Table 3-12). These patterns are also consistent with findings presented by other researchers regarding the relative decrease in concentration with increasing distance from roadways, though the magnitude of the relationship can vary. Two studies summarized in the ISA (Zhu et al., 2002; Baldauf et al., 2008) indicate that near-road CO concentrations measured within 20 meters of an interstate highway can range from 2 – 10 times greater than CO concentrations measured as far as 300 meters from a major road possibly influenced by wind direction and on-road vehicle density (ISA, Figures 3-29 and 3-30).

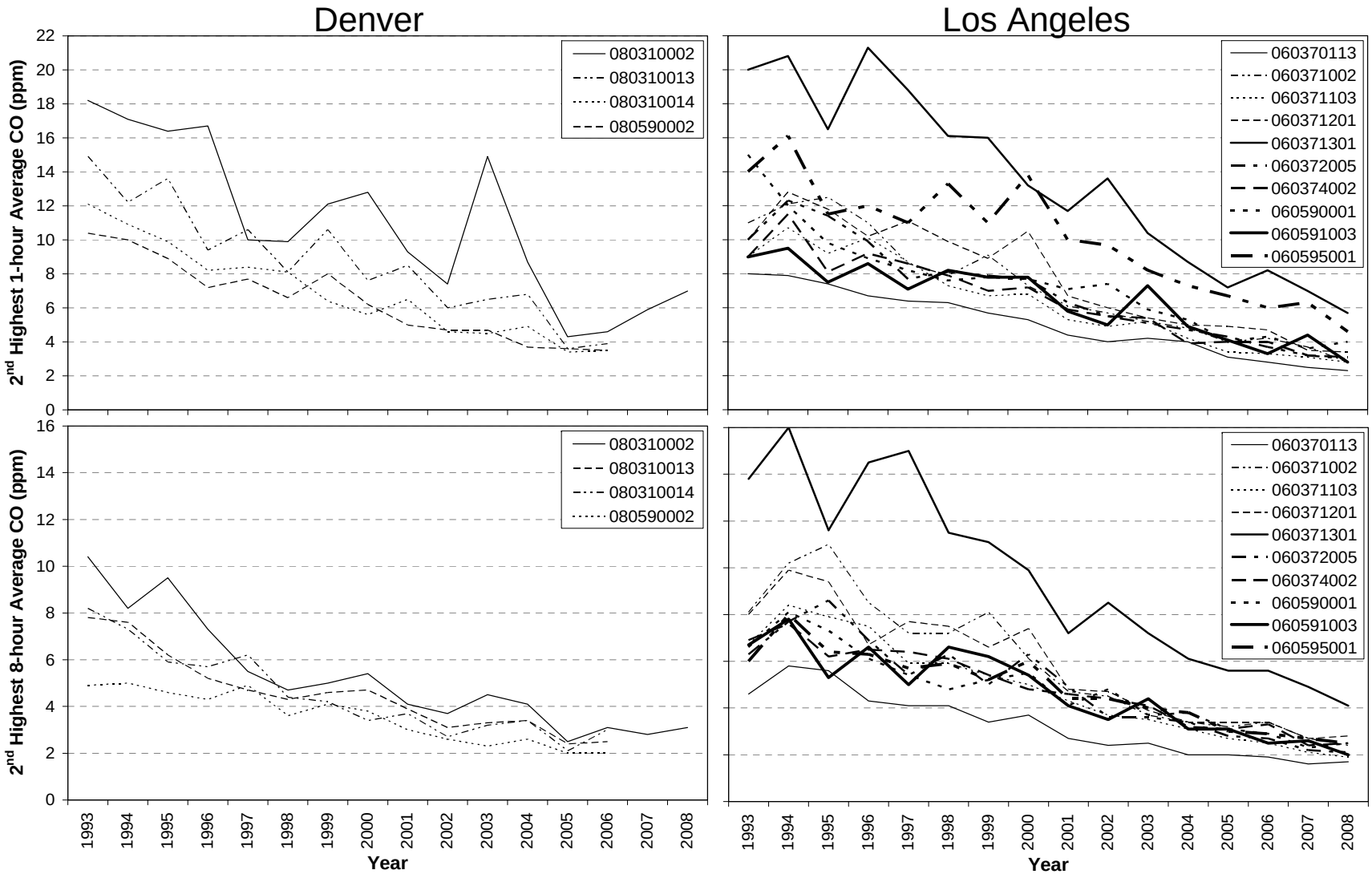

Figure 3-1. Spatial and temporal trends in the 2nd highest 1-hour (top) and 8-hour average (bottom) CO ambient monitoring concentrations in Denver, Colorado (left) and Los Angeles, California (right), Years 1993 – 2008.

While recognizing that monitoring site attributes are not available for all monitors in the current network and that data for some attributes may not reflect current conditions,[8] the ISA also evaluated the average annual daily traffic (AADT) data available for each ambient monitor. The ISA noted that only two microscale monitors and two middle scale monitors in the existing network are sited at roads with ≥100,000 AADT, although it is not uncommon for roadways within Consolidated Statistical Areas (CSAs) to have several roads with AADT > 100,000. The AADT ranged from 160,000-178,000 for the near-road monitors used in the aforementioned study by Zhu et al. (2002) where CO concentrations were up to 10 times greater than monitors sited at 300 m from a major road.[9] Existing microscale sites near roads having only moderate traffic count data (<100,000 AADT) may record concentrations that are not substantially different from those obtained from neighborhood scale measurements (ISA, section 3.5.1.3).

Within a specific urban area, however, consideration of only monitor scale or other attributes reported in AQS, such as AADT estimates, may be of limited use in efforts to characterize the monitoring data as to its representation of local near-road CO concentrations. For example, of the five monitors meeting a 75% completeness criterion in the Denver CSA, three were microscale and two were neighborhood scale (ISA, section 3.5.1.2). While one of the microscale monitors sited within downtown Denver measured the highest hourly ambient CO concentrations (ID 080310002), another microscale monitor (ID 080130009) located outside the urban core measured the lowest hourly ambient CO concentrations (ISA, Figure 3-19). Further, the AADT estimate for a major road near the microscale monitor within the urban core (ID 080310002, AADT=17,200) was lower than that listed for the microscale monitor outside the urban core (ID 080130009, AADT=20,000) (ISA, Table A-2). And, a third microscale monitor located 1.3 km from monitor ID 080310002, within the urban core, and measuring somewhat lower CO concentrations (but not lower than the monitor outside the urban core) had only 500 AADT listed for the nearest major road. It is likely that the higher CO concentrations measured at the downtown monitor reflect influences of the denser roadway network surrounding that monitor in the downtown Denver area (ISA, Figure 3-17).[10]

Thus, to better characterize the representation of near-road CO concentrations for many of the existing ambient monitors, additional analyses would need to be performed that go beyond

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[8] Recorded AQS monitoring site attributes are not always available for each monitor or may not always reflect potential source influences. For example, of 24 CO monitors in the Los Angeles CSA, AQS had no information regarding the monitoring scale for 16 monitors (ISA, Figure 3-22).

[9] Local-scale meteorology may have also contributed to the heightened concentrations, given that the Zhu et al. (2000) study was designed to capture CO concentrations downwind of the roadway.

[10] We also recognize there is uncertainty in how well the AQS estimated AADT reflects current conditions at this monitor site.

the AQS standard list of monitoring site attributes. Such analyses could include local-scale meteorological data, using GIS to determine detailed monitor-to-roadway characteristics (e.g., monitor distance from roadways, the number and type of roads within close proximity of the monitor), and obtaining current traffic count data for all roads.

Carbon monoxide also exhibits hourly variability within a day, with two distinct temporal patterns noted for weekdays and weekends (ISA, section 3.5.2.2). The diurnal variation is inherently linked to the typical commute times-of-day that occur within urban locations. In general, in recent years observed mean and median concentrations for all hours of the day and across all monitors within urban areas demonstrated limited variability, however 90th and 95th percentile hourly concentrations generally exhibit early-morning and late afternoon peak CO concentrations during weekdays (ISA, Figure 3-36). The weekend diurnal variation in ambient CO concentrations was much lower than that occurring during weekdays as expected due to the relative absence of commuter vehicle traffic during the morning and evening hours of the day. Most urban areas have relatively stable concentrations throughout weekend days at each of the selected percentiles, though a few locations (e.g., Phoenix, Los Angeles, Seattle) did have a more pronounced late afternoon peak (ISA, Figure 3-37).

We investigated local hourly variation at two separate CO monitors located in Denver and Los Angeles to illustrate similar trends. The monitor in Denver is a microscale monitor located in downtown Denver and expected to reflect concentrations resulting from dense downtown traffic in that city; it is the monitor measuring the highest ambient CO concentrations in the Denver area. The monitor in Los Angeles is a middle scale monitor located in Lynwood; it is also the monitor measuring the highest ambient CO concentrations in the Los Angeles area. Figure 3-2 indicates that on average, peak ambient CO concentrations that occur during typical commute times in Denver ranged from about 1 to 5 ppm during weekdays in 1995, while currently, ambient CO concentrations during morning and afternoon commutes range from about 1 to 2 ppm. Weekends tend to exhibit less variability throughout the day. On average, CO ambient concentrations generally ranged from 1 to 3 ppm throughout the day in 1995, while current weekend concentrations are less than 1 ppm for most hours of the day. In Los Angeles, both the concentration levels and variability are greater than when compared with similar years and times of day in Denver (Figure 3-3). Peak ambient CO concentrations are more prominent during morning commutes and generally ranged from 2 to 10 ppm in 1995, while when considering more recent ambient monitor concentration (2006), most commuting times are associated with hourly concentrations ranging from between 1 and 5 ppm. The weekend profile exhibits some variation when considering either year, with maximum concentration levels and variability commonly exhibited during the late-night/early morning hours.

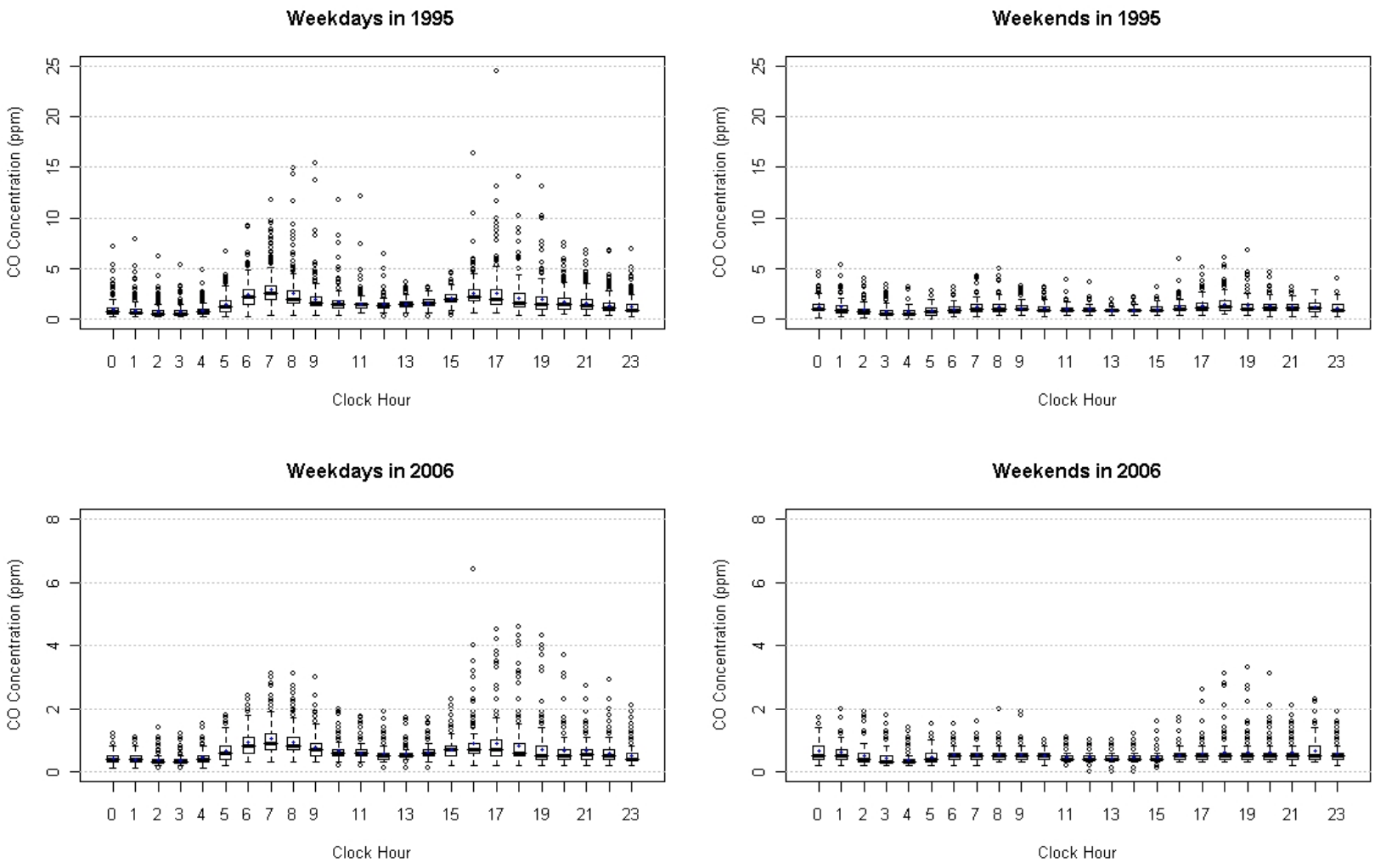

Figure 3-2. **Diurnal distribution of 1-hour CO concentrations in Denver (Monitor 080310002) by day-type (weekdays-left; weekends-right), Years 1995 (top) and 2006 (bottom).** The box encompasses concentrations from the 25th to 75th percentiles or Interquartile range (IQR), the line bisecting the box is the median, the solid dot within the box is the mean, the whiskers represent 1.5 times the IQR, and concentrations outside the whiskers are indicated by open circles. Note there are differences in the y-axis scale for the two monitoring years.

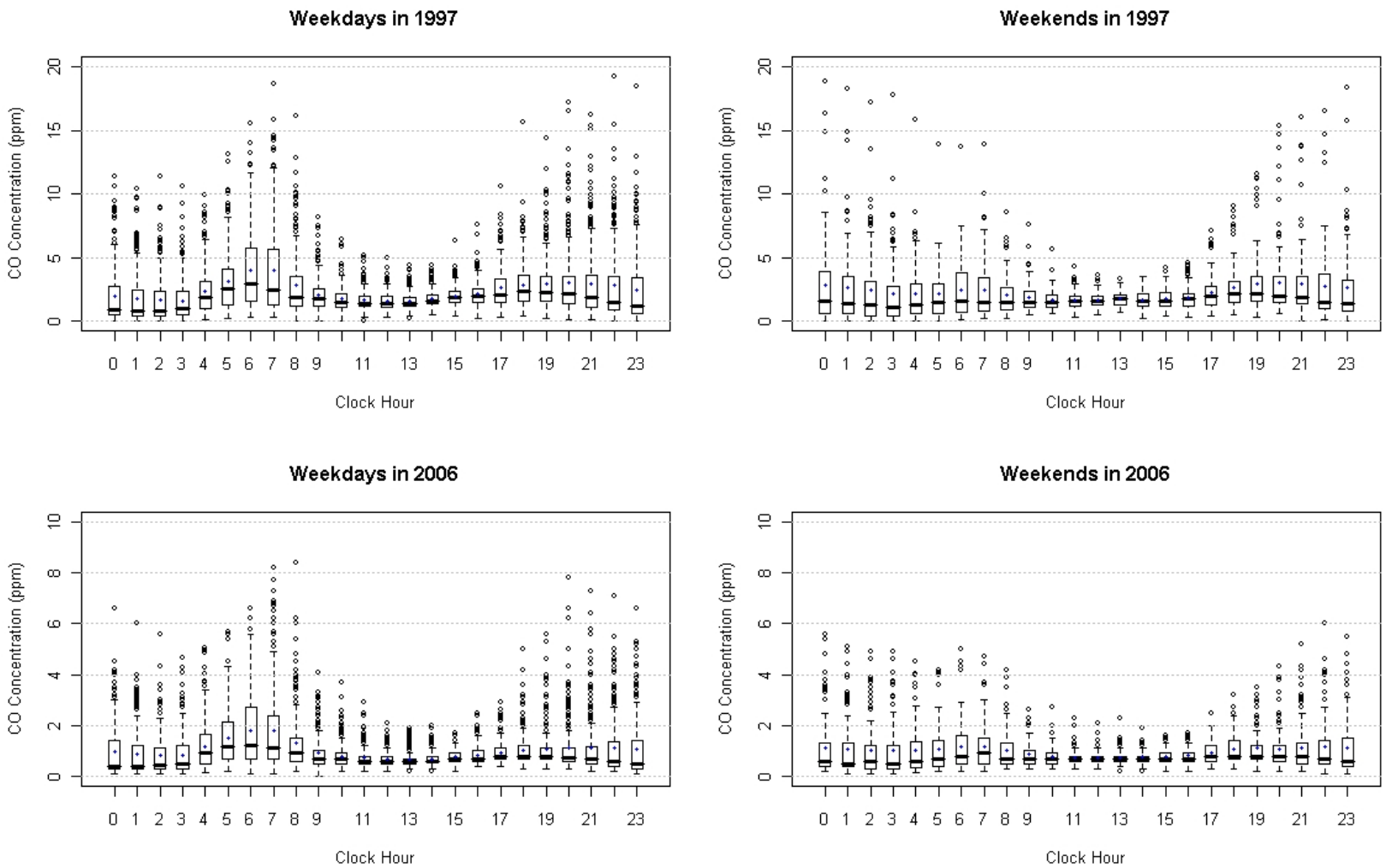

Figure 3-3. Diurnal distribution of 1-hour CO concentrations in Los Angeles (Monitor 060371301) by day-type (weekdays-left; weekends-right), years 1997 (top) and 2006 (bottom). The box encompasses concentrations from the 25th to 75th percentiles or IQR, the line bisecting the box is the median, the solid dot within the box is the mean, the whiskers represent 1.5 times the IQR, and concentrations outside the whiskers are indicated by open circles. Note there are differences in the y-axis scale for the two monitoring years.

3.1.4 Policy-Relevant Background Concentrations

EPA has generally conducted NAAQS risk assessments that focus on the risks associated with ambient levels of a pollutant that are in excess of policy-relevant background (PRB). Policy-relevant background levels are defined, for purposes of this document, as concentrations of a pollutant that would occur in the US in the absence of anthropogenic emissions in the US, Canada, and Mexico.

Over the continental US (CONUS), the 3-year (2005-2007) average CO PRB concentration is estimated to range from 0.118 to 0.146 ppm (ISA, section 3.5.4). Outside the CONUS, the 3-year average CO PRB in three Alaskan sites is estimated to range from 0.127 to 0.135 ppm, and from 0.095 to 0.103 ppm in two Hawaiian monitoring locations. The estimated PRB concentrations exhibit significant within-location seasonal variation, with minimum concentrations observed in the summer and fall and maximum concentrations occurring in the winter and spring. For example, PRB in two California sites is estimated to range from about 0.085 to 0.170 ppm, and PRB in one site in Colorado ranged from about 0.080 to 0.140 ppm (ISA, Figure 3-43).

Given that ambient concentrations of interest in this REA are well above the estimated PRB levels discussed above and, thus the contribution of PRB to overall ambient CO concentrations is very small, EPA is characterizing risks associated with ambient CO levels without regard to estimated PRB levels.

3.1.5 Within-Monitor CO Concentration Trends

The previous section addressed general trends in ambient concentrations. Of particular interest in this assessment is how concentrations have changed at a specific monitor over time. This is an important consideration in determining how best to address alternative air quality conditions. These alternative air quality conditions are useful in evaluating how varying distributions of air quality might affect different exposure scenarios. In other recent NAAQS reviews for NO_2 (US EPA, 2008) and SO_2 (US EPA, 2009) it was determined that the relationship between high concentration and low concentration years of ambient monitoring data was mainly proportional (Rizzo, 2008, 2009), that is all concentrations across the entire distribution at a single monitor changed in equivalent amounts over time. We needed the relationship to adjust current air quality because, at the time of the NAAQS reviews, the current ambient NO_2 and SO_2 concentrations were far below that expected to just meet the current standards.

Knowledge of this relationship for ambient CO concentrations is also needed to develop alternative air quality conditions for use in some of the exposure scenarios investigated in this REA. Ambient CO concentration data were obtained from AQS for several monitors in Los

Angeles for two years: 1997 – representing a high concentration year and 2006 – representing a low concentration year. In Denver, the year 1995 was selected to represent a high concentration year, while 2006 was selected to represent a low concentration year. As was done for prior NAAQS reviews (Rizzo, 2008, 2009), 75% completeness criteria were applied in selecting valid monitoring data,[11] the 1-hour daily maximum concentration for each day was identified, and the 0 through 100th percentiles of the distribution were calculated (by 1% increments). Then the percentiles for the low concentration year were paired and plotted against those calculated for the high concentration year at each individual monitor. Figure 3-4 illustrates the results for four monitors in Denver, while Figure 3-5 illustrates a similar comparison for four monitors in Los Angeles. A simple linear regression was also calculated and plotted, along with the regression slope, intercept, and fit statistic (R^2). As shown by the relationships and fit statistics in each location, there is a very strong linear relationship when comparing each year of data within each monitor. In general, the regression slopes and intercepts are similar for monitors within each location, indicating a similarity in the rate of change in concentration occurring at the monitors within each location. There are however, at most of the sites, instances where upper percentile values deviate from linearity (i.e., ≥ 99th percentile 1-hour daily maximum concentration). Concentrations deviating above the best fit line indicate that these upper percentile concentrations have not declined at the same rate as the middle of the distribution at that particular monitor (e.g., Figure 3-5, monitor ID 060370113). In addition, many of the estimated regression intercepts are positive, though most are ≤ 0.1 ppm. A positive intercept also indicates a larger percentage decline between high and low year concentrations in the upper end of the distribution relative to that of the middle and lower percentiles. However, given that there are a limited number of points deviating from linearity and that regression slopes and intercepts are similar for most of the monitors within each location and having mainly small intercepts, this analysis provides adequate support for adjusting air quality by a proportional method.

[11] Monitoring sites first had to have 75% of hours reported in each day to be considered as a valid day. Then each quarter had to have at least 75% valid days to be complete and all four quarters had to be complete across the year for the site to be retained.

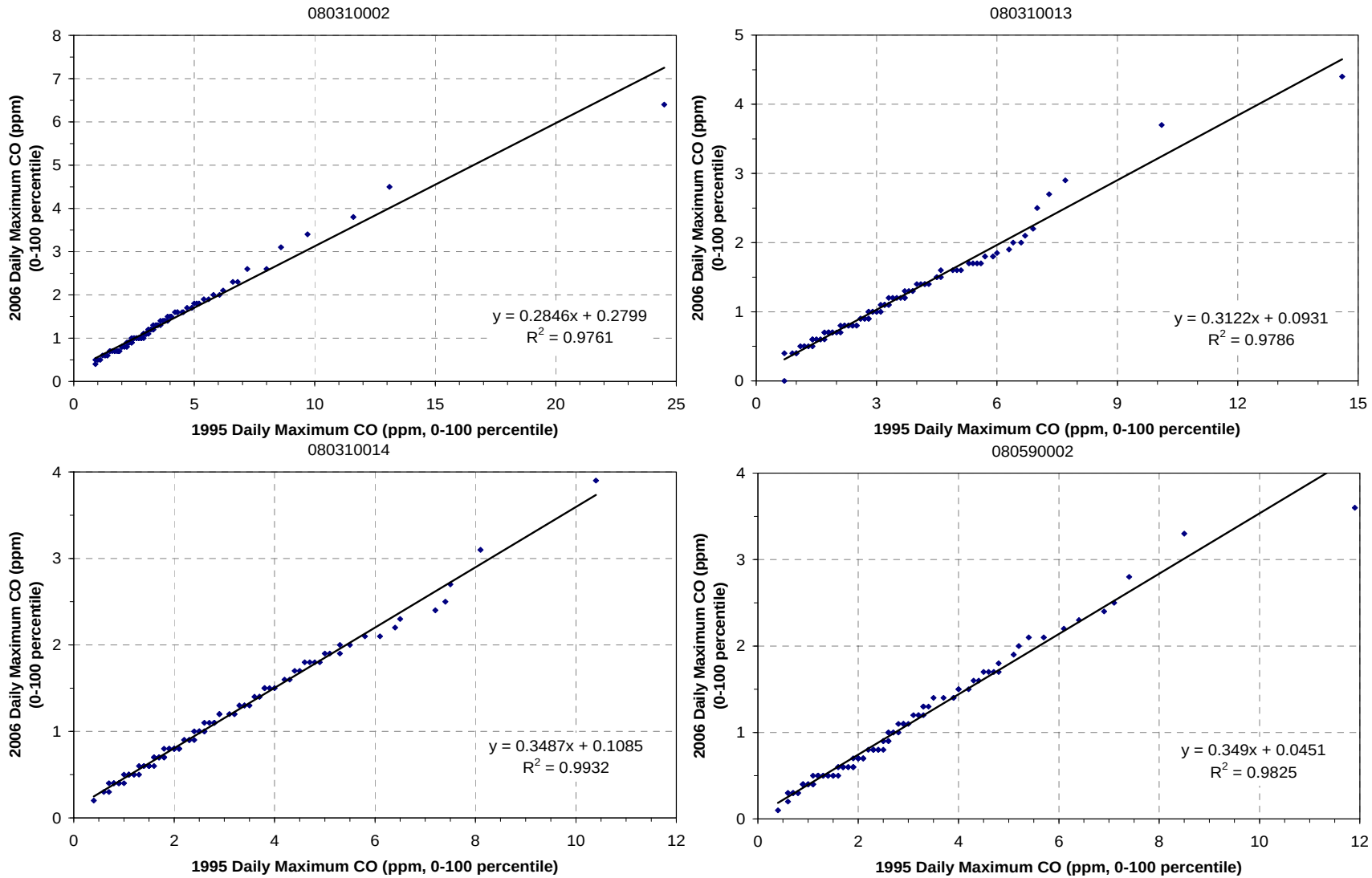

Figure 3-4. Comparison of a high concentration year (1995) versus a low concentration year (2006) at four ambient monitors in Denver. The 0 through 100th percentiles of the 1-hour daily maximum CO are plotted for each monitor-year.

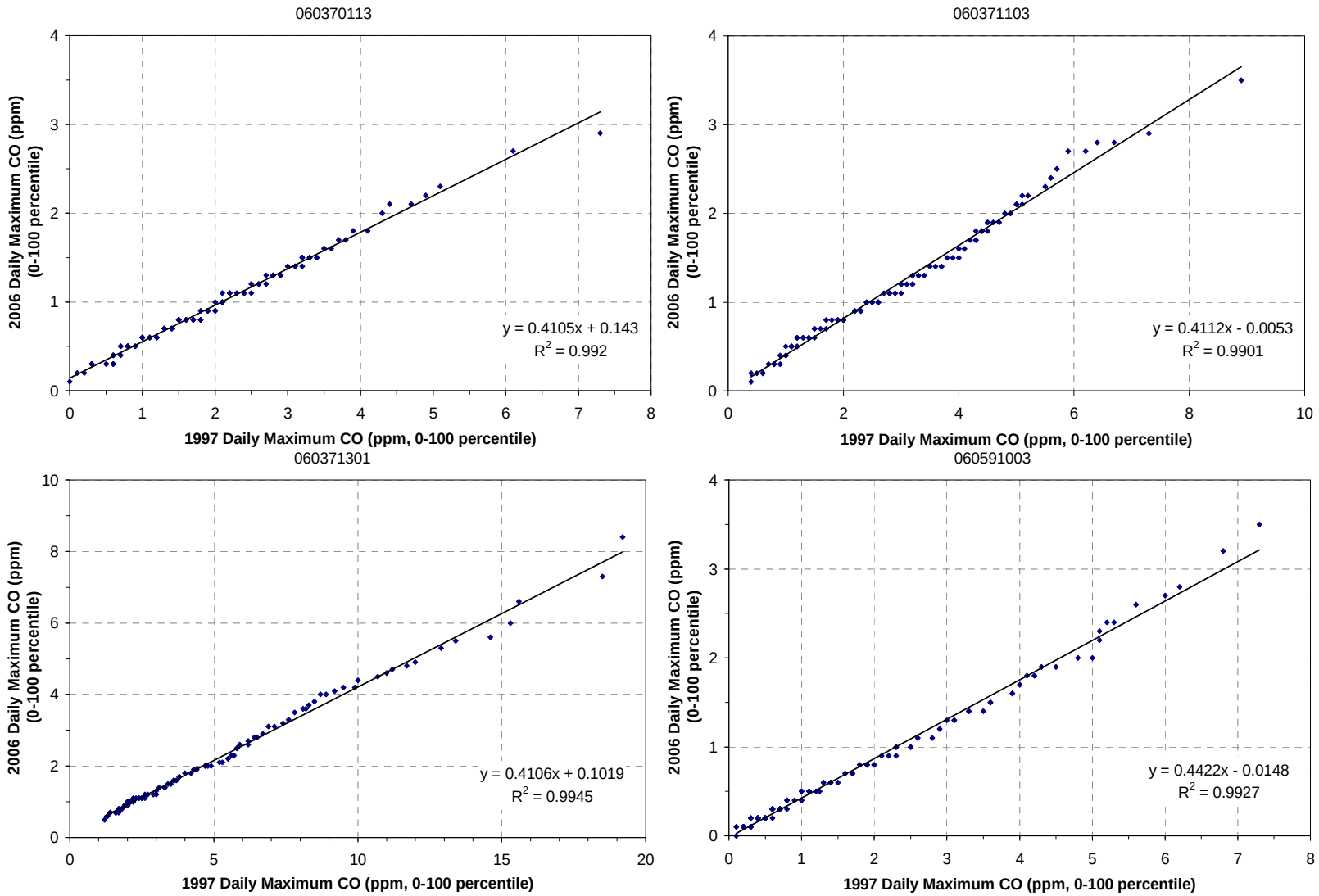

Figure 3-5. Comparison of a high concentration year (1997) versus a low concentration year (2006) at four ambient monitors in Los Angeles. The 0 through 100th percentiles of the 1-hour daily maximum CO are plotted for each monitor-year.

We were also interested in estimating the within-monitor temporal variability for three air quality metrics. The first air quality metric was the current design value, that is, the 2nd highest 8-hour average CO concentration in a year. The next two air quality metrics we compared were the 99th percentile 1-hour and 8-hour daily maximum CO concentrations. We evaluated the within-monitor temporal variability using two comparisons: one using historical versus current air quality data and the other comparing year-to-year variability of these upper percentile concentrations within the air quality distribution. Two three-year periods (1995-1997 and 2005-2007) were chosen to represent historical and recent air quality, respectively. We limited the analysis to four monitors within the Denver CSA and ten monitors within the Los Angeles CSA, with all monitor data meeting standard requirements for data completeness. In addition to the temporal evaluation of the air quality metrics, a limited analysis of the spatial variability across the two periods is also provided for the selected monitors in each area.

Tables 3-1 and 3-2 provide results for the current design value in Denver and Los Angeles, respectively. As shown by the Tables, there is a wide range in the temporal variability of the 2nd highest 8-hour average CO concentration in both locations, however, the relative variability, as indicated by the coefficient of variation (COV),[12] is slightly less for the recent air quality when compared with the historical air quality. For example, in Denver the COV ranges from 4-27 percent (mean = 13%) for the historical data, while the recent data temporal COV ranges from 3-23 percent (mean = 10%) (Table 3-1). Note also that the design value decreases with increasing monitoring year over the selected three-year periods in both Denver and Los Angeles (and of course is consistent with Figures 3-1 and 3-2), though this trend is more prevalent when considering the historical air quality data. In addition, the magnitude of the spatial variability tends to vary from year-to-year as indicated by the COV, though there are differences in the historical versus recent air quality pattern by location. In Denver, there was generally less spatial variability in the 2nd highest 8-hour concentration when comparing the recent to historical air quality data. There was no apparent trend in year-to-year spatial variability for Los Angeles as both air quality periods had a mean COV of about 31% (Table 3-2).

Similar temporal trends are observed with the 99th percentile 1-hour daily maximum concentrations when comparing historical versus recent air quality (Tables 3-3 and 3-4 for Denver and Los Angeles, respectively). The temporal variability in the recent air quality data was also less than that of the prior air quality metric (i.e., the 2nd highest 8-hour average), averaging about 4% COV in Denver and 7% COV in Los Angeles across that 3-year period. The

[12] The COV is calculated here by dividing the standard deviation (std) by the mean, then multiplying by 100.

year-to-year spatial variability for this metric is also consistent with that stated above. In Denver, the COV on average was less for the recent air quality when compared to that of the historical data. There was little difference in the year-to-year spatial variability in Los Angeles when considering the two air quality periods. Results for the 99th percentile 8-hour daily maximum concentrations were more similar to the results for the 2nd highest 8-hour average concentration than the 99th percentile 1-hour daily maximum (Tables 3-5 and 3-6, for Denver and Los Angeles, respectively).

Table 3-1. Within monitor temporal variability in Denver using historical (1995-97) and recent (2005-07) air quality data - 2nd highest 8-hour average.

Monitor	Historical Air Quality – 2nd highest 8-hour average						Recent Air Quality – 2nd highest 8-hour average					
	1995	1996	1997	mean	std	COV	2005	2006	2007	mean	std	COV
31-0002	9.5	7.3	5.5	7.4	2.0	**27**	2.6	3.1	2.8	2.8	0.3	**9**
31-0013	6.2	5.2	4.7	5.4	0.8	**14**	2.4	2.5		2.4	0.1	**3**
31-0014	5.9	5.7	6.2	5.9	0.2	**4**	2.1	3.0		2.5	0.6	**23**
59-0002	4.6	4.3	4.9	4.6	0.3	**7**	1.8	2.0		1.9	0.1	**6**
mean	6.6	5.6	5.3	5.8			2.2	2.6	2.8	2.4		
std	2.1	1.3	0.6	1.2			0.3	0.5		0.4		
COV	**32**	**22**	**12**	**20**			**14**	**19**		**16**		

Table 3-2. Within monitor temporal variability in Los Angeles using historical (1995-97) and recent (2005-07) air quality data - 2nd highest 8-hour average.

Monitor	Historical Air Quality – 2nd highest 8-hour average						Recent Air Quality – 2nd highest 8-hour average					
	1995	1996	1997	mean	std	COV	2005	2006	2007	mean	std	COV
37-0113	9.4	8.5	4.1	7.3	2.8	**39**	1.9	1.9	1.6	1.8	0.2	**10**
37-1002	10.9	8.5	7.2	8.9	1.9	**21**	3.2	3.4	2.7	3.1	0.4	**12**
37-1103	7.9	7.5	5.9	7.1	1.1	**15**	2.6	2.5	2.1	2.4	0.3	**12**
37-1201	9.4	6.7	7.7	7.9	1.3	**17**	3.4	3.4	2.7	3.2	0.4	**12**
37-1301	11.7	14.3	15.0	13.6	1.7	**13**	5.6	5.6	4.9	5.3	0.4	**8**
37-2005	8.6	6.9	5.4	7.0	1.6	**23**	2.8	2.7	2.2	2.6	0.3	**13**
37-4002	6.3	6.2	6.4	6.3	0.1	**2**	2.9	3.3	2.5	2.9	0.4	**15**
59-0001/7	7.3	6.1	5.4	6.3	1.0	**16**	3.1	2.9	2.3	2.8	0.4	**15**
59-1003	5.3	6.5	5.0	5.6	0.8	**14**	3.1	2.5	2.5	2.7	0.3	**12**
59-5001	6.4	6.3	5.7	6.1	0.4	**6**	2.9	2.9	2.5	2.8	0.2	**8**
mean	8.3	7.7	6.8	7.6			3.1	3.1	2.6	3.0		
std	2.1	2.5	3.1	2.3			0.9	1.0	0.9	0.9		
COV	**25**	**32**	**45**	**31**			**30**	**32**	**33**	**31**		

Table 3-3. Within monitor temporal variability in Denver using historical (1995-97) and recent (2005-07) air quality data – 99th percentile 1-hour daily maximum.

Monitor	Historical Air Quality – 99th percentile 1-hour daily maximum						Recent Air Quality – 99th percentile 1-hour daily maximum					
	1995	1996	1997	mean	std	COV	2005	2006	2007	mean	std	COV
31-0002	13.5	13.4	9.1	12.0	2.5	**21**	3.8	4.5	4.4	4.2	0.4	**9**
31-0013	11.1	9.0	8.6	9.6	1.3	**14**	3.5	3.7		3.6	0.1	**3**
31-0014	8.2	7.3	7.8	7.8	0.5	**6**	3.3	3.2		3.2	0.1	**3**
59-0002	8.6	6.8	7.2	7.5	0.9	**12**	3.4	3.4		3.4	0.0	**0**
mean	10.4	9.1	8.2	9.2			3.5	3.7	4.4	3.6		
std	2.5	3.0	0.9	2.1			0.2	0.6		0.4		
COV	**24**	**32**	**10**	**22**			**6**	**16**		**12**		

Table 3-4. Within monitor temporal variability in Los Angeles using historical (1995-97) and recent (2005-07) air quality data – 99th percentile 1-hour daily maximum.

Monitor	Historical Air Quality – 99th percentile 1-hour daily maximum						Recent Air Quality – 99th percentile 1-hour daily maximum					
	1995	1996	1997	mean	std	COV	2005	2006	2007	mean	std	COV
37-0113	13.9	7.5	6.1	9.2	4.2	**45**	2.6	2.7	2.1	2.5	0.3	**13**
37-1002	11.6	9.7	8.2	9.9	1.7	**17**	3.9	4.1	3.6	3.9	0.3	**7**
37-1103	9.0	9.4	7.4	8.6	1.1	**13**	3.1	2.9	2.6	2.9	0.3	**9**
37-1201	10.6	8.4	8.4	9.1	1.3	**14**	4.0	3.9	3.4	3.8	0.3	**8**
37-1301	16.2	20.2	18.5	18.3	2.0	**11**	7.1	7.4	6.8	7.1	0.3	**4**
37-2005	10.3	8.8	6.2	8.4	2.0	**24**	3.4	3.3	3.0	3.2	0.2	**6**
37-4002	7.6	8.4	7.6	7.9	0.5	**6**	3.8	3.8	3.1	3.6	0.4	**12**
59-0001/7	9.1	8.2	7.7	8.4	0.7	**9**	3.6	3.6	3.2	3.5	0.2	**6**
59-1003	7.3	8.4	6.9	7.5	0.8	**11**	3.6	3.2	3.2	3.3	0.2	**6**
59-5001	10.7	11.6	10.3	10.9	0.7	**6**	5.2	5.4	5.2	5.3	0.1	**2**
mean	10.6	10.1	8.7	9.8			4.0	4.0	3.6	3.9		
std	2.8	3.7	3.6	3.1			1.3	1.4	1.4	1.3		
COV	**26**	**37**	**42**	**32**			**32**	**35**	**38**	**34**		

Table 3-5. Within monitor temporal variability in Denver using historical (1995-97) and recent (2005-07) air quality data – 99th percentile 8-hour daily maximum.

Monitor	Historical Air Quality – 99th percentile 8-hour daily maximum						Recent Air Quality – 99th percentile 8-hour daily maximum					
	1995	1996	1997	mean	std	COV	2005	2006	2007	mean	std	COV
31-0002	7.3	7.2	5.2	6.6	1.2	**18**	2.4	2.8	2.7	2.6	0.2	**9**
31-0013	5.4	5.2	4.7	5.1	0.4	**7**	2.2	2.1		2.2	0.0	**2**
31-0014	5.7	5.5	5.8	5.7	0.1	**2**	2.1	2.8		2.4	0.5	**22**
59-0002	4.1	3.8	4.8	4.2	0.5	**12**	1.8	1.8		1.8	0.0	**2**
mean	5.6	5.4	5.1	5.4			2.1	2.4	2.7	2.3		
std	1.3	1.4	0.5	1.0			0.3	0.5		0.4		
COV	**24**	**26**	**10**	**18**			**12**	**21**		**16**		

Table 3-6. Within monitor temporal variability in Los Angeles using historical (1995-97) and recent (2005-07) air quality data – 99th percentile 8-hour daily maximum.

Monitor	Historical Air Quality – 99th percentile 8-hour daily maximum						Recent Air Quality – 99th percentile 8-hour daily maximum					
	1995	1996	1997	mean	std	COV	2005	2006	2007	mean	std	COV
37-0113	8.6	5.2	3.7	5.8	2.5	**43**	1.9	1.8	1.5	1.8	0.2	**12**
37-1002	9.7	8.3	6.8	8.3	1.4	**17**	3.0	3.2	2.6	3.0	0.3	**11**
37-1103	7.5	7.0	5.6	6.7	1.0	**15**	2.6	2.4	2.0	2.4	0.3	**13**
37-1201	9.0	6.7	7.3	7.6	1.2	**15**	3.2	3.1	2.6	2.9	0.3	**12**
37-1301	11.2	13.9	13.1	12.7	1.4	**11**	4.9	5.1	4.5	4.8	0.3	**7**
37-2005	8.5	6.8	5.0	6.7	1.8	**26**	2.8	2.6	2.1	2.5	0.3	**14**
37-4002	5.9	6.2	5.9	6.0	0.2	**3**	2.9	2.7	2.4	2.7	0.2	**9**
59-0001	6.5	5.7	5.1	5.8	0.7	**12**	2.7	2.7	2.1	2.5	0.3	**14**
59-1003	4.7	6.4	4.9	5.3	0.9	**17**	3.0	2.2	2.4	2.6	0.4	**16**
59-5001	6.3	5.9	5.3	5.8	0.5	**9**	2.6	2.7	2.5	2.6	0.1	**5**
mean	7.8	7.2	6.3	7.1			3.0	2.9	2.5	2.8		
std	2.0	2.5	2.6	2.2			0.8	0.9	0.8	0.8		
COV	**25**	**35**	**42**	**31**			**25**	**31**	**31**	**29**		

3.2 STUDY AREAS SELECTED FOR CURRENT CO REA

We identified several criteria to select the exposure assessment study areas drawing from information discussed in the earlier sections of this Chapter and additional scientific evidence in the ISA. We selected Denver and Los Angeles as areas to focus the current assessment because (1) both cities have been included in prior CO NAAQS exposure assessments and thus serve as an important connection with past assessments, (2) they have historically had among the highest CO ambient concentrations among urban areas in the U.S., and (3) Denver is at high altitude and represents a scenario of interest due to the potentially increased susceptibility of visitors to high altitude locations from exposure to CO. In addition, of ten urban areas across the US having monitors meeting a 75% completeness criteria, the two locations were ranked 1st (Los Angeles) and 2nd (Denver) regarding percent of elderly population within 5, 10, and 15 km of monitor locations, and ranked 1st (Los Angeles) and 5th (Denver) regarding number of 1-hour and 8-hour daily maximum CO concentration measurements (ISA, section 3.5.1.1).

3.3 KEY OBSERVATIONS

Presented below are key observations resulting from the air quality considerations.

- Mobile sources (i.e., gasoline powered vehicles) are the primary contributor to CO emissions, particularly in urban areas due to greater vehicle and roadway densities.
- Recent (2005-2007) ambient CO concentrations across the US are lower than those reported in the previous CO NAAQS review and are also well below the current CO NAAQS levels. Further, a large proportion of the reported concentrations are below the conventional instrument lower detectable limit of 1 ppm.
- The currently available information for CO monitors indicates that siting of microscale and middle scale monitors in the current network is primarily associated with roads having moderate traffic density (<100,000 AADT), however, factors other than reported AADT (e.g., orientation with regard to dense urban roadway networks) can contribute to sites reporting higher CO concentrations.
- Ambient CO concentrations are highest at monitors sited closest to roadways (i.e., microscale and middle scale monitors) and exhibit a diurnal variation linked to the typical commute times of day, with peak concentrations generally observed during early morning and late afternoon during weekdays.
- Policy relevant background (PRB) concentrations across the US are generally less than 0.2 ppm, far below that of interest in this REA with regard to ambient CO exposures.
- Historical trends in ambient monitoring data indicate that at individual sites, ambient concentrations have generally decreased in a proportional manner. This comparison included air quality distributions with concentrations at or above the current 8-hour standard and those reflecting current (*as is*) conditions.

- The temporal variability in selected upper percentile ambient concentrations (e.g., 99th percentile 1-hour daily maximum) at individual monitors in Denver and Los Angeles is relatively small across a three-year monitoring period, particularly when considering recent air quality. Much of the within-monitor temporal variability is due to a trend in decreasing concentration from year-to-year.
- There is greater spatial variability in selected upper percentile ambient concentrations (e.g., 99th percentile 1-hour daily maximum) at ten selected monitoring sites in Los Angeles when compared with four selected monitoring sites Denver, particularly when considering the recent air quality.

REFERENCES

Baldauf R, Thoma E, Hays M, Shores R, Kinsey J, Gullett B, Kimbrough S, Isakov V, Long T, Snow R, Khlystov A, Weinstein J, Chen FL, Seila R, Olson D, Gilmour I, Cho SH, Watkins N, Rowley P, Bang J. (2008). Traffic and meteorological impacts on near-road air quality: Summary of methods and trends from the Raleigh near-road study. *J Air Waste Manag Assoc*. 58:865-878.

Michie Jr RM, McElroy FF, Sokash JA, Thompson VL, Dayton DP, Sutcliffe CR. (1983). Performance Test Results and Comparative for Designated Equivalence Methods for Carbon Monoxide. EPA-600/S4-83-013.

Rizzo M. (2008). Investigation of how distributions of hourly nitrogen dioxide concentrations have changed over time in six cities. Nitrogen Dioxide NAAQS Review Docket. Docket ID no. EPA–HQ–OAR–2006–0922). Available at: http://www.epa.gov/ttn/naaqs/standards/nox/s_nox_cr_rea.html.

Rizzo M. (2009). Investigation of How Distributions of Hourly Sulfur Dioxide Concentrations Have Changed Over Time in Six Cities. Sulfur Dioxide Review Docket. Docket ID no. EPA-HQ-OAR-2007-0352. Available at: www.regulations.gov.

US EPA. (2000). Air Quality Criteria for Carbon Monoxide. National Center for Environmental Assessment, Office of Research and Development, U.S. Environmental Protection Agency, Research Triangle Park, NC 27711; report no. EPA/600/P-99/001F. June 2000. Available at: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=18163.

US EPA. (2006). 2002 National Emissions Inventory Data and Documentation. U.S. Environmental Protection Agency, Office of Air and Radiation, Office of Air Quality Planning and Standards, Research Triangle Park, NC. Available at: http://www.epa.gov/ttn/chief/net/2002inventory.html.

US EPA. (2008). Risk and Exposure Assessment to Support the Review of the NO_2 Primary National Ambient Air Quality Standard. EPA-452/R-08-008a. November 2008. Available at: http://www.epa.gov/ttn/naaqs/standards/nox/data/20081121_NO2_REA_final.pdf.

US EPA. (2009). Risk and Exposure Assessment to Support the Review of the SO_2 Primary National Ambient Air Quality Standard. EPA-452/R-09-007. August 2009. Available at: http://www.epa.gov/ttn/naaqs/standards/so2/data/200908SO2REAFinalReport.pdf.

US EPA. (2010). Integrated Science Assessment for Carbon Monoxide. U.S. Environmental Protection Agency, Washington, DC, report no. EPA/600/R-09/019F. Available at: http://www.epa.gov/ttn/naaqs/standards/co/s_co_cr_isa.html.

Zhu Y, Hinds WC, Kim S, Shen S, Sioutas C. (2002). Study of ultrafine particles near a major highway with heavy-duty diesel traffic. *Atmos Environ*. 36:4323-4335.

4 OVERVIEW OF APEX MODELING SYSTEM FOR ESTIMATING CO EXPOSURES AND COHB DOSE LEVELS

4.1 PURPOSE

This chapter presents an overview and description of the overall approach to estimating human exposure and dose for past and recent NAAQS reviews. Section 4.2 provides a brief overview of EPA's Air Pollutants Exposure model (APEX), the model used in this assessment to estimate population exposure and dose. This overview is followed by a short history that explains the evolution of exposure and dose models used by OAQPS to conduct exposure and dose assessments for CO and other NAAQS reviews (section 4.3). Section 4.4 provides a generalized description of the APEX simulation process, though having detailed focus on a few of the important approaches used for modeling CO exposure and COHb dose. This includes expanded discussion on the approach used to estimate microenvironmental concentrations (section 4.4.4) and COHb dose levels (section 4.4.7).

4.2 MODEL OVERVIEW

The Air Pollutants Exposure model (APEX) is a personal computer (PC)-based program designed to estimate human exposure to criteria and air toxic pollutants at the local, urban, and consolidated metropolitan levels. APEX, also known as TRIM.Expo, is the human inhalation exposure module of EPA's Total Risk Integrated Methodology (TRIM) model framework (US EPA, 1999), a modeling system with multimedia capabilities for assessing human health and ecological risks from hazardous and criteria air pollutants.[1]

APEX estimates human exposure using a stochastic, *microenvironmental* approach (see caption). The model randomly selects data for a sample of hypothetical individuals from an actual population database and simulates each individual's movements through time and space (e.g., indoors at home, inside vehicles) to estimate his or her exposure to a pollutant. APEX can account for travel to and from work locations (i.e., commuting) and provide estimates of exposures at both home and work locations for individuals who work away from home.

> A **microenvironment** is a three-dimensional space in which human contact with an environmental pollutant takes place and which can be treated as a well characterized, relatively homogeneous location with respect to pollutant concentrations for a specified time period.

[1] Additional information on the TRIM modeling system, as well as downloads of the APEX Model, user guides (US EPA 2008a, 2008b), and other supporting documentation, can be found at http://www.epa.gov/ttn/fera.

4.3 MODEL HISTORY AND EVOLUTION

APEX was derived from the National Ambient Air Quality Standards (NAAQS) Exposure Model (NEM) series of models. The NEM series was developed to estimate population exposures to the criteria pollutants (e.g., CO, ozone). In 1988, OAQPS first incorporated probabilistic elements into the NEM methodology and used activity pattern data based on available human activity diary studies to create an early version of probabilistic NEM for ozone (i.e., pNEM/O_3). In 1991, a probabilistic version of NEM was developed for CO (pNEM/CO) that included a one-compartment mass-balance model to estimate CO concentrations in indoor microenvironments. The first application of this model to Denver, Colorado is summarized in Johnson et al. (1992). Between 1999 and 2001, updated versions of pNEM/CO (versions 2.0 and 2.1) were developed that relied on detailed activity diary data compiled in EPA's Consolidated Human Activities Database (CHAD) (McCurdy et al., 2000; US EPA, 2002) and enhanced algorithms for simulating gas stove usage, estimating alveolar ventilation rate (a measure of human respiration), and modeling home-to-work commuting patterns. A draft report by Johnson et al. (2000) describes the application of Version 2.1 of pNEM/CO to Denver and Los Angeles.

The first version of APEX was essentially identical to pNEM/CO (version 2.0) except that it ran on a personal computer (PC) instead of a mainframe. The next version, APEX2, was substantially different, particularly in the use of a personal profile approach rather than the previously used cohort simulation approach. APEX3 introduced a number of new features including automatic site selection from national databases, a series of new output tables providing summary exposure and dose statistics, and a thoroughly reorganized method of describing microenvironments and their variable parameters. Johnson and Capel (2003) describe a case study in which the PC-based Version 3.1 of APEX was used to estimate population exposure to CO in Los Angeles.

The current version of APEX (Version 4.3) (US EPA, 2008a; 2008b) was used to estimate CO exposure and dose as described in chapter 5 of this document. This version was also recently used to estimate O_3 exposures in 12 urban areas for the O_3 NAAQS review (US EPA, 2007), to estimate population exposures to nitrogen dioxide (NO_2) in Atlanta as part of the NO_2 NAAQS review (US EPA, 2008c), and to estimate sulfur dioxide (SO_2) exposures for asthmatics and asthmatic children in two study areas in Missouri as part of the SO_2 NAAQS review (US EPA, 2009a). There have been several recent enhancements to APEX since the prior 1994 CO NAAQS review, including:

- Algorithms for the assembly of multi-day (longitudinal) activity diaries that model intra-individual variance, inter-individual variance, and day-to-day autocorrelation in diary properties;

- Methods for adjusting diary-based energy expenditures for fatigue and excess post-exercise oxygen (EPOC) consumption;
- New equations for estimation of ventilation (i.e., breathing rate);
- The ability to use air quality data and model exposures over flexible time scales;
- New output files containing diary event-level, time-step level, and hourly-level exposure, dose, and ventilation data, and hourly-level microenvironmental data;
- The ability to model the prevalence of disease states such as asthma or heart disease;
- New output exposure tables that report exposure statistics for population groups and life-stages such as children and active people at varying ventilation rates;
- The inclusion of tract-level commuting data from the 2000 census; and
- Expanded options for modeling microenvironments.

4.4 MODEL SIMULATION PROCESS

APEX4.3 is designed to simulate population exposure to criteria and air toxic pollutants at local, urban, and regional scales. The user specifies the geographic area to be modeled and the number of individuals to be simulated to represent a population of interest. APEX4.3 then generates a personal profile for each simulated person that specifies various parameter values required by the model to estimate their exposure and dose. The model next uses diary-derived time/activity data matched to each personal profile to generate an exposure event sequence (also referred to as a *time-location-activity pattern* or *composite diary*) for the modeled individual that spans a specified time period, such as a calendar year. Each event in the sequence specifies a start time, exposure duration, a geographic location, a microenvironment inhabited, and an activity performed. Probabilistic algorithms are used to estimate the pollutant concentration and ventilation (respiration) rate associated with each exposure event. The estimated pollutant concentrations account for the effects of ambient (outdoor) pollutant concentration, penetration factor, air exchange rate, decay/deposition rate, and proximity to emission sources, each depending on the microenvironment, available data, and the estimation method selected by the user. The ventilation rate is derived from an energy expenditure rate estimated for each individual when performing the specified activity. Because the simulated individuals represent a random sample of the population of interest and are proportionally derived from actual population distributions, the distribution of modeled individual exposures can then be extrapolated to the larger population of interest.

The model simulation generally includes up to seven steps as follows:

- **Characterize study area:** APEX4.3 selects sectors (e.g., census tracts) within a study area—and thus identifies the potentially exposed population — usually based on the

user-defined center and radius of the study area and availability of air quality and meteorological input data for the area (section 4.4.1).

- **Generate simulated individuals:** APEX4.3 stochastically generates a sample of simulated individuals based on the census data for the study area and human profile distribution data (such as age-specific employment probabilities or disease prevalence) (section 4.4.2)
- **Construct activity sequences:** APEX4.3 constructs an exposure event sequence (time-location-activity pattern) spanning the simulation period for each of the simulated persons based on the CHAD diaries (section 4.4.3).
- **Calculate microenvironmental concentrations:** APEX4.3 enables the user to define microenvironments that people in a study area would visit (e.g., by grouping location codes included in the activity pattern database). The model then calculates time-averaged concentrations (e.g., hourly) of each pollutant in each of the microenvironments for each simulated person for the period of simulation based on the user-provided ambient air quality data (section 4.4.4).
- **Estimate energy expenditure and ventilation rates:** APEX4.3 constructs a time-series of energy expenditures for each individual's exposure profile based on the sequence of activities performed. The sequence of energy expenditures are adjusted to ensure that they are physiologically realistic and then used to estimate activity-specific alveolar ventilation rates (section 4.4.5).
- **Calculate exposure:** APEX4.3 assigns a concentration to each exposure event based on the microenvironment occupied during the event and the person's activity. These values are time-averaged (e.g., hourly) to produce a sequence of exposures spanning the specified exposure period (typically one year). The hourly values may be further aggregated to produce 8-hour, daily, monthly, and annual average exposure values (section 4.4.6).
- **Calculate dose:** APEX4.3 optionally calculates hourly, daily, monthly, and annual average dose values for each of the simulated individuals. For the application of APEX to CO, a module within the model estimates the percent COHb level in the blood at the end of each hour based on the time-series of CO concentrations and alveolar ventilation rates experienced by the simulated person (section 4.4.7).

The model simulation continues until exposures (and associated COHb dose levels) are calculated for the user-specified number of simulated individuals. Figure 4-1 presents a conceptual model and simplified data flow diagram illustrating the implementation of APEX4.3 to estimate CO exposure and dose. The following sections provide additional details on the general procedures and algorithms used in each of the seven simulation steps listed above, though more complete discussion can be found in US EPA (2008a, 2008b). The specific input data and microenvironmental factors used in applying APEX4.3 to CO for the current assessment are further described in section 5.1.

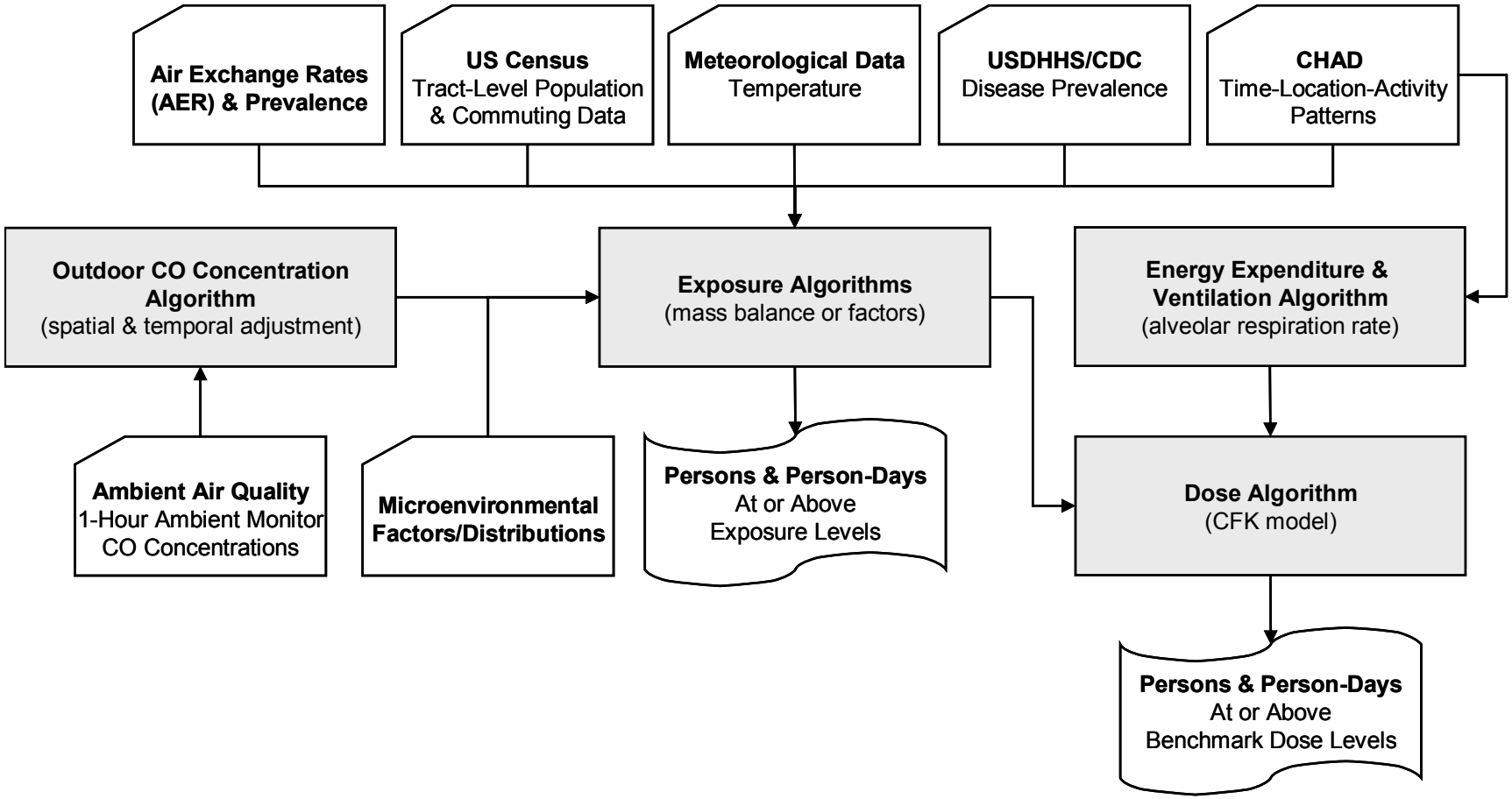

Figure 4-1. Conceptual model and simplified data flow for estimating population exposure and dose using APEX4.3.

4.4.1 Characterize Study Area

An initial study area in an APEX4.3 assessment consists of a set of basic geographic units called sectors, typically defined by US census data reported at the census tract level. The user may provide the geographic center (latitude/longitude) and radius of the study area. Then APEX4.3 calculates the distances to the center of the study area of all the sectors included in the sector location database and selects the sectors within the radius of the study area. APEX4.3 then maps the user-provided air quality and meteorological data for specified monitoring districts to the selected sectors. The sectors identified as having acceptable air quality and meteorological data within the radius of the study area are selected to comprise a final study area for the APEX4.3 simulation analysis. This final study area determines the population make-up of the simulated persons (profiles) to be modeled.

4.4.2 Generate Simulated Individuals

APEX4.3 stochastically generates a user-specified number of simulated persons to represent the population in the study area. Each simulated person is represented by a personal profile. APEX4.3 generates the simulated person by probabilistically selecting values for a set of profile variables. The profile variables include:

- Demographic variables that are generated based on US census data (e.g., age, gender, home sector, work sector);
- Residential variables that are generated based on sets of distribution data (e.g., air conditioning prevalence);
- Physiological variables that are generated based on age- and gender-specific distribution data (e.g., blood volume, body mass, resting metabolic rate); and
- Daily varying variables that are generated based on distribution data that change daily during the simulation period (e.g., daily work status).

APEX4.3 first selects and calculates demographic, residential, and physiological variables (except for daily values) for each of the user-specified number of simulated individuals. APEX4.3 then follows each simulated individual over time and calculates exposures (and optionally doses) for the individual over the duration of the assessment period. The complete listing of profile variables used by APEX4.3 and detailed description can be found in section 5 of US EPA (2008b). An overview of the data sources used and their implementation in APEX4.3 is provided below.

4.4.2.1 Population Demographics

APEX4.3 takes population characteristics into account to develop accurate representations of study area demographics. Specifically, population counts by area and

employment probability estimates are used to develop representative profiles of hypothetical individuals for the simulation.

APEX4.3 is flexible in the resolution of population data provided. As long as the data are available, any resolution can be used (e.g., county, census tract, census block). For this application of the model, census tract level data were used. Census tract level population counts are obtained from the 2000 Census of Population and Housing Summary File 1 (SF-1). This file contains data compiled from the questions asked of all respondents and about every housing unit.

As part of the population demographics inputs, it is important to integrate working patterns into the assessment. In the 2000 US Census, estimates of employment were developed by census information (US Census Bureau, 2007). The employment statistics are broken down by gender and age group, so that each gender/age group combination is given an employment probability fraction (ranging from 0 to 1) within each census tract. The age groupings used are: 16-19, 20-21, 22-24, 25-29, 30-34, 35-44, 45-54, 55-59, 60-61, 62-64, 65-69, 70-74, and >75. Children under 16 years of age were assumed by the model to not be employed.

4.4.2.2 Commuting Database

In addition to using estimates of employment by census tract, APEX4.3 also incorporates home-to-work commuting data. Commuting data were derived from the 2000 Census and were collected as part of the Census Transportation Planning Package (CTPP) (US DOT, 2007). The data used contain counts of individuals commuting from home to work locations at a number of geographic scales. These data were processed to calculate fractions for each tract-to-tract flow to create the national commuting data distributed with APEX4.3. This database contains commuting data for each of the 50 states and Washington, D.C.

Several assumptions were made in the development of the database and with the modeling of a person's commute in this assessment as follows.

- **Commutes within tracts and home workers:** There is no differentiation between people that work at home from those that commute within their home tract.
- **Commute distance cutoff:** All persons in home-work flows up to 120 km are assumed to be daily commuters and no persons in more widely separated flows would commute daily. This means that the list of destinations for each home tract was restricted to only those work tracts that are within 120 km of the home tract. This distance is based on the presence of a near-constant relationship between commute flows and distance traveled up to 120 km.
- **Eliminated Records:** Tract-to-tract pairs representing workers who either worked outside of the US (9,631 tract pairs with 107,595 workers) or worked in an unknown location (120,830 tract pairs with 8,940,163 workers) were eliminated from the database. An additional 515 workers in the commuting database whose data were

missing from the original files, possibly due to privacy concerns or errors, were also deleted.

- **Commuting outside the study area:** APEX4.3 allows for some flexibility in the treatment of persons in the modeled population who commute to destinations outside the study area. Users can either retain these persons and include them as part of the population exposed or have them eliminated from the model simulation. In the first instance (i.e., "KeepLeavers = Yes"), APEX4.3 can assign input concentrations based on the available ambient concentration data within the model domain. For the second option (i.e., "KeepLeavers = No") , people who work inside the study area but live outside of it are not modeled, nor are people who live in the study area but work outside of it.

4.4.2.3 Profile Functions File

A *Profile Functions* file contains settings used to generate results for variables related to simulated individuals. While certain settings for individuals are generated automatically by APEX4.3 based on other input files, including demographic characteristics, others can be specified using this file. For example, the file may contain settings for determining whether the profiled individual's residence has an air conditioner, a gas stove, etc.

4.4.2.4 Physiology File

The APEX4.3 *physiology.txt* file contains age- and gender-based information for several physiological parameters used in human exposure modeling. This information includes various equations, distributional shapes, and parameters for all age and gender cohorts from age 0 to 100 years for variables such as normalized maximal oxygen uptake, body mass, resting metabolic rate (RMR), and blood hemoglobin content. Appendix A provides an evaluation of a few important variables used by APEX4.3 in this exposure and dose assessment as well as their updated values or distributions (e.g., new age-gender body mass distributions derived from 1999-2004 National Health and Nutrition Examination Survey data). Details regarding any other physiology variable distributions and their parameters not discussed in this CO REA and associated appendices can be found in US EPA (2008a, 2008b).

4.4.3 Construct Activity Sequences

Different human activities, such as spending time outdoors, indoors, or driving, will be associated with varying pollutant concentrations. Therefore, to accurately model individuals and their exposure to pollutants, it is critical to understand people's daily activities and use such data in the exposure model. EPA's Consolidated Human Activity Database (CHAD) provides diary-derived data indicating where people spend time and the activities they perform at each location (US EPA, 2002). CHAD was designed to provide a basis for conducting multi-route, multi-media exposure assessments (McCurdy et al., 2000). The data contained within CHAD originate

from multiple activity pattern surveys with varied structures (Table 4-1), however the surveys have commonality in that they contain daily diaries of human activities performed, locations visited, and the personal attributes of survey participants (e.g., age and gender).

There are four CHAD-related input files used in APEX4.3. The first three can be considered standard input files for most model simulations; the user typically does not modify their contents. These include the human activity diaries file, the personal data file, and a metabolic information file, each of which are discussed briefly below. The fourth CHAD-related input file maps the five-digit location codes used in the diary file to APEX4.3 microenvironments; this file is commonly modified by the user and is discussed in section 5.8 (i.e., it is most relevant for the specific microenvironments modeled in this CO REA). And finally, section 4.4.3.4 discusses how these diaries are linked together to form a continuous time-location-activity pattern for each individual across the entire simulation period.

Table 4-1. Summary of activity pattern studies comprising the recent version of CHAD.

Study Name	CHAD Prefix	Study Years	Number of Diary Days	Reference
Baltimore	BAL	1997-1998	391	Williams et al. (2000)
CARB: Adults	CAA	1987-1988	1579	Wiley et al. (1991a)
CARB: Adolescents	CAY	1987-1988	183	Wiley et al. (1991a)
CARB: Children	CAC	1989-1990	1200	Wiley et al. (1991b)
Cincinnati (EPRI)	CIN	1985	2614	Johnson (1989)
Denver (EPA)	DEN	1982-1983	805	Johnson (1984); Akland et al. (1985)
Los Angeles: Elementary	LAE	1989	51	Spier et al. (1992)
Los Angeles: High School	LAH	1990	43	Spier et al. (1992)
NHAPS A	NHA	1992-1994	4723	Klepeis et al. (1996); Tsang and Klepeis (1996)
NHAPS B	NHW	1992-1994	4663	Klepeis et al. (1996); Tsang and Klepeis (1996)
PSID 1 (U Michigan I)	UMC	1997	5616	University of Michigan (2010)
PSID 2 (U Michigan II)	ISR	2002-2003	4782	University of Michigan (2010)
Valdez	VAL	1990-1991	397	Goldstein et al. (1992)
Washington, DC	WAS	1982-1983	699	Hartwell et al. (1984); Akland et al. (1985)
RTI Ozone Averting Behavior	OAB	2002-2003	2907	Mansfield and Corey (2003); Mansfield et al. (2004; 2006)
RTP Panel Study	RTP	2000-2001	1003	Williams et al. (2003a, 2003b)
Seattle Study	SEA	1999-2002	1693	Liu et al. (2003)
Internal EPA Study 2006-2007	EPA	2006-2007	434	Isaacs et al. (2009)
EPA Longitudinal 1	EPA	1999,2002	736	Isaacs et al. (2009)
EPA Longitudinal 2	EPA	2000	197	Isaacs et al. (2009)
EPA Longitudinal 3	EPA	2008	62	Isaacs et al. (2009)

4.4.3.1 Personal Information file

Personal attribute data are contained in the CHAD questionnaire file that is distributed with APEX4.3. This file also has information for each day individuals have diaries. The different variables in this file are:

- The study, person, and diary day identifiers
- Day of week

- Gender
- Employment status
- Age in years
- Maximum temperature in degrees Celsius for the diary day
- Mean temperature in degrees Celsius for the diary day
- Occupation code (if requested in survey)
- Time, in minutes, during this diary day for which no data are included in the database

4.4.3.2 Diary Events File

The human activity diary data are contained in the events file that is distributed with APEX4.3. This file contains the locations visited and the activities performed for the nearly 35,000 person-days of data with event intervals ranging from a minimum of one minute upwards to a one hour maximum duration. Typically, a study individuals' diary can vary in length from one to 15 days (i.e., referring to the number of person-days) though a few recent surveys have upwards of hundreds of diary days for a few individuals. Nevertheless, the diary events file contains the following variables:

- The study, person, and diary day identifiers
- Start time of the event
- Number of minutes for the event
- Activity code (a record of what the individual was doing)
- Location code (a record of where the individual was)

4.4.3.3 Activity-Specific Metabolic File

The metabolic file contains the distributional forms and parameters for the activity-specific metabolic equivalents (METs) used to quantitatively assign exertion levels to each activity performed by simulated individuals (McCurdy, 2000). Some activities are specified as a single point value (for instance, watching TV), while others, such as athletic endeavors or manual labor, are represented by normal, lognormal, or other statistical distributions. APEX4.3 samples from these distributions and calculates values to simulate the variable nature of activity levels among different people. The CHAD User's guide provides details on the distributions used, parameters, and sources for each activity (US EPA, 2002).

4.4.3.4 Longitudinal Diary Processing

APEX4.3 probabilistically creates a composite longitudinal diary for each of the simulated persons by selecting a 24-hour diary record – or diary day – from an activity database for each day of the simulation period. The EPA's CHAD data (US EPA, 2002) are supplied with

APEX4.3 for this purpose. A composite diary is a sequence of events that simulates the movement of a modeled person through varying geographical locations and microenvironments for the duration of the simulation period. Each diary event is defined by geographic location, start time, duration, microenvironment visited, and an activity performed.

The activity database input to APEX4.3 contains the following information for each diary day: age, gender, employment status, occupation, day-of-week (or day-type), and maximum hourly average temperature. This information enables APEX4.3 to select data from the activity database that tend to match the characteristics of the simulated person, the study area, and the specified time period. APEX4.3 develops a composite diary for each of the simulated individuals according to the following steps.

- Divide diary days in the CHAD database into user-defined activity pools, based on day-type and temperature categories.
- Assign an activity pool number to each day of the simulation period, based on the user-provided daily maximum/average temperature data.
- Calculate a selection probability for each of the diary days in each of the activity pools, based on age/gender/employment similarity of a simulated person to a diary day.
- Probabilistically select a diary day from available diary days in the activity pool assigned to each day of the simulation period.
- Estimate a MET value for each activity performed while in a location, based on a random sampling of the particular distribution of each specific activity. The METs values are used to calculate an activity-specific ventilation rate (see section 4.4.5) for the simulated person.
- Map the CHAD locations in the selected diary to the user-defined modeled microenvironments.
- Concatenate the selected diary days into a sequential longitudinal diary for a simulated individual covering all days in the simulated period.

APEX4.3 provides an optional longitudinal diary-assembly algorithm that enables the user to create composite diaries that reflect the tendency of individuals to repeat activities on a day-to-day basis. The user specifies values for two statistical variables (i.e., D and A) that relate to a key daily variable, typically the time spent per day in a particular microenvironment (e.g., in a motor vehicle). The D statistic reflects the relative importance of within-person variance and between-person variance in the key variable. The A statistic quantifies the lag-one (day-to-day) variable autocorrelation. APEX4.3 then constructs composite diaries that exhibit the statistical properties defined by the specified values of D and A. The longitudinal diary assembly algorithm is described in greater detail by Glen et al. (2008) and in section 6.3 of US EPA (2008b).

4.4.4 Calculate Microenvironmental Concentrations

Probabilistic algorithms are used by APEX4.3 to estimate the pollutant concentration associated with each exposure event. The estimated pollutant concentrations account for the effects of ambient (outdoor) pollutant concentration, penetration factor, air exchange rate, decay/deposition rate, and proximity to emission sources, depending on the microenvironment, available data, and the estimation method selected by the user.

APEX4.3 calculates air concentrations in the various microenvironments visited by the simulated person by using the ambient air data for the relevant census tracts and the user-specified method and parameters that are specific to each microenvironment. In typical applications, APEX4.3 calculates hourly concentrations in all the microenvironments at each hour of the simulation for each of the simulated individuals, based on the hourly ambient air quality data specific to the geographic locations visited by the individual. APEX4.3 provides two methods for calculating microenvironmental concentrations: the mass balance method and the transfer factors method (each are described briefly below). The user is required to specify a calculation method for each of the microenvironments; there are no restrictions on the method specified for each microenvironment (e.g., some microenvironments can use the mass balance method while the others can use the transfer factors method). Each of these approaches is described in sections 4.4.4.1 and 4.4.4.2, respectively.

When using an exposure model to estimate population exposures to CO based on exposures to concentrations in microenvironments, it is best to use estimates of the outdoor (ambient) CO concentration in the immediate vicinity of each microenvironment to address the ambient contribution to that microenvironment. These concentrations may need to be derived because concentrations measured at a fixed-site monitor may not adequately represent the spatial and temporal heterogeneity in concentrations expected with distance from the ambient monitor location. There can be different ways to derive the ambient concentration in the immediate vicinity of the microenvironment. For example, one can use an emission-based dispersion model to estimate ambient concentrations at a fine temporal (e.g., hourly) and spatial scale (e.g., census block-level or 500 meter grid cells). Another method is to use a statistically-based approach that addresses the variability in concentrations in a similar manner as a dispersion model, only that important physical factors that influence concentration levels are represented by and/or possibly combined with a series of regression equation coefficients and are related to an ambient monitor CO concentration. Ultimately, it is this estimated outdoor CO concentration that is then used as input to the microenvironmental algorithm (either the mass balance model or factors method) employed to estimate CO microenvironmental concentrations.

For this APEX application, staff selected a statistically-based approach to estimate ambient concentrations in the immediate vicinity of each microenvironment based on the

ambient monitor concentrations. The approach was designed to reflect both the spatial and temporal variability expected to occur outside microenvironments, while also appropriately linking the estimated microenvironmental concentrations to observed concentrations at a fixed-site ambient monitor. The approach was developed using personal exposure, fixed-site monitor, and outdoor concentration measurement data and first implemented in the pNEM/CO model for use in the most recent CO exposure assessment (Johnson et al., 2000). This approach was proposed as a method to address spatial and temporal variability in outdoor and microenvironmental concentrations in the draft scope and methods plan (US EPA, 2009b), though not fully described there as is done here.

To provide both historical perspective and context regarding the current application, this microenvironmental algorithm and the data that were used in the past with pNEM/CO to estimate values for the algorithm variables is described in section 4.4.4.3. The pNEM/CO approach was then adapted and implemented in APEX3.1, a model more similar in structure to the current version of APEX (version 4.3) than pNEM/CO. This approach as applied to APEX3.1 is then described in section 4.4.4.4. The details regarding selection of specific microenvironments and parameters used by APEX4.3 in this assessment is provided in section 5.9.

4.4.4.1 Overview of the Mass Balance Model

The mass balance method models an enclosed microenvironment as a well-mixed volume in which the air concentration is spatially uniform at any specific time. The concentration of an air pollutant in such a microenvironment is estimated using the following four processes:

- Inflow of air into the microenvironment;
- Outflow of air from the microenvironment;
- Removal of a pollutant from the microenvironment due to deposition, filtration, and/or chemical degradation; and
- Emissions from sources of a pollutant inside the microenvironment.

Table 4-2 lists the parameters required by the mass balance method to calculate concentrations in a microenvironment. The *proximity factor* ($f_{proximity}$) is used to account for differences in ambient concentrations between the geographic location represented by the ambient air quality data (e.g., a fixed-site monitor) and the geographic location of the microenvironment (e.g., near a roadway). This factor could take a value either greater than or less than 1. *Emission source* (*ES*) represents the emission rate for the emission source, and *concentration source* (*CS*) is the mean air concentration resulting from the source (these are not used in the current assessment. The factor $R_{removal}$ is defined as the removal rate of a pollutant

from a microenvironment due to deposition, filtration, and chemical reaction. The *air exchange rate* ($R_{air\ exchange}$) is expressed in air changes per hour.

Table 4-2. Variables used by APEX4.3 in the mass balance model.

Variable	Definition	Units	Value Range
$f_{proximity}$	Proximity factor	unitless	$f_{proximity} > 0$
CS	Concentration source	ppm	$CS \geq 0$
ES	Emission source	µg/hr	$ES \geq 0$
$R_{removal}$	Removal rate due to deposition, filtration, and chemical reaction	1/hr	$R_{removal} \geq 0$
$R_{air\ exchange}$	Air exchange rate	1/hr	$R_{air\ exchange} \geq 0$
V	Volume of microenvironment	m^3	$V > 0$

The mass balance equation for a pollutant in a microenvironment is described by the differential equation

$$\frac{dC_{ME}(t)}{dt} = \Delta C_{in} - \Delta C_{out} - \Delta C_{removal} + \Delta C_{source} \qquad (4\text{-}1)$$

where:

$dC_{ME}(t)$ = Change in concentration in a microenvironment at time t (ppm),

ΔC_{in} = Rate of change in microenvironmental concentration due to influx of air (ppm/hour),

ΔC_{out} = Rate of change in microenvironmental concentration due to outflux of air (ppm/hour),

$\Delta C_{removal}$ = Rate of change in microenvironmental concentration due to removal processes (ppm/hour), and

ΔC_{source} = Rate of change in microenvironmental concentration due to an emission source inside the microenvironment (ppm/hour).

Within the time period of an hour each of the rates of change, ΔC_{in}, ΔC_{out}, $\Delta C_{removal}$, and ΔC_{source}, is assumed to be constant. The change in microenvironmental concentration due to influx of air is represented by the following equation:

$$\Delta C_{in} = \frac{dC_{in}(t)}{dt} = C_{ambient}\ x\ f_{proximity}\ x\ f_{penetration}\ x\ R_{air\ exchange} \qquad (4\text{-}2)$$

where:

$C_{ambient}$	=	Ambient hourly outdoor concentration (ppm)
$f_{proximity}$	=	Proximity factor
$f_{penetration}$	=	Penetration factor
$R_{air\ exchange}$	=	Air exchange rate (1/hour)

The change in microenvironmental concentration due to outflux of air is described by:

$$\Delta C_{out} = \frac{dC_{out}(t)}{dt} = R_{air\ exchange} \times C_{ME}(t) \qquad (4\text{-}3)$$

The change in concentration due to deposition, filtration, and chemical degradation in a microenvironment is simulated by a first-order equation:

$$\Delta C_{removal} = \frac{dC_{removal}(t)}{dt} = (R_{deposition} + R_{filtration} + R_{chemical})C_{ME}(t) = R_{remova} \times C_{ME}(t) \qquad (4\text{-}4)$$

where:

$R_{deposition}$	=	Removal rate of a pollutant from a microenvironment due to deposition (1/hour)
$R_{filtration}$	=	Removal rate of a pollutant from a microenvironment due to filtration (1/hour)
$R_{chemical}$	=	Removal rate of a pollutant from a microenvironment due to chemical degradation (1/hour)
$R_{removal}$	=	Removal rate of a pollutant from a microenvironment due to overall removal (1/hour)

As discussed in Section 2.2, EPA has not modeled indoor emissions of CO in the current exposure assessment; consequently, the optional term ΔC_{source} was uniformly set equal to 0.0 for this study.

Combining equation 4-1 with equations 4-2, 4-3, and 4-4 yields

$$\frac{dC_{ME}(t)}{dt} = \Delta C_{in} - R_{air\ exchange} \times C_{ME}(t) - R_{removal} \times C_{ME}(t) \tag{4-5}$$

The solution to this differential equation is

$$C_{ME}(t) = \frac{\Delta C_{in}}{R_{combined}} + (C_{ME}(0) - \frac{\Delta C_{in}}{R_{combined}}) \exp(-R_{combined} t) \tag{4-6}$$

where:

$C_{ME}(0)$	=	Concentration of a pollutant in a microenvironment at the beginning of a hour (ppm)
$C_{ME}(t)$	=	Concentration of a pollutant in a microenvironment at time *t* within the time period of a hour (ppm)
$R_{combined}$	=	$R_{air\ exchange} + R_{removal}$ (1/hour)

Based on equation 4-6, the following three hourly concentrations in a microenvironment are calculated:

$$C_{ME}^{equil} = C_{ME}(t \to \infty) = \frac{\Delta C_{in}}{R_{combined}} \tag{4-7}$$

$$C_{ME}^{hourly\ end} = C_{ME}^{equil} + (C_{ME}(0) - C_{ME}^{equil}) \exp(-R_{combined}) \tag{4-8}$$

$$C_{ME}^{hourlymean} = \frac{\int_0^1 C(t)dt}{\int_0^1 dt} = C_{ME}^{equil} + (C_{ME}(0) - C_{ME}^{equil}) \frac{1 - \exp(-R_{combined})}{R_{combined}} \tag{4-9}$$

where:

C_{ME}^{equil}	=	Equilibrium concentration in a microenvironment (ppm)
$C_{ME}(0)$	=	Concentration in a microenvironment at the beginning of an hour (ppm)

$C_{ME}^{hourly\,end}$ = Concentration in a microenvironment at the end of an hour (ppm)

$C_{ME}^{hourlymean}$ = Hourly mean concentration in a microenvironment (ppm)

At each hour time step of the simulation period, APEX4.3 uses equations 4-7, 4-8, and 4-9 to calculate the hourly equilibrium, hourly ending, and hourly mean concentrations. APEX4.3 reports hourly mean concentration as the hourly concentration for a specific hour. The calculation continues to the next hour by using $C_{ME}^{hourly\,end}$ for the previous hour as $C_{ME}(0)$.

4.4.4.2 Overview of the Factors Model

The factors model approach is conceptually simpler than the mass balance method and has fewer user-specified parameters. It estimates the concentration in a microenvironment as a linear function of ambient concentration of that hour, regardless of the concentration in the microenvironment during the preceding hour. Table 4-3 lists the parameters required by the factors model approach to calculate concentrations in a microenvironment in the absence of indoor emissions sources.

Table 4-3. Variables used by APEX4.3 in the factors model.

Variable	Definition	Units	Value Range
$f_{proximity}$	Proximity factor	unitless	$f_{proximity} > 0$
$f_{penetration}$	Penetration factor	unitless	$0 \le f_{penetration} \le 1$

The factors model approach uses the following equation to calculate hourly mean concentration in a microenvironment from the user-provided hourly air quality data:

$$C_{ME}^{hourlymean} = C_{ambient} \times f_{proximity} \times f_{penetration} \qquad (4\text{-}10)$$

where

$C_{ME}^{hourlymean}$ = Hourly concentration in a microenvironment (ppm)

$C_{ambient}$ = Hourly concentration in ambient environment (ppm)

$f_{proximity}$ = Proximity factor (unitless)

$f_{penetration}$ = Penetration factor (unitless)

The proximity factor ($f_{proximity}$) is used to account for differences in ambient concentrations between the geographic location represented by the ambient air quality data (e.g., a fixed-site monitor) and the geographic location of the particular microenvironment. For example, persons travelling inside motor vehicles may be located on a heavily-trafficked

roadway, whereby the ambient air outside the vehicle would likely have elevated levels of mobile source pollutants such as carbon monoxide relative to the ambient monitor. In this case, a value greater than one for the proximity factor would be appropriate to represent the increase in concentrations outside the vehicle relative to the ambient monitor. Additionally, for some pollutants the process of infiltration may remove a fraction of the pollutant from the air. The fraction that is retained in the indoor/enclosed microenvironment is given by the penetration factor ($f_{penetration}$) and is dependent on the particular pollutant's physical and chemical removal rates.

4.4.4.3 Description of the Original pNEM/CO Microenvironmental Algorithm

Version 2.1 of pNEM/CO determined the hourly outdoor CO concentration applicable to each microenvironment through a Monte Carlo process based on the following equation

$$CO_{out}(c,m,d,h) = M(m) \times L(c, m, d) \times T(c,m,d,h) \times [CO_{mon}(d,h)]^{A} \qquad (4\text{-}11)$$

where,

$CO_{out}(c,m,d,h)$	=	outdoor CO concentration (ppm) for cohort *c* with respect to microenvironment *m* in district *d* during hour *h*,
$M(m)$	=	multiplier (> 0) specific to microenvironment *m*,
$L(c,m,d)$	=	location factor (> 0) specific to cohort *c*, microenvironment *m*, and district *d* (held constant for all hours),
$T(c,m,d,h)$	=	time-of-day factor (> 0) specific to cohort *c*, microenvironment *m*, district *d*, and hour *h*,
$CO_{mon}(d,h)$	=	ambient monitor-derived CO concentration (ppm) for hour *h* in district *d*, and
A	=	exponent (A > 0).

This equation was used to generate a year-long sequence of outdoor one-hour CO concentrations for each combination of cohort (*c*), microenvironment (*m*), and district (*d*) by Johnson et al. (2000). The exponent *A* was set equal to 0.621 and held constant for all sequences. The value of *M(m)* varied only with microenvironment as indicated in Table 4-4 [and is identical to Table 2-6 in Johnson et al. (2000)].

A value of the location factor *L(c, m, d)* was specified for each individual sequence and held constant for all hours in the sequence. The value was randomly selected from a lognormal distribution with geometric mean (GM_L) equal to 1.0 and geometric standard deviation (GSD_L)

equal to 1.5232. The natural logarithms of this distribution can be characterized by a normal distribution with an arithmetic mean (μ_L) equal to 0 and an arithmetic standard deviation (σ_L) equal to 0.4208.

A value of the time-of-day factor *T(c, m, d, h)* was randomly selected for each hour within a sequence from a lognormal distribution with geometric mean (GM_T) equal to 1.0 and geometric standard deviation (GSD_T) equal to 1.6289. The natural logarithms of this distribution follow a normal distribution with an arithmetic mean (μ_T) equal to 0 and an arithmetic standard deviation (σ_T) equal to 0.4879.

The $CO_{out}(c, m, d, h)$ term is interpreted as the outdoor CO concentration in the immediate vicinity of microenvironment *m* in district *d* during hour *h*. $CO_{mon}(d, h)$ is the CO concentration reported for hour *h* by a nearby fixed-site monitor selected to represent district *d*.

The mass balance model in pNEM/CO included a penetration factor that was set equal to 1.0 for CO. Consequently, this predicts no change in CO concentration associated ambient (outdoor) air as it moves into a microenvironment, though the CO concentration within the microenvironment will be affected by inputs for air exchange rate and indoor sources.

Table 4-4. Estimated values of distribution parameters and variables in equation 4-11 as implemented in the application of pNEM/CO to Denver and Los Angeles (Johnson et al., 2000).

Microenvironment[a]			Activity diary locations included in microenvironment	Parameter Estimates for Equation 4-11			
Code	General location	Specific location		A	σ_L	σ_T	M(m)
1	Indoors	Residence	Indoors - residence	0.621	0.4208	0.4879	1.034
2	Indoors	Nonresidence A	Service station Auto repair	0.621	0.4208	0.4879	2.970
3	Indoors	Nonresidence B	Other repair shop Shopping mall	0.621	0.4208	0.4879	1.213
4	Indoors	Nonresidence C	Restaurant	0.621	0.4208	0.4879	1.213
5	Indoors	Nonresidence D	Bar	0.621	0.4208	0.4879	1.213
6	Indoors	Nonresidence E	Other indoor location Auditorium	0.621	0.4208	0.4879	1.213
7	Indoors	Nonresidence F	Store Office Other public building	0.621	0.4208	0.4879	1.213
8	Indoors	Nonresidence G	Health care facility School Church Manufacturing facility	0.621	0.4208	0.4879	0.989
9	Indoors	Residential garage	Residential garage	0.621	0.4208	0.4879	1.034
10	Outdoors	Near road	Near road Bicycle Motorcycle	0.621	0.4208	0.4879	1.607
11	Outdoors	Other locations	Outdoor res. garage Construction site Residential grounds School grounds Sports arena Park or golf course Other outdoor	0.621	0.4208	0.4879	1.436
12	Vehicle	Automobile	Automobile	0.621	0.4208	0.4879	3.020
13	Vehicle	Truck	Truck	0.621	0.4208	0.4879	3.020
14	Vehicle	Mass transit vehicles	Bus Train/subway Other vehicle	0.621	0.4208	0.4879	3.020
15	Outdoor	Public parking or fueling facility	Indoor parking garage Outdoor parking garage Outdoor parking lot Outdoor service station	0.621	0.4208	0.4879	2.970

Notes:
[a] Aggregate microenvironments defined for statistical analysis of Denver PEM data: residence (1 and 9), service/parking (2 and 15), commercial (3 through 7), and vehicle (12 through 14).

4.4.4.3.1 Data Used To Estimate pNEM/CO Microenvironmental Algorithm Parameters

The parameter values for the location factor (σ_L), time-of-day (σ_T), and ambient concentration exponent (A) were based on data collected during a residential monitoring study described by Wilson et al. (1995). Ten-minute CO concentrations were measured outside 293 residences throughout California in 1992 including customers of Pacific Gas and Electricity (PG&E) (129 residences in Northern California), San Diego Gas and Electric Company (89 residences in the San Diego area), and Southern California Gas Corporation (75 residences in the Los Angeles area). After excluding the PG&E data (i.e., not part of the Los Angeles study area) and homes for which valid CO data were not available, analysts used a remaining subset of 156 residences, 70 from Los Angeles and 86 from San Diego, as the basis for estimating values of σ_L, σ_T, and A applicable to the Los Angeles study area.[2] This data subset contained 44,726 valid 10-minute averages measured outside of residences, of which less than 1% were negative (smallest value = -1.0 ppm), 14,817 (33%) were equal to 0 ppm, and the remainder were positive (maximum = 68.7 ppm). These valid 10-minute CO concentrations were then averaged by clock hour to permit comparison with hourly CO concentrations reported by nearby fixed-site monitors.

An assumption was made by the original data analysts to maximize the number of hourly averaged outdoor residential samples available to use in determining the algorithm parameters. It was proposed that the negative concentrations in this data set were most likely caused by the subtraction of an offset from all measured values to account for monitor drift. To adjust for this offset and to prevent the occurrence of negative and zero values in the hourly-averaged data (which could not be used in fitting equation 4-11), analysts added a constant offset of 0.5 ppm to all hourly-averaged values measured outside a residence. In addition, seventeen (0.2%) of the original hourly averages ≤ -0.5 ppm were removed from the data set (i.e., the offset adjustment would still yield a concentration of ≤0 ppm). Each of the resulting one-hour outdoor residential CO concentrations was paired with the one-hour CO concentration measured simultaneously at the nearest fixed-site monitor [based on data obtained from EPA's Aerometric Information Retrieval System (AIRS)]. The fixed-site ambient monitoring data were used as reported. This approach yielded a final database containing 6,330 pairs of hourly average CO concentrations, in

[2] Note these same coefficient values derived from the California measurement data were also applied to estimate exposures in the pNEM/CO Denver study area, as researchers were unable to identify a usable data set specific to Denver.

which each pair was indexed by date, time, residence identifier, fixed-site monitor identifier, and fixed-site monitor scale (e.g., neighborhood scale).

The parameters for the microenvironmental factors (or *M(m)*) in equation 4-11 were derived from data generated through the Denver Personal Monitoring Study (Akland et al, 1985; Johnson, 1984). During this study, each of approximately 450 subjects carried a personal exposure monitor (PEM) for two 24-hour periods. Each PEM measured CO concentration continuously. The PEM readings were averaged by exposure event such that each event was associated with a single microenvironment and a single clock hour (e.g., 1 pm to 2 pm). Event durations ranged from one minute to one hour. The microenvironment assigned to each PEM reading was determined from entries made in a real-time diary carried by the subject.

Researchers created a database in which each PEM CO concentration was matched to the corresponding hourly-average CO concentration reported by the nearest fixed-site monitor. The data were first processed by excluding data with missing measurements, where measurements failed a quality control check, and instances in which applicable diary data indicated the presence of smokers or gas stoves. Each PEM CO concentration was then assigned to a microenvironment, *m*, based on entries in the activity dairy. In some cases, data for two or more similar microenvironments were aggregated to provide more stable estimates than those based on the very limited amount of data available for specific microenvironments (see Table 4-4 footnote). For consistency with the above described Wilson et al. (1995) database, all cases with a zero PEM measurement were excluded, as were all cases in which the fixed-site monitor concentration was zero after rounding to the nearest integer ppm. Note that the Denver fixed-site data were recorded to the nearest 0.1 ppm, whereas the Los Angeles fixed-site data were only recorded to the nearest integer.

4.4.4.3.2 Development of the pNEM/CO Microenvironmental Algorithm Form

Equation 4-11 was based on the results of data analyses that suggested that the relationship between $CO_{out}(c, m, d, h)$ and $CO_{mon}(d, h)$ should account for the specific microenvironment, the geographic location of the microenvironment, and the time-of-day. Analysts recognized that numerous statistical algorithms could have been developed. In specifying the algorithm that was ultimately used (i.e., equation 4-11), the analysts attempted to balance the need for simplicity and parsimony with the need to represent the patterns in concentration variability observed in the available data. The bulk of the algorithm development was based on the Wilson et al. (1995) database, that is, hourly average 10-minute CO concentrations measured outside residences in southern California paired with hourly average CO concentrations measured at the nearest fixed-site monitor. For this case and consistent with equation 4-11 nomenclature, *m* represented the residence microenvironment in the district *d*.

The district *d* was initially taken to be the entire study region where measurements were collected (i.e., San Diego and Los Angeles areas).

Analysts began by considering a simple linear regression model of the form

$$CO_{out}(c,m,d,h) = a(m,d) + A \times [CO_{mon}(d,h)] + e(c,m,d,h) \quad (4\text{-}12)$$

where the residual term $e(c,m,d,h)$ was assumed to be independent and normally distributed with a mean of zero. For simplicity and parsimony, the slope coefficient A was assumed to be the same for all microenvironments (m) and districts (d).

Although the coefficient of determination (R^2) for this linear regression model was moderate (0.53),[3] the model was found to be unacceptable because it does not properly reflect the strong correlations that were observed between concentrations measured outside the same location. Instead, this form of regression model assumes that the residuals associated with a particular residential location are independent. In other words, this model does not properly separate out the variation between locations from the variation within locations. Analysts identified two other deficiencies in this model: (1) large negative values of the randomly-selected $e(c,m,d,h)$ term could produce negative outdoor concentrations, an unrealistic exposure scenario, and (2) the model did not generate outdoor concentrations characterized by lognormal distributions. Various researchers (e.g., Ott, 1995) have demonstrated that ambient CO concentrations tend to be characterized by lognormal distributions rather than normal distributions.

To better address these latter concerns, analysts evaluated an alternative model where the natural logarithm of outdoor concentration was expressed as a linear function of the natural logarithm of monitor concentration:

$$\mathrm{LN}[CO_{out}(c,m,d,h)] = a(m,d) + A \times \mathrm{LN}[CO_{mon}(d,h)] + e(c,m,d,h) \quad (4\text{-}13)$$

In this equation and those that follow, *LN[ ]* indicates the natural logarithm of the quantity in brackets. To properly separate the variability between and within locations, the intercept term $a(m,d)$ was also permitted to vary with the cohort location, c, leading to the final selected algorithm:

$$\mathrm{LN}[CO_{out}(c,m,d,h)] = a(c,m,d) + A \times \mathrm{LN}[CO_{mon}(d,h)] + e(c,m,d,h) \quad (4\text{-}14)$$

---

[3] Note that the R^2 goodness-of-fit statistic is not an appropriate measure of model adequacy when the true, underlying errors are highly correlated.

Exponentiating both sides of equation 4-14 yields the equivalent formulation to that presented above in equation 4-11:

$$CO_{out}(c,m,d,h) = M(m) \times L(c,m,d) \times T(c,m,d,h) \times [CO_{mon}(d,h)]^{A} \qquad (4\text{-}15)$$

where

$M(m)$ = exp{mean [$a(c,m,d)$]}, averaged over cohorts,

$L(c,m,d)$ = exp{$a(c,m,d)$ - mean [$a(c,m,d)$]}, and

$T(c,m,d,h)$ = exp[$e(c,m,d,h)$].

Several alternative statistical models were considered by analysts during the development of the selected algorithm formulation. Early in the process, analysts evaluated a series of autoregressive time series models, in which model predictions were influenced by the past history of CO concentrations at the monitor and outdoors of the microenvironment. These models were rejected for several reasons: (1) they were inherently complex, (2) they yielded a wide variation in model coefficients which did not always produce reasonable estimates when applied to specific California residences, and (3) they required microenvironment-specific time series data for coefficient estimation which were not readily available for non-residential microenvironments.

Analysts also evaluated algorithms similar to equation 4-11 in which the exponent A varied with microenvironment. These algorithms were rejected due to the need for parsimony and perhaps more importantly, the lack of sufficient, suitable data for estimating microenvironment-specific values of A. A simpler model in which the exponent A is fixed at 1 was rejected because fits of equation 4-11 to the California data indicated that A differed significantly from 1 ($p<0.01$). In addition, the assumption that $A = 1$ produced unrealistically high predictions for outdoor CO concentrations when the model was applied to monitoring data obtained from the Denver Broadway site (ID 08310002). These high values were found to be a direct result of setting $A = 1$, which forced the geometric standard deviation of the estimated outdoor concentrations to significantly exceed the geometric standard deviation of the monitor values.

Analysts ultimately arrived at equation 4-11 (equivalent to equation 4-15), which permits the A exponent to differ from 1.0. The model was fitted using statistical software for a mixed (random and fixed effects) model which employed restricted maximum likelihood estimation.

The fit yielded estimates of $\sigma_L = 0.4208$, $\sigma_T = 0.4879$, and $A = 0.621$, the values subsequently used in the pNEM/CO runs described by Johnson et al. (2000). The fitted value of *M(m)*, representing residences in Los Angeles during 1992, was actually 0.9706. An alternative value (1.034), based on the additional analyses described below, was applied to the indoor-residence microenvironment in the pNEM/CO runs (see Table 4-4).

This algorithm, considered a reasonable compromise between model simplicity and performance, is completely specified by four parameters [*M(m)*, σ_L, σ_T, and A]. Note that σ_L, σ_T, and A are defined to be independent of the microenvironment, whereas *M(m)* is microenvironment-specific. At the time of the initial algorithm development, researchers were unable to find a single data source capable of providing estimates of all four parameters. Consequently, values for σ_L, σ_T, and A were estimated by analyzing data obtained from the Wilson et al. (1995) database, whereas the specific *M(m)* values were based on data provided by the Denver PEM database (Akland et al, 1985; Johnson, 1984).

Researchers conducted a series of sensitivity analyses to evaluate the potential effects on parameter estimates of variations in the regional location and scale of the fixed-site monitor. Equation 4-11 was fitted to a series of data subsets defined by region (Los Angeles or San Diego) or by the scale of the fixed-site monitor (based on the estimated maximum distance from the monitor represented by the measured concentrations: micro, middle, neighborhood, or urban scale). The fitted values of σ_L, σ_T, A, and *M(m)* were very similar across the different subsets, supporting the assumption that these parameters can be assumed to be representative of concentration patterns outside residences in other regions and for other time periods, and can be chosen to be the same value for all monitoring scales. Due to a lack of additional suitable data, the values of σ_L, $\underline{\sigma_T}$, and A are also assumed to be applicable to concentrations outside all other microenvironments, although *M(m)* varies with the particular microenvironment (see below).

In equation 4-11, the $CO_{out}(c, m, d, h)$ term represents the outdoor CO concentration associated with a particular microenvironment *m*, even when the microenvironment is an indoor location. Few of the Denver outdoor PEM concentrations could be reliably associated with particular indoor microenvironments. Consequently, researchers employed a simplified procedure for estimating *M(m)* values which assumed that the mean of the indoor PEM values associated with each indoor microenvironment was approximately equal to the mean of the outdoor concentration for the microenvironment.[4] This assumption is consistent with the results of applying mass-balance modeling to non-reactive pollutants in enclosed spaces where the only

[4] Because the simplified approach was also less sensitive to the wide variation in averaging times exhibited by the PEM values (i.e., one minute to 60 minutes), analysts were able to use the majority of PEM values in the statistical analysis. Limiting the analysis to one-hour PEM values would have significantly reduced the pool of usable data.

source of the pollutant is the outside air. In such cases, the mean indoor concentration approximates the mean outdoor concentration, with the instantaneous indoor concentration exhibiting a lower degree of variability than the corresponding outdoor concentration.

When equation 4-11 is expressed in a logarithmic form (i.e., as in equation 4-14) and averaged over cohorts, one obtains the equation

$$\begin{aligned}\text{Mean}\{\text{LN}[CO_{out}(c, m, d, h)\}\\ &= \text{Mean}[a(c, m, d)] + \text{A} \times \text{Mean}\{\text{LN}[CO_{mon}(d, h)]\} + \text{Mean}[e(c, m, d, h)]\\ &= \text{LN}[M(m)] + A \times \text{Mean}\{\text{LN}[CO_{mon}(d, h)]\}.\end{aligned}$$

Therefore, the value of $M(m)$ equals

$$M(m) = \exp\{\text{Mean LN}[COout(c, m, d, h)] - A \times \text{Mean LN}[COmon(d, h)]\} \quad (4\text{-}16)$$

where $A = 0.621$ (as above). This equation was then used to obtain estimates of $M(m)$ for each particular microenvironment, or aggregate of microenvironments, as indicated in Table 4-4 using the available Denver PEM study data (Akland et al, 1985; Johnson, 1984). The same value of $M(m)$ was applied to each specific microenvironment within an aggregate.

4.4.4.4 The Micronenvironmental Algorithm as Implemented by APEX3.1

As discussed in section 4-3, the pNEM/CO model effectively evolved into what is known today as the APEX model. In APEX3.1, the portion of the outdoor concentration affecting the indoor concentration is determined by the formula

$$CO_{out} = Ambient \times Proximity \times Penetration \quad (4\text{-}17)$$

Note that we can represent *Proximity* and *Penetration* as distributions in APEX3.1. These distributions can be sampled hourly, daily, or yearly. Let us make the following substitutions of the variables used to estimate the outdoor concentrations:

$$Ambient = [CO_{mon}(d,h)]^{A} \quad (4\text{-}18)$$

$$Proximity = M(m) \times L(c, m, d) \quad (4\text{-}19)$$

$$Penetration = T(c,m,d,h) \quad (4\text{-}20)$$

which yields

$$CO_{out} = M(m) \times L(c, m, d) \times T(c,m,d,h) \times [CO_{mon}(d,h)]^{A} \quad (4\text{-}21)$$

and is identical to equation 4-11 above.

To obtain results from APEX3.1 that are comparable to that generated by pNEM/CO, Johnson and Capel (2003) preprocessed the hourly ambient monitor data assigned to the district containing the microenvironment using the formula

$$Ambient = [CO_{mon}(d,h)]^{0.621} \quad (4\text{-}22)$$

where $CO_{mon}(d,h)$ is expressed in ppm. For each profile, a value for the *Proximity* term was selected for each microenvironment from a lognormal distribution with geometric mean equal to $M(m)$ and geometric standard deviation equal to 1.5232. The natural logarithms of this distribution were characterized by a normal distribution with an arithmetic mean (μ_L) equal to LN[$M(m)$] and an arithmetic standard deviation (σ_L) equal to 0.4208. Consistent with the pNEM/CO algorithm, *Proximity* values were not permitted to fall below the 5th percentile of the specified distribution or above the 95th percentile of the distribution. Table 4-5 lists the parameter values applicable to the 15 microenvironments defined by Johnson and Capel (2003).

Penetration values were randomly selected for each hour from a lognormal distribution with geometric mean (GM_T) equal to 1.0 and geometric standard deviation (GSD_T) equal to 1.6289. As indicated above, the natural logarithms of this distribution followed a normal distribution with an arithmetic mean (μ_T) equal to zero and an arithmetic standard deviation (σ_T) equal to 0.4879. In agreement with the pNEM/CO algorithm, *Penetration* values were not permitted to fall below the 5th percentile of the specified distribution (0.4482) or above the 95th percentile of the distribution (2.2313).[5]

[5] Note the *Penetration* factor was not used according to its originally intended purpose in the APEX model. As discussed in Volume I of the APEX3.1 User's Guide (US EPA, 2003), the *Penetration* factor is typically used to account for removal of pollutants during the transfer of outdoor air to a microenvironment. The Penetration factor was used to represent the $T(c,m,d,h)$ term in equation 4-11 because *Penetration* is the only APEX3.1 parameter available for this purpose, given that the *Proximity* factor is being used to represent the product of $M(m)$ and $L(c,m,d)$. The product of $M(m)$, $L(c,m,d)$, and $T(c,m,d,h)$ could not be represented by a single term because $L(c,m,d)$ and $T(c,m,d,h)$ have different averaging times (day vs. hour).

Table 4-5. Parameters of bounded lognormal distributions defined for proximity factors used in applications of APEX3.1 to Los Angeles (Johnson and Capel, 2003).

Microenvironment			Activity diary locations included in microenvironment	Parameters of bounded lognormal distribution			
Code	General Location	Specific location		GM	GSD	Lower Bound (5th pct)	Upper Bound (95th pct)
1	Indoors	Residence	Indoors - residence	1.034	1.5232	0.5175	2.0661
2	Indoors	Nonresidence A	Service station Auto repair	2.970	1.5232	1.4864	5.9345
3	Indoors	Nonresidence B	Other repair shop Shopping mall	1.213	1.5232	0.6071	2.4237
4	Indoors	Nonresidence C	Restaurant	1.213	1.5232	0.6071	2.4237
5	Indoors	Nonresidence D	Bar	1.213	1.5232	0.6071	2.4237
6	Indoors	Nonresidence E	Other indoor location Auditorium	1.213	1.5232	0.6071	2.4237
7	Indoors	Nonresidence F	Store Office Other public building	1.213	1.5232	0.6071	2.4237
8	Indoors	Nonresidence G	Health care facility School Church Manufacturing facility	0.989	1.5232	0.4950	1.9762
9	Indoors	Residential garage	Residential garage	1.034	1.5232	0.5175	2.0661
10	Outdoors	Near road	Near road Bicycle Motorcycle	1.607	1.5232	0.8042	3.2110
11	Outdoors	Other locations	Outdoor res. garage Construction site Residential grounds School grounds Sports arena Park or golf course Other outdoor	1.436	1.5232	0.7187	2.8693
12	Vehicle	Automobile	Automobile	3.020	1.5232	1.5114	6.0344
13	Vehicle	Truck	Truck	3.020	1.5232	1.5114	6.0344
14	Vehicle	Mass transit vehicles	Bus Train/subway Other vehicle	3.020	1.5232	1.5114	6.0344
15	Outdoor	Public parking or fueling facility	Indoor parking garage Outdoor parking garage Outdoor parking lot Outdoor service station	2.970	1.5232	1.4864	5.9345

4.4.5 Estimate Energy Expenditure and Ventilation Rates

APEX4.3 includes a module that estimates COHb levels in the blood as a function of alveolar ventilation rate, the CO concentration of the respired air, endogenous CO production rate, and various physiological variables such as blood volume and pulmonary CO diffusion rate. Alveolar ventilation rate is estimated as a function of oxygen uptake rate, which in turn is estimated as a function of energy expenditure rate. This section provides a brief summary of the algorithm used to estimate alveolar ventilation rate. A detailed description of the algorithm, based on the nonlinear solution to the Coburn-Forster-Kane (CFK) equation (Coburn et al., 1965), together with the distributions and estimating equations used in determining the value of each parameter in the algorithm, can be found in Appendix B of this document.

4.4.5.1 Energy Expenditure

McCurdy (2000) has recommended that measures of human ventilation (respiration) rate be estimated as functions of energy expenditure rate. The energy expended by an individual during a particular activity can be expressed as

$$EE = METS \times RMR \qquad (4\text{-}23)$$

where *EE* is the average energy expenditure rate (kcal min^{-1}) during the activity and RMR is the resting metabolic rate of the individual expressed in terms of number of energy units expended per unit of time (kcal min^{-1}). *METS* (i.e., metabolic equivalent of work) is a ratio specific to the activity and is dimensionless.

The *METS* concept provides a means for estimating the alveolar ventilation rate associated with each activity. For convenience, let $EE(i,j,k)$ indicate the energy expenditure rate associated with the ith activity on day j for person k. Equation 4-23 can now be expressed as

$$EE(i,j,k) = METS(i,j,k) \times RMR(k) \qquad (4\text{-}24)$$

where $RMR(k)$ is the average value for resting metabolic rate specific to person k. Note that $METS(i,j,k)$ is specific to a particular activity performed by person k.

4.4.5.2 Oxygen Requirements for Energy Expenditure

Energy expenditure requires oxygen which is supplied by ventilation (respiration). $ECF(k)$ represents an energy conversion factor defined as the volume of oxygen required to produce one kilocalorie of energy in person k. The oxygen uptake rate (VO_2) associated with a particular activity can be expressed as

$$VO_2(i,j,k) = ECF(k) \times EE(i,j,k) \qquad (4\text{-}25)$$

where $VO_2(i,j,k)$ has units of liters oxygen min^{-1}, $ECF(k)$ has units of liters oxygen $kcal^{-1}$, and $EE(i,j,k)$ has units of kcal min^{-1}. The value of $VO_2(i,j,k)$ can now be determined from $MET(i,j,k)$ by substituting equation 4-24 into equation 4-25 to produce the relationship

$$VO_2(i,j,k) = ECF(k) \times METS(i,j,k) \times RMR(k) \quad (4\text{-}26)$$

4.4.5.3 Excess Post-Exercise Oxygen Consumption

At the beginning of exercise, there is a lag between work expended and oxygen consumption. During this work/ventilation mismatch, an individual's energy needs are met by anaerobic processes. The magnitude of the mismatch between expenditure and consumption is termed the *oxygen deficit*. During heavy exercise, further oxygen deficit (in addition to that associated with the start of exercise) may be accumulated. At some point, oxygen deficit reaches a maximum value, and performance and energy expenditure deteriorate. After exercise ceases, ventilation and oxygen consumption will remain elevated above baseline levels. This increased oxygen consumption was historically labeled the *oxygen debt* or *recovery oxygen consumption*. However, the term *excess post-exercise oxygen consumption* (EPOC) has been adopted here to represent this phenomenon. APEX4.3 has an algorithm for adjusting the MET values to account for EPOC. This algorithm is described in detail in section 7.2 of US EPA (2008b).

4.4.5.4 Alveolar Ventilation Rate

Alveolar ventilation (V_A) represents the portion of the minute ventilation that is involved in gaseous exchange with the blood. VO_2 is the oxygen uptake that occurs during this exchange. The absolute value of V_A is known to be affected by total lung volume, lung dead space, and respiration frequency – parameters that vary according to the person and/or exercise rate. However, it is reasonable to assume that the ratio of V_A to VO_2 is relatively constant regardless of a person's physiological characteristics or energy expenditure rate. Consistent with this assumption, APEX4.3 converts each estimate of $VO_2(i,j,k)$ to an estimate of $V_A(i,j,k)$ by the proportional relationship

$$V_A(i,j,k) = 19.63 \times VO_2(i,j,k) \quad (4\text{-}27)$$

where both V_A and VO_2 are expressed in units of liters min^{-1}. This relationship was obtained from Joumard et al. (1981), who based it on research by Galetti (1959). Equation 4-15 can also be expressed by the equivalent equation

$$V_A(i,j,k) = 19.63 \times METS(i,j,k) \times ECF(k) \times RMR(k) \quad (4\text{-}28)$$

If *ECF* and *RMR* are specified for an individual, then equation 4-28 requires only an activity-specific estimate of *METS* to produce an estimate of the energy expenditure rate for a given activity. APEX4.3 processes time-location-activity data obtained from the CHAD to create a sequence of activity-specific *METS* values for each simulated individual. APEX4.3 estimates *RMR* as a function of body mass based on probabilistic equations specific to age and gender using equations reported by Schofield (1985). A value of *ECF* is selected for each individual from a uniform distribution (minimum = 0.20, maximum = 0.21) based on data provided by Esmail et al. (1995). Using equation 4-28 and these inputs, APEX4.3 calculates a sequence of V_A values for each simulated individual. These values are provided to the algorithm that estimates the percent COHb in the blood resulting from the simulated exposure (see section 4.4.7 and Appendix B).

4.4.6 Calculate Exposure

APEX4.3 calculates exposure as a time series of exposure concentrations that a simulated individual experiences during the simulation period. APEX4.3 determines the exposure using hourly ambient air concentrations, calculated concentrations in each microenvironment based on these ambient air concentrations, and the minutes spent in a sequence of microenvironments visited according to the composite diary. The hourly exposure concentration at any clock hour during the simulation period is determined using the following equation:

$$C_i = \frac{\sum_{j=1}^{N} C_{ME(j)}^{hourlymean} \; t_{(j)}}{T} \qquad (4\text{-}29)$$

where

C_i = Hourly exposure concentration at clock hour *i* of the simulation period (ppm)

N = Number of events (i.e., varied microenvironments visited/activities performed) in clock hour *i* of the simulation period.

$C_{ME(j)}^{hourlymean}$ = Hourly mean concentration in microenvironment *j* (ppm)

$t_{(j)}$ = Time spent in microenvironment *j* (minutes)

T = 60 minutes

From the hourly exposures, APEX4.3 calculates time series of 8-hour and daily average exposure concentrations that a simulated individual would experience during the simulation period. APEX4.3 then statistically summarizes and tabulates the number of persons and person-days at or above selected hourly, 8-hour, and daily average exposure concentrations in a series of output tables.

4.4.7 Calculate Dose

Using time-location-activity pattern data obtained from several diary studies, APEX4.3 constructs a composite diary for each simulated person in the specified population. The composite diary consists of a sequence of events spanning the specified period of the exposure assessment (typically one calendar year). Each event is defined by a start time, duration, a geographic location, a microenvironment, and an activity. Using the algorithms described above in sections 4.4.4, 4.4.5, and 4.4.6, APEX4.3 provides estimates of CO microenvironmental concentrations and the persons' alveolar ventilation rate for each event in the composite diary, for each simulated individual. APEX4.3 then uses these data, together with estimates of various physiological parameters specific to the simulated individual, to estimate the percent COHb in the blood at the end of each event. The percent COHb calculation is based on the solution to the nonlinear Coburn-Forster-Kane (CFK) equation (Coburn et al., 1965), as detailed in Appendix B. Briefly, the CFK module in APEX4.3 describes the rate of change in COHb blood levels as a function of the following quantities:

- Inspired CO pressure;
- COHb level;
- Oxyhemoglobin (O_2Hb) level;
- Hemoglobin (Hb) content of blood;
- Blood volume;
- Alveolar ventilation rate;
- Endogenous CO production rate;
- Mean pulmonary capillary oxygen pressure;
- Pulmonary diffusion rate of CO;
- Haldane coefficient (M);
- Barometric pressure; and
- Vapor pressure of water at body temperature (47 torr).

If all of the listed quantities except COHb level are constant over some time interval, the CFK equation has a linear form over the interval and is readily integrated. The solution to the linear form gives reasonably accurate results for lower levels of COHb (ISA section 4.2.1). However, CO and oxygen can compete for binding with the available hemoglobin and, therefore, are not independent of each other. If this dependency is taken into account, the resulting differential equation is no longer linear. Peterson and Stewart (1975) proposed a heuristic approach to account for this dependency which assumed the linear form and then adjusted the

O_2Hb level iteratively based on the assumption of a linear relationship between COHb and O_2Hb. This approach was used in the COHb module of the original CO-NEM exposure model (Biller and Richmond, 1982; Johnson and Paul, 1983).

Alternatively, it is possible to determine COHb at any time by numerical integration of the nonlinear CFK equation if one assumes a particular relationship between COHb and O_2Hb. Muller and Barton (1987) demonstrated that assuming a linear relationship between COHb and O_2Hb leads to a form of the CFK equation equivalent to the Michaelis-Menten kinetic model that can be analytically integrated. However, the analytical solution in this case cannot be solved explicitly for COHb. Muller and Barton (1987) demonstrated a binary search method for determining the COHb value.

The COHb module used in pNEM/CO employed a linear relationship between COHb and O_2Hb which was consistent with the basic assumptions of the CFK model. The approach differed from the linear forms used by other modelers in that the Muller and Barton (1987) solution was employed. However, instead of the simple binary search described in the Muller and Barton paper, a combination of the binary search and Newton-Raphson root finding methods was used to solve for COHb (Press et al., 1986).

As mentioned above, the current COHb module included in APEX4.3 is based on the solution to the nonlinear CFK equation using the assumption adopted by Muller and Barton (1987) which employs a linear relationship between O_2Hb and COHb. The CFK equation does not have an explicit solution, so an iterative solution or approximation is needed to calculate each percent COHb value. APEX4.3 solves the CFK equation using a 4th-order Taylor's series with subintervals. This method, first incorporated in APEX3 (Glen, 2002), is summarized in Appendix B. The selected method (4th-order Taylor series with subintervals) was chosen because of its simplicity, fast execution speed, and ability to produce relatively accurate estimates of percent COHb at both low and high levels of CO exposure.

While there may be other approaches proposed as improvements to the standard CFK equation (e.g., Bruce and Bruce (2003) multi-compartment model), at this time both the nonlinear and linear CFK models remain the most widely accepted and validated approaches used to estimate COHb levels (ISA, section 4.2.3). Before any such future module modifications could be planned and implemented, a more thorough and balanced evaluation of the uncertainties needs to be performed to include those uncertainties that may be reduced, as well as those uncertainties introduced by the model modification,. Briefly as an example, the Bruce and Bruce (2003) model accounts for distribution of CO to five modeled compartments: the lungs, arterial blood, mixed venous blood, muscle tissue, and other soft tissues. In accounting for these additional compartments in a new APEX/COHb module, a number of variables would need to be introduced. Some of these variables may have data or equations available in the extant literature

to parameterize the variable (e.g., Q or cardiac output), while others may not be measureable or are unknown (i.e., the distribution of Q between two tissue compartments). When data do become available to support such model modifications, one would need to evaluate the appropriateness of these data sets for estimating the parameter values used for the selected at-risk population. Further, a comparison of estimated COHb levels using the standard CFK equation with that of the 5-compartment model indicated that, consistently, the estimated COHb levels would be lower when considering uptake and storage within muscle tissue, however these differences were very small, particularly at the lowest (and most relevant) exposure concentration level evaluated (see Figure 7 of Bruce and Bruce, 2003). This preliminary comparison indicates that while adding multiple compartments to the COHb model may be more physiologically representative, the extent of any overall benefit in adding such modeling complexity to the current approach used is unclear at this time. Given the extremely tight timeframe for this assessment and the relative strength of the dose modeling approach used, we elected to use the nonlinear CFK model to best approximate population-based end-of-hour COHb levels for this current CO NAAQS review.

And finally, the current structure of APEX allows the user to control the random sampling of model input parameters, such that, the same persons, their personal attributes, and microenvironmental factors will be identical from one simulation to another. Modelers can then vary a particular input to evaluate the impact to exposure and dose results. This is being used in this REA to develop estimates of the contribution of ambient exposure to an individual's COHb levels, an additional metric of interest in this current APEX application. Results for simulations that are identical in all respects except their CO exposure can be used to separate the contribution of endogenous CO production to an individual's maximum end-of-hour COHb level from that of the ambient exposure contribution. For such an analysis, two simulations are performed: the first is a typical simulation that generates exposure and dose in the presence of ambient CO and the second simulation uses ambient concentrations equal to zero at all monitors and all hours of the day. In this first simulation, the exposures persons experience will be a result of their contact with ambient and microenvironmental CO concentrations, while end-of-hour dose levels will reflect both the contribution from CO exposure and endogenous CO production. In the second simulation, exposure concentrations will be zero for all hours and for all persons, while end-of-hour COHb dose levels will be that resultant from endogenous CO production alone. The difference in the event-level time series for each individual (and entire population) can thus be used to approximate the contribution from ambient CO for all exposure events throughout the simulation period. See section 5.10 and Appendix B for details.

4.4.8 Model Output

All of the output files written by APEX4.3 are ASCII text files; the complete list and their descriptions can be found in Table 5-1 of the APEX4.3 User's Guide (US EPA, 2008a). In general, the simulation output files most relevant to results generated for the assessment include summary tabulations of population exposure concentrations and maximum end-of-hour COHb levels. Detailed event-level (minute to 1-hour in duration) or hourly-average information can also be output for each of the exposure and dose metrics of interests as well as activity specific ventilation rates and energy expenditures. For example, both the *hourly* and *events* APEX files were needed to estimate a distribution of microenvironmental-to-ambient concentration ratios (see section 5.10). However, given the potential size of the files that can be generated for a large population and assessment duration, it is not common to generate event-level files outside of research purposes. Specific outputs generated for the purposes of the current CO exposure and dose assessment are discussed in section 6.1.

4.5 KEY OBSERVATIONS

Presented below are key observations related to the modeling system used for the population assessment of CO exposure and dose.

- APEX, an EPA human exposure and dose model, has a long history of use in estimating exposure and dose for many of the criteria pollutants including CO, O_3, SO_2, and NO_2. Over time, EPA has improved and developed new model algorithms, incorporated newer available input data and parameter distributions, as well as performed several model evaluations, sensitivity analyses, and uncertainty characterizations for the above pollutants. Based on this analysis, APEX was judged to be an appropriate model to use for assessing CO exposure and dose.

4.6 REFERENCES

Akland GG, Hartwell TD, Johnson TR, Whitmore RW. (1985). Measuring human exposure to carbon monoxide in Washington, D. C. and Denver, Colorado during the winter of 1982-83. *Environ Sci Technol*. 19:911-918.

Biller WF and Richmond HM. (1982). Sensitivity Analysis on Coburn Model Predictions of COHb Levels Associated with Alternative CO Standards. Report to Strategies and Air Standards Division of the Office of Air quality Planning and Standards, U.S. Environmental Protection Agency, Research Triangle Park, NC. November, 1982.

Bruce EN and Bruce MC. (2003). A multicompartment model of carboxyhemoglobin and carboxymyoglobin responses to inhalation of carbon monoxide. *J Appl Physiol*. 95:1235-1247.

Coburn RF, Forster RE, Kane RB. (1965). Considerations of the physiology and variables that determine blood carboxyhemoglobin concentration in man. *J Clin Invest*. 44:1899-1910.

Esmail S, Bhambhani Y, Brintnell S. (1995). Gender differences in work performance on the Baltimore therapeutic equipment work simulator. *Amer J Occup Therapy*. 49:405-411.

Galetti PM. (1959). Respiratory exchanges during muscular effort. *Helv Physiol Acta*. 17:34-61.

Glen G. (2002). Programmer's Guide for the APEX3 Model. Prepared by ManTech Environmental Technology, Inc., for the U.S. Environmental Protection Agency, Research Triangle Park, NC. April, 2002.

Glen G, Smith L, Isaacs K, McCurdy T, Langstaff J. (2008). A new method of longitudinal diary assembly for human exposure modeling. *J Expos Sci Environ Epidem*. 18:299-311.

Goldstein BR, Tardiff G, Hoffnagle G, Kester R. (1992). Valdez Health Study: Summary Report. Alyeska Pipeline Service Company, Anchorage AK.

Hartwell TD, Clayton CA, Ritchie RM, Whitmore RW, Zelon HS, Jones SM, Whitehurst DA. (1984). Study of Carbon Monoxide Exposure of Residents of Washington, DC and Denver, Colorado. Research Triangle Park, NC: U.S. Environmental Protection Agency, Office of Research and Development, Environmental Monitoring Systems Laboratory. EPA-600/4-84-031.

Isaacs K, McCurdy T, Errickson A, Forbes S, Glen G, Graham S, McCurdy L, Nysewander M, Smith L, Tulve N, Vallero D. (2009). Statistical properties of longitudinal time-activity data for use in EPA exposure models. Poster presented at the American Time Use Research Conference; College Park MD, June 26, 2009.

Johnson T and Capel J. (2003). Total Risk Integrated Methodology. TRIM ExpoInhalation User's Document. Volume III: Air Pollutant Exposure Model Criteria Air Pollutants Case Study (Carbon Monoxide Exposures in Los Angeles). Report prepared by TRJ Environmental, Inc., for the Office of Air Quality Planning and Standards, U.S. Environmental Protection Agency, Research Triangle Park, North Carolina.

Johnson T and Paul R. (1983). The NAAQS Exposure Model (NEM) Applied to Carbon Monoxide. EPA Report No. 450/5-83-003. Prepared by PEDCo Environmental, Inc. for the Office of Air Quality Planning and Standards, U.S. Environmental Protection Agency, Research Triangle Park, NC.

Johnson T. (1984). A Study of Personal Exposure to Carbon Monoxide in Denver, Colorado. Research Triangle Park, NC: U.S. Environmental Protection Agency, Environmental Monitoring Systems Laboratory. EPA-600/4-84-014.

Johnson T. (1989). Human Activity Patterns in Cincinnati, Ohio. Palo Alto, CA: Electric Power Research Institute. EPRI EN-6204.

Johnson T, Capel J, Olaguer E, Wijnberg L. (1992). Estimation of Carbon Monoxide Exposures and Associated Carboxyhemoglobin Levels in Denver Residents Using a Probabilistic Version of NEM. Report prepared for the Office of Air Quality Planning and Standards, U.S. Environmental Protection Agency, Research Triangle Park, North Carolina.

Johnson T, Mihlan G, LaPointe J, Fletcher K, Capel J. (2000). Estimation of Carbon Monoxide Exposures and Associated Carboxyhemoglobin Levels for Residents of Denver and Los Angeles Using pNEM/CO (Version 2.1). Report prepared by ICF Consulting and TRJ Environmental, Inc., under EPA Contract No. 68-D6-0064. U.S. Environmental Protection Agency, Research Triangle Park, North Carolina. Available at: http://www.epa.gov/ttn/fera/human_related.html. June 2000.

Joumard R, Chiron M, Vidon R, Maurin M, Rouzioux JM. (1981). Mathematical models of the uptake of carbon monoxide on hemoglobin at low carbon monoxide levels. *Environ Health Persp*. 41:277-289.

Klepeis NE, Tsang AM, Behar JV. (1996). Analysis of the National Human Activity Pattern Survey (NHAPS) Respondents from a Standpoint of Exposure Assessment. Washington, DC: U.S. Environmental Protection Agency, Office of Research and Development. EPA/600/R-96/074.

Liu L-JS, Box M, Kalman D, Kaufman J, Koenig J, Larson T, Lumley T, Sheppard L, Wallace L. (2003). Exposure assessment of particulate matter for susceptible populations in Seattle. *Environ Health Persp*. 111:909-918.

Mansfield CA and Corey C. (2003). Analysis of Survey Data on Ozone Alert Days. Research Triangle Park: Research Triangle Institute. (Task 4 Report).

Mansfield C, Johnson FR, Van Houtven G. (2006). The missing piece: averting behavior for children's ozone exposures. *Resource Energy Econ*. 28:215-228.

Mansfield C, Van Houtven G, et al. (2004). Parental Averting Behavior With Respect To Ozone Alerts. Research Triangle Park NC: Research Triangle Institute.

McCurdy T. (2000). Conceptual basis for multi-route intake dose modeling using an energy expenditure approach. *J Expos Anal Environ Epidemiol*. 10:1-12.

McCurdy T, Glen G, Smith L, and Lakkadi Y. (2000). The National Exposure Research Laboratory's Consolidated Human Activity Database. *J Expos Anal and Environ Epidemiol*. 10:566-578.

Muller KE and Barton CN. (1987). A nonlinear version of the Coburn, Forster and Kane model of blood carboxyhemoglobin. *Atmos Environ*. 21:1963-1967.

Ott W. (1995). Environmental Statistics and Data Analysis. CRC Press, Boca Raton.

Peterson JE and Stewart RD. (1975). Predicting the carboxyhemoglobin levels resulting from carbon monoxide exposures. *J Appl Physiol*. 39(4):633-638.

Press WH, Flannery BP, Teukolsky SA, Vettering WT. (1986). Numerical Recipes. Cambridge University Press.

Schofield WN. (1985). Predicting basal metabolic rate, new standards, and review of previous work. *Hum Nutr Clin Nutr*. 39C(S1):5-41.

Spier CE, Little DE, Trim SC, Johnson TR, Linn WS, Hackney JD. (1992). Activity patterns in elementary and high school students exposed to oxidant pollution. *J Expo Anal Environ Epidemiol*. 2:277-293.

Tsang AM and Klepeis NE. (1996). Descriptive Statistics Tables from a Detailed Analysis of the National Human Activity Pattern Survey (NHAPS) Data. U.S. Environmental Protection Agency. EPA/600/R-96/148.

US Census Bureau. (2007). Employment Status: 2000- Supplemental Tables. Available at: http://www.census.gov/population/www/cen2000/phc-t28.html.

US DOT. (2007). Part 3-The Journey To Work files. Bureau of Transportation Statistics (BTS). Available at: http://transtats.bts.gov/.

US EPA. (1999). Total Risk Integrated Methodology. Available at: http://www.epa.gov/ttnatw01/urban/trim/trimpg.html.

US EPA. (2002). EPA's Consolidated Human Activities Database. Data and associated documentation available at: http://www.epa.gov/chad/.

US EPA. (2007). Ozone Population Exposure Analysis for Selected Urban Areas (July 2007). Office of Air Quality Planning and Standards, Research Triangle Park, NC. EPA-452/R-07-010. Available at: http://epa.gov/ttn/naaqs/standards/ozone/s_o3_cr_td.html.

US EPA. (2008a). Total Risk Integrated Methodology (TRIM) Air Pollutants Exposure Model Documentation (TRIM.Expo/APEX, Version 4.3). Volume 1: Users Guide. Report no. EPA-452/B-08-001a. Office of Air Quality Planning and Standards, U.S. Environmental Protection Agency, Research Triangle Park, NC. Available at: http://www.epa.gov/ttn/fera/human_apex.html

US EPA. (2008b). Total Risk Integrated Methodology (TRIM) Air Pollutants Exposure Model Documentation (TRIM.Expo/APEX, Version 4.3). Volume 2: Technical Support Document. Report no. EPA-452/B-08-001b. Office of Air Quality Planning and Standards, U.S. Environmental Protection Agency, Research Triangle Park, NC. Available at: http://www.epa.gov/ttn/fera/human_apex.html

US EPA. (2008c). Risk and Exposure Assessment to Support the Review of the NO_2 Primary National Ambient Air Quality Standard. Report no. EPA-452/R-08-008a. November 2008. Available at: http://www.epa.gov/ttn/naaqs/standards/nox/data/20081121_NO2_REA_final.pdf.

US EPA. (2009a). Risk and Exposure Assessment to Support the Review of the SO_2 Primary National Ambient Air Quality Standard. Report no. EPA-452/R-09-007. August 2009. Available at: http://www.epa.gov/ttn/naaqs/standards/so2/data/200908SO2REAFinalReport.pdf.

US EPA. (2009b). Carbon Monoxide National Ambient Air Quality Standards: Scope and Methods Plan for Health Risk and Exposure Assessment. Report no. EPA-452/R-09-004. Available at: http://www.epa.gov/ttn/naaqs/standards/co/s_co_cr_pd.html.

University of Michigan. (2010). The Panel Study of Income Dynamics (PSID). Data and documentation Available at: http://www.psidonline.isr.umich.edu/Data/.

Wiley JA, Robinson JP, Piazza T, Garrett K, Cirksena K, Cheng Y-T, Martin G. (1991a). Activity Patterns of California Residents: Final Report. California Air Resources Board, Sacramento, CA. ARB/R93/487. Available from: NTIS, Springfield, VA., PB94-108719.

Wiley JA, Robinson JP, Cheng Y-T, Piazza T, Stork L, Pladsen K. (1991b). Study of Children's Activity Patterns: Final Report. California Air Resources Board, Sacramento, CA. ARB-R-93/489.

Williams R, Suggs J, Creason J, Rodes C, Lawless P, Kwok R, Zweidinger R, Sheldon L. (2000). The 1998 Baltimore particulate matter epidemiology-exposure study: Part 2. Personal exposure associated with an elderly population. *J Expo Anal Environ Epidemiol*. 10(6):533-543.

Williams R, Suggs J, Rea A, Leovic K, et al. (2003a). The Research Triangle particulate panel study: PM mass concentrations relationships. *Atmos Environ*. 37:5349-5363.

Williams R, Suggs J, Rea A, Sheldon L, et al. (2003b). The Research Triangle particulate panel study: modeling ambient source contributions to personal and residential PM mass concentrations. *Atmos Environ*. 37:5365-5378.

Wilson AL, Colome SD, Tian Y. (1995). California Residential Indoor Air Quality Study. Volume III: Ancillary and Exploratory Analysis. Integrated Environmental Services, Irvine, California.

5 APPLICATION OF APEX4.3 IN THIS ASSESSMENT

5.1 PURPOSE

This chapter presents detailed information regarding the varied input data sources, the APEX model settings, and input variable parameterizations used in estimating population exposure and dose in the Denver and Los Angeles study areas. In particular, this chapter (and its associated appendices) describes the:

- geographic study areas and time periods defined for the exposure and dose analyses,
- method and parameters used to construct a composite diary for each simulated individual,
- study area population, the modeled at-risk population and associated CHD prevalence rates,
- exposure scenarios under evaluation,
- air quality and meteorological data used for each study area and exposure scenario,
- method used to estimate local outdoor and microenvironmental CO concentrations, and
- additional output data files generated for this particular assessment.

Note that the APEX model version used in this assessment was APEX4.3, but for simplicity will be referred to as APEX in much of the discussion that follows.

5.2 OVERVIEW

As summarized above in section 1.3, the previous analysis of population CO exposure employed the pNEM/CO model in Denver and Los Angeles study areas, comprising the majority of census tracts within those metropolitan areas (Johnson et al., 2000). In this earlier exposure assessment, air quality data were obtained from multiple fixed-site monitors within the study areas, and the exposure assessment accounted for the effects of geographic location, a diverse set of microenvironments, commuting within the study area, and selected indoor sources (e.g., passive smoking, gas stoves). In the specific application of APEX described in this CO REA, a similar exposure and dose modeling approach has been developed by staff, though without inclusion of indoor source emissions. The detailed approach presented here was designed in consideration of comments and recommendations made by the CASAC and public regarding the earlier draft CO REAs (US EPA, 2009a; 2010).

The general description of APEX, the standard databases used, modeling capabilities, as well as the history of the pNEM/APEX series of exposure models, can be found in chapter 4. This includes use of the national data files obtained from the US Census Bureau (i.e., the 2000 Census data) for the following types of information:

- Population data and employment probabilities by gender, age, and census tract;
- Locations of census tracts (latitude and longitude); and
- Commuting flows for combinations of home and work census tracts.

Other default input files provided within APEX include tables of age- and gender-specific physiological parameters (e.g., body weight) and activity-specific metabolic equivalents (METs). The contents of each of these default files and their use were summarized in chapter 4. They are described in greater detail in the APEX Users Guide (US EPA, 2008a) and the APEX Technical Support Document (US EPA, 2008b). The typical output files (e.g., number of persons at or above a selected exposure or dose level) were also summarized in chapter 4, though additional exposure and dose outputs were generated for this assessment using the APEX *hourly* and *events* files (US EPA, 2008a, 2008b) and are described in section 5.10.

5.3 STUDY AREAS

As discussed in section 3.2, areas within Denver, Colorado, and Los Angeles, California, were selected for the current exposure and dose assessment. Briefly, considerations in selection of these areas included: the prior analysis of these locations in CO NAAQS reviews, the areas having historically elevated CO concentrations, and the areas currently having some of the most complete ambient monitoring data available. The monitors selected for use in defining the air quality in each urban area are listed in Tables 5-1 (Denver) and 5-2 (Los Angeles).

The actual study areas were defined as including all census tracts within 10 km of the selected fixed-site monitors. These areas are illustrated in Figures 5-1 and 5-2, which indicate the locations of the fixed-site monitors and the circular 10-km region surrounding each ambient monitor. Each 10 km region defines the aforementioned *air district* that includes the geographic area (i.e., the census tracts) represented by data from the associated CO monitor. Note that all air districts have the same radius (10 km), a value specified by the "AirRadius" input parameter of APEX. Any tracts residing within overlapping monitor radii were assigned to the closest monitor.

In addition to defining the air districts, the model user must specify a location for the center of the study area and a value for "CityRadius." The circular area defined by the city center location and the value of "CityRadius" must be large enough to include all census tracts included in the air districts. For Denver, staff used the location of monitor ID 08310014 (Denver -Carriage) for the city center and set the "CityRadius" equal to 20 km (Figure 5-1). Staff used the location of monitor ID 06371103 (Los Angeles) for the center city of Los Angeles and set the "CityRadius" equal to 65 km (Figure 5-2).

5.4 EXPOSURE PERIODS

EPA selected the following calendar years as the study periods for each area:

Denver: 1995 and 2006

Los Angeles: 1997 and 2006

The year 2006 was selected for both cities because it was the most recent year of monitoring data that met the 75% completeness requirement for the ambient monitors listed above. Note, the CO levels reported for 2006 were well below the 8-hour NAAQS (see Tables 5-1 and 5-2) and are considered representative of the *as is* air quality in each study area for purposes of this assessment. The year 1995 for Denver and the year 1997 for Los Angeles were selected as periods for which the ambient monitor concentrations were near or exceeding the 8-hour average CO NAAQS of 9 ppm. Staff judged that these historical monitoring data would be most useful in representing air quality that just meets the current or alternative CO standards and, following an appropriate concentration level adjustment, would represent a particular air quality scenario (see sections 5.6 and 5.7.3).

Table 5-1. Attributes of fixed-site monitors selected for the Denver study area.

Monitor ID	031-0002[a]	031-0013[a]	031-0014[a]	059-0002[a]
City	Denver	Denver	Denver	Arvada
Local Name	CAMP	NJH-E	Carriage	-
Latitude	39.751184	39.738578	39.800333	39.751761
Longitude	-104.987625	-104.939925	-105.099973	-105.030681
Elevation (m)	1593	1620	1640	1621
Scale	Microscale	Neighborhood	-	Neighborhood
Objective	Highest Concentration	Population Exposure	Unknown	Population Exposure
1995 2nd Highest 8-hour avg. CO (ppm)	9.5	6.2	5.9	4.6
2006 2nd Highest 8-hour avg. CO (ppm)	3.1	2.5	3	2

Notes:
[a] Identified monitor was used in the 2000 pNEM/CO analysis (Johnson et al., 2000).

Table 5-2. Attributes of fixed-site monitors selected for the Los Angeles study area.

Monitor ID	037-0113[a]	037-1002[a]	037-1103[a]	037-1201	037-1301[a]	037-2005[a]	037-4002[a]	059-0001/7[a,b]	059-1003	059-5001[a]
City	West LA	Burbank	Los Angeles	Reseda	Lynwood	Pasadena	Long Beach	Anaheim	Costa Mesa	La Habra
Local Name	-	-	-	-	-	-	-	-	-	-
Latitude	34.05111	34.17605	34.06659	34.19925	33.92899	34.1326	33.82376	33.83062	33.67464	33.92513
Longitude	-118.45636	-118.31712	-118.22688	-118.53276	-118.21071	-118.1272	-118.18921	-117.93845	-117.92568	-117.95264
Elevation (m)	91	168	87	226	27	250	6	45	0	82
Scale	-	-	-	-	Middle	-	-	Neighborhood	Middle	-
Objective	Unknown	Unknown	Unknown	Unknown	Highest Conc.	Unknown	Unknown	Population Exposure	Unknown	Population Exposure
1997 2nd Highest 8-hour avg. CO (ppm)	4.1	7.2	5.9	7.7	15	5.4	6.4	5.4	5	5.7
2006 2nd Highest 8-hour avg. CO (ppm)	1.9	3.4	2.5	3.4	5.6	2.7	3.3	2.9	2.5	2.9

Notes:
[a] Identified monitor was used in the 2000 pNEM/CO analysis (Johnson et al., 2000).
[b] When considering the two monitoring periods (1997 and 2006), two separate ambient monitor IDs were noted (059-0001 and 059-0007) though effectively the locations of both monitors were the same.

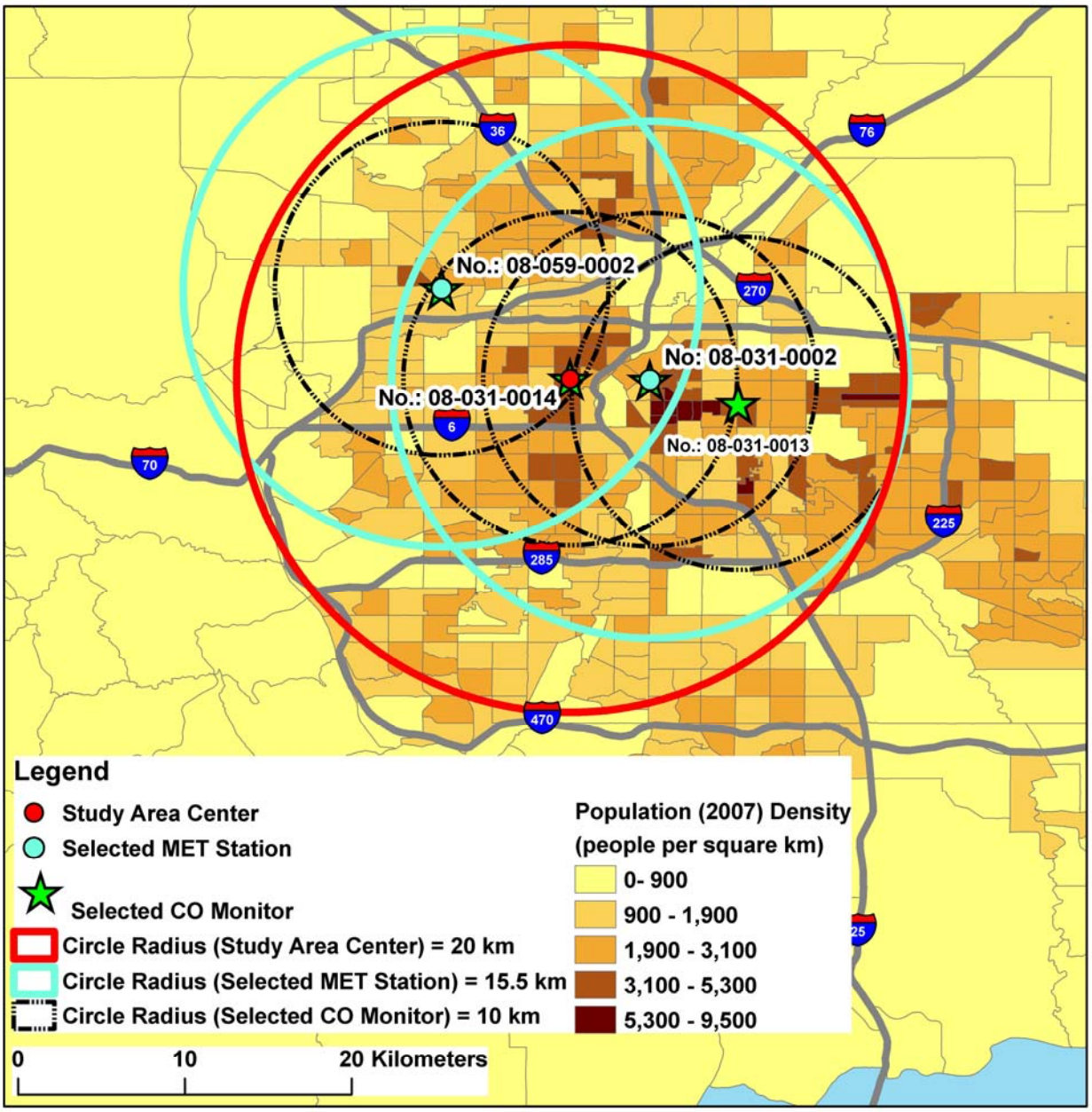

Figure 5-1. Ambient monitor locations, air districts (black circles), meteorological zones (blue circles), and study area (red circle) for the Denver exposure modeling domain.

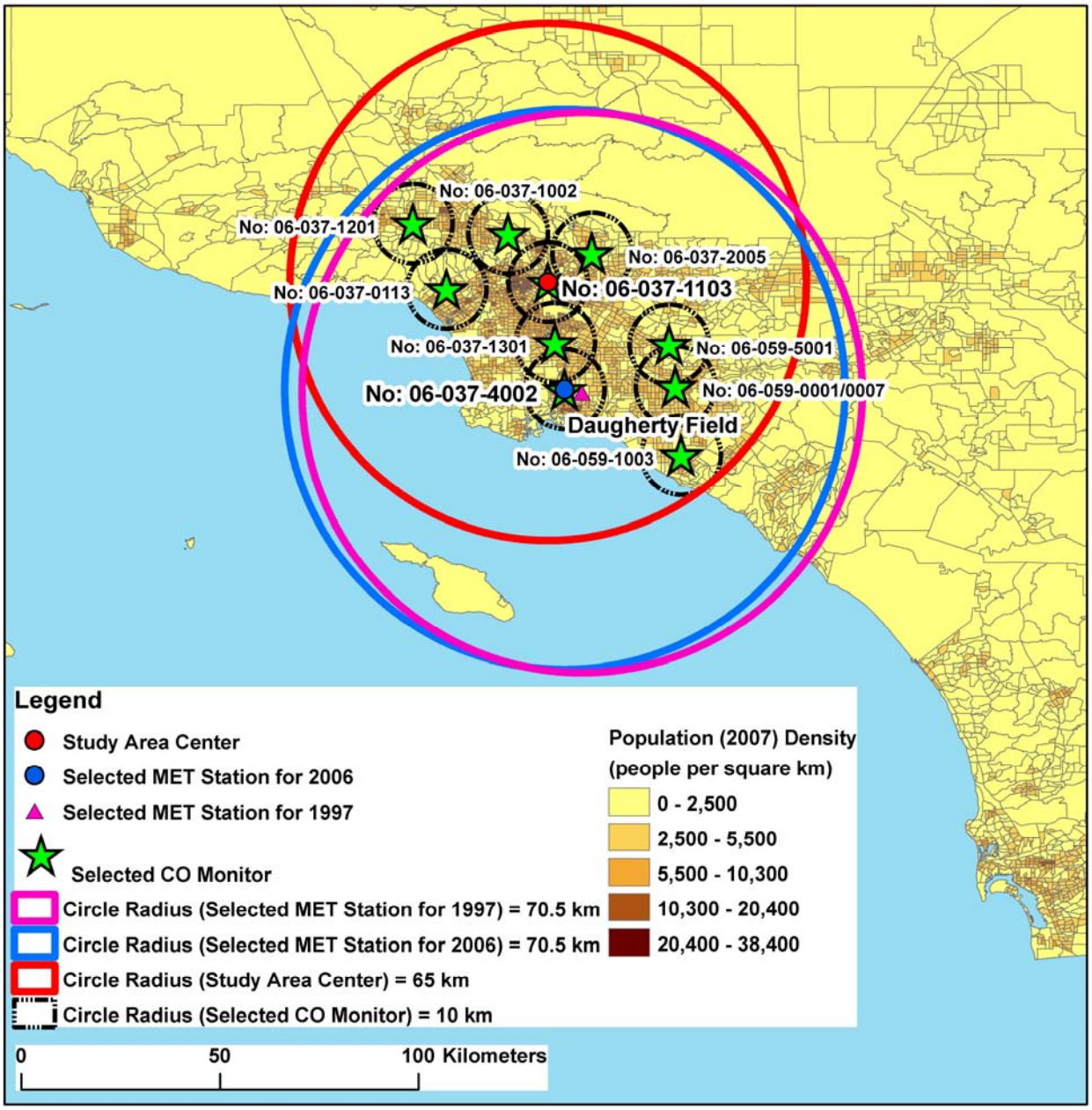

Figure 5-2. Ambient monitor locations, air districts (black circles), meteorological zones (blue and pink circles), and study area (red circle) for the Los Angeles exposure modeling domain.

5.5 STUDY POPULATION

Population estimates were obtained from the 2000 US Census for Denver and Los Angeles study areas.[1] In light of the health outcome of interest and characteristics of the susceptible population, the population in each area was first restricted to persons aged 18 years or older. Next, the populations were adjusted to remove residents commuting outside of the study area. The resulting population for the Denver study area was 617,020 persons (or 81.1% of the total population ≥18 years of age residing in modeled census tracts). The corresponding figure for Los Angeles was 5,017,551 persons (or 88.5% of the total population ≥18 years old within the modeled census tracts). These populations are referred to below as the total simulated population in each area. To obtain adequate representation of the simulated population while also keeping the model runs tractable, fifty-thousand exposure profiles (or simulated individuals) were run by APEX for each study area and exposure scenario.[2]

5.5.1 Simulated at-Risk Subpopulations

As mentioned above, the simulated at-risk populations within each study area focused on adults (ages 18 and older), consistent with the previous CO exposure assessment (Johnson et. al, 2000) and the completed 1994 CO NAAQS review (US EPA, 1992), as the incidence of heart disease in younger individuals is extremely small (CDC, 2009). For this assessment, we identified two at-risk subpopulations using disease prevalence rates characterized in the National Health Interview Survey (NHIS): (1) the potential population comprised of persons with "coronary heart disease" and (2) the potential population comprised of persons with "all types of heart disease".

This first category (i.e., coronary heart disease) is limited to those persons with diagnosed coronary heart disease, angina pectoris, and heart attack (CDC, 2009) in addition to an estimate of those persons having undiagnosed CHD (US EPA, 2010). The second category (i.e., all types of heart disease) is inclusive of those with diagnosed coronary heart disease, angina pectoris, heart attack, and any other heart condition or disease (CDC, 2009), in addition to an estimate of those persons with undiagnosed coronary heart disease. The specific data and method used to estimate the prevalence rates for each of these subpopulations is provided in the following subsections.

The disease prevalence rates (stratified by age and gender) are used to generate a population-weighted representative sample of simulated individuals that are then used to calculate exposure and associated COHb for the simulated at-risk subpopulations. While this

[1] No adjustments were made to census estimates to reflect alternate years.

[2] There were a few APEX simulations performed for purposes of obtaining the exposure and dose time-series for each individual. These runs were 5,000 persons only. See section 5.10 for details.

provides estimates of exposure and COHb levels for subpopulations in the two study areas having the *demographic* characteristics (i.e., age and gender) of the two at-risk populations of interest, we note that the simulation does not include any other characteristics specific to the at-risk populations of interest. For example, the CHAD diaries used to represent the simulated individuals are not exclusively drawn from a pool of diaries of persons identified by the original activity pattern survey as having the disease state(s) of interest.[3] This limitation and its effect on exposure and dose estimates for representing the simulated at-risk subpopulations are discussed in chapter 7 below.

5.5.1.1 Coronary Heart Disease

For estimates of adults with diagnosed CHD, staff obtained CHD prevalence data from the NHIS for 2007 (CDC, 2009). The CHD prevalence for the population at or above 18 years of age is about 6% (ISA, section 5.7.2.1).[4] We assumed the national prevalence rates for CHD were appropriate to use in each of the two study areas because there was a general similarity in the reported regional rates. Although we desired the prevalence rates to be stratified by age *and* gender, the available data were stratified by age *or* gender. Table 5-3 provides national prevalence data for CHD by age and Table 5-4 provides CHD stratified by gender. The gender-only data were used to estimate gender-specific adjustment factors to apply to the age-only data set. For males, the adjustment factor = 0.080/0.061 = 1.31; for females, the adjustment factor = 0.045/0.061 = 0.74. Table 5-5 provides the estimated national prevalence rates for CHD by age range adjusted for gender using these adjustment factors.

Table 5-3. National prevalence rates for diagnosed coronary heart disease by age range.

Age range	Prevalence rate (fraction) for diagnosed coronary heart disease[a]
18 to 44	0.009
45 to 64	0.067
65 to 74	0.186
75+	0.236

Notes:
[a] Source: Coronary heart disease statistics in Table 2 of NHIS (CDC, 2009), which include coronary heart disease, angina pectoris and heart attack.

[3] Note though, that the activity database did include a few activity pattern studies (e.g., NHAPS) where a disease state was identified (including having a lung or heart condition). Therefore, in sampling for diaries using attributes such as age and gender, some of the APEX simulated individuals would have their activity sequence constructed of diaries obtained from persons having a heart condition.

[4] Note that in the last CO NAAQS review completed in 1994, the estimated number of individuals with CHD represented about 3% of the entire (all ages) US population (US EPA, 1992).

Table 5-4. National prevalence rates for diagnosed coronary heart disease by gender.

Age range	Prevalence rate (fraction) for diagnosed coronary heart disease[a]		
	Total	Males	Females
18+	0.061	0.080	0.045

Notes:
[a] Source: Coronary heart disease statistics in Table 2 of NHIS (CDC, 2009), which include coronary heart disease, angina pectoris and heart attack.

Table 5-5. Estimated national prevalence rates for diagnosed coronary heart disease, stratified by age and gender.

Age range	Prevalence rate (fraction) for diagnosed coronary heart disease	
	Males[a]	Females[b]
18 to 44	0.012	0.007
45 to 64	0.088	0.050
65 to 74	0.244	0.138
75+	0.310	0.175

Notes:
[a] Values listed in Table 5-3 were multiplied by 1.31.
[b] Values listed in Table 5-4 were multiplied by 0.74.

The selected at-risk population was then expanded to also include undiagnosed cases of coronary heart disease using a method similar to that developed by OAQPS for use in the 2000 exposure assessment (see Appendix F of Johnson et al., 2000). Briefly, in the prior assessment the prevalence estimates of diagnosed IHD[5] were stratified by age and sex (Adams and Marano, 1995) and constituted approximately 8.0 million individuals in the civilian, non-institutionalized population.[6] In addition, as many as three to four million persons were estimated by the American Heart Association as having silent ischemia or undiagnosed IHD (AHA, 1990).[7] We used this information to provide estimates of the undiagnosed IHD population for use in the pNEM/CO model. We assumed 3.5 million persons had undiagnosed IHD and assumed the prevalence to be distributed by age and gender in the same manner as diagnosed IHD. These data yield an adjustment factor of 0.438 (i.e., 3.5 million/8.0 million) to apply to the diagnosed

[5] The NHIS prevalence rates used in the 2000 assessment used the term IHD, rather than CHD (Adams and Marano, 1995).

[6] These estimates did not include individuals in the military or individuals in nursing homes or other institutions.

[7] Note that the size of this undiagnosed IHD population (i.e., 3-4 million persons) is the same as that reported by AHA (2003).

prevalence for use in estimating the undiagnosed prevalence. Consequently, this factor can be interpreted as the undiagnosed cases may be 43.8% of the diagnosed prevalence.

Table 5-6 lists the results of applying the 0.438 factor to the age and gender stratified prevalence rates listed in Table 5-5. This assumes that CHD and IHD are identical with respect to the ratio of undiagnosed cases to diagnosed cases and this ratio has not changed since reported in 1990 (and 2003) and assumes that undiagnosed prevalence rates would not vary by gender.[8] This total prevalence for coronary heart disease (diagnosed and undiagnosed combined) stratified by gender was used by APEX in estimating the first simulated at-risk subpopulation.

When using these CHD prevalence rates in the APEX model runs, there were 383,040 simulated persons (or 7.6% of the total simulated population) with either diagnosed or undiagnosed CHD in the Los Angeles study area, while in Denver there were 53,656 simulated persons (or 8.7% of the total simulated population) within the CHD simulated at-risk population.

Table 5-6. Estimated national prevalence rates for coronary heart disease, including diagnosed and undiagnosed cases, stratified by age and gender.

Age range	Prevalence rate (fraction) for coronary heart disease					
	Males			Females		
	Diagnosed	Undiagnosed[a]	Total	Diagnosed	Undiagnosed[a]	Total
18 to 44	0.012	0.005	0.017	0.007	0.003	0.010
45 to 64	0.088	0.038	0.127	0.050	0.022	0.072
65 to 74	0.244	0.107	0.351	0.138	0.060	0.198
75+	0.310	0.135	0.446	0.175	0.077	0.252

Notes:
[a] Values listed in Table 5-5 (diagnosed CHD) were multiplied by 0.438 to estimate the undiagnosed prevalence. This calculation assumed CHD and IHD are identical with respect to the ratio of undiagnosed cases (3.5 million) to diagnosed cases (8.0 million), that this ratio has been constant since reported in 1990 and 2003, and that there is no gender difference in undiagnosed prevalence rates.

5.5.1.2 All Heart Disease

For estimates of adults with heart disease (HD), we also obtained prevalence data from the NHIS for 2007 (CDC, 2009). The HD prevalence for the population above 18 years of age is about 11% (Table 2, CDC, 2009). The national prevalence rates for HD were used in each of the two study areas because there was a general similarity in the reported regional rates. As described in section 5.5.2.1, although staff desired the prevalence rates to be stratified by age *and* gender, the available data were stratified by age *or* gender. Table 5-7 provides national

[8] Specific data on which to base development of differing prevalence estimates by gender for undiagnosed CHD as compared to diagnosed CHD were not identified in the limited time available for this assessment.

prevalence data for HD by age and Table 5-8 provides HD stratified by gender. These gender-only data were used to estimate gender-specific adjustment factors to apply to the age-only data set. For males, the adjustment factor = 0.125/0.112 = 1.12; for females, the adjustment factor = 0.102/0.112 = 0.91. Table 5-9 provides the estimated national prevalence rates for HD by age range adjusted for gender using these adjustment factors.

Table 5-7. National prevalence rates for all types of diagnosed heart disease by age range.

Age range	Prevalence rate (fraction) for all types of diagnosed heart disease[a]
18 to 44	0.041
45 to 64	0.122
65 to 74	0.271
75+	0.358

Notes:
[a] Source: Statistics for all types of heart disease listed in Table 2 of NHIS (CDC, 2009), which include coronary heart disease, angina pectoris, heart attack, or any other heart condition or disease.

Table 5-8. National prevalence rates for all types of diagnosed heart disease by gender.

Age range	Prevalence rate (fraction) for all types of diagnosed heart disease[a]		
	Total	Males	Females
18+	0.112	0.125	0.102

Notes:
[a] Source: Statistics for all types of heart disease listed in Table 2 of NHIS (CDC, 2009), which include coronary heart disease, angina pectoris, heart attack, or any other heart condition or disease.

Table 5-9. Estimated national prevalence rates for all types of diagnosed heart disease, stratified by age and gender.

Age range	Prevalence rate (fraction) for all types of diagnosed heart disease[a]	
	Males	Females
18 to 44	0.046	0.037
45 to 64	0.137	0.111
65 to 74	0.304	0.247
75+	0.401	0.326

Notes:
[a] Values listed in Table 5-7 were multiplied by 1.12 for males and 0.91 for females using data from Table 5-8.

The same approach described in section 5.5.2.1 was used to include an estimate of the

percent of persons with undiagnosed coronary heart disease in addition to the estimate of population estimated having HD. The undiagnosed CHD prevalence from Table 5-6 was simply added to the HD to generate the prevalence rates summarized in Table 5-10. The total prevalence listed for each gender was used by APEX to estimate the second simulated at-risk population.

When using these prevalence rates in the APEX model runs, there were 630,807 simulated persons (or 12.6% of the total simulated population) with HD in the Los Angeles study area, while in Denver there were 85,926 simulated persons (or 13.9% of the total simulated population) comprising the same simulated at-risk population.

Table 5-10. Estimated national prevalence rates for all types of diagnosed heart disease plus undiagnosed coronary heart disease, stratified by age and gender.

Age range	Prevalence rate (fraction) for all types of heart disease					
	Males			Females		
	Diagnosed heart disease	Undiagnosed coronary heart disease[a]	Total	Diagnosed heart disease	Undiagnosed coronary heart disease[a]	Total
18 to 44	0.046	0.005	0.051	0.037	0.003	0.040
45 to 64	0.137	0.038	0.175	0.111	0.022	0.133
65 to 74	0.304	0.107	0.410	0.247	0.060	0.307
75+	0.401	0.135	0.536	0.326	0.077	0.402

Notes:
[a] Values obtained from Table 5-6 (i.e., undiagnosed CHD).

5.5.2 Time-Location-Activity Patterns

APEX constructs a 365-day longitudinal diary for each simulated individual by selecting 24-hour diaries from those available in CHAD. In performing the exposure assessments described in this report, all available diaries for persons above age 17 in the CHAD database were used.

5.5.3 Construction of Longitudinal Diaries

As discussed in section 4.4.3.4, APEX provides a longitudinal diary assembly algorithm that enables the user to create composite diaries that reflect the tendency of individuals to repeat day-to-day activities (Glen et al., 2008). The user specifies values for two statistical variables (*D* and *A*) that relate to a key daily variable, typically the time spent per day in a particular microenvironment (e.g., in a motor vehicle). The *D* statistic reflects the relative importance of intra- and inter-personal variance within the selected key daily variable. The *A* variable

quantifies the day-to-day autocorrelation in the selected key daily variable. APEX then constructs composite diaries that exhibit the statistical properties defined by the specified values of *D* and *A*.

In this exposure assessment, we used the longitudinal diary algorithm to construct year-long activity patterns for each simulated individual to reflect the day-to-day correlation of time spent inside motor vehicles. Each diary day in the CHAD database was tagged with the number of minutes spent in the vehicle microenvironment. Parameter settings of $D = 0.31$ and $A = 0.19$ were specified to control the day-to-day repetition of time spent in motor vehicles in the constructed composite diaries. These particular *D* and *A* values were obtained from Isaacs et al. (2009) (see Appendix C).

In selecting particular diaries to represent the simulated population, the CHAD data are categorized or separated by APEX into data pools. The pools were defined by three ranges for the maximum temperature of the diary day (< 55.0 °F, between 55.0 and 83.9 °F, and ≥84.0 °F) and two day-types (i.e., weekend and weekday); thus, there were 3 × 2 = 6 diary pools. The window for age was set at 15%. For example, diaries can be selected for a simulated individual of age 60 from CHAD individuals ranging from ages 51 though 69 (i.e., 60 +/- 15 percent).

5.6 EXPOSURE SCENARIOS

In this CO REA, the exposure scenario refers to the air quality conditions considered for each APEX simulation. Staff evaluated five exposure scenarios for each study area. The first exposure scenario used unadjusted 2006 ambient air quality as input to APEX; this is designated as the *as is* air quality exposure scenario. The purpose of this scenario is to determine the number of persons that may experience COHb levels at or above selected benchmarks when considering current air quality conditions. The next four exposure scenarios used ambient data from a high concentration year in each location (i.e., the 1995 monitoring data in Denver and the 1997 monitoring data in Los Angeles) adjusted to represent different air quality conditions. The purpose of these scenarios is to determine the number of persons that may experience COHb levels at or above selected benchmark levels when considering air quality conditions that just meet a selected level, form, and averaging time of interest. This is not the same as considering exposures associated with the *as is* air quality conditions.

The first of these four adjusted air quality exposure scenarios considered ambient concentrations adjusted to just meet the current 8-hour CO NAAQS of 9 ppm. The 8-hour standard was selected when considering the two current standards (8-hour and 1-hour) because it

is the controlling standard.[9] The second of these exposure scenarios using the historical monitoring data also considered the form of the current 8-hour CO standard, but with the ambient concentrations in each study adjusted to meet an alternative standard level of 5 ppm. The next two scenarios considered percentile forms of potential alternative standards, consistent with the alternative standards investigated for other criteria pollutants (e.g., NO_2 (US EPA, 2008c); and SO_2 (US EPA, 2009b)). The first of these potential percentile forms considered a 99th percentile daily maximum 8-hour average CO concentration of 5.0 ppm, while the second considered the same form though with a 1-hour averaging time and a 1-hour level of 8.0 ppm. Details regarding the concentration adjustments associated with each of the current and potential alternative standards are provided in section 5.7.3.

Tables 5-11 and 5-12 provide perspective on the selected levels and the air quality used to represent each scenario in Denver and Los Angeles, respectively. An array was constructed using the varying air quality scenarios to indicate how a single APEX run using a particular air quality input data set might reflect different levels and forms of potential alternative standards. For example, in Denver, the exposure and dose results for the *as is* scenario would be the same as a standard level of 3.1 ppm in terms of second highest non-overlapping 8-hour average (Table 5-11). The generated results would also represent exposures and doses experienced considering a 99th percentile 1-hour daily maximum concentration of 4.5 ppm.

[9] The controlling standard by definition would be the standard that allows air quality to have either a 2nd highest 8-hour average concentration of ≤ 9.4 ppm (i.e., the 8-hour standard is the controlling standard) or to have a 2nd highest 1-hour concentration of ≤ 35.4 ppm (i.e., the 1-hour standard is the controlling standard).

Table 5-11. Array of alternative standard forms and levels informed by modeled exposure scenarios in Denver.

Denver Design Values (ppm)				
Averaging Time & Form	8-hour		1-hour	
Air Quality Scenario	2nd highest[a]	99th percentile daily max	2nd highest[a]	99th percentile daily max
As Is	3.1	2.8	4.6	4.5
Current 8-hour standard (9 ppm)[b]	9.4	7.2	16.2	13.3
2nd highest 8-hour average (5 ppm)[b]	5.4	4.1	9.3	7.7
99th percentile daily max 8-hour (5.0 ppm)	6.5	5.0	11.2	9.2
99th percentile daily max 1-hour (8.0 ppm)	5.6	4.3	9.7	8.0

Notes:
[a] This is the form of the current standards.
[b] Note that the rounding convention for the current standard allows for concentrations of up to the given standard level plus 0.4 ppm.

Table 5-12. Array of alternative standard forms and levels informed by modeled exposure scenarios in Los Angeles.

Los Angeles Design Values (ppm)				
Averaging Time & Form	8-hour		1-hour	
Air Quality Scenario	2nd highest[a]	99th percentile daily max	2nd highest[a]	99th percentile daily max
As Is	5.6	5.1	8.2	7.4
Current 8-hour standard (9 ppm)[b]	9.4	8.2	11.8	11.6
2nd highest 8-hour average (5 ppm)[b]	5.4	4.7	6.8	6.7
99th percentile daily max 8-hour (5.0 ppm)	5.7	5.0	7.2	7.1
99th percentile daily max 1-hour (8.0 ppm)	6.5	5.7	8.1	8.0

Notes:
[a] This is the form of the current standards.
[b] Note that the rounding convention allows for concentrations of up to the given standard level plus 0.4 ppm.

5.7 AMBIENT AIR QUALITY DATA

5.7.1 Unadjusted 1-Hour Ambient Concentrations

Ambient monitoring data serve as an important input in estimating CO exposure and dose. Descriptive statistics were generated for the hourly CO concentrations measured at the identified ambient monitors in each study area and monitoring year (Tables 5-13 to 5-16). As expected, CO concentrations in the high concentration year (1995 or 1997) are about a factor of two or greater than the more recent year (2006) of ambient monitoring data in either study area. In general, there is similarity in the concentration distribution for both study areas within a given year, with the following exceptions. There is one monitor in Los Angeles (ID 06371301) that consistently reported exceptionally high concentrations when compared with the other Los Angeles monitors for either year. In addition, there is a sharper rate of increase in the upper percentile concentrations (i.e., $\geq$95th percentiles) in Denver when compared with the Los Angeles ambient concentration distribution, for either year.

5.7.2 Method for Estimating Missing 1-Hour Ambient Concentrations

APEX requires that each site-year of monitoring data be complete (i.e., it is free of hourly gaps in concentration levels). The missing values in each data set were estimated by the sequential application of the following four methods.

1) If the data gap was less than six continuous missing values, the missing values were estimated by linear interpolation using the valid values at the ends of the gap.
2) Where possible, data gaps of at least six hours were estimated as linear functions of hourly values reported by other ambient CO monitors in the area. Linear regression was used to develop a set of models that were specific to time-of-day and monitor. The model selected to estimate missing values for a particular time of day was the model that maximized the variance explained (R^2) for that hour, subject to the constraints that regression model R^2 was greater than 0.5 and the number of available measurements used in constructing the model was at least 50.
3) In cases where method 2 (above) could not be used (i.e., no regression models were available for a particular time-of-day) and the gap was less than nine hours, the missing values were estimated by linear interpolation between the valid values at the ends of the gap.
4) All remaining missing values were substituted with the 1-hour concentration from the same day and hour as the nearest monitor. The hourly concentration used was normalized to the respective monitors' monthly mean concentrations.

Tables 5-13 to 5-16 provide the descriptive statistics for 1-hour CO concentrations in each data set, before and after estimating missing values, and considering the two years of ambient monitoring data in each study area. The excellent agreement between concentrations at the various percentiles of the distribution (before and after substitution) indicates that the addition of the estimated missing-value concentrations did not significantly affect the overall distributions of the hourly CO concentrations.

Table 5-13. Descriptive statistics for hourly carbon monoxide concentrations before and after estimation of missing values – Denver 1995.

Monitor ID	Missing values filled?	1-hour values (n)		CO concentration (ppm)										
							Percentile							
		Present	Missing	Mean	SD	Min	25th	50th	75th	90th	95th	99th	99.9th	Max
31-0002	No	8697	63	1.50	1.20	0.0	0.8	1.2	1.8	2.7	3.4	6.1	13.1	24.5
	Yes	8760	0	1.50	1.20	0.0	0.8	1.2	1.8	2.7	3.4	6.1	13.1	24.5
31-0013	No	8647	113	1.25	1.08	0.1	0.6	0.9	1.5	2.5	3.4	5.5	8.9	14.6
	Yes	8760	0	1.25	1.08	0.1	0.6	0.9	1.5	2.5	3.4	5.5	8.8	14.6
31-0014	No	8701	59	1.09	1.05	0.0	0.5	0.7	1.3	2.3	3.2	5.3	7.7	10.4
	Yes	8760	0	1.09	1.05	0.0	0.5	0.7	1.3	2.3	3.2	5.3	7.8	10.4
59-0002	No	8680	80	0.96	0.93	0.1	0.4	0.6	1.1	2.0	2.7	4.8	7.5	11.9
	Yes	8760	0	0.96	0.93	0.1	0.4	0.6	1.1	2.0	2.7	4.8	7.5	11.9

Table 5-14. Descriptive statistics for hourly carbon monoxide concentrations before and after estimation of missing values – Denver 2006.

Monitor ID	Missing values filled?	1-hour values (n)		CO concentration (ppm)										
							Percentile							
		Present	Missing	Mean	SD	Min	25th	50th	75th	90th	95th	99th	99.9th	Max
31-0002	No	8672	88	0.62	0.39	0.0	0.4	0.5	0.7	1.0	1.3	2.2	4.1	6.4
	Yes	8760	0	0.62	0.39	0.0	0.4	0.5	0.7	1.0	1.3	2.1	4.1	6.4
31-0013	No	8635	125	0.49	0.36	0.0	0.3	0.4	0.6	0.9	1.2	1.8	3.4	4.4
	Yes	8760	0	0.49	0.36	0.0	0.3	0.4	0.6	0.9	1.2	1.8	3.4	4.4
31-0014	No	8557	203	0.47	0.38	0.0	0.3	0.4	0.5	0.9	1.2	2.0	3.1	3.9
	Yes	8760	0	0.47	0.38	0.0	0.3	0.4	0.5	0.9	1.2	2.0	3.1	3.9
59-0002	No	8603	57	0.40	0.37	0.0	0.2	0.3	0.5	0.8	1.1	1.9	2.8	3.6
	Yes	8760	0	0.40	0.37	0.0	0.2	0.3	0.5	0.8	1.1	1.9	2.8	3.6

Table 5-15. Descriptive statistics for hourly carbon monoxide concentrations before and after estimation of missing values – Los Angeles 1997.

Monitor ID	Missing values filled?	1-hour values (n)		CO concentration (ppm)										
							Percentile							
		Present	Missing	Mean	SD	Min	25th	50th	75th	90th	95th	99th	99.9th	Max
37-0113	No	8360	400	0.84	0.86	0.0	0.2	0.6	1.2	2.0	2.6	3.7	5.1	7.3
	Yes	8760	0	0.84	0.85	0.0	0.2	0.6	1.2	2.0	2.6	3.6	5.1	7.3
37-1002	No	8025	735	1.75	1.27	0.0	0.9	1.4	2.2	3.5	4.5	6.1	7.8	8.8
	Yes	8760	0	1.73	1.24	0.0	0.9	1.4	2.1	3.5	4.4	6.0	7.7	8.8
37-1103	No	8292	468	1.36	1.19	0.0	0.5	0.9	1.9	3.1	3.9	5.4	7.2	8.9
	Yes	8760	0	1.36	1.17	0.0	0.5	1.0	1.9	3.0	3.8	5.4	7.1	8.9
37-1201	No	8245	515	1.15	1.25	0.0	0.4	0.7	1.5	2.8	3.8	6.0	8.4	11.7
	Yes	8760	0	1.17	1.24	0.0	0.4	0.7	1.5	2.8	3.8	5.9	8.3	11.7
37-1301	No	8302	458	2.35	2.19	0.0	1.1	1.7	2.8	4.9	6.8	11.3	17.2	19.2
	Yes	8760	0	2.34	2.17	0.0	1.1	1.7	2.8	4.9	6.7	11.2	17.2	19.2
37-2005	No	8250	510	1.11	0.84	0.0	0.6	0.9	1.4	2.1	2.8	4.2	6.1	8.1
	Yes	8760	0	1.10	0.83	0.0	0.6	0.9	1.4	2.1	2.8	4.2	6.0	8.1
37-4002	No	8347	413	1.11	1.10	0.0	0.4	0.7	1.3	2.7	3.6	5.2	7.3	9.0
	Yes	8760	0	1.11	1.11	0.0	0.4	0.7	1.4	2.7	3.6	5.2	7.2	9.0
59-0001/7	No	8354	406	1.11	0.91	0.0	0.6	0.8	1.4	2.3	2.9	4.6	6.9	8.4
	Yes	8760	0	1.11	0.90	0.0	0.6	0.8	1.4	2.3	2.9	4.6	6.9	8.4
59-1003	No	8325	435	0.74	1.01	0.0	0.2	0.3	0.9	2.1	3.0	4.7	6.3	7.3
	Yes	8760	0	0.74	1.00	0.0	0.2	0.3	0.9	2.1	3.0	4.6	6.2	7.3
59-5001	No	8230	530	1.36	1.21	0.0	0.6	1.0	1.7	2.8	3.7	6.2	9.9	11.9
	Yes	8760	0	1.36	1.19	0.0	0.6	1.0	1.7	2.8	3.7	6.2	9.9	11.9

Table 5-16. Descriptive statistics for hourly carbon monoxide concentrations before and after estimation of missing values – Los Angeles 2006.

Monitor	Missing values filled?	1-hour values (n)		CO concentration (ppm)										
							Percentile							
		Present	Missing	Mean	SD	Min	25th	50th	75th	90th	95th	99th	99.9th	Max
37-0113	No	8365	395	0.42	0.37	0.0	0.2	0.3	0.6	0.9	1.2	1.7	2.5	2.9
	Yes	8760	0	0.43	0.37	0.0	0.2	0.3	0.6	0.9	1.2	1.7	2.5	2.9
37-1002	No	8345	415	0.67	0.61	0.0	0.3	0.5	0.8	1.5	2.0	2.9	4.0	4.3
	Yes	8760	0	0.67	0.61	0.0	0.3	0.5	0.8	1.5	2.0	2.9	3.9	4.3
37-1103	No	8265	495	0.55	0.50	0.0	0.2	0.4	0.7	1.3	1.6	2.3	2.9	3.5
	Yes	8760	0	0.56	0.50	0.0	0.2	0.4	0.8	1.3	1.6	2.2	2.9	3.5
37-1201	No	8375	385	0.55	0.54	0.0	0.2	0.4	0.6	1.2	1.7	2.7	3.8	4.8
	Yes	8760	0	0.56	0.53	0.0	0.2	0.4	0.7	1.2	1.7	2.7	3.7	4.8
37-1301	No	8275	485	1.00	0.89	0.0	0.5	0.7	1.1	2.0	2.9	4.7	6.9	8.4
	Yes	8760	0	1.01	0.90	0.0	0.5	0.7	1.1	2.0	2.9	4.6	6.8	8.4
37-2005	No	8258	502	0.73	0.49	0.0	0.4	0.6	1.0	1.4	1.7	2.4	3.2	4.1
	Yes	8760	0	0.73	0.49	0.0	0.4	0.6	1.0	1.3	1.7	2.4	3.1	4.1
37-4002	No	8216	544	0.74	0.55	0.0	0.4	0.6	0.9	1.5	1.9	2.7	3.7	4.2
	Yes	8760	0	0.75	0.54	0.0	0.4	0.6	0.9	1.5	1.9	2.7	3.7	4.2
59-0001/7	No	8342	418	0.43	0.47	0.0	0.1	0.3	0.5	1.0	1.4	2.3	3.4	4.5
	Yes	8760	0	0.43	0.47	0.0	0.1	0.3	0.5	1.0	1.4	2.3	3.4	4.5
59-1003	No	8358	402	0.33	0.45	0.0	0.1	0.1	0.4	0.9	1.4	2.1	3.1	3.5
	Yes	8760	0	0.33	0.45	0.0	0.1	0.1	0.4	0.9	1.4	2.1	3.0	3.5
59-5001	No	8227	533	0.64	0.57	0.0	0.3	0.4	0.7	1.3	1.8	3.0	4.7	6.0
	Yes	8760	0	0.64	0.56	0.0	0.3	0.4	0.7	1.3	1.8	2.9	4.6	6.0

5.7.3 Adjusted 1-Hour Ambient Concentrations

In addition to modeling exposures based on recent *as is* air quality (i.e., ambient monitoring data for year 2006), exposures and resulting dose were estimated for air quality conditions that just meet the current 8-hour CO NAAQS and various alternative standards under evaluation. Because CO concentrations in recent years were significantly lower than the current NAAQS, staff first selected an earlier year for each city (1995 for Denver and 1997 for Los Angeles) to represent air quality conditions that were near the current 8-hour CO standard. Consistent with the data adjustment approach employed in the previous draft CO exposure assessment (Johnson et al., 2000), and approaches used in prior REAs supporting other pollutant NAAQS reviews (e.g., US EPA, 2008c; US EPA, 2009b), staff concluded (1) that the policy-relevant background levels of CO were negligible in each area (section 3.1.4), and (2) that the fixed-site monitoring data could be adjusted to simulate just meeting the current CO standards by use of a simple proportional adjustment of all hourly values (section 3.1.5). Consequently, the following adjustment equation was employed:

$$CO_{adj}(m,h) = (NAAQS/DV) \times CO(m,h). \qquad (5\text{-}1)$$

$CO(m,h)$ is the 1-hour CO concentration at hour h for monitor m. It follows that $CO_{adj}(m,h)$ is the adjusted CO concentration for hour h at monitor m through the use of the specific design value (DV) for monitor m. Although the current 8-hour NAAQS for CO specifies a maximum concentration of 9 ppm, which is not to be exceeded more than one time in a year, the NAAQS term in Equation 5-1 is equivalent to 9.4 ppm due to the application of a standard data rounding convention used in calculating design values (DVs) for CO.[10]

The DVs for Denver (1995) and for Los Angeles (1997) were 9.5 ppm and 15 ppm, respectively. The Denver DV is calculated as the second-highest 8-hour average CO concentration reported by monitor ID 080310002 for 1995. The adjustment factor (or NAAQS/DV) that was applied equally to all 8,760 hourly ambient CO concentrations at that monitor is thus 9.4/9.5, or 0.989. In a similar manner, the DV used in Los Angeles is the second-highest 8-hour average CO concentration reported at monitor ID 060371301 for 1997, giving an ambient concentration adjustment factor of 9.4/15, or 0.627 which was applied equally to all 8,760 hourly ambient CO concentrations from the Los Angeles monitor.

[10] A design value is a statistic that describes the air quality status of a given area or monitor relative to the level of the NAAQS. For the CO 8-hour NAAQS, the design value is the highest annual second maximum non-overlapping 8-hour concentration during the most recent two years. The design value for the 1-hour CO NAAQS is the highest annual second maximum 1-hour concentration during the most recent two years. The latest update (2007-2008) on the CO design values can be found at: http://www.epa.gov/airtrends/pdfs/dv_co_2006_2008.pdf

Staff evaluated three additional air quality scenarios considering potential alternative standard levels, averaging times, and forms. Assuming a similar form and averaging time of the current 8-hour standard (2nd highest non-overlapping 8-hour average CO concentration), staff selected a level of 5 ppm for the first potential alternative standard.[11] As was done for other recent NAAQS reviews (US EPA, 2008c; US EPA, 2009b), staff selected percentiles of the air quality distribution and averaging times to identifying potential levels associated with alternative standards. The second potential alternative standard considered by staff also uses an 8-hour average concentration, though having a 99th percentile daily maximum CO concentration of 5.0 ppm.[12] The final potential alternative standard that staff evaluated was a 99th percentile daily maximum 1-hour CO concentration of 8.0 ppm. Table 5-17 summarizes the adjustment factors that were developed from equation 5-1 and used to adjust the high concentration year air quality data in each study area.

Table 5-17. Design values and adjustment factors used to represent air quality just meeting the current and potential alternative standards.

Study Area	Standard			Design Value[a] (ppm)	Adjustment Factor
	Averaging Time	Form	Level (ppm)		
Denver	8-hour	2nd highest	9	9.5	0.989[b]
			5		0.568
		99th pct daily max	5.0	7.3	0.685
	1-hour	99th pct daily max	8.0	13.5	0.593
Los Angeles	8-hour	2nd highest	9	15	0.627[b]
			5		0.360
		99th pct daily max	5.0	13.1	0.382
	1-hour	99th pct daily max	8.0	18.5	0.432

Notes:
[a] All design values were obtained from monitor ID monitor ID 080310002 in Denver (1995 data) and monitor ID 060371301 in Los Angeles (1997 data).
[b] Adjustment factor for just meeting the current 8-hour average CO standard.

[11] Note that this would allow a 2nd highest non-overlapping 8-hour concentration up to 5.4 ppm (hence the design value).

[12] It was assumed that there are an infinite number of zeros, that is, the level is exactly 5.0 ppm. This rounding convention also applies to the other potential alternative standard selected; the level of the 99th percentile 1-hour daily maximum is exactly 8.0 ppm.

Tables 5-18 and 5-19 provide the descriptive statistics for the Denver and Los Angeles ambient monitor 1-hour CO concentrations, respectively, after applying the appropriate adjustment factor to simulate just meeting the current standard. As expected, the adjusted monitoring concentrations for Denver 1995 are very similar to the unadjusted data set given that the adjustment factor used was close to unity. For example, the maximum concentration at the design monitor was reduced from 24.5 ppm to 24.2 ppm. The change in CO concentrations was much greater in Los Angeles compared with that of Denver as a result of differences in the adjustment factor used in each study area. For example, the maximum CO concentration at the design monitor in Los Angeles was reduced from 19.2 ppm to 12.0 ppm. Considering the patterns described above in section 5.7.1 for the unadjusted air quality and given that the concentration adjustment was proportional, additional remarks can be made regarding differences in the air quality adjusted to just meet the current 8-hour CO NAAQS. When comparing the adjusted concentrations in Denver and Los Angeles, there is still a sharper rate of increase in CO concentrations at and above the 95th percentiles of the distribution, only now all of the Denver monitors have greater CO concentrations at these upper percentiles when compared with concentrations observed at all of the Los Angeles monitors (excluding concentrations at the Los Angeles design monitor).

Given the proportional approach used to adjust ambient concentrations for each of the other exposure scenarios (e.g., 99th percentile daily maximum 1-hour concentration of 8.0); similar patterns in concentrations were expected and are therefore not summarized here.

Table 5-18. Descriptive statistics for hourly carbon monoxide concentrations after adjusting to just meet the current 8-hour standard – Denver (adjusted 1995 data).

Monitor ID	Hourly-average CO concentration (ppm)											DV (ppm)
	Mean	SD	25.0	50.0	75.0	90.0	95.0	99.0	99.5	99.9	Max	
31-0002	1.5	1.2	0.8	1.2	1.8	2.7	3.4	6.0	7.6	13.0	24.2	9.4
31-0013	1.2	1.1	0.6	0.9	1.5	2.5	3.4	5.4	6.4	8.7	14.4	6.1
31-0014	1.1	1.0	0.5	0.7	1.3	2.3	3.2	5.3	6.4	7.7	10.3	5.8
59-0002	1.0	0.9	0.4	0.6	1.1	2.0	2.7	4.8	5.7	7.4	11.8	4.5

Table 5-19. Descriptive statistics for hourly carbon monoxide concentrations after adjusting to just meet the current 8-hour standard – Los Angeles (adjusted 1997 data).

Monitor ID	Hourly-average CO concentration (ppm)											DV (ppm)
	Mean	SD	25.0	50.0	75.0	90.0	95.0	99.0	99.5	99.9	Max	
37-0113	0.5	0.5	0.1	0.4	0.8	1.3	1.6	2.3	2.6	3.2	4.6	2.6
37-1002	1.1	0.8	0.6	0.9	1.3	2.2	2.8	3.8	4.1	4.8	5.5	4.5
37-1103	0.9	0.7	0.3	0.6	1.2	1.9	2.4	3.4	3.6	4.5	5.6	3.7
37-1201	0.7	0.8	0.3	0.4	0.9	1.8	2.4	3.7	4.3	5.2	7.3	4.8
37-1301	1.5	1.4	0.7	1.1	1.7	3.1	4.2	7.0	8.5	10.8	12.0	9.4
37-2005	0.7	0.5	0.4	0.6	0.9	1.3	1.8	2.6	2.9	3.8	5.1	3.4
37-4002	0.7	0.7	0.3	0.4	0.8	1.7	2.3	3.3	3.7	4.5	5.6	4.0
59-0001	0.7	0.6	0.4	0.5	0.9	1.4	1.8	2.9	3.4	4.3	5.3	3.4
59-1003	0.5	0.6	0.1	0.2	0.6	1.3	1.9	2.9	3.2	3.9	4.6	3.1
59-5001	0.9	0.7	0.4	0.6	1.1	1.8	2.3	3.8	4.5	6.1	7.5	3.6

5.8 METEOROLOGICAL DATA

A few algorithms within APEX require meteorological data (primarily temperature) from stations located within the study area. For example, in selecting a CHAD diary to simulate an individual's daily activities, a range of daily maximum temperatures is used to categorize diaries for sampling purposes so as to best match the temperature observed on the simulation day within the study area (section 5.5.4). In addition, mean temperatures are used by APEX to select from an appropriate air exchange rate distribution to estimate indoor microenvironmental concentrations (section 5.8). For the analyses described in this report, hourly temperature data were obtained from meteorological stations located at or near the fixed-site CO monitor specified for each study area.

Tables 5-20 and 5-21 list the meteorological stations we used in modeling the Denver and Los Angeles study areas, respectively. Ideally, staff would have used the same station (Long Beach: 37-4002) matched for both monitoring years (1997 and 2006) in Los Angeles. Because this station did not report a complete year of data for 1997, we substituted data reported by the Long Beach Daugherty Field station located approximately 3.6 km from the 37-4002 station. The same two stations (31-0002 and 59-0002) were used for the Denver study area for 1995 and Denver 2006, because there were adequate data for both years for both sites.

To run APEX, a "ZoneRadius" is specified by the user as the maximum radius for the region surrounding each meteorological station that will be represented by the temperature data provided by the station. In this assessment, we set this to a value that includes all census tracts within the air districts. A radius of 15.5 km met this requirement for Denver (Figure 5-1), while Los Angeles required a larger radius of 70.5 km (Figure 5-2).

Table 5-20. Locations of meteorological stations selected for Denver.

Meteorological station		Location coordinates		Monitoring Year			
				1995		2006	
Monitor ID	County	Latitude	Longitude	1-hour values (n)	Mean temp (◦F)	1-hour values (n)	Mean temp (◦F)
31-0002	Denver	39.751184	-104.987625	8742	53.3	8749	55.2
59-0002	Jefferson	39.800333	-105.099973	8702	49.7	8758	51.5

Table 5-21. Locations of meteorological stations selected for Los Angeles.

Meteorological station		Coordinates		Monitoring Year			
				1997		2006	
Monitor ID	County	Latitude	Longitude	1-hour values (n)	Mean temp (°F)	1-hour values (n)	Mean temp (°F)
Daugherty Field	Long Beach	33.81667	-118.15	8751	65.8	--	--
37-4002	Long Beach	33.82376	-118.18921	--	--	8759	63.8

5.8.1 Method for Estimating Missing 1-Hour Temperature Data

APEX also requires a complete (full) meteorological data set to run properly. In checking the meteorological data for completeness, staff noted all stations and years had at least one missing hourly value for temperature (Tables 5-20 and 5-21). To generate the complete one-year temperature data sets, we estimated the missing values for the selected meteorological (MET) stations in Denver and Los Angeles as follows.

For the Denver study area, we selected two MET stations for use in 1995 and 2006. All missing values in year 2006 were filled using linear interpolation. For the missing values in 1995, staff used linear interpolation to fill in short gaps. Where there were long gaps in the data (e.g., more than 16 continuous hours of missing values), linear interpolation was judged as inappropriate because this method would likely not produce reasonable estimates of the potential variability in temperature (particularly the daily maximum) that might occur during the gap. In these instances, staff applied an alternative approach in which the average temperature of the previous day and the latter day were averaged and then substituted for the corresponding hours. For example, if the temperature data were missing from 1 am to 11 pm on 2/8/1995, staff averaged the hourly temperature of 2/7/1995 and 2/9/1995 for 1 am, 2 am …, 11 pm to fill the missing hours (all eleven hours have an individual value).[13]

For Los Angeles, we evaluated the two sites identified here as site 1 (ID 037-4002) and site 2 (located at Daugherty Field). Both locations reported temperature in both years of interest; however, the degree of completeness for each varied. Given their close proximity to one another (3.6 km), we decided that a complete data set would be best generated by using a composite of the two monitors, using the monitor with the greatest number of measurements as the primary

[13] Calculating the average temperature using this method does not apply if 1) the long gap occurs on January 1 or December 31, or if 2) the temperature data in the previous day or the latter day are not available. In such cases, we used the non-missing values in the previous day or the latter day, whichever was available.

data set. Because site 1 had fewer missing values than site 2 for 2006, site 1 was selected as the primary meteorological site to represent the Los Angeles area for that year. For the one missing value on Site 1 in 2006, the corresponding temperature from Site 2 was used to fill the missing value for 2006. For 1997, there were 2,263 missing values on Site 1 while only 9 missing values on Site 2. As a result, Site 2 was selected as the primary meteorological station for 1997. Two of the nine missing values from Site 2 were available from Site 1. Therefore, these temperatures were directly substituted with values from the corresponding hours of the Site 1 data set. To fill the remaining seven missing values, we used linear interpolation by connecting successive straight line segments and fitting a continuous curve to the data.[14]

The temperature distributions before and after filling missing values were compared at for each station in each year to assess the impact (if any) of the substitution method. Given the limited number of missing values in the original data sets, there were negligible differences when comparing mean, median, variance and percentile statistics.

5.9 MICROENVIRONMENTS MODELED

This section briefly discusses the approach and specific factors used to estimate CO microenvironmental concentrations in the current assessment. As described in section 4.4.4.3, the approach was originally developed for pNEM/CO and used in the previous assessment (Johnson et al., 2000).

5.9.1 The Microenvironmental Model as Implemented by APEX4.3

Section 8.2.2 of US EPA (2008b) indicates that the mass balance model in APEX4.3 models the portion of outdoor air that enters the microenvironment as

$$CO_{out} = f_{proximity} \times f_{penetration} \times CO_{ambient} \qquad (5\text{-}2)$$

Since this is effectively equivalent to the method used by APEX3.1 described in section 4.4.4.4, we used the same method here with respect to application of the proximity and penetration factors in APEX4.3 to implement equation 4-11. First, to obtain the appropriate CO concentrations outside each microenvironment, ambient CO concentration were adjusted by an exponential factor of 0.621 (see equation 4-22). Then for each profile, a value for $f_{proximity}$ term would be sampled for each microenvironment from a lognormal distribution with geometric mean (GM) equal to $M(m)$ and geometric standard deviation (GSD) equal to 1.5232. A value for $f_{penetration}$ for each hour would also be sampled from a lognormal distribution with geometric

[14] This was done in SAS using a procedure, PROC EXPAND, along with the JOIN option.

mean (GM_T) equal to 1.0 and geometric standard deviation (GSD_T) equal to 1.6289. As described in section 4.4.4.4, the $f_{penetration}$ values were bounded at the lower and upper tails of the distribution by 0.4482 and 2.2313, respectively.

Table 5-16 presents the algorithm parameters proposed for the eight microenvironments currently defined for the application of APEX to Los Angeles and Denver. These eight microenvironments were selected rather than the fifteen selected in earlier assessments (see Tables 4-4 and 4-5) based on the locations having the same proximity factors and air exchange rates distributions, or when using a similar microenvironmental approach (see section 5.9.5).

Note that when this algorithm is implemented within the APEX framework, the application of Equation 4-11 will produce a "compression" effect in which the ratio of CO_{out} to CO_{mon} tends to become smaller (on average) as CO_{mon} increases. This effect is consistent with data reported by field studies such as Wilson et al. (1995) which have compared outdoor concentrations with simultaneously measured fixed-site concentrations. Note also that the effective microenvironment-to-ambient concentration ratios will differ from the proximity factor distributions provided in Table 5-22 given the influence of other variables used in equation 4-11. An analysis of these ratios (e.g., in-vehicle to ambient monitor concentration) is provided in section 6.1.

Table 5-22. Parameters of bounded lognormal distributions defined for proximity factors used in the application of APEX4.3 to Los Angeles and Denver.

Microenvironment			Activity diary locations included in microenvironment	Parameters of bounded lognormal distribution for proximity factor			
Code	General location	Specific location		GM	GSD	Minimum (5th pct)	Maximum (95th pct)
1	Indoors	Residence	Indoors - residence	1.034	1.5232	0.5175	2.0661
2	Indoors	Service station and auto repair	Service station Auto repair	2.970	1.5232	1.4864	5.9345
3	Indoors	Other indoor locations A	Other repair shop Shopping mall Other indoor location Auditorium Store Office Other public building Bars Restaurants	1.213	1.5232	0.6071	2.4237
4	Indoors	Other indoor locations B	Health care facility School Church Manufacturing facility	0.989	1.5232	0.4950	1.9762
5	Outdoors	Near road locations	Bus stop Bicycle Motorcycle Other near road	1.607	1.5232	0.8042	3.2110
6	Outdoor	Public parking or fueling facility	Indoor parking garage Outdoor parking garage Outdoor parking lot Outdoor service station	2.970	1.5232	1.4864	5.9345
7	Outdoors	Other outdoor locations	Outdoor res. garage Construction site Residential grounds School grounds Sports arena Park or golf course Other outdoor	1.436	1.5232	0.7187	2.8693
8	Vehicle	Automobile and mass transit	Automobile Truck Bus Train/subway Other vehicle	3.020	1.5232	1.5114	6.0344

5.9.2 Microenvironmental Mapping

In APEX, microenvironments represent the exposure locations for simulated individuals. For exposures to be estimated accurately, it is important to have realistic microenvironments that match closely to the locations where actual people spend time on a daily basis. It is necessary to map the CHAD location codes to one of the eight specific microenvironments selected for this exposure assessment or to a supplemental category (either *-1* or *0*). As a reminder, these eight microenvironments were selected based on having suitable data to use for proximity factors and air exchange rates (when using a mass balance approach). The *-1* code is assigned to events where the location code is missing (X) or the location is classified as uncertain (U); the *-1* code instructs APEX to use the last known microenvironment for that person's diary in determining the exposure concentration. The *0* code is assigned to an airplane microenvironment (CHAD location code: 31160) and instructs APEX to set the exposure concentration equal to 0 ppm. Figure D-1 in Appendix D describes the specific mapping of CHAD codes to microenvironments.

The microenvironment mapping file also permits the user to assign a home/work/other (H/W/O) location to each CHAD location code. The home/work/other location determines the source of the hourly-average monitoring data that will represent the ambient CO concentration for the microenvironment: the home district monitor, the work district monitor, or other.

The initial APEX assignments of H/W/O to the CHAD location codes were used as a starting point (see Figure D-1 in Appendix D) and modified using a few of the options available in APEX. First, staff overrode the H/W/O designations listed in the microenvironment mapping file for selected activities by compiling a list of CHAD activity codes that will always be associated with the work district (regardless of the CHAD location code). This list is inserted in the "CustomWork" parameter found in the simulation control file. The default list of work activity codes, which were used in this application, includes codes 10000 through 10300 (see Appendix D Table D-1). As a result of using this option, APEX will assign the simulated person to the work district whenever the *activity code* falls between 10000 and 10300. This assignment will override the home/work/assignment associated with the applicable CHAD *location code*.

There will still be exposure events in which the simulated person is assigned to the "other" location. In the default mode, APEX uses an average of all monitor values to determine the ambient concentration for these events. Note that this averaging approach will tend to smooth the data; that is, it will produce ambient CO concentrations that have slightly less variance than a comparable set of ambient concentrations obtained from a single monitor. To avoid this effect, staff chose to specify the option OtherDistricts = 1, so that only one monitor is used to represent "other." The monitor used in the model application is randomly selected from the set of all monitors.

5.9.3 Selection of Microenvironmental Method Used

As discussed in chapter 4, the two approaches available in APEX for calculating pollutant levels within microenvironments are (1) the mass balance method and (2) the factors method. Table 5-23 lists the microenvironments used in this study and the calculation method used.

Table 5-23. List of microenvironments modeled and calculation methods used.

Microenvironment			Calculation Method
Code	Location	Name	
1	Indoors	Residence	Mass balance
2	Indoors	Service station and auto repair	Mass balance
3	Indoors	Other indoor locations A	Mass balance
4	Indoors	Other indoor locations B	Mass balance
5	Outdoors	Near road locations	Factors
6	Outdoors	Public parking or fueling facility	Factors
7	Outdoors	Other outdoor locations	Factors
8	Vehicle	Automobile and mass transit	Factors

5.9.4 Air Exchange Rates and Air Conditioning Prevalence

For the microenvironments using the mass balance method (i.e., all indoor microenvironments), air exchange rate (AER) and air conditioning prevalence data are needed to estimate microenvironmental concentrations. Air exchange rate data used for the indoor residential microenvironment were the same used in APEX for the most recent O_3 NAAQS review (US EPA, 2007). As part of that earlier review, AER data were reviewed, compiled, and evaluated from the extant literature to generate location-specific AER distributions[15] categorized by influential factors, namely temperature and presence of air conditioning. In general, lognormal distributions provided the best fit, and are defined by a geometric mean (GM) and standard deviation (GSD). To avoid unusually extreme simulated AER values, bounds of 0.1 and 10 were selected for minimum and maximum AER, respectively. Tables 5-24 and 5-25

[15] There were AER measurement data specific to the Los Angeles study area; these were used by US EPA (2007) to develop AER distributions. Denver was not a location of interest in US EPA (2007); therefore there were no Denver-specific AER developed for this study area. Consistent with what was done in US EPA (2007) for cities not having location-specific AER data available, the composite AER distributions developed using data from cities outside California were applied in this study to Denver.

summarize the AER distributions used in modeling indoor exposures in Denver and Los Angeles, respectively, each classified by A/C prevalence and temperature categories. For all other indoor microenvironments, the AER distributions used here (Tables 5-24 and 5-25) were based on data provided by an indoor air quality study (Persily et al., 2005). These are the same AER distributions used for the APEX assessments in the most recent O_3 NAAQS review (US EPA, 2007), NO_2 REA (US EPA, 2008c) and SO_2 REA (US EPA, 2009b).

Because the selection of an air exchange rate distribution is conditioned on the presence or absence of an air-conditioner (A/C), the air conditioning status of the residential microenvironments in each modeled area is simulated randomly using the probability that a residence has an air conditioner. A value of 55% was used to represent the A/C prevalence rate in Los Angeles, based on data obtained from US EPA (2007). For Denver, residential A/C prevalence was estimated to be 69% of homes, a value obtained from AHS (2005). Air conditioning prevalence is noted as being distinct from usage rate, the latter being represented by the air exchange rate distribution and dependent on temperature.

Table 5-24. Lognormal distributions of indoor air exchange rates used in Denver.

Micro-environment	Classification category		Parameters of bounded lognormal distribution[a]			
	A/C present?	Mean Temp (degrees F)	GM	GSD	Minimum[c]	Maximum[c]
Indoors - residence	Yes[b]	≤ 50	0.919	1.859	0.1	10.0
		50 – 68	0.564	1.940	0.1	10.0
		68 – 77	0.468	2.201	0.1	10.0
		77 – 86	0.424	2.037	0.1	10.0
		86+	0.567	1.945	0.1	10.0
	No	≤ 50	0.926	2.084	0.1	10.0
		50 – 68	0.733	2.330	0.1	10.0
		68+	1.378	2.276	0.1	10.0
Indoors - other	-	-	1.109	3.015	0.1	10.0

Notes:
[a] Obtained from Table D-4 of US EPA (2007) and derived from locations outside California.
[b] Estimated air conditioning prevalence rate for Denver = 69% (see Table 1-4 in AHS, 2005).
[c] Assumed here to be consistent with other approximated lower and upper bounds.

Table 5-25. Lognormal distributions of indoor air exchange rates used in Los Angeles.

Micro-environment	Classification category		Parameters of bounded lognormal distribution[a]			
	A/C present?	Mean Temp (degrees F)	GM	GSD	Minimum	Maximum
Indoors - residence	Yes[b]	≤ 50	0.589	1.894	0.1	10.0
		50 – 67	0.589	1.894	0.1	10.0
		68 – 76	1.100	2.365	0.1	10.0
		77 – 85	0.813	2.415	0.1	10.0
		86+	0.266	2.790	0.1	10.0
	No	< 50	0.543	3.087	0.1	10.0
		50 – 67	0.747	2.085	0.1	10.0
		68 – 76	1.372	2.283	0.1	10.0
		77 – 85	0.988	1.967	0.1	10.0
		86+	0.988	1.967	0.1	10.0
Indoors - other	-	-	1.109	3.015	0.1[c]	10.0[c]

Notes:
[a] Obtained from Table D-4 of US EPA (2007).
[b] Estimated air conditioning prevalence rate for Los Angeles = 55 percent (see page 47 and Table A-3 of US EPA, 2007).
[c] Assumed here to be consistent with other approximated lower and upper bounds.

5.10 ADDITIONAL EXPOSURE AND DOSE OUTPUT GENERATED USING REDUCED APEX SIMULATIONS

In a typical model run, APEX generates a complete time-series of exposure and dose for each simulated individual based on the microenvironmental concentrations they contact and the activities they perform. Because there are usually thousands of simulated persons and thus thousands of exposure and dose profiles, it is common practice that only summary output data are generated. As there are 8,760 hours in a year and potentially multiple events within an hour, the large size of these time-series profile files presents computational challenges for the data analyst, and increases the model run time. In this assessment however, we were interested in additional exposure and dose output data not summarized by the typical APEX output files. The APEX *events* and *hourly* files provide event-level and hourly-level exposure and dose profiles for all simulated individuals (US EPA, 2008a, 2008b). The time-series of exposure and dose for each individual are useful in performing three important analyses in this assessment, each described in the following sections.

5.10.1 Estimate of Microenvironment Contribution to At-Risk Population Exposure Levels

The first analysis using the individual-level exposure and dose output was designed to identify the microenvironments that are most influential to different levels of population exposure.[16] To simplify the presentation of the data in this analysis, the total time spent in each of the modeled eight microenvironments was aggregated into five microenvironments to evaluate time spent by simulated persons at selected exposure levels. The aggregation was based on microenvironments having similar proximity factors (see Table 5-22), resulting in aggregated microenvironments defined as follows: indoors-low (indoor-residence and indoor-other A&B), indoors-high (indoors-auto service/repair), outdoors-low (outdoors-other and near-road), outdoors-high (outdoor-parking/gas station), inside-vehicles. In addition, the total time the CHD population spent at or above each exposure level was calculated.

5.10.2 Estimate of Microenvironment-to-Ambient Concentration Ratios

The second analysis using the individual-level exposure and dose output was designed to estimate the effective microenvironmental factors, or the ratio of modeled microenvironmental concentrations to associated ambient monitor concentrations. The distributions of these effective microenvironmental factors are then compared to commonly reported microenvironment-to-ambient concentration ratios that are based on measurement data. The use of these estimated microenvironmental factors for comparison is more informative than simply using the distribution of proximity factors given in Table 5-22. As noted earlier, the series of factors in equation 4-11 are designed to spatially and temporally adjust the ambient concentrations to reflect concentrations immediately proximal to the microenvironment. The proximity factors listed in Table 5-22 would effectively reflect microenvironment-to-spatially and temporally adjusted ambient concentration ratios, not microenvironment-to-fixed site ambient monitor concentration ratios commonly reported in the extant human exposure literature.

The microenvironment-to-ambient concentration ratios were calculated by dividing each estimated event-level microenvironmental CO concentration by its corresponding hourly CO ambient monitor concentration.[17] In summarizing these microenvironment-to-ambient concentration ratios, we excluded those ratios that were associated with ambient concentrations

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[16] The standard APEX summary output table only generates microenvironment contributions for the general population (i.e., it is not necessarily representative of the demographics of the CHD or HD population).

[17] Note that event-level ambient concentration is not a variable that can be output from APEX at the time of analysis. The 1-hour ambient concentration in the APEX hourly file does account for when a person might experience ambient concentrations outside their home tract (e.g., when commuting). When this does occur, the 1-hour concentration would be time-averaged based on the time spent in each air quality district for each event during the hour, effectively approximating an average event-level ambient concentration.

less than 1 ppm. These calculated ratios using the event-level modeled concentrations tended to be extremely large, particularly when considering the *as is* air quality, as a result of dividing by extremely low ambient concentrations rather than the calculation method employed in estimating the microenvironmental concentrations. Inclusion of these ratios (while valid) would be of little practical use in interpreting the microenvironment-to-ambient concentration ratios and high microenvironmental concentrations because the design of the microenvironmental algorithm results in the highest concentrations being driven largely by the high ambient concentrations, not by these extreme ratios. For example, Figure 5-3b illustrates an inverse relationship between the microenvironment-to-ambient concentration ratios and estimated microenvironmental concentration. Any large proximity factors that might have occurred when randomly sampling from the distributions used in Table 5-22 were effectively modified by the ambient concentration exponential adjustment (equation 4-11), thus controlling for extreme ratio and high concentration combinations in estimating the microenvironmental concentrations. Although the calculated ratios can reach extremely high values (> 100), they are not responsible for estimating the highest microenvironmental concentrations. The full distribution representing all event-level microenvironmental concentrations estimated to be experienced by the CHD population is also included in this analysis.

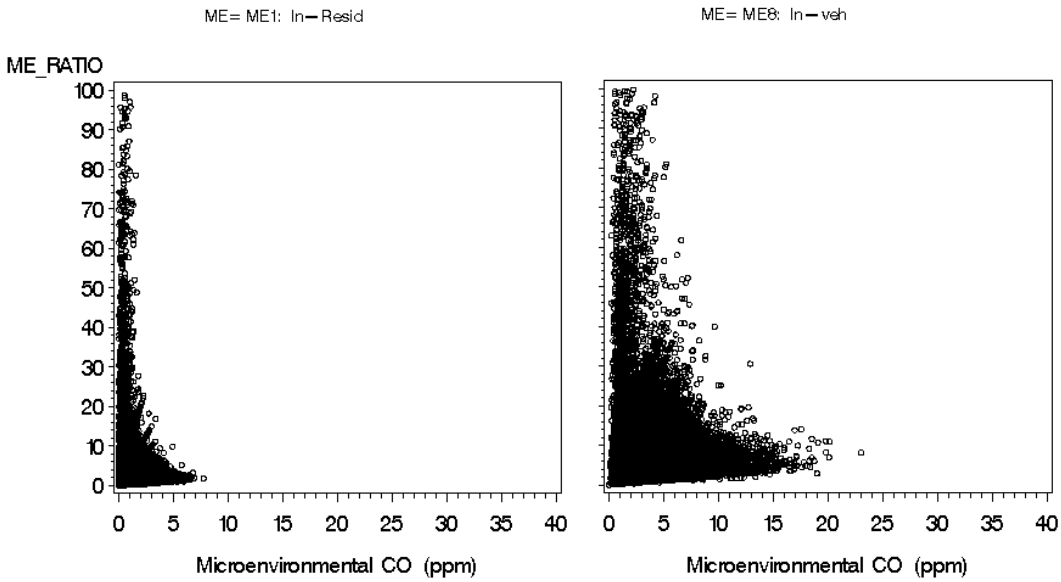

Figure 5-3. Relationship between microenvironment-to-ambient concentration ratios using estimated indoor-residential concentrations (left panel) and inside-vehicle concentrations (right panel) in Denver – *as is* air quality.

5.10.3 Estimate of Ambient Exposure Contribution to Total COHb Level

In the third analysis, we were interested in the contribution of ambient CO exposure to each individual's COHb dose level above their endogenous CO production. As summarized in section 4.4.7 and described fully in Appendix B, we estimated COHb levels in each simulated individual using the CFK dose module within APEX. Theoretically, in the absence of ambient concentrations or other sources of CO, one can perform an APEX simulation to estimate endogenous CO production and its effect on COHb levels. Two APEX model simulations were performed for each location and air quality scenario evaluation: one using ambient concentrations and the second using ambient concentrations equal to zero. Each of the new runs simulated the complete dose time-series for each individual. By design, the simulated persons in each of these two model runs line up perfectly in terms of physiology and activities performed, enabling staff to compare the COHb levels experienced across the two runs event-by-event. We calculated all event-by-event ambient contributions (*COHb ambient contribution*) to corresponding COHb levels (i.e., *COHb ambient contribution* = % COHb with ambient exposure minus % COHb for zero exposure), effectively giving the ambient contribution to estimated COHb levels. Consistent with the dose metric of interest in this assessment, the daily maximum end-of-hour COHb level is calculated using each individual's entire dose profile, only in this instance it is the daily maximum end-of-hour contribution to COHb associated with ambient CO exposure.

5.10.4 Comparison of the Exposure and Dose Results Generated Using 50,000 Persons *Versus* 5,000 Persons Simulation

For each of these particular model runs, APEX generated the complete time-series of exposure and dose for 5,000 persons, of which there were approximately 400 CHD simulated individuals.[18] The CHD prevalence rates were used to simulate the at-risk population for two air quality scenarios in each study area: *as is* air quality and just meeting the current standard. The complete output and analysis of these data are provided in chapter 6; however, a comparison of the summary results is provided here to demonstrate the representativeness of the smaller sample run size. The summary exposure and dose results from the smaller sample size runs (i.e., the percent of persons and person-days at or above selected levels) were very similar to the results generated using a 50,000 person simulation for either exposure scenario and study area. Table 5-26 summarizes the exposure output using *as is* air quality, while Table 5-27 summarizes the summary dose output for air quality just meeting the current standard; as noted above, little difference can be observed when comparing the 50,000 person simulation to the 5,000 person

[18] Of the 5,000 person model simulations, APEX simulated 438 CHD persons in Denver and 394 CHD persons in Los Angeles.

simulation for either exposure scenario. Therefore, the time-series results generated for the smaller sample size simulations are considered representative of the larger modeled CHD population.[19]

Table 5-26. Comparison of exposure summary output generated when simulating 50,000 persons *versus* that of simulating 5,000 persons – *as is* air quality.

Daily Maximum Exposure (ppm)		Denver CHD Population[a,b,c]				Los Angeles CHD Population[a,b,c]			
		Percent of Persons		Percent of Person-days		Percent of Persons		Percent of Person-days	
		50K Run[d]	5K Run	50K Run[d]	5K Run	50K Run[e]	5K Run	50K Run[e]	5K Run
1-hour	≥ 0	100	100	100	100	100	100	100	100
	≥ 3	99.5	99.3	11.2	10.5	99.9	100	16.9	17.1
	≥ 6	60.6	59.6	0.9	0.8	75.1	78.2	1.7	1.7
	≥ 9	19.9	16.4	0.1	0.1	32.0	28.4	0.3	0.3
	≥ 12	5.7	5.0	< 0.1	< 0.1	11.2	10.9	< 0.1	< 0.1
	≥ 15	1.6	1.1	< 0.1	< 0.1	3.6	4.3	< 0.1	< 0.1
	≥ 20	0.1	0	< 0.1	0	0.6	1.0	< 0.1	< 0.1
	≥ 30	0	0	0	0	< 0.1	0	< 0.1	0
	≥ 40	0	0	0	0	0	0	0	0
8-hour	≥ 0	100	100	100	100	100	100	100	100
	≥ 3	57.8	55.3	1.0	0.9	76.9	78.4	2.7	2.7
	≥ 6	3.2	3.0	< 0.1	< 0.1	9.5	9.1	< 0.1	< 0.1
	≥ 9	0.1	0.2	< 0.1	< 0.1	0.8	0.8	< 0.1	< 0.1
	≥ 12	< 0.1	0	< 0.1	0	< 0.1	0.3	< 0.1	< 0.1
	≥ 15	0	0	0	0	0	0	0	0
	≥ 20	0	0	0	0	0	0	0	0
	≥ 30	0	0	0	0	0	0	0	0
	≥ 40	0	0	0	0	0	0	0	0

Notes:
[a] Persons with diagnosed coronary heart disease, angina pectoris, and heart attack (CDC, 2009).
[b] Includes estimate of persons with undiagnosed ischemia developed by EPA (see section 5.5.1).
[c] Unadjusted ambient concentrations from four monitors (Denver) and ten monitors (Los Angeles) in 2006 were used to represent the *As Is* air quality scenario.
[d] Exposure results obtained from Table 6-1.
[e] Exposure results obtained from Table 6-4.

[19] Given that the results generated using the CHD and HD populations were also generally similar when comparing the percent of persons and person-days (e.g., see Table 6-1), the microenvironmental contributions (and microenvironmental factors) estimated from the smaller sample size CHD population simulations are considered representative estimated exposures for the simulated HD population.

Table 5-27. Comparison of dose summary output generated when simulating 50,000 persons *versus* that of simulating 5,000 persons – just meeting the current standard.

	Denver CHD Population[a,b,c]				Los Angeles CHD Population[a,b,c]			
COHb Level (%)	Percent of Persons		Percent of Person-days		Percent of Persons		Percent of Person-days	
	50K Run[d]	5K Run	50K Run[d]	5K Run	50K Run[e]	5K Run	50K Run[e]	5K Run
0.0	100	100	100	100	100	100	100	100
1.0	82.3	82.6	6.8	6.1	41.2	44.4	1.8	2.1
1.5	23.4	21.2	0.4	0.4	4.7	5.1	< 0.1	< 0.1
1.75	10.8	10.0	< 0.1	< 0.1	1.6	1.3	< 0.1	< 0.1
2.0	4.2	4.1	< 0.1	< 0.1	0.6	0.8	< 0.1	< 0.1
2.5	0.8	0.7	< 0.1	< 0.1	< 0.1	0.3	< 0.1	< 0.1
3.0	0.2	0	< 0.1	0	< 0.1	0.3	< 0.1	< 0.1
4.0	< 0.1	0	< 0.1	0	0	0	0	0

Notes:
[a] Persons with diagnosed coronary heart disease, angina pectoris, and heart attack (CDC, 2009).
[b] Includes estimate of persons with undiagnosed ischemia developed by EPA (see section 5.5.1).
[c] Ambient concentrations from 1995 (Denver) and 1997 (Los Angeles) were adjusted to just meet a 2nd highest 8-hour average concentration of 9.4 ppm.
[d] Dose results obtained from Table 6-18.
[e] Dose results obtained from Table 6-19.

5.11 KEY OBSERVATIONS

The following presents the key observations for this chapter:

- Two exposure model domains (Denver and Los Angeles study areas) were defined by overlaying ambient monitor locations having 10 km radii with US census tract population data. Monitors selected comprised the bulk of the urban core in each location, where ambient monitoring data exist.
- Two simulated at-risk subpopulations were identified by combining the census tract-specific age and gender population distributions with HD and CHD prevalence rates, each also stratified by age and gender. In using this approach, staff can represent the variability that exists in the simulated at-risk HD and CHD subpopulations that reside in each census tract and within each study area.
    - Both simulated at-risk subpopulations include an estimate of persons with undiagnosed CHD.
- To represent spatial variability in ambient concentrations in Denver, a total of four monitors were used; in Los Angeles, the total number of monitors was ten. Temporal variability was represented by use of hourly ambient concentrations in each study area.

- The exposure and dose model simulations included 8 microenvironments in each location to represent the expected variability in microenvironmental CO concentrations.
- All indoor microenvironments were modeled using a mass balance model to represent temporal variability in indoor CO concentrations with respect to the outdoor CO concentration variability. In addition, distributions of microenvironmental factors were used for all microenvironments rather than point estimates. Using distributions of microenvironmental factors will better represent both spatial and temporal variability in estimated microenvironmental CO concentrations.
- Additional analyses using output from individual-level simulations were performed to provide information on the microenvironments most influential to population exposure at different exposure levels. This included an analysis of the effective ratios of microenvironment to ambient concentrations and the contribution of ambient CO exposure to total COHb level estimates. The smaller sample sizes generated for these analyses were found to be representative of the larger simulations employed for estimating exposure and dose in the different air quality exposure scenarios.

5.12 REFERENCES

AHS. (2005). American Housing Survey for the Denver Metropolitan Area: 2004. Available at: http://www.census.gov/prod/2005pubs/h170-04-46.pdf

Adams PF and Marano MA. (1995). Current Estimates from the National Health Interview Survey, 1994. National Center for Health Statistics. Vital Health Stat. 10(193).

American Heart Association. (1990). Heart and Stroke Facts. American Heart Association, Dallas, TX. p.13. As cited by Johnson et al. (2000).

American Heart Association. (2003). Heart and Stroke Facts. American Heart Association, Dallas, TX. p.14. Available at: http://www.americanheart.org/downloadable/heart/1056719919740HSFacts2003text.pdf

CDC. (2009). Summary Health Statistics for U.S. Adults: National Health Interview Survey, 2007. Series 10, Number 240. U.S. Department of Health and Human Services, Hyattsville, MD, May 2009.

Glen G, Smith L, Isaacs K, McCurdy T, Langstaff J. (2008). A new method of longitudinal diary assembly for human exposure modeling. *J Expos Sci Environ Epidem*. 18:299-311.

Isaacs K, McCurdy T, Erickson A, Forbes S, Glen G, Graham S, McCurdy L, Nysewander, M, Smith L, Tulve N, Vallero D. (2009). Statistical properties of longitudinal time-activity data for use in EPA exposure models. Poster presented at the American Time Use Research Conference; College Park MD, June 26, 2009.

Johnson T, Mihlan G, LaPointe J, Fletcher K, Capel J. (2000). Estimation of Carbon Monoxide Exposures and Associated Carboxyhemoglobin Levels for Residents of Denver and Los Angeles Using pNEM/CO (Version 2.1). Report prepared by ICF Consulting and TRJ Environmental, Inc., under EPA Contract No. 68-D6-0064. U.S. Environmental Protection Agency, Research Triangle Park, North Carolina. Available at: http://www.epa.gov/ttn/fera/human_related.html. June 2000.

Persily A, Gorfain J, Brunner G. (2005). Ventilation design and performance in U.S. Office buildings. *ASHRAE Journal*. April 2005, 30-35.

US EPA. (1992). Review of the National Ambient Air Quality Standards for Carbon Monoxide: Assessment of Scientific and Technical Information. Office of Air Quality Planning and Standards Staff Paper. Report no. EPA/452/R-92-004.

US EPA. (2003). Total Risk Integrated Methodology TRIM.ExpoInhalation User's Document. Volume I: Air Pollutants Exposure Model (APEX, version 3). Available at: http://www.epa.gov/ttn/fera/data/apex322/apexusersguidevoli4-24-03.pdf

US EPA. (2007). Ozone Population Exposure Analysis for Selected Urban Areas. Office of Air Quality Planning and Standards, Research Triangle Park, NC. July 2007. Report no. EPA-452/R-07-010. Available at: http://www.epa.gov/ttn/naaqs/standards/ozone/data/2007_07_o3_exposure_tsd.pdf.

US EPA. (2008a). Total Risk Integrated Methodology (TRIM) Air Pollutants Exposure Model Documentation (TRIM.Expo/APEX, Version 4.3). Volume 1: Users Guide. Report no. EPA-452/B-08-001a. Office of Air Quality Planning and Standards, U.S. Environmental Protection Agency, Research Triangle Park, NC.

US EPA. (2008b). Total Risk Integrated Methodology (TRIM) Air Pollutants Exposure Model Documentation (TRIM.Expo/APEX, Version 4.3). Volume 2: Technical Support Document. Report no. EPA-452/B-08-001b. Office of Air Quality Planning and Standards, U.S. Environmental Protection Agency, Research Triangle Park, NC.

US EPA. (2008c). Risk and Exposure Assessment to Support the Review of the NO_2 Primary National Ambient Air Quality Standard. Report no. EPA-452/R-08-008a. November 2008. Available at: http://www.epa.gov/ttn/naaqs/standards/nox/data/20081121_NO2_REA_final.pdf.

US EPA. (2009a). Risk and Exposure Assessment to Support the Review of the Carbon Monoxide Primary National Ambient Air Quality Standard. First External Review Draft. Report no. EPA-452/P-09-008. Available at: http://www.epa.gov/ttn/naaqs/standards/co/data/COREA1stDraftOct2009.pdf

US EPA. (2009b). Risk and Exposure Assessment to Support the Review of the SO_2 Primary National Ambient Air Quality Standard. Report no. EPA-452/R-09-007. August 2009. Available at http://www.epa.gov/ttn/naaqs/standards/so2/data/200908SO2REAFinalReport.pdf.

US EPA. (2010). Risk and Exposure Assessment to Support the Review of the Carbon Monoxide Primary National Ambient Air Quality Standard. Second External Review Draft. Report no. EPA-452/P-10-004. Available at: http://www.epa.gov/ttn/naaqs/standards/co/data/COREA2ndDraftFeb2010.pdf

Wilson AL, Colome SD, Tian Y. (1995). California Residential Indoor Air Quality Study. Volume III: Ancillary and Exploratory Analysis. Integrated Environmental Services, Irvine, California.

6 SIMULATED EXPOSURE AND COHB RESULTS

This chapter summarizes the CO exposure and dose results for the Denver and Los Angeles study areas that were generated using EPA's APEX model described in chapters 4 and 5. Staff considered exposures associated with five air quality scenarios; air quality (1) unadjusted or *as is*, (2) adjusted to just meet the current 8-hour standard of 9 ppm, (3) adjusted to just meet a 2nd highest 8-hour average concentration of 5 ppm, (4) adjusted to just meet a 99th percentile daily maximum 8-hour average of 5.0 ppm, and (5) adjusted to just meet a 99th percentile daily maximum 8-hour average of 8.0 ppm (see section 5.7 for details regarding the air quality adjustment procedure). This chapter is divided into four main sections, with each described briefly below.

The first section (6.1) summarizes the estimated exposures associated with each of the five air quality scenarios. As described in section 5.5.1, two at-risk subpopulations were simulated in this assessment. The first simulated at-risk subpopulation includes individuals with diagnosed CHD as well as those persons with potentially undiagnosed CHD.[1] For simplicity, they will be combined and referred to as the *CHD population* in this chapter. The second simulated at-risk population includes individuals with diagnosed heart disease (HD) as well as those persons with potentially undiagnosed CHD. For simplicity, this subpopulation will be combined and referred to as the *HD population* in this chapter. The primary exposure metrics of interest in this REA and generated by APEX include the number and percent of persons at or above staff-selected exposure levels and the corresponding number of person-days.[2] Two exposure averaging times were also selected: 1-hour and 8-hour daily maximum exposures.

Section 6.2 summarizes the estimated COHb levels for persons in the simulated at-risk population residing in each study area. The primary dose metric of interest in this REA and generated by APEX includes the number and percent of persons at or above staff selected COHb levels and the corresponding number of person-days. Consistent with prior CO exposure assessments, the daily maximum end-of-hour COHb level was reported. This section also

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[1] As described in section 5.5.2, in characterizing the population of interest with regard to demographics (age and gender), the assessment drew from estimates of the prevalence of coronary heart disease (CHD, which includes CHD, angina pectoris and heart attack) and all types of heart disease (HD, which includes coronary heart disease, angina pectoris, heart attack, or any other heart condition or disease) provided by the National Health Interview Survey, each combined with estimates of undiagnosed ischemia developed by EPA.

[2] Because the duration of the exposure assessment is one year, there are opportunities for individuals to experience more than one day in the year above a selected exposure concentration, hence use of the term *person-days*.

presents an evaluation of the ambient contribution to COHb levels for APEX simulated individuals for three of the air quality scenarios.

In section 6.3, staff compares the dose estimates in this CO REA with those estimated in the 2000 exposure assessment (Johnson et al., 2000). Finally, key observations are presented in the final section (6.4). As mentioned in Chapter 1, due to the extremely tight timeline for this NAAQS review, the exposure and risk results are provided here without substantial interpretation. Rather, interpretative discussion of these results is provided in the CO Policy Assessment.

6.1 ESTIMATED EXPOSURES

This section summarizes the estimated exposures for the simulated individuals in a series of tables, classified by the five air quality scenarios and two study areas considered. Given the complexity of the simulations and output data requirements, a limited number of additional modeling runs were added to this final assessment. First, in expanding the at-risk population to include persons with all types of heart disease, the standard APEX output data (i.e., number and percent of persons and person-days at selected exposure levels) were generated for all five air quality scenarios and summarized. Additional exposure output data sets (i.e., microenvironmental contributions to selected exposure levels and the evaluation of microenvironmental factors distributions) were generated using a smaller simulation size (i.e., 5,000 persons) and the CHD population for two air quality scenarios (i.e., *as is* and just meeting the current standard). The smaller simulation size was used to reduce the size of the output file under analysis. See section 5.10 for details on the approach used and evaluation of the representativeness of the simulation size and at-risk population used.

6.1.1 Air Quality "As Is"

As described in section 5.6, ambient monitoring data from each study area for the year 2006 were used to represent the *as is* air quality. Table 6-1 summarizes the distribution of the 1-hour and 8-hour daily maximum CO exposures experienced by the CHD and HD populations in the Denver Study area. About 80% of the simulated CHD population did not experience a 1-hour daily maximum exposure at or above 9 ppm; 99.9% did not experience a 1-hour daily maximum exposure concentration at or above 20 ppm. Of the nearly 20 million CHD person-days, over 99% were associated with a 1-hour daily maximum exposure below 6 ppm. Very few individuals were estimated to experience an 8-hour daily maximum exposure at or above 9 ppm (0.1% of the CHD population). Approximately 99% of simulated CHD person-days were associated with 8-hour daily maximum exposure concentrations of less than 3 ppm.

While there were a greater number of persons and person-days at each of the exposure levels for the HD as compared to the CHD population, consistent with the larger size of that population, there was little difference when considering the percentages of each population at or above selected exposure levels and for either averaging time. For example, about 20% of both the CHD and HD populations experienced a 1-hour daily maximum exposure at or above 9 ppm. About 89% of person-days for either population were associated with 1-hour daily maximum exposures of less than 3 ppm.

Table 6-1. Estimated daily maximum 1-hour or 8-hour exposure for simulated at-risk populations in the Denver study area – *as is* air quality.

Daily Maximum Exposure (ppm)		Coronary Heart Disease[a,c]				All Heart Disease[b,c]			
		Persons		Person-days		Persons		Person-days	
		Number	Percent	Number	Percent	Number	Percent	Number	Percent
1-hour	≥ 0	53,656	100	19,580,000	100	85,926	100	31,360,000	100
	≥ 3	53,397	99.5	2,188,000	11.2	85,494	99.5	3,582,000	11.4
	≥ 6	32,517	60.6	170,400	0.9	52,274	60.8	281,700	0.9
	≥ 9	10,662	19.9	24,560	0.1	17,412	20.3	39,550	0.1
	≥ 12	3,048	5.7	4,677	<0.1	5,010	5.8	7,441	<0.1
	≥ 15	876	1.6	1,061	<0.1	1,431	1.7	1,666	<0.1
	≥ 20	62	0.1	62	<0.1	99	0.1	99	<0.1
	≥ 30	0	0	0	0	0	0	0	0
	≥ 40	0	0	0	0	0	0	0	0
8-hour	≥ 0	53,656	100	19,580,000	100	85,926	100	31,360,000	100
	≥ 3	31,036	57.8	189,500	1.0	50,361	58.6	309,400	1.0
	≥ 6	1,715	3.2	2,851	<0.1	2,604	3.0	4,171	<0.1
	≥ 9	62	0.1	86	<0.1	99	0.1	136	<0.1
	≥ 12	12	<0.1	12	<0.1	12	<0.1	12	<0.1
	≥ 15	0	0	0	0	0	0	0	0
	≥ 20	0	0	0	0	0	0	0	0
	≥ 30	0	0	0	0	0	0	0	0
	≥ 40	0	0	0	0	0	0	0	0

Notes:
Unadjusted ambient concentrations from four monitors in 2006 were used to represent the *As Is* air quality scenario.
[a] Persons with diagnosed coronary heart disease, angina pectoris, and heart attack (CDC, 2009).
[b] Inclusive of those persons with diagnosed coronary heart disease, angina pectoris, heart attack, and any other heart condition or disease (CDC, 2009).
[c] Includes estimate of persons with undiagnosed ischemia developed by EPA (see section 5.5.1).

These exposure results are consistent with the ambient concentration distributions used to represent this scenario, where upper percentile concentrations range from about 2 to 6.4 ppm (see Table 5-14). Note also that the highest estimated 1-hour daily maximum exposures are likely a function of microenvironmental concentrations (e.g., exposures occurring while inside vehicles or immediately near roads) that, in general, may be a factor of two to five times higher than

ambient CO concentrations at monitors that are not immediately near roads (2000 AQCD; ISA section 3.6.1).

As mentioned above, a smaller subset of the at-risk CHD population was simulated to generate additional exposure results. First, we were interested in determining the important microenvironments that contribute to CHD population exposures at each of the selected levels.[3] Figure 6-1 illustrates such an analysis, beginning with the total minutes per year spent by the simulated CHD population in Denver at or above each exposure level. Note that total time spent at or above a particular exposure concentration decreases with increasing exposure level. This pattern is consistent with the exposure results above (Table 6-1); that is, for most of the time, the population is exposed to concentrations less than 6 ppm (about 99.9% of the total time), with very little time spent exposed to concentrations at or above 20 ppm. For this scenario, in fact, there were 50 total minutes out of the 230 million minutes in the year simulated where the population was exposed at or above a level of 20 ppm. Note that when considering the zero exposure concentration level, the distribution of microenvironmental contributions effectively approximates the time spent by the population in each of the microenvironments across the simulation period. Not surprisingly, the simulated population spends over 85% of their time within indoor microenvironments and is consistent with the reported activity pattern survey data (Graham and McCurdy, 2004). At the lowest exposure levels (e.g., < 2 ppm), much of the estimated population exposure occurs within indoor microenvironments. For exposure concentrations at or above 2 ppm, most of the population exposure occurs while inside vehicles or during time spent within outdoor high-concentration microenvironments. These two aggregate microenvironments predominantly contribute to exposure concentrations at or above 4 ppm (> 90% of all personal time at these levels).

These smaller CHD population simulations also served to approximate the effective microenvironmental factors, the distributions of which are more useful to compare with literature reported microenvironment-to-ambient concentration ratios rather than simply using the distribution of proximity factors given in Table 5-22. Table 6-2 summarizes these ratios that were calculated by dividing the estimated event-level microenvironmental concentration by its corresponding ambient concentration. Values for the estimated microenvironmental ratios correspond reasonably well with reported personal exposure to ambient concentration ratios (ISA, Figure 3-46). The distribution of estimated microenvironmental concentrations (Table 6-3) also generally reflect the range of concentrations reported in personal exposure studies,

[3] The default APEX summary output table only generates microenvironmental contributions for the general population.

particularly those where measurements were made inside-vehicles and near-roadways (ISA section 3.6.6.2).

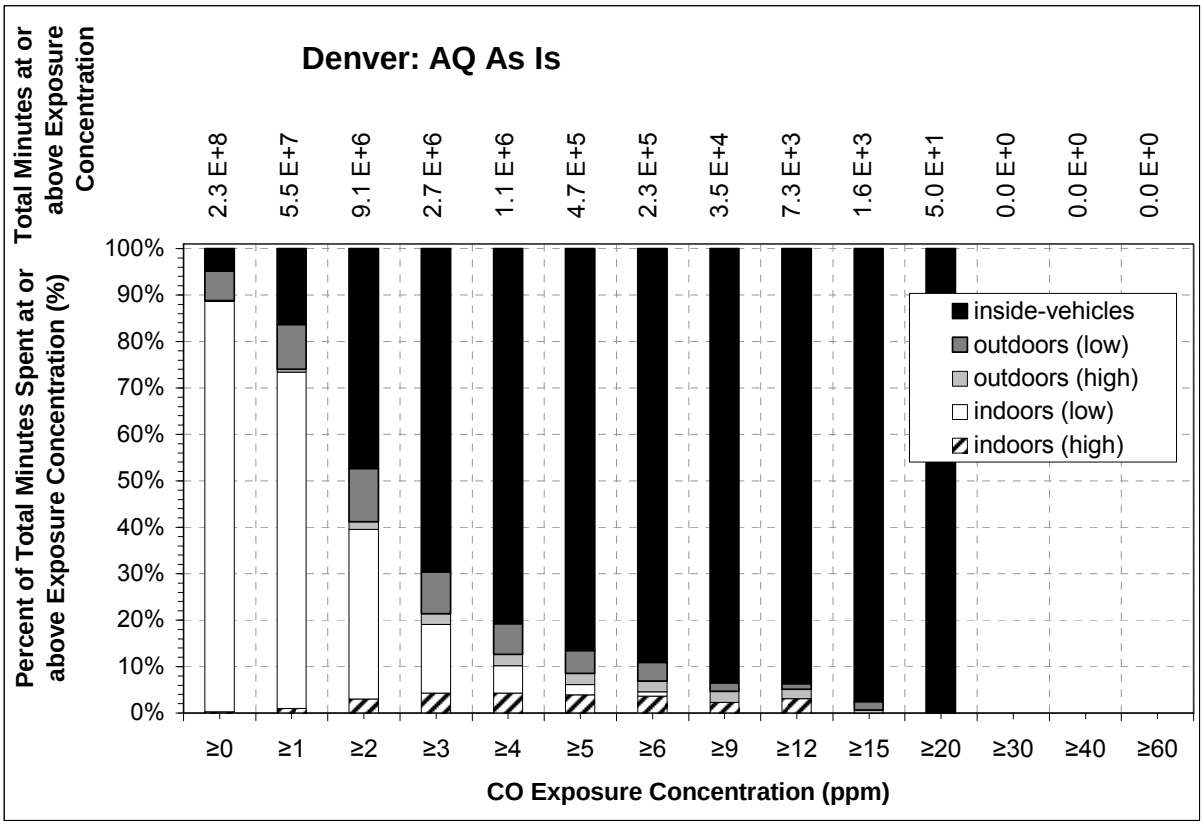

Figure 6-1. Estimated microenvironmental contributions to time spent at or above selected exposure concentrations using the Denver CHD population – *as is* air quality. The total minutes spent at or above each exposure concentration are presented above each bar.

Table 6-2. Estimated distribution of microenvironment-to-ambient concentration ratios using the Denver CHD population – *as is* air quality.

Microenvironment[a]	Events[b,c] (n)	Mean Ratio[c,d] (unitless)	std	Distribution Percentiles[c,d] (unitless)						
				min	p1	p5	p50	p95	p99	max
1: In-Residence	401,098	0.9	0.4	0	0.3	0.4	0.8	1.8	2.4	5.1
2: In-Service Station	1,425	2.9	1.3	0.5	0.9	1.3	2.7	5.4	6.6	10.0
3: In-Other A	39,348	1.1	0.5	0.1	0.4	0.5	1.0	2.1	2.6	4.2
4: In-Other B	15,956	0.9	0.4	0.1	0.3	0.4	0.9	1.7	2.2	4.2
5: Out-Near Road	8,822	1.6	0.8	0.1	0.5	0.6	1.5	3.1	4.1	6.1
6: Out-Parking Lot/ Refueling	3,079	2.9	1.4	0.4	0.8	1.2	2.6	5.5	7.4	10.2
7: Out-Other	24,515	1.5	0.8	0	0.4	0.6	1.3	2.9	3.9	6.1
8: In-Vehicle	44,998	2.9	1.4	0	0.8	1.2	2.6	5.7	7.5	14.1

Notes:
[a] See section 5.9 and Table 5-22 for details.
[b] This is the number of times the population experienced an exposure event in that microenvironment.
[c] Data set used to calculate the ratios represent the CHD population extracted from a 5,000 person simulation and was screened to eliminate ambient concentrations less than 1 ppm. See section 5.10 for details.
[d] The mean, standard deviation, and percentiles (p) were calculated using all events regardless of event duration. Note that based on the activity pattern diaries used, the length of an event can range from 1 minute to 1 hour.

Table 6-3. Estimated distribution of microenvironmental concentrations using the Denver CHD population – *as is* air quality.

Microenvironment[a]	Events[b,c] (n)	Mean CO[c,d] (ppm)	Std[c,d]	Distribution Percentiles[c,d] (ppm)						
				min	p1	p5	p50	p95	p99	Max
1: In-Residence	4,046,011	0.7	0.4	0	0.1	0.2	0.6	1.5	2.2	7.8
2: In-Service Station	17,715	2.2	1.2	0	0.3	0.8	1.9	4.5	6.4	14.3
3: In-Other A	486,641	0.8	0.5	0	0.1	0.3	0.7	1.7	2.5	7.3
4: In-Other B	183,535	0.7	0.4	0	0.1	0.2	0.6	1.5	2.1	6.2
5: Out-Near Road	100,303	1.1	0.8	0	0	0.3	1.0	2.6	3.8	15.4
6: Out-Parking Lot/ Refueling	39,801	2.0	1.3	0	0	0.6	1.7	4.4	6.7	16.6
7: Out-Other	354,654	1.0	0.7	0	0	0.3	0.8	2.2	3.4	12.3
8: In-Vehicle	546,573	2.0	1.4	0	0	0.6	1.7	4.6	6.9	23.0

Notes:
[a] See section 5.9 and Table 5-22 for details.
[b] This is the number of times the population experienced an exposure event in that microenvironment.
[c] These include all exposure events for the CHD population extracted from a 5,000 person simulation. See section 5.10 for details.
[d] The mean, standard deviation, and percentiles (p) were calculated using all events regardless of event duration. Note that based on the activity pattern diaries used, the length of an event can range from 1 minute to 1 hour.

In Los Angeles, there was a greater number of individuals experiencing exposures at or above each of the selected exposure levels (Table 6-4) when compared with exposures in Denver (Table 6-1) and considering either simulated at-risk population. This is expected given that the exposure modeling domain in Los Angeles encompasses a larger area than Denver and therefore comprises a larger total simulated population. The estimated percentage of persons exposed in Los Angeles is also greater when compared with the corresponding exposure levels evaluated for the Denver study area. For example, approximately 32% of the CHD population was estimated to experience a 1-hour daily maximum exposure of at least 9 ppm in Los Angeles (Table 6-6) while in Denver this same level was experienced by approximately 20% of the CHD population (Table 6-1). This result is likely driven by the differences noted in the *as is* air quality data, where in Los Angeles, the 2006 ambient concentrations were generally higher than those observed for Denver (see section 5.7.1; Tables 5-14 and 5-16).

In addition, the highest 1-hour daily maximum exposure was estimated to be at or above 30 ppm (but less than 40 ppm) in the Los Angeles study area, though limited to a small fraction of either simulated at-risk population (<0.1%). The corresponding highest 1-hour daily maximum exposure in the Denver study area was at or above 20 ppm (but less than 30 ppm) and was experienced by approximately 0.1% of either simulated at-risk population. Therefore, the overall range of the exposure distribution was wider in Los Angeles when compared with that of Denver when considering the *as is* air quality scenario.

Similar to that estimated for either at-risk population in Denver, over 98% of the person-days in Los Angeles were associated with 1-hour daily maximum exposures below 6 ppm and very few persons (<1%) experienced 8-hour daily maximum exposures at or above 9 ppm. These exposure results are also consistent with the distributions of ambient air quality used to represent this scenario, where the ambient monitor upper percentile concentrations extend from about 2 to 8.4 ppm (Table 5-16).

Table 6-4. Estimated daily maximum 1-hour or 8-hour exposure for simulated at-risk populations in the Los Angeles study area – *as is* air quality.

Daily Maximum Exposure (ppm)		Coronary Heart Disease[a,c]				All Heart Disease[b,c]			
		Persons		Person-days		Persons		Person-days	
		Number	Percent	Number	Percent	Number	Percent	Number	Percent
1-hour	≥ 0	383,040	100	139,800,000	100	630,807	100	230,200,000	100
	≥ 3	382,739	99.9	23,620,000	16.9	630,305	99.9	38,680,000	16.8
	≥ 6	287,606	75.1	2,423,000	1.7	471,951	74.8	3,880,000	1.7
	≥ 9	122,428	32.0	408,300	0.3	194,681	30.9	651,500	0.3
	≥ 12	42,850	11.2	83,990	< 0.1	65,730	10.4	133,500	< 0.1
	≥ 15	13,949	3.6	20,170	< 0.1	21,074	3.3	31,510	< 0.1
	≥ 20	2,208	0.6	2,509	< 0.1	3,211	0.5	3,613	< 0.1
	≥ 30	100	< 0.1	100	< 0.1	100	< 0.1	100	< 0.1
	≥ 40	0	0	0	0	0	0	0	0
8-hour	≥ 0	383,040	100	139,800,000	100	630,807	100	230,200,000	100
	≥ 3	294,430	76.9	3,793,000	2.7	481,986	76.4	6,178,000	2.7
	≥ 6	36,528	9.5	72,150	< 0.1	57,100	9.1	114,300	< 0.1
	≥ 9	3,011	0.8	3,412	< 0.1	4,616	0.7	5,319	< 0.1
	≥ 12	301	< 0.1	301	< 0.1	301	< 0.1	301	< 0.1
	≥ 15	0	0	0	0	0	0	0	0
	≥ 20	0	0	0	0	0	0	0	0
	≥ 30	0	0	0	0	0	0	0	0
	≥ 40	0	0	0	0	0	0	0	0

Notes:
Unadjusted ambient concentrations from ten monitors in 2006 were used to represent the *As Is* air quality scenario.
[a] Persons with diagnosed coronary heart disease, angina pectoris, and heart attack (CDC, 2009).
[b] Inclusive of those persons with diagnosed coronary heart disease, angina pectoris, heart attack, and any other heart condition or disease (CDC, 2009).
[c] Includes estimate of persons with undiagnosed ischemia developed by EPA (see section 5.5.1.1).

The microenvironmental contributions to time spent at or above selected exposure levels in Los Angeles (Figure 6-2) are also similar to that estimated for Denver, though indoor microenvironments contribute a somewhat greater percentage in Los Angeles at each of the exposure levels. This is likely the result of generally higher *as is* ambient concentrations across the entire distribution in Los Angeles when compared with the Denver ambient concentrations distribution (Table 5-14). As expected, the distributions of event-level microenvironment-to-ambient concentration ratios (Table 6-5) are also similar to those calculated for Denver (Table 6-3), though estimated microenvironmental concentrations are slightly higher in Los Angeles (Table 6-6). This is also a function of the generally higher ambient concentrations measured at the Los Angeles monitors when compared with ambient monitor concentrations in Denver.

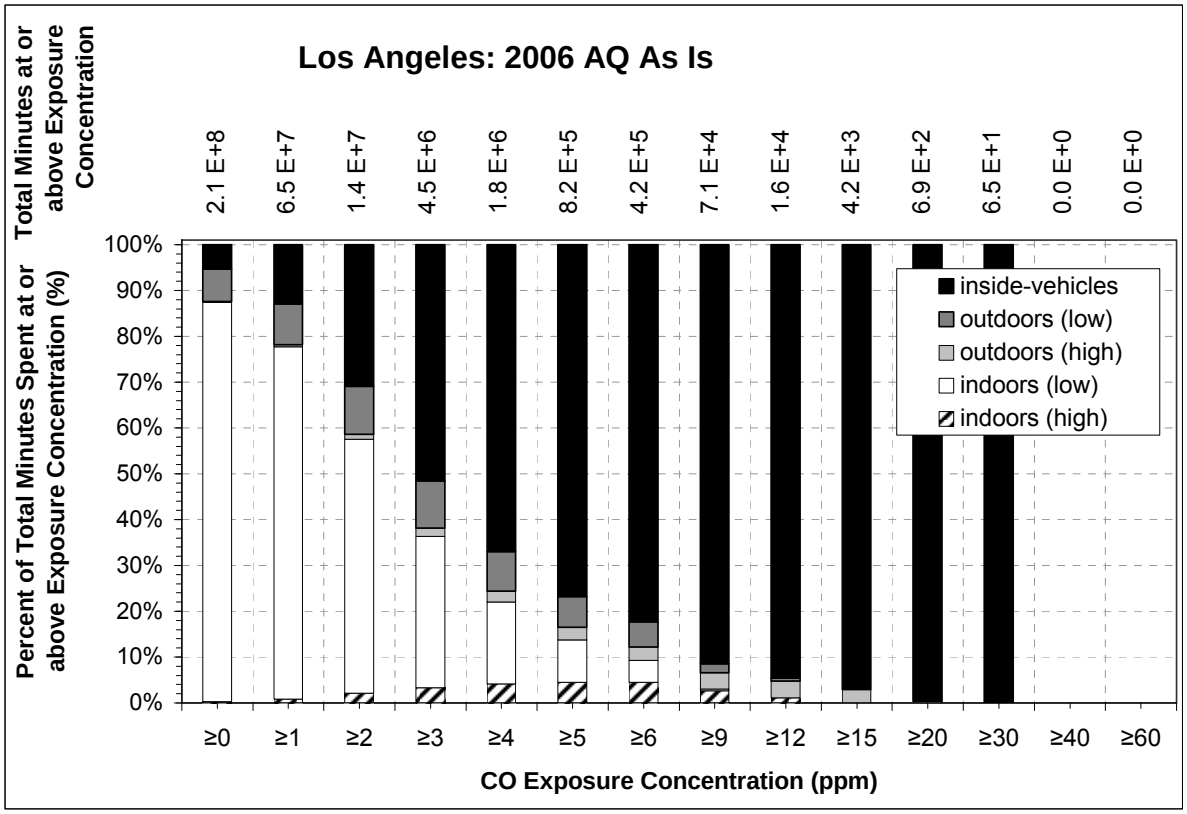

Figure 6-2. Estimated microenvironmental contributions time spent at or above selected exposure concentrations using the Los Angeles CHD population – *as is* air quality. The total minutes spent at or above each exposure concentration are presented above each bar.

Table 6-5. Estimated distribution of microenvironment-to-ambient concentration ratios using the Los Angeles CHD population – *as is* air quality.

Microenvironment[a]	Events[b,c] (n)	Mean Ratio[c,d] (unitless)	Std	Distribution Percentiles[c,d] (unitless)						
				min	p1	p5	p50	p95	p99	max
1: In-Residence	631,366	0.9	0.4	0	0.3	0.4	0.9	1.8	2.3	5.7
2: In-Service Station	2,190	2.8	1.2	0.4	1.0	1.3	2.6	5.1	6.6	9.4
3: In-Other A	45,134	1.2	0.5	0	0.4	0.5	1.0	2.2	2.8	5.4
4: In-Other B	18,735	1.0	0.4	0.1	0.3	0.4	0.9	1.8	2.3	3.8
5: Out-Near Road	12,954	1.5	0.8	0	0.3	0.6	1.4	3.0	3.9	9.0
6: Out-Parking Lot/ Refueling	4,307	2.9	1.5	0.3	0.7	1.1	2.6	5.9	7.6	10.8
7: Out-Other	40,000	1.4	0.7	0.1	0.4	0.5	1.3	2.9	3.8	7.0
8: In-Vehicle	59,191	2.9	1.5	0	0.7	1.1	2.5	5.7	7.5	21.1

Notes:
[a] See section 5.9 and Table 5-22 for details.
[b] This is the number of times the population experienced an exposure event in that microenvironment.
[c] Data set used to calculate the ratios represents the CHD population extracted from a 5,000 person simulation and was screened to eliminate ambient concentrations less than 1 ppm. See section 5.10 for details.
[d] The mean, standard deviation, and percentiles (p) were calculated using all events regardless of event duration. Note that based on the activity pattern diaries used, the length of an event can range from 1 minute to 1 hour.

Table 6-6. Estimated distribution of microenvironmental concentrations using the Los Angeles CHD population – *as is* air quality.

Microenvironment[a]	Events[b,c] (n)	Mean CO[c,d] (ppm)	Std	Distribution Percentiles[c,d] (ppm)						
				min	p1	p5	p50	p95	p99	max
1: In-Residence	3,620,332	0.8	0.6	0	0	0.2	0.7	1.9	2.9	9.7
2: In-Service Station	19,825	2.2	1.5	0	0	0.6	1.8	5.1	7.5	14.6
3: In-Other A	433,366	0.9	0.6	0	0	0.2	0.7	2.0	3.0	10.7
4: In-Other B	164,167	0.8	0.5	0	0	0.2	0.6	1.7	2.6	7.8
5: Out-Near Road	102,844	1.2	0.9	0	0	0.3	0.9	2.9	4.5	14.7
6: Out-Parking Lot/ Refueling	41,611	2.1	1.6	0	0	0.5	1.6	5.2	8.2	26.8
7: Out-Other	359,727	1.0	0.8	0	0	0.2	0.8	2.6	4.1	14.1
8: In-Vehicle	523,967	2.1	1.6	0	0	0.5	1.7	5.3	8.1	34.3

Notes:
[a] See section 5.9 and Table 5-22 for details.
[b] This is the number of times the population experienced an exposure event in that microenvironment.
[c] These include all exposure events for the CHD population extracted from a 5,000 person simulation. See section 5.10 for details.
[d] The mean, standard deviation, and percentiles (p) were calculated using all events regardless of event duration. Note that based on the activity pattern diaries used, the length of an event can range from 1 minute to 1 hour.

6.1.2 Air quality adjusted to just meet the current 8-hour standard

As described in section 5.6, historical ambient monitoring data from each study area were adjusted to represent air quality that just meets the current 8-hour standard. For both Denver (year 1995) and Los Angeles (year 1997), air quality data were adjusted downwards to meet a 2nd highest 8-hour average concentration of 9.4 ppm. Note that even with a downward proportional adjustment, these adjusted ambient concentrations remain much higher than *as is* ambient air quality. Table 6-7 summarizes the exposure results for the simulated at-risk populations in the Denver study area when using these adjusted ambient CO concentrations as an input to APEX and using the same modeling assumptions and parameter distributions described in chapters 4 and 5.

Over half of the Denver at-risk population was estimated to experience a 1-hour daily maximum exposure at or above 12 ppm. This is nearly a factor of 10 greater than that estimated when using the *as is* air quality (Table 6-1). The highest 1-hour daily maximum exposure was estimated to be at or above 40 ppm (but below 60 ppm) when considering air quality adjusted to just meet the current standard, though only experienced by less than 0.2% of the simulated at-risk populations. Thus, there is a wider range in the exposure levels experienced by the simulated at-risk populations when considering this exposure scenario.

The number and percent of persons experiencing 8-hour daily maximum exposures is also greater for this scenario when compared with corresponding levels using the *as is* air quality. Nearly 10% of the simulated at-risk population was estimated to experience an 8-hour daily maximum exposure at or above 9 ppm (Table 6-7) when considering air quality just meeting the current 8-hour standard. Most of the CHD or HD population (>99%) would not experience an 8-hour daily maximum concentration at that same level when considering the *as is* air quality scenario (Table 6-1).

Indoor microenvironments simulated in Denver were estimated to contribute to a greater percentage of time spent at each selected exposure level using the adjusted air quality when compared with the results using *as is* air quality, though the difference is most notable at exposures less than 9 ppm (Figure 6-3). For example, about 50% of exposures that occurred at or above 3 ppm were experienced within indoor microenvironments when air quality just meets the current standard (Figure 6-3), while indoor microenvironments account for less than 20% of exposures when considering *as is* air quality (Figure 6-1). Indoor microenvironments would be expected to play a larger role in low level exposures when using air quality adjusted to just meet the current standard given the higher ambient concentrations across the entire air quality distribution when compared with *as is* air quality.

As was observed for both locations using *as is* air quality, the distributions of microenvironment to ambient concentration ratios are largely the same when comparing microenvironments (Table 6-8), likely a function of the same algorithm and parameter inputs used for each scenario and location. Also as expected, the estimated microenvironmental concentrations (Table 6-9) are higher across the entire distribution when compared with those estimated when considering the *as is* exposure scenario (Table 6-3).

Table 6-7. Estimated daily maximum 1-hour and 8-hour exposures for simulated at-risk populations in the Denver study area – air quality just meeting the current 8-hour standard.

Daily Maximum Exposure (ppm)		Coronary Heart Disease[a,c]				All Heart Disease[b,c]			
		Persons		Person-days		Persons		Person-days	
		Number	Percent	Number	Percent	Number	Percent	Number	Percent
1-hour	≥ 0	53,656	100	19,580,000	100	85,926	100	31,360,000	100
	≥ 3	53,656	100	8,638,000	44.1	85,926	100	13,960,000	44.5
	≥ 6	53,039	98.9	1,625,000	8.3	84,964	98.9	2,660,000	8.5
	≥ 9	44,598	83.1	404,800	2.1	71,426	83.1	666,400	2.1
	≥ 12	28,469	53.1	127,300	0.7	45,919	53.4	206,700	0.7
	≥ 15	16,610	31.0	46,710	0.2	26,840	31.2	75,350	0.2
	≥ 20	6,022	11.2	10,290	< 0.1	9,885	11.5	16,500	< 0.1
	≥ 30	691	1.3	802	< 0.1	1,283	1.5	1,493	< 0.1
	≥ 40	86	0.2	86	< 0.1	136	0.2	136	< 0.1
	≥ 60	0	0	0	0	0	0	0	0
8-hour	≥ 0	53,656	100	19,580,000	100	85,926	100	31,360,000	100
	≥ 3	52,706	98.2	2,690,000	13.7	84,445	98.3	4,318,000	13.8
	≥ 6	23,879	44.5	97,760	0.5	38,132	44.4	157,000	0.5
	≥ 9	5,060	9.4	9,724	< 0.1	7,861	9.1	14,850	< 0.1
	≥ 12	1,037	1.9	1,382	< 0.1	1,666	1.9	2,197	< 0.1
	≥ 15	309	0.6	346	< 0.1	457	0.5	531	< 0.1
	≥ 20	37	< 0.1	37	< 0.1	62	< 0.1	62	< 0.1
	≥ 30	0	0	0	0	0	0	0	0
	≥ 40	0	0	0	0	0	0	0	0
	≥ 60	0	0	0	0	0	0	0	0

Notes:
Ambient concentrations from 1995 were adjusted to just meet a 2nd highest 8-hour average concentration of 9.4 ppm using a relationship derived from the design monitor (ID 080310002).
[a] Persons with diagnosed coronary heart disease, angina pectoris, and heart attack (CDC, 2009).
[b] Inclusive of those persons with diagnosed coronary heart disease, angina pectoris, heart attack, and any other heart condition or disease (CDC, 2009).
[c] Includes estimate of persons with undiagnosed ischemia developed by EPA (see section 5.5.1.1).

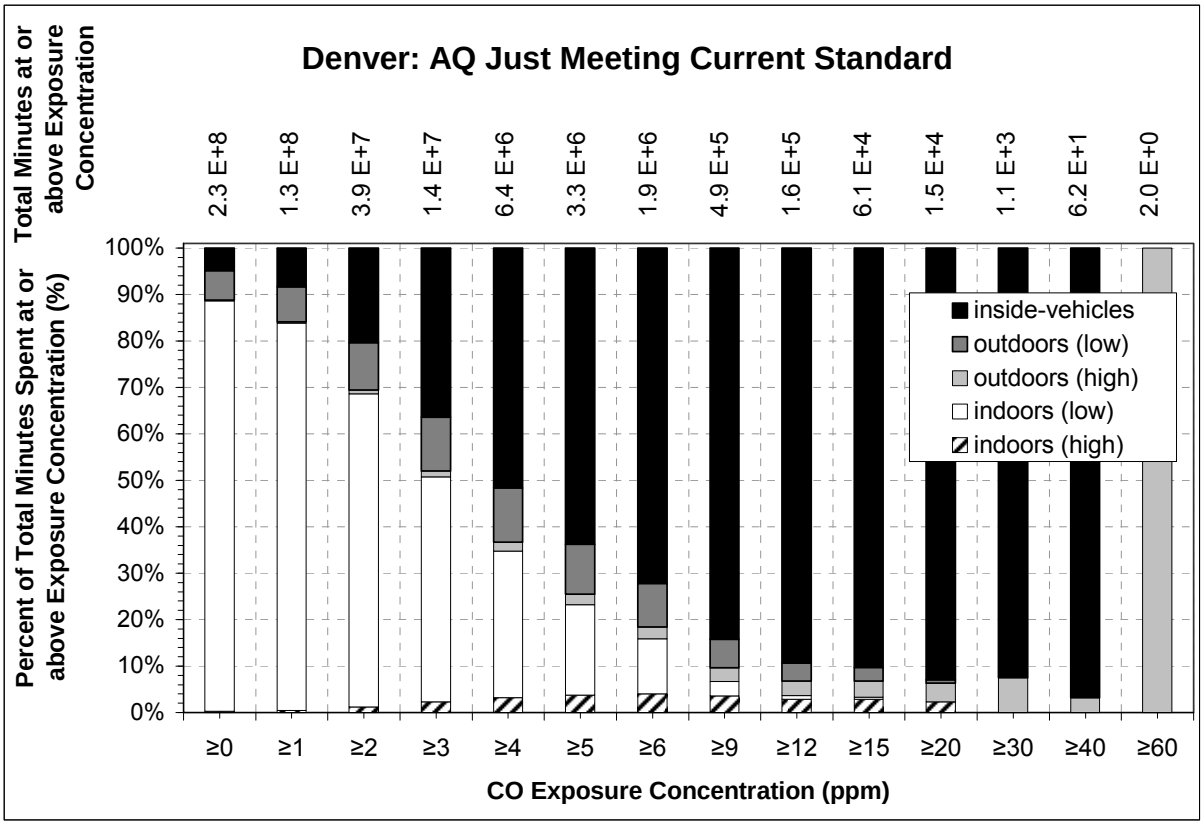

Figure 6-3. Estimated microenvironmental contributions to time spent at or above selected exposure concentrations using the Denver CHD population – air quality just meeting the current 8-hour standard. The total minutes spent at or above each exposure concentration are presented above each bar.

Table 6-8. Estimated distribution of microenvironment-to-ambient concentration ratios using the Denver CHD population – air quality just meeting the current 8-hour standard.

Microenvironment[a]	Events[b,c] (n)	Mean Ratio[c,d] (unitless)	Std	Distribution Percentiles[c,d] (unitless)						
				min	p1	p5	p50	p95	p99	max
1: In-Residence	1,633,520	0.9	0.5	0.1	0.2	0.3	0.8	1.8	2.3	5.5
2: In-Service Station	7,342	2.8	1.3	0.4	0.8	1.2	2.6	5.3	7.0	10.5
3: In-Other A	202,514	1.1	0.5	0.1	0.3	0.5	1.0	2.1	2.7	6.2
4: In-Other B	76,797	0.9	0.4	0.1	0.3	0.4	0.8	1.7	2.3	6.0
5: Out-Near Road	43,108	1.5	0.8	0.1	0.4	0.6	1.3	2.9	4.0	9.6
6: Out-Parking Lot/ Refueling	16,563	2.6	1.3	0.2	0.7	1.0	2.4	5.2	6.9	13.6
7: Out-Other	130,733	1.4	0.7	0.1	0.4	0.5	1.2	2.7	3.7	8.5
8: In-Vehicle	228,813	2.6	1.4	0	0.7	1.0	2.3	5.3	7.1	17.7

Notes:
[a] See section 5.9 and Table 5-22 for details.
[b] This is the number of times the population experienced an exposure event in that microenvironment.
[c] Data set used to calculate the ratios represents the CHD population extracted from a 5,000 person simulation and was screened to eliminate ambient concentrations less than 1 ppm. See section 5.10 for details.
[d] The mean, standard deviation, and percentiles (p) were calculated using all events regardless of event duration. Note that based on the activity pattern diaries used, the length of an event can range from 1 minute to 1 hour.

Table 6-9. Estimated distribution of microenvironmental concentrations using the Denver CHD population – air quality just meeting the current 8-hour standard.

Microenvironment[a]	Events[b,c] (n)	Mean CO[c,d] (ppm)	Std	Distribution Percentiles[c,d] (ppm)						
				min	p1	p5	p50	p95	p99	max
1: In-Residence	4,047,786	1.2	0.8	0	0.3	0.4	1.0	2.7	4.0	16.6
2: In-Service Station	17,781	3.7	2.2	0.4	1.0	1.3	3.2	8.0	11.4	25.0
3: In-Other A	489,984	1.4	0.9	0.1	0.4	0.5	1.2	3.2	4.7	16.6
4: In-Other B	186,897	1.2	0.8	0.1	0.3	0.4	1.0	2.6	3.9	11.4
5: Out-Near Road	100,520	2.0	1.4	0.1	0.4	0.6	1.6	4.7	7.1	22.5
6: Out-Parking Lot/ Refueling	39,895	3.5	2.5	0	0.7	1.0	2.8	8.0	12.4	63.4
7: Out-Other	351,163	1.7	1.3	0	0.3	0.5	1.3	4.1	6.4	25.5
8: In-Vehicle	548,978	3.5	2.5	0	0.8	1.1	2.8	8.2	12.8	56.9

Notes:
[a] See section 5.9 and Table 5-22 for details.
[b] This is the number of times the population experienced an exposure event in that microenvironment.
[c] These include all exposure events for the CHD population extracted from a 5,000 person simulation. See section 5.10 for details.
[d] The mean, standard deviation, and percentiles (p) were calculated using all events regardless of event duration. Note that based on the activity pattern diaries used, the length of an event can range from 1 minute to 1 hour.

Similarly in Los Angeles, the number and percent of persons exposed above selected exposure concentrations is greater when considering the air quality adjusted to just meet the current standard than when using *as is* air quality. For example, nearly 50% of the CHD population was estimated to experience a 1-hour daily maximum exposure of 9 ppm when considering air quality just meeting the current standard (Table 6-8), while only 32% were estimated to experience a similar concentration using *as is* air quality (Table 6-2). The range of the 1-hour daily maximum exposure distribution extends upward to 30 ppm, but less than 40 ppm for this scenario in Los Angeles. This estimate of an upper level is below the maximum in-vehicle concentration of 46 ppm measured by Shikiya (1989) during 112 southern California commutes in wintertime in 1987-88, of average duration shorter than an hour.[4] For a time period closer to the present scenario, Rodes et al. (1998) reported maximum in-vehicle and on-road CO concentrations of only 7.6 and 9.0 ppm, respectively during Los Angeles commutes in 1997. Note however the scripted commutes in this latter study are not necessarily directly comparable to this modeled data, as the measurements were time-averaged for two hours, the sample size was limited to about 30 total samples, and data were collected over nine days in the fall.

When comparing the overall population exposure distribution for Los Angeles to Denver for this exposure scenario, there are greater percentages of persons and person-days estimated for the Denver simulated at-risk populations at each corresponding exposure level. For example, only 2.7% of the CHD population was estimated to experience an 8-hour daily maximum exposure at or above 9 ppm in Los Angeles (Table 6-10), while in Denver, the estimated percent of the CHD population exposed at this level was over a factor of three greater (9.4%) (Table 6-7). This result is likely driven by differences observed at the upper tails of the air quality distribution noted in section 5.7.3, even though both study areas have ambient concentrations adjusted to just meet the same 8-hour average CO concentration of 9.4 ppm.

[4] On average, the commute time associated with the collection of these samples was 33 minutes. The reported mean 4-hour integrated ambient monitor concentrations was 3.6 ppm (std = 2.1; max = 8.6 ppm).

Table 6-10. Estimated daily maximum 1-hour and 8-hour exposures for simulated at-risk populations in the Los Angeles study area – air quality just meeting the current 8-hour standard.

Daily Maximum Exposure (ppm)		Coronary Heart Disease[a,c]				All Heart Disease[b,c]			
		Persons		Person-days		Persons		Person-days	
		Number	Percent	Number	Percent	Number	Percent	Number	Percent
1-hour	≥ 0	383,040	100	139,800,000	100	630,807	100	230,200,000	100
	≥ 3	383,040	100	36,430,000	26.1	630,807	100	59,960,000	26.0
	≥ 6	335,975	87.7	4,826,000	3.5	553,536	87.8	7,828,000	3.4
	≥ 9	189,563	49.5	982,300	0.7	305,268	48.4	1,550,000	0.7
	≥ 12	83,693	21.9	257,200	0.2	130,356	20.7	396,600	0.2
	≥ 15	36,126	9.4	80,180	< 0.1	55,293	8.8	119,900	< 0.1
	≥ 20	8,731	2.3	14,450	< 0.1	13,547	2.1	20,970	< 0.1
	≥ 30	803	0.2	803	< 0.1	1,004	0.2	1,004	< 0.1
	≥ 40	0	0	0	0	0	0	0	0
	≥ 60	0	0	0	0	0	0	0	0
8-hour	≥ 0	383,040	100	139,800,000	100	630,807	100	230,200,000	100
	≥ 3	342,598	89.4	8,655,000	6.2	562,166	89.1	14,190,000	6.2
	≥ 6	75,966	19.8	262,600	0.2	122,328	19.4	405,100	0.2
	≥ 9	10,336	2.7	18,670	< 0.1	16,157	2.6	28,600	< 0.1
	≥ 12	1,505	0.4	2,308	< 0.1	2,007	0.3	3,011	< 0.1
	≥ 15	301	0.1	401	< 0.1	502	< 0.1	602	< 0.1
	≥ 20	100	<0.1	100	< 0.1	100	< 0.1	100	< 0.1
	≥ 30	0	0	0	0	0	0	0	0
	≥ 40	0	0	0	0	0	0	0	0
	≥ 60	0	0	0	0	0	0	0	0

Notes:
Ambient concentrations from 1997 were adjusted to just meet a 2nd highest 8-hour average concentration of 9.4 ppm using a relationship derived from the design monitor (ID 060371301).
[a] Persons with diagnosed coronary heart disease, angina pectoris, and heart attack (CDC, 2009).
[b] Inclusive of those persons with diagnosed coronary heart disease, angina pectoris, heart attack, and any other heart condition or disease (CDC, 2009).
[c] Includes estimate of persons with undiagnosed ischemia developed by EPA (see section 5.5.1.1).

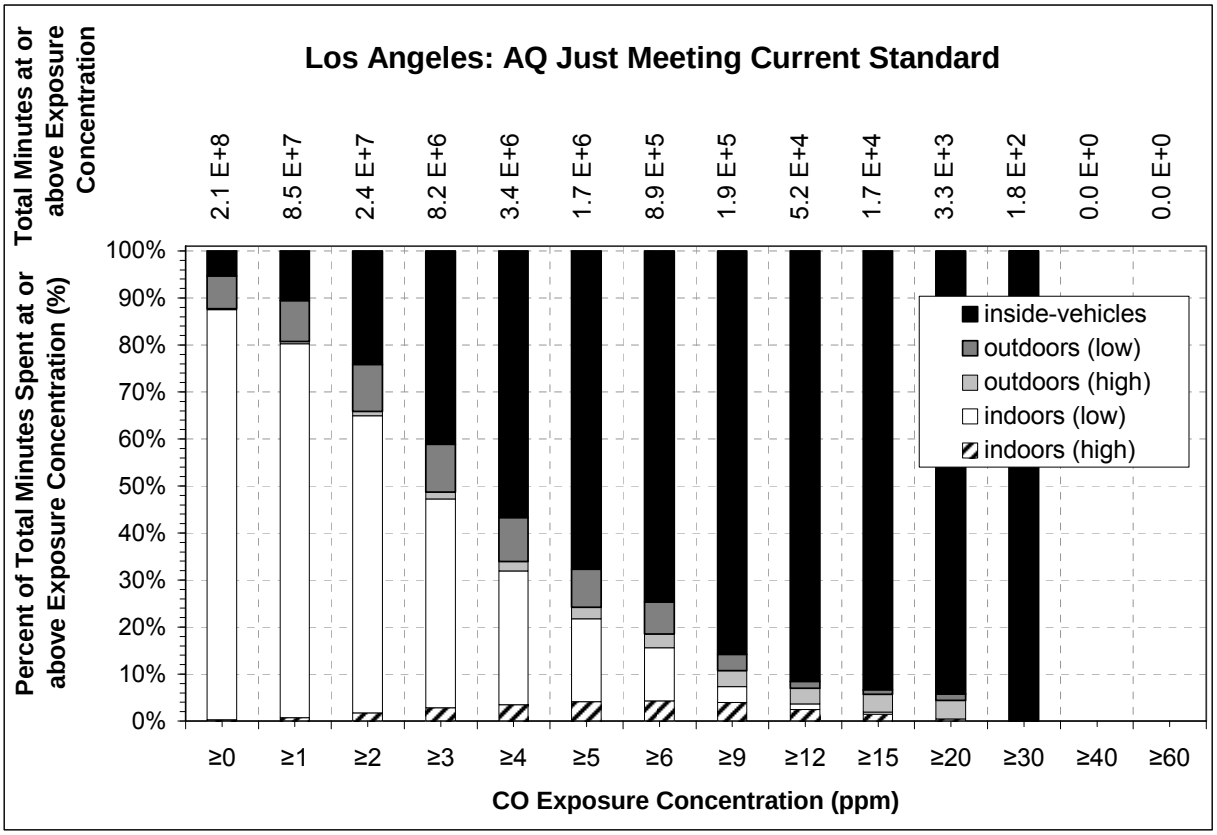

Figure 6-4. Estimated microenvironmental contributions to time spent at or above selected exposure concentrations using the Los Angeles CHD population – air quality just meeting the current 8-hour standard. The total minutes spent at or above each exposure concentration are presented above each bar.

The percent contribution of the aggregated microenvironments to the selected exposure levels in Los Angeles (Figure 6-4) is nearly identical to that estimated for Denver, given air quality adjusted to just meeting the current standard. The Los Angeles data differ in that upper-level exposure concentrations only extend upwards to about 30 ppm (occurring for about 180 event-level minutes), while in Denver there were a greater number of exposure events with concentrations at or above 40 ppm (occurring for about 1,100 event-level minutes). Not surprisingly, estimated microenvironment-to-ambient concentration ratios for this scenario (Table 6-11) were also similar to those for the Denver air quality scenarios (Tables 6-2 and 6-8) and those derived for the Los Angeles *as is* air quality (Table 6-5). Note also that estimated upper level concentrations here for the in-vehicle microenvironment are within the maximum measured peak level (one minute average) concentration reported by Rodes et al. (1998) of 67 ppm during rush hour commutes in Los Angeles (ISA, section 3.6.6.2).

Table 6-11. Estimated distribution of microenvironment-to-ambient concentration ratios using the Los Angeles CHD population – air quality just meeting the current 8-hour standard.

Microenvironment[a]	Events[b,c] (n)	Mean Ratio[c,d] (unitless)	Std	Distribution Percentiles[c,d] (unitless)						
				min	p1	p5	p50	p95	p99	max
1: In-Residence	1,087,377	1.0	0.5	0	0.3	0.4	0.9	1.8	2.4	6.6
2: In-Service Station	4,516	2.8	1.4	0.4	0.8	1.2	2.6	5.4	7.0	12.6
3: In-Other A	92,255	1.1	0.5	0	0.4	0.5	1.0	2.2	2.9	6.4
4: In-Other B	37,297	1.0	0.4	0	0.3	0.4	0.9	1.8	2.4	4.2
5: Out-Near Road	23,676	1.5	0.8	0	0.3	0.5	1.3	2.9	4.0	7.4
6: Out-Parking Lot/ Refueling	8,614	2.9	1.5	0	0.7	1.1	2.5	5.8	7.7	16.9
7: Out-Other	78,546	1.4	0.7	0	0.3	0.5	1.2	2.9	3.8	10.8
8: In-Vehicle	112,592	2.8	1.5	0	0.7	1.0	2.5	5.7	7.7	18.9

Notes:
[a] See section 5.9 and Table 5-22 for details.
[b] This is the number of times the population experienced an exposure event in that microenvironment.
[c] Data set used to calculate the ratios represents the CHD population extracted from a 5,000 person simulation and was screened to eliminate ambient concentrations less than 1 ppm. See section 5.10 for details.
[d] The mean, standard deviation, and percentiles (p) were calculated using all events regardless of event duration. Note that based on the activity pattern diaries used, the length of an event can range from 1 minute to 1 hour.

Table 6-12. Estimated distribution of microenvironmental concentrations using the Los Angeles CHD population – air quality just meeting the current 8-hour standard.

Microenvironment[a]	Events[b,c] (n)	Mean CO[c,d] (ppm)	Std	Distribution Percentiles[c,d] (ppm)						
				min	p1	p5	p50	p95	p99	max
1: In-Residence	3,621,050	1.0	0.7	0	0	0.2	0.8	2.4	3.5	15.7
2: In-Service Station	19,803	2.7	1.8	0	0	0.6	2.2	6.1	9.0	25.2
3: In-Other A	432,894	1.0	0.7	0	0	0.2	0.9	2.4	3.6	12.0
4: In-Other B	162,031	0.9	0.6	0	0	0.2	0.8	2.1	3.1	9.6
5: Out-Near Road	102,771	1.4	1.1	0	0	0.2	1.2	3.5	5.4	15.2
6: Out-Parking Lot/ Refueling	41,803	2.5	2.0	0	0	0.4	2.0	6.3	10.1	25.4
7: Out-Other	358,006	1.3	1.0	0	0	0.2	1.0	3.1	4.9	22.5
8: In-Vehicle	522,406	2.6	2.0	0	0	0.4	2.1	6.4	9.9	39.8

Notes:
[a] See section 5.9 and Table 5-22 for details.
[b] This is the number of times the population experienced an exposure event in that microenvironment.
[c] These include all exposure events for the CHD population extracted from a 5,000 person simulation. See section 5.10 for details.
[d] The mean, standard deviation, and percentiles (p) were calculated using all events regardless of event duration. Note that based on the activity pattern diaries used, the length of an event can range from 1 minute to 1 hour.

6.1.3 Air quality adjusted to just meet alternative air quality scenarios

Three potential alternative air quality scenarios were investigated to observe how the averaging times, forms, and levels for the simulated alternative standards would affect the estimated exposure concentrations (section 5.6). The data for the 1-hour and 8-hour daily maximum exposure concentrations are presented here, with a focus on the number and percent of persons exposed at selected concentrations. As observed in the above two sections summarizing exposures associated with *as is* air quality and air quality adjusted to just meet the current 8-hour standard, the distributions of the microenvironment–to-ambient concentration ratios are expected to be the same and are thus not provided here for the alternative air quality scenarios. The air quality associated with these alternative standards is generally similar to *as is* conditions. Therefore, the microenvironmental contributions to exposure and microenvironmental concentrations associated with these alternative standard scenarios are expected to be similar to those estimated for the *as is* scenario and are not included here.

Table 6-13 summarizes the 1-hour and 8-hour daily maximum exposures for each of the three alternative standards scenarios in the Denver study area, while Table 6-14 presents the same information for the Los Angeles study area. In comparing the exposure results for each potential alternative scenario within each study area and exposure averaging time, generally similar numbers of persons and their respective percentages of the simulated at-risk populations are observed at the same level. This was by general design, that is, to investigate differing forms of the potential alternative standards that would generate potentially similar exposure (and dose) results. Again, there is a wider range in the 1-hour exposure levels experienced by the simulated at-risk populations in Denver (Table 6-13) when compared with those of Los Angeles (Table 6-14) when considering the same potential alternative standard, consistent with the differing distribution of CO concentrations. There are also consistent patterns in the estimated distribution of 8-hour daily maximum exposures experienced by the simulated at-risk populations, though the upper range of that 8-hour maximum exposure is of course less than that of the 1-hour daily maximum in each respective location.

There is some variability in the percent of persons exposed when considering a particular level, form, and study area. For example, the 2nd highest 8-hour CO concentration of 5 ppm most limited the number and percent of exposed persons in each location when compared to results for the other potential alternative standard, though in Denver there were still a few persons estimated to experience a 1-hour daily maximum at or above 30 ppm (Table 6-13). In Los Angeles, the upper level of the 1-hour daily maximum exposure concentration experienced by the simulated CHD population was just at or above 20 ppm, though below 30 ppm.

Table 6-13. Estimated daily maximum 1-hour and 8-hour exposures for simulated at-risk populations in the Denver study area – alternative air quality scenarios.

Daily Maximum Exposure (ppm)		2nd highest 8-hour average of 5 ppm				99th pct 8-hour Daily Max of 5.0 ppm				99th pct 1-hour Daily Max of 8.0 ppm			
		CHD Persons[a,c]		HD Persons[b,c]		CHD Persons[a,c]		HD Persons[b,c]		CHD Persons[a,c]		HD Persons[b,c]	
		Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
1-hour	≥ 0	53,656	100	85,926	100	53,656	100	85,926	100	53,656	100	85,926	100
	≥ 3	53,656	100	85,926	100	53,656	100	85,926	100	53,656	100	85,926	100
	≥ 6	47,264	88.1	75,671	88.1	50,534	94.2	80,928	94.2	48,239	89.9	77,263	89.9
	≥ 9	25,174	46.9	40,489	47.1	32,147	59.9	51,645	60.1	26,877	50.1	43,241	50.3
	≥ 12	11,082	20.7	18,140	21.1	16,326	30.4	26,384	30.7	12,192	22.7	19,917	23.2
	≥ 15	4,850	9.0	7,886	9.2	7,676	14.3	12,501	14.5	5,282	9.8	8,688	10.1
	≥ 20	975	1.8	1,802	2.1	1,888	3.5	3,209	3.7	1,222	2.3	2,123	2.5
	≥ 30	62	0.1	74	< 0.1	136	0.3	247	0.3	74	0.1	111	0.1
	≥ 40	0	0	0	0	0	0	0	0	0	0	0	0
	≥ 60	0	0	0	0	0	0	0	0	0	0	0	0
8-hour	≥ 0	53,656	100	85,926	100	53,656	100	85,926	100	53,656	100	85,926	100
	≥ 3	44,574	83.1	71,488	83.2	48,819	91.0	78,189	91.0	45,808	85.4	73,376	85.4
	≥ 6	6,590	12.3	10,637	12.4	10,650	19.8	17,412	20.3	7,380	13.8	11,995	14.0
	≥ 9	839	1.6	1,296	1.5	1,555	2.9	2,369	2.8	926	1.7	1,469	1.7
	≥ 12	111	0.2	173	0.2	296	0.6	432	0.5	123	0.2	197	0.2
	≥ 15	25	< 0.1	37	< 0.1	49	< 0.1	74	< 0.1	25	< 0.1	37	< 0.1
	≥ 20	0	0	0	0	0	0	0	0	0	0	0	0
	≥ 30	0	0	0	0	0	0	0	0	0	0	0	0
	≥ 40	0	0	0	0	0	0	0	0	0	0	0	0
	≥ 60	0	0	0	0	0	0	0	0	0	0	0	0

Notes:
Ambient concentrations from 1995 were adjusted to just meet the level of the potential alternative standard indicated using a relationship derived from the design monitor (ID 080310002).
[a] Persons with diagnosed coronary heart disease, angina pectoris, and heart attack (CDC, 2009).
[b] Inclusive of those persons with diagnosed coronary heart disease, angina pectoris, heart attack, and any other heart condition or disease (CDC, 2009).
[c] Includes estimate of persons with undiagnosed ischemia developed by EPA (see section 5.5.1.1).

Table 6-14. Estimated daily maximum 1-hour and 8-hour exposures for simulated at-risk populations in the Los Angeles study area – alternative air quality scenarios.

Daily Maximum Exposure (ppm)		2nd highest 8-hour average of 5 ppm				99th pct 8-hour Daily Max of 5.0 ppm				99th pct 1-hour Daily Max of 8.0 ppm			
		CHD Persons[a,c]		HD Persons[b,c]		CHD Persons[a,c]		HD Persons[b,c]		CHD Persons[a,c]		HD Persons[b,c]	
		Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
1-hour	≥ 0	383,040	100	630,807	100	383,040	100	630,807	100	383,040	100	630,807	100
	≥ 3	378,624	98.8	624,183	99.0	379,728	99.1	626,090	99.3	381,535	99.6	628,498	99.6
	≥ 6	215,454	56.2	348,720	55.3	229,302	59.9	373,105	59.1	260,913	68.1	426,090	67.5
	≥ 9	68,540	17.9	105,469	16.7	77,571	20.3	120,321	19.1	98,244	25.6	154,641	24.5
	≥ 12	19,769	5.2	30,507	4.8	24,285	6.3	36,728	5.8	34,721	9.1	53,186	8.4
	≥ 15	6,322	1.7	9,533	1.5	7,827	2.0	11,841	1.9	10,738	2.8	16,759	2.7
	≥ 20	903	0.2	1,606	0.3	1,305	0.3	2,208	0.3	2,709	0.7	4,315	0.7
	≥ 30	0	0	0	0	0	0	0	0	0	0	0	0
	≥ 40	0	0	0	0	0	0	0	0	0	0	0	0
	≥ 60	0	0	0	0	0	0	0	0	0	0	0	0
8-hour	≥ 0	383,040	100	630,807	100	383,040	100	630,807	100	383,040	100	630,807	100
	≥ 3	214,149	55.9	350,626	55.6	230,807	60.3	376,918	59.8	264,425	69.0	430,707	68.3
	≥ 6	17,060	4.5	26,192	4.2	20,672	5.4	31,811	5.0	28,801	7.5	44,355	7.0
	≥ 9	903	0.2	1,204	0.2	1,204	0.3	1,706	0.3	2,007	0.5	3,011	0.5
	≥ 12	301	< 0.1	502	< 0.1	301	< 0.1	502	< 0.1	301	< 0.1	502	< 0.1
	≥ 15	0	0	0	0	100	< 0.1	100	< 0.1	100	< 0.1	201	< 0.1
	≥ 20	0	0	0	0	0	0	0	0	0	0	0	0
	≥ 30	0	0	0	0	0	0	0	0	0	0	0	0
	≥ 40	0	0	0	0	0	0	0	0	0	0	0	0
	≥ 60	0	0	0	0	0	0	0	0	0	0	0	0

Notes:
Ambient concentrations from 1997 were adjusted to just meet the level of the potential alternative standard indicated using a relationship derived from the design monitor (ID 060371301).
[a] Persons with diagnosed coronary heart disease, angina pectoris, and heart attack (CDC, 2009).
[b] Inclusive of those persons with diagnosed coronary heart disease, angina pectoris, heart attack, and any other heart condition or disease (CDC, 2009).
[c] Includes estimate of persons with undiagnosed ischemia developed by EPA (see section 5.5.1.1).

6.2 ESTIMATED COHB LEVELS

Consistent with section 6.1, this section summarizes the estimated COHb levels for the simulated at-risk populations in a series of tables, classified by the air quality scenarios and study areas considered. As was done in presenting the exposure results, we summarized the dose results corresponding to both the CHD and HD populations. For all five air quality scenarios, we report the number and percentage of persons and person-days estimated to have experienced selected levels of the dose metric of interest (daily maximum end-of-hour COHb level). In addition, we include an evaluation of the number of days in the year that individuals are estimated to experience a dose at or above the selected COHb level. For three of the scenarios (i.e., *as is* conditions, air quality adjusted to just meet the current 8-hour standard, and air quality adjusted to just meet a 99th percentile daily maximum 8-hour average concentration of 5.0 ppm), additional dose output data sets were generated using a smaller simulation size (i.e., 5,000 persons) and for the CHD population, to estimate the contribution of ambient CO exposure alone to selected COHb levels. See section 5.10 for details on the approach used and evaluation of the representativeness of the simulation size and at-risk population used.

6.2.1 Air Quality "As Is"

Table 6-15 provides the COHb levels (%) for the simulated at-risk populations in Denver when considering the *as is* air quality. No persons were estimated to have experienced a daily maximum end-of-hour COHb level at or above 2.5%, while only a few (<0.1%) were estimated to have experienced a COHb level ≥2.0%. Nearly 99% of the simulated at-risk populations had their highest daily maximum end-of-hour COHb level below 1.5%. Most of the simulated person-days (about 97.5%) were associated with daily maximum end-of-hour COHb levels below 1.0%.

Similarly in Los Angeles, very few persons (1.6%) were estimated to experience a daily maximum end-of-hour COHb level at or above 1.5% when considering the *as is* air quality (Table 6-16). Similar to that observed for the at-risk population in Denver, very few persons (<0.1%) were estimated to experience at least one daily maximum end-of-hour COHb levels at or above 2.0% in Los Angeles. Of these few hundred simulated individuals, all were estimated to have only one person-day per person at that level (i.e., to have experienced this COHb level on only one day in the year). As was observed with the Denver dose results, the majority of the simulated person-days (>98%) were limited to COHb levels at or below 1.0%.

Table 6-15. Portion of the simulated at-risk populations in the Denver study area estimated to experience a daily maximum end-of-hour COHb at or above specified levels– *as is* air quality.

COHb Level (%)	Coronary Heart Disease[a,c]				All Heart Disease[b,c]			
	Persons		Person-days		Persons		Person-days	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
≥ 0.0	53,656	100	19,580,000	100	85,926	100	31,360,000	100
≥ 1.0	10,773	20.1	494,600	2.5	17,807	20.7	781,100	2.5
≥ 1.5	654	1.2	17,170	< 0.1	1,074	1.2	29,050	< 0.1
≥ 1.75	111	0.2	2,616	< 0.1	234	0.3	3,579	< 0.1
≥ 2.0	12	< 0.1	86	< 0.1	12	< 0.1	86	< 0.1
≥ 2.5	0	0	0	0	0	0	0	0
≥ 3.0	0	0	0	0	0	0	0	0
≥ 4.0	0	0	0	0	0	0	0	0

Notes:
Unadjusted ambient concentrations from four monitors in 2006 were used to represent the *As Is* air quality scenario.
[a] Persons with diagnosed coronary heart disease, angina pectoris, and heart attack (CDC, 2009).
[b] Inclusive of those persons with diagnosed coronary heart disease, angina pectoris, heart attack, and any other heart condition or disease (CDC, 2009).
[c] Includes estimate of persons with undiagnosed ischemia developed by EPA (see section 5.5.1.1).

Table 6-16. Portion of the simulated at-risk populations in the Los Angeles study area estimated to experience a daily maximum end-of-hour COHb at or above specified levels – *as is* air quality.

COHb Level (%)	Coronary Heart Disease[a,c]				All Heart Disease[b,c]			
	Persons		Person-days		Persons		Person-days	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
≥ 0.0	383,040	100	139,800,000	100	630,807	100	230,200,000	100
≥ 1.0	99,348	25.9	1,725,000	1.2	165,880	26.3	3,112,000	1.4
≥ 1.5	6,021	1.6	91,120	< 0.1	9,834	1.6	165,200	< 0.1
≥ 1.75	1,907	0.5	18,870	< 0.1	3,011	0.5	28,100	< 0.1
≥ 2.0	301	< 0.1	301	< 0.1	502	< 0.1	502	< 0.1
≥ 2.5	0	0	0	0	0	0	0	0
≥ 3.0	0	0	0	0	0	0	0	0
≥ 4.0	0	0	0	0	0	0	0	0

Notes:
Unadjusted ambient concentrations from four monitors in 2006 were used to represent the *As Is* air quality scenario.
[a] Persons with diagnosed coronary heart disease, angina pectoris, and heart attack (CDC, 2009).
[b] Inclusive of those persons with diagnosed coronary heart disease, angina pectoris, heart attack, and any other heart condition or disease (CDC, 2009).
[c] Includes estimate of persons with undiagnosed ischemia developed by EPA (see section 5.5.1.1).

The population-based person-day dose metric was evaluated further by analyzing the number of days in the year each individual experiences a daily maximum end-of hour COHb at or above a selected level. As observed in the above analyses, there were little differences between the two simulated at-risk populations in the percentage estimated to experience a %COHb at or above selected levels. Therefore, we have chosen to use the CHD population as a base case for this analysis. Figure 6-5 presents the percent of the CHD populations in Denver (top) and Los Angeles (bottom) experiencing repeated COHb levels using *as is* air quality. As a point of reference in the figure, the percent of persons with the number of occurrences ≥ 1 corresponds to the data summarized in Tables 6-15 and 6-16.[5] Note that we have included only those COHb levels between 1.5 and 2.0%, though in 0.1% COHb increments.

Consistent with the summary tables, a small percentage of the CHD population (about 1.2% in Denver; 1.6% in Los Angeles) was estimated to experience a single COHb level at or above 1.5% (Figure 6-15). Even fewer persons experienced two or more occurrences of COHb above 1.5% (about 0.7% of the CHD population in Denver; 0.5% in Los Angeles), generally about a factor of two or three lower than when considering persons experiencing at least one COHb dose at or above that level. There were very few persons experiencing 3 or more COHb levels at or above 1.5% in either study area. Even fewer persons experienced multiple occurrences of higher COHb levels. For example less than 0.1% of the population experienced 3 or more COHb levels at or above 1.8% in either study area.

As discussed in chapter 2, we also evaluated the contribution of ambient CO exposure alone to each simulated person's COHb level. The complete time-series of exposure for each individual was used to generate each person's maximum end-of-hour COHb level attributable to ambient CO exposure. This analysis also focused on the CHD population as a base-case in each study area, given the limited differences between the percentage of persons at or above specific COHb levels for either simulated at-risk population. Table 6-17 summarizes the estimated COHb levels experienced by the CHD population for both study areas, using the *as is* air quality. None of the persons experienced a COHb level at or above 1.8% due to ambient CO exposure alone for this scenario in either study area. Estimated levels of maximum end-of-hour COHb attributable to ambient CO exposure were at or below 1.3% COHb for approximately 99% of the simulated CHD population. This is consistent with the above results for total COHb (Tables 6-15 and 6-16)[6] and the finding that endogenous CO production, on average, can contribute to an

[5] The number of occurrences in Figure 6-5 corresponds to the number of days per year each person(s) experienced a maximum end-of-hour COHb dose at or above the given level.

[6] We used the term total COHb here as the combined dose from ambient CO exposure and endogenous CO production.

end-of-hour COHb level of approximately 0.3% for the simulated at-risk population in either study area (Appendix B, Table B-4).

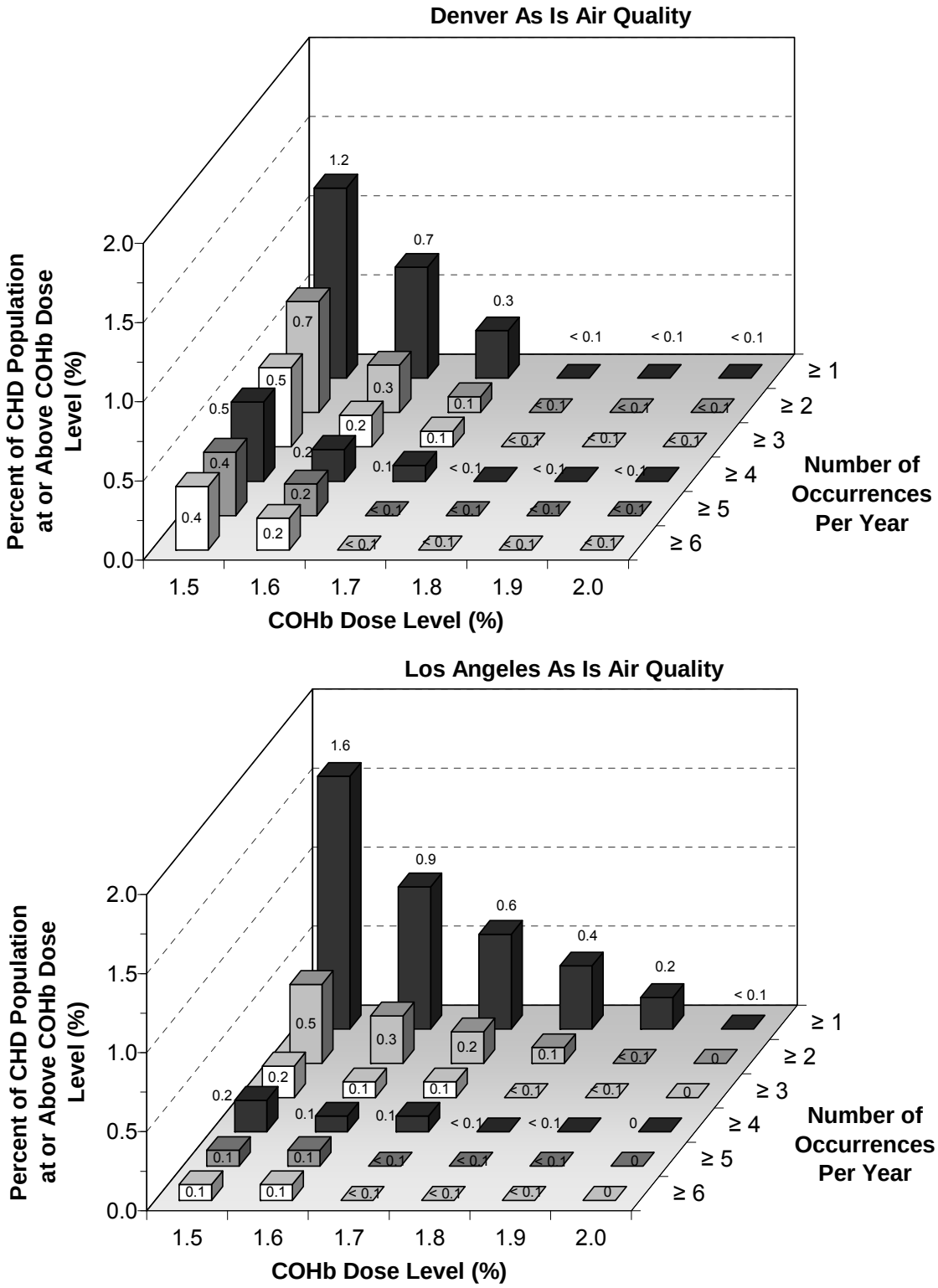

Figure 6-5. Estimated percent of the CHD population in Denver (top) and Los Angeles (bottom) experiencing repeated COHb levels – as is air quality.

Table 6-17. Percentages of the simulated CHD populations in the Denver and Los Angeles study areas estimated to experience a daily maximum end-of-hour COHb contribution from ambient exposure alone at or above specified levels – *as is* air quality.

Ambient-Exposure Contribution to COHb Level (%)	Percent of CHD Population[a]	
	Denver	Los Angeles
≥ 1.0	2.1	7.1
≥ 1.1	1.4	5.3
≥ 1.2	0.9	3.0
≥ 1.3	0.7	1.5
≥ 1.4	0.2	0.5
≥ 1.5	0.2	0.5
≥ 1.6	0.2	0.5
≥ 1.7	0	0.3
≥ 1.8	0	0
≥ 1.9	0	0
≥ 2.0	0	0

Notes:
Unadjusted ambient concentrations from 2006 were used to represent the *As Is* air quality scenario.
[a] Persons with diagnosed coronary heart disease, angina pectoris, and heart attack (CDC, 2009). Includes estimate of persons with undiagnosed ischemia developed by EPA (see section 5.5.1.1).

6.2.2 Air Quality Adjusted to Just Meet the Current 8-hour Standard

Consistent with the estimated exposure concentrations, COHb levels estimated to be experienced by the simulated at-risk populations in each study area were greater when considering exposures associated with air quality adjusted to just meet the current standard than when using *as is* air quality. For example, in Denver, just over 4% of the simulated at-risk populations were estimated to have experienced a daily maximum end-of-hour COHb level at or above 2.0% (Table 6-18). Note there were fewer than 0.1% of persons in Denver estimated to have experienced COHb at a level above 2.0% based on estimated ambient exposures associated with *as is* air quality (Table 6-15). A similar pattern is observed for the simulated at-risk population in Los Angeles (Table 6-19), though a lower percentage of persons (0.6%) were estimated to have experienced a daily maximum end-of-hour COHb level at or above 2.0% when compared to the results for Denver. In both study areas, a few persons were estimated to have experienced a daily maximum end-of-hour COHb levels as high as 3.0%. However, most of the persons that did experience these higher COHb levels (≥2.0%) experienced them for fewer than 2 days in a year (Table 6-19). A general pattern in experiencing multiple days at or above selected COHb levels is evident in Figure 6-6. The percent of the population that experiences two or more occurrences of %COHb at or above selected levels is reduced by about a factor of two when compared with those experiencing at least one. Even fewer persons experience three

or more days per year, also reduced by about a factor of about 2 when compared with those experiencing at least two. When considering three or more occurrences in a year, the reduction rate in the percent of persons at or above the selected COHb levels lessens with increasing number of occurrences. In general, this pattern indicates a few simulated individuals, given specific conditions of their estimated exposure and dose, experienced multiple days (e.g., possibly 6 or more) at or above selected COHb levels.

Table 6-18. Portion of the simulated at-risk populations in the Denver study area estimated to experience a daily maximum end-of-hour COHb at or above specified levels – air quality just meeting the current 8-hour standard.

COHb Level (%)	Coronary Heart Disease[a,c]				All Heart Disease[b,c]			
	Persons		Person-days		Persons		Person-days	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
≥ 0.0	53,656	100	19,580,000	100	85,926	100	31,360,000	100
≥ 1.0	44,166	82.3	1,330,000	6.8	71,710	83.5	2,125,000	6.8
≥ 1.5	12,563	23.4	79,050	0.4	21,028	24.5	124,800	0.4
≥ 1.75	5,800	10.8	15,240	< 0.1	9,502	11.1	24,820	< 0.1
≥ 2.0	2,258	4.2	3,677	< 0.1	3,826	4.5	6,047	< 0.1
≥ 2.5	444	0.8	494	< 0.1	802	0.9	901	< 0.1
≥ 3.0	111	0.2	111	< 0.1	222	0.3	247	< 0.1
≥ 4.0	12	< 0.1	12	< 0.1	25	< 0.1	25	< 0.1

Notes:
Ambient concentrations from 1995 were adjusted to just meet a 2nd highest 8-hour average concentration of 9.4 ppm using a relationship derived from the design monitor (ID 080310002).
[a] Persons with diagnosed coronary heart disease, angina pectoris, and heart attack (CDC, 2009).
[b] Inclusive of those persons with diagnosed coronary heart disease, angina pectoris, heart attack, and any other heart condition or disease (CDC, 2009).
[c] Includes estimate of persons with undiagnosed ischemia developed by EPA (see section 5.5.1.1).

Table 6-19. Portion of the simulated at-risk populations in the Los Angeles study area estimated to experience a daily maximum end-of-hour COHb at or above specified levels – air quality just meeting the current 8-hour standard.

COHb Level (%)	Coronary Heart Disease[a,c]				All Heart Disease[b,c]			
	Persons		Person-days		Persons		Person-days	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
≥ 0.0	383,040	100	139,800,000	100	630,807	100	230,200,000	100
≥ 1.0	157,852	41.2	2,584,000	1.8	260,612	41.3	4,598,000	2.0
≥ 1.5	17,963	4.7	125,400	< 0.1	31,410	5.0	227,400	< 0.1
≥ 1.75	6,222	1.6	30,510	< 0.1	10,537	1.7	50,280	< 0.1
≥ 2.0	2,107	0.6	3,211	< 0.1	3,613	0.6	4,716	< 0.1
≥ 2.5	301	< 0.1	401	< 0.1	401	< 0.1	502	< 0.1
≥ 3.0	100	< 0.1	100	< 0.1	100	< 0.1	100	< 0.1
≥ 4.0	0	0	0	0	0	0	0	0

Notes:
Ambient concentrations from 1997 were adjusted to just meet a 2nd highest 8-hour average concentration of 9.4 ppm using a relationship derived from the design monitor (ID 060371301).
[a] Persons with diagnosed coronary heart disease, angina pectoris, and heart attack (CDC, 2009).
[b] Inclusive of those persons with diagnosed coronary heart disease, angina pectoris, heart attack, and any other heart condition or disease (CDC, 2009).
[c] Includes estimate of persons with undiagnosed ischemia developed by EPA (see section 5.5.1.1).

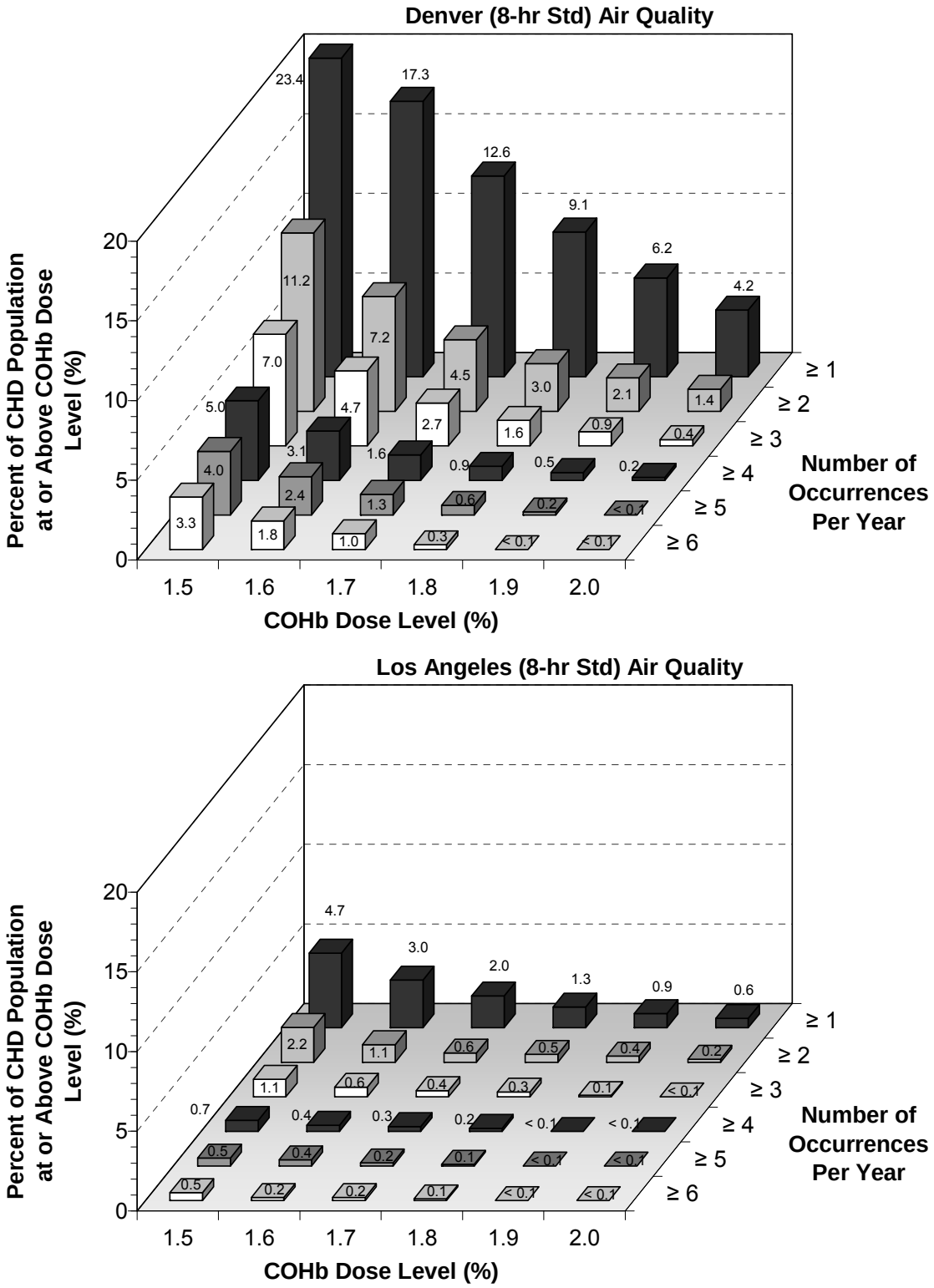

Figure 6-6. Estimated percent of the CHD population in Denver (top) and Los Angeles (bottom) experiencing repeated COHb levels – air quality just meeting the current 8-hour standard.

Table 6-20. Percentage of simulated CHD populations in the Denver and Los Angeles study areas estimated to experience daily maximum end-of-hour COHb contribution from ambient exposure alone at or above specified levels – air quality just meeting the current 8-hour standard.

Ambient-Exposure Contribution to COHb Level (%)	Percent of CHD Population[a]	
	Denver	Los Angeles
≥ 1.0	43.6	17.3
≥ 1.1	30.4	11.2
≥ 1.2	21.0	7.6
≥ 1.3	16.0	4.1
≥ 1.4	12.8	2.0
≥ 1.5	9.4	1.8
≥ 1.6	6.8	1.3
≥ 1.7	4.1	0.8
≥ 1.8	3.4	0.8
≥ 1.9	3.0	0.5
≥ 2.0	2.7	0.5

Notes:
Ambient concentrations from were adjusted to just meet a 2nd highest 8-hour average concentration of 9.4 ppm.
[a] Persons with diagnosed coronary heart disease, angina pectoris, and heart attack (CDC, 2009). Includes estimate of persons with undiagnosed ischemia developed by EPA (see section 5.5.1.1).

Table 6-20 summarizes the percentages of the CHD population for both study areas estimated to have experienced COHb levels at or above selected levels, when considering ambient CO exposure alone (i.e., COHb level in the absence of endogenous CO production) and using air quality adjusted to just meet the current 8-hour standard. As observed above (Tables 6-18 and 6-19), there are differences between the two study areas when comparing the percent of the CHD population estimated to experience a given COHb level. Approximately 9% of the Denver population is estimated to have experienced a daily maximum end-of-hour COHb level at or above 1.5% due to ambient CO exposure alone, while it was estimated that about 2% of the simulated at-risk population in Los Angeles had at least one occurrence at this level.

6.2.3 Air Quality Adjusted to Just Meet Alternative Air Quality Scenarios

Consistent with the exposure results described above, the percentage of persons estimated to experience a daily maximum end-of-hour COHb at or above the selected levels is generally similar across the three potential alternative standard scenarios. For example, in Denver most of the population (≥99%) was estimated to not experience a daily maximum end-of-hour COHb level at or above 2.0% (Table 6-21). Further, the potential alternative standard of a 2nd highest 8-

hour average of 5 ppm resulted in the lowest number and percent of the simulated population experiencing at least one occurrence of %COHb at or above the selected levels.

There are a few study area differences worthy of note. As expected, the corresponding estimated percent of the CHD population experiencing a particular dose level in Denver is greater than that estimated for Los Angeles, even when considering the same potential alternative standard form and air quality level. For example, when considering a 99th percentile daily maximum 8-hour average CO concentration of 5.0 ppm, 1.0% of the CHD population in the Denver study area was estimated to have experienced an estimated daily maximum end-of-hour COHb level at or above 2.0% (Table 6-21); in Los Angeles this dose level was estimated to have been experienced by fewer than 0.1% of the CHD population (Table 6-22). Again, this is largely a function of the differences observed between the upper percentile ambient concentrations used to simulate these air quality scenarios in each study area (i.e., greater spatial variability in ambient concentrations in the larger Los Angeles study area) and the large differences in altitude between the two study areas.

Table 6-23 summarizes the percentage of the CHD population in both study areas estimated to have experienced selected levels of COHb, when considering ambient CO exposure alone (i.e., COHb level in the absence of endogenous CO production) and using air quality adjusted to just meet a 99th percentile daily maximum 8-hour average concentration of 5.0 ppm. As observed above (Tables 6-21 and 6-22), there is a similar pattern when comparing the two study areas and the percent of the CHD population estimated to have experienced a given COHb level. Approximately 3.2% of the Denver population experienced a daily maximum end-of-hour COHb level at or above 1.5% due to ambient CO exposure alone, while in Los Angeles, it was estimated that about 0.3% of the simulated at-risk population had at least one occurrence at this level.

Table 6-21. Portion of the simulated at-risk populations in the Denver study area estimated to experience a daily maximum end-of-hour COHb at or above specified levels– air quality just meeting potential alternative standards.

COHb Level (%)	2nd highest 8-hour average of 5 ppm				99th pct 8-hour Daily Max of 5.0 ppm				99th pct 1-hour Daily Max of 8.0 ppm			
	CHD Persons[a,c]		HD Persons[b,c]		CHD Persons[a,c]		HD Persons[b,c]		CHD Persons[a,c]		HD Persons[b,c]	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
≥ 0.0	53,656	100	85,926	100	53,656	100	85,926	100	53,656	100	85,926	100
≥ 1.0	24,212	45.1	39,773	46.3	31,690	59.1	51,459	59.9	25,656	47.8	42,031	48.9
≥ 1.5	2,764	5.2	4,640	5.4	4,961	9.2	8,256	9.6	3,171	5.9	5,282	6.1
≥ 1.75	802	1.5	1,382	1.6	1,703	3.2	2,789	3.2	1,074	2.0	1,740	2.0
≥ 2.0	284	0.5	494	0.6	555	1.0	975	1.1	284	0.5	518	0.6
≥ 2.5	62	0.1	86	0.1	111	0.2	210	0.2	74	0.1	111	0.1
≥ 3.0	0	0	12	< 0.1	12	< 0.1	37	< 0.1	12	< 0.1	25	< 0.1
≥ 3.5	0	0	0	0	0	0	12	< 0.1	0	0	12	< 0.1
≥ 4.0	0	0	0	0	0	0	0	0	0	0	0	0

Notes:
Ambient concentrations from 1995 were adjusted to just meet the level of the potential alternative standard indicated using a relationship derived from the design monitor (ID 080310002).
[a] Persons with diagnosed coronary heart disease, angina pectoris, and heart attack (CDC, 2009).
[b] Inclusive of those persons with diagnosed coronary heart disease, angina pectoris, heart attack, and any other heart condition or disease (CDC, 2009).
[c] Includes estimate of persons with undiagnosed ischemia developed by EPA (see section 5.5.1.1).

Table 6-22. Portion of the simulated at-risk populations in the Los Angeles study area estimated to experience a daily maximum end-of-hour COHb at or above specified levels – air quality just meeting potential alternative standards.

COHb Level (%)	2nd highest 8-hour average of 5 ppm				99th pct 8-hour Daily Max of 5.0 ppm				99th pct 1-hour Daily Max of 8.0 ppm			
	CHD Persons[a,c]		HD Persons[b,c]		CHD Persons[a,c]		HD Persons[b,c]		CHD Persons[a,c]		HD Persons[b,c]	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
≥ 0.0	383,040	100	630,807	100	383,040	100	630,807	100	383,040	100	630,807	100
≥ 1.0	54,491	14.2	91,319	14.5	62,017	16.2	102,258	16.2	78,776	20.6	130,858	20.7
≥ 1.5	2,509	0.7	4,917	0.8	3,613	0.9	6,121	1.0	5,319	1.4	9,232	1.5
≥ 1.75	803	0.2	1,305	0.2	1,004	0.3	1,706	0.3	1,706	0.4	3,011	0.5
≥ 2.0	301	< 0.1	401	< 0.1	301	< 0.1	401	< 0.1	401	0.1	502	< 0.1
≥ 2.5	0	0	0	0	0	0	0	0	0	0	0	0
≥ 3.0	0	0	0	0	0	0	0	0	0	0	0	0
≥ 3.5	0	0	0	0	0	0	0	0	0	0	0	0
≥ 4.0	0	0	0	0	0	0	0	0	0	0	0	0

Notes:
Ambient concentrations from 1997 were adjusted to just meet the level of the potential alternative standard indicated using a relationship derived from the design monitor (ID 060371301).
[a] Persons with diagnosed coronary heart disease, angina pectoris, and heart attack (CDC, 2009).
[b] Inclusive of those persons with diagnosed coronary heart disease, angina pectoris, heart attack, and any other heart condition or disease (CDC, 2009).
[c] Includes estimate of persons with undiagnosed ischemia developed by EPA (see section 5.5.1.1).

Table 6-23. Percentage of simulated CHD populations in the Denver and Los Angeles study areas estimated to experience daily maximum end-of-hour COHb contribution from ambient exposure alone at or above specified levels – air quality just meeting a 99th percentile daily maximum 8-hour average concentration of 5.0 ppm.

Ambient-Exposure Contribution to COHb Level (%)	Percent of CHD Population[a]	
	Denver	Los Angeles
≥ 1.0	18.0	2.8
≥ 1.1	13.2	1.8
≥ 1.2	8.9	1.3
≥ 1.3	5.9	0.8
≥ 1.4	3.7	0.5
≥ 1.5	3.2	0.3
≥ 1.6	2.7	0.3
≥ 1.7	2.1	0.3
≥ 1.8	0.9	0.3
≥ 1.9	0.7	0.3
≥ 2.0	0.2	0.3

Notes:
Ambient concentrations from were adjusted to just meet a 99th percentile daily maximum 8-hour average concentration of 5.0 ppm.
[a] Persons with diagnosed coronary heart disease, angina pectoris, and heart attack (CDC, 2009). Includes estimate of persons with undiagnosed ischemia developed by EPA (see section 5.5.1.1).

6.3 COMPARISON OF COHB ESTIMATES OBTAINED FROM THE 2000 PNEM/CO AND 2010 APEX/CO ASSESSMENTS

As described above in chapters 2 and 4, population exposure and dose were estimated in 2000 using pNEM/CO, a predecessor to APEX, for adults with ischemic heart disease (IHD) residing in a defined study area within the same two urban areas (Johnson et al., 2000). As described in section 1.2 above, IHD is also termed CHD, and with regard to characterizing the population of interest with regard to demographics (age and gender), the 2000 assessment, like the current assessment, drew from estimates of the prevalence provided by the NHIS (which includes CHD or IHD, angina pectoris, and heart attack) and corresponding estimates of undiagnosed ischemia developed by EPA. As part of this current (2010) CO REA, staff has used APEX to estimate CO exposures and resulting COHb levels using a largely similar approach,

modeling domains, years of ambient concentration data,[7] and defined at-risk population.[8] There are some differences that exist when comparing details of the methodologies and data sets used:

- number of ambient monitors used (e.g., previously six in Denver versus four used here),[9]
- location of ambient monitors used (e.g., eight of the same monitors used previously were used here for Los Angeles),
- number of microenvironments modeled (previously 15 versus the 8 modeled here),
- use of mass balance modeling (previously all 12 enclosed microenvironments used mass balance, here only indoor microenvironments used a mass balance approach)
- use of a cohort approach (pNEM) versus individual approach (APEX), and
- inclusion of two indoor emission sources of CO in the 2000 pNEM/CO assessment for residential microenvironments: gas stoves and passive smoking.

Despite these differences and a few others not listed, staff still did not expect to see greatly different results when comparing the two assessments given the similarities in the most likely influential variables (i.e., ambient CO concentrations, microenvironmental approach, CFK module used, etc.). Table 6-24 presents estimates for the percentage of Denver adults with CHD estimated to experience a daily maximum end-of-hour %COHb at or above the selected level under the specified air quality conditions for 1995. Table 6-25 presents similar estimates for Los Angeles using the 1997 ambient air quality data adjusted to just meet the current 8-hour standard. Each table provides two sets of COHb level estimates for the 2000 pNEM/CO assessment (one with and the other without indoor source emissions) and one set generated from the current (2010) APEX/CO REA.

As expected, the estimated percent of persons at or above selected COHb levels from the 2000 pNEM/CO assessment is greatest when indoor source emissions are included in the exposure modeling simulation. It is clear by comparing the two estimates from Johnson et al. (2000) that the presence of indoor sources had a significant impact on COHb levels – much more so than the ambient air contributions, as the percent of persons at selected COHb levels increased by large margins (about 10-30 percentage points) where data are available and comparable from both model simulations. The range of COHb levels also extends upwards to at or above 6.0%

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[7] When considering the exposure scenario that uses air quality just meeting the current standard.

[8] When considering the CHD population.

[9] The actual number of monitors used in the 2000 assessment was seven, though air quality data from two monitors in Boulder CO (monitor IDs 080130010 and 080131001) were averaged to create a composite air quality district (Johnson et al., 2000).

COHb for 0.2% of the CHD population when considering indoor source emissions and air quality adjusted to just meet the current 8-hour standard.

While these results regarding indoor sources from Johnson et al. (2000) are generally informative, they cannot be directly applied to the current dose assessment results. This is because the data used for simulating the indoor source emissions, while some of it may be readily available for use in the currently used APEX model, are considered not necessarily reflective of current conditions. For example, the indoor gas stove emissions data used were generated at a time where pilot lights (a continuous low-level combustion scenario) and limited external ventilation conditions existed. In addition, while tobacco smoking prevalence rates have not necessarily changed much over the past two decades, the prevalence of smoking indoors has been substantially reduced in public buildings and likely within many residential microenvironments. It is these important changes in indoor source emissions, the limited availability of current and relevant input data, and the limited time and resources allocated for this assessment, that preclude a current quantitative assessment of the impact of indoor source emissions on population COHb levels.

The range of dose estimates without simulated indoor sources are generally similar in both study areas when comparing results from the Johnson et al. (2000) assessment with those generated in the current CO REA. However at selected COHb levels in Denver, the current approach estimated a higher percent of the CHD population than when compared with the previous Johnson et al. (2000) assessment. For example, approximately 4.2% of the CHD population was estimated to have a daily maximum end-of-hour COHb level at or above 2.0% in this current assessment. The corresponding value estimated in the Johnson et al. (2000) assessment was approximately 0.5% of the IHD population. One factor contributing to the difference in the results for Denver at this benchmark level is the air quality data used for each assessment. The two additional air quality districts used in the 2000 assessment had consistently lower hourly CO concentrations when compared with concentrations measured at the other four ambient monitors that were consistent for both assessments. For example, at selected upper percentiles of the air quality distribution for these two monitoring sites, concentrations are reduced by a factor of 1.5 to 6.8 (Table 3-8 of Johnson et al., 2000). As a result, the simulated persons residing within these low CO concentration air quality districts[10] would have consistently lower estimated exposure concentrations and thus experience lower COHb levels. While there were differences in two of the ten monitors used to define the Los Angeles study

[10] These persons comprised 20.6% of the total simulated IHD population in the Denver study area (see Table 2-8 of Johnson et al., 2000).

areas in each assessment, a 1.5 to 6.8 factor difference in the upper percentiles of the air quality distributions used is not present.

Table 6-24. Percentage of Denver adults with coronary heart disease (CHD) estimated to experience a daily maximum end-of-hour COHb level – air quality just meeting the current 8-hour standard.

COHb Level (%)	Percentage of CHD Adults at or Above COHb Level		
	Johnson et al. (2000) pNEM/CO[a]		2010 REA APEX/CO[b]
	Includes Indoor Source Emissions	No Indoor Source emissions	No Indoor Source Emissions
≥ 0.0	100	100	100
≥ 1.0	83.2	65.0	82.3
≥ 1.5	37.6	6.7	23.4
≥ 2.0	19.9	0.5	4.2
≥ 2.5	10.4	0.2	0.8
≥ 3.0	5.5	< 0.1	0.2
≥ 4.0	1.6	0	< 0.1
≥ 5.0	0.6	0	na
≥ 6.0	0.2	0	na

Notes:
[a] Used Denver 1995 CO ambient concentrations with no adjustment (2nd highest 8-hour CO concentration was 9.5 ppm, close in value to the design value of 9.4 ppm).
[b] Denver 1995 ambient CO concentrations adjusted to just meet the current 8-hour standard (9.4 ppm).
na - benchmark level was not evaluated in the current exposure and dose simulations.

Table 6-25. Percentage of Los Angeles adults with coronary heart disease (CHD) estimated to experience a daily maximum end-of-hour COHb level – air quality just meeting the current 8-hour standard.

COHb Level (%)	Percentage of CHD Adults at or Above COHb Level		
	Johnson et al. (2000) pNEM/CO[a]		2010 REA APEX/CO[a]
	Includes Indoor Source Emissions	No Indoor Source emissions	No Indoor Source Emissions
≥ 0.0	100	100	100
≥ 1.0	79.0	58.1	41.2
≥ 1.5	32.3	5.2	4.7
≥ 2.0	16.8	0.5	0.6
≥ 2.5	9.0	<0.1	< 0.1
≥ 3.0	5.1	<0.1	< 0.1
≥ 4.0	2.2	0	0
≥ 5.0	0.9	0	0
≥ 6.0	0.3	0	0

Notes:
[a] Los Angeles 1997 ambient CO concentrations adjusted to just meet the current 8-hour standard (9.4 ppm).

6.4 KEY OBSERVATIONS

Presented below are key observations resulting from the exposure and dose assessment for ambient CO.

- Ambient CO exposures and resulting COHb levels in the blood of two simulated at-risk populations in the Los Angeles and Denver study areas were estimated considering five air quality scenarios: *as is* air quality, air quality adjusted to simulate *just meeting* the current 8-hour CO NAAQS, and air quality adjusted to just meet three potential alternative standards.
- The two at-risk populations simulated were: (1) persons with diagnosed CHD, including those estimated to have undiagnosed CHD, and (2) the larger group of persons with any type of HD including those estimated to have undiagnosed CHD. While the number of persons and person-days at or above selected COHb levels differed between the two populations, reflecting their differing size, the percentage of each population's persons and person-days were similar.
- The relative contribution of various microenvironments to exposure concentrations was generally similar between the two study areas. When considering *as is* air quality, indoor microenvironments contributed mostly to low level exposures (at or above 1 ppm and 2 ppm), comprising between 40 – 80% of the time spent at those exposure levels, while time spent inside vehicles contributed to most exposures at or above 3 ppm (70 – 100%). In comparison, when considering air quality just meeting the current standard, the percent contribution from indoor microenvironments was generally higher for low level exposures (about 65 – 85% of exposure concentrations at or above 1 ppm and 2 ppm), though again higher level exposures were dominated by the contributions from inside-vehicle microenvironments.
- The relationship between the two study areas with regard to estimated distribution of maximum end-of-hour COHb levels differed with the different air quality scenarios. Under *as is* air quality conditions, the simulated at-risk populations in the Los Angeles study area were estimated to experience a slightly higher distribution of maximum end-of-hour COHb levels than the Denver populations. Under conditions of air quality adjusted from historical air quality data to just meet the current or alternative standards, however, appreciably larger percentages of the Denver populations were estimated to experience COHb at or above specific levels than the Los Angeles populations.
- For *as is* air quality conditions, the highest daily maximum end-of-hour COHb estimated to be experienced over the course of the simulated year was below 1.5% for more than 98% of the at-risk populations simulated in each study area; it was below 2% COHb for more than 99.9% of these simulated populations. A lower percentage of the simulated at-risk populations in Denver were estimated to experience daily maximum end-of hour COHB below these benchmarks than were the populations in Los Angeles.
    - Under *as is* air quality conditions, the highest incremental contribution of ambient CO exposure to maximum end-of-hour COHb levels estimated in the simulated populations was 1.7% COHb, and more than 99% of both study area populations were estimated to have ambient CO contributions to COHb below

1.4%. As with estimates of total COHb (i.e., COHb from endogenous CO production and ambient exposure together), a larger percentage of the Los Angeles population was estimated to experience the higher ambient contributions to maximum end-of-hour COHb compared to the Denver population. For example, the percentage of the population estimated to experience ambient contributions to COHb at or above COHb levels above 1.0% was approximately 2 to 3 times as high in Los Angeles than in Denver.

- For simulations of air quality adjusted to just meet the current 8-hour standard of 9 ppm, the highest estimated daily maximum end-of-hour COHb over the course of the simulated year was below 1.5% for 95% of both simulated at-risk populations in the Los Angeles study area, and was below 2% COHb for 99.4% of these populations. In contrast, the percentage of the simulated at-risk populations in the Denver study area estimated to experience daily maximum end-of-hour COHb levels that did not exceed 1.5% was about 80%. The percentage of the Denver populations with their highest estimated daily maximum end-of-hour COHb below 2% was approximately 95%.
    - As with estimates of total COHb (i.e., COHb from endogenous CO production and ambient exposure together), the percentage of the simulated population estimated to experience the higher ambient contributions to maximum end-of hour COHb was appreciably greater in Denver as compared to Los Angeles. While estimated ambient CO contributions to daily maximum end-of-hour COHb were below 1.4% for nearly 98% of the Los Angeles simulated population, the corresponding percentage of the Denver population was about 87%.
- In addition to the simulations for *as is* and just meeting the current 8-hour standard air quality conditions, three simulations of air quality just meeting potential alternative standards were performed. The alternatives comprise different combinations of form, averaging time and level which were expected to achieve somewhat similar exposure and dose results. The combinations that were selected were based on consideration of exposure and dose results obtained for the *as is* air quality conditions and the higher just meeting the current 8-hour standard conditions. The combinations of form, averaging time and level that were simulated include: (1) a second-highest 8-hour average of 5 ppm, (2) a 99th percentile daily maximum 8-hour average of 5.0 ppm, and (3) a 99th percentile daily maximum 1-hour average of 8.0 ppm.
    - These three simulations generated generally similar percentages of the at-risk populations estimated to be exposed at selected concentrations and experience maximum end-of hour COHb levels at or above selected levels. Each of these three simulations generated fewer persons and a lower percent of the at-risk populations at or above selected COHb levels than did simulations for air quality adjusted to just meet the current 8-hour standard. For example, about 1% or less of the Denver populations had a highest daily maximum end-of-hour COHb at or above the 2.0% COHb level in the alternative standards' simulations as compared to approximately 4.2% in simulations of air quality just meeting the current standard. When considering the potential alternative standards in Los Angeles, generally fewer than 0.1% of the simulated at-risk populations were estimated to experience a maximum end-of-hour COHb level

at or above 2.0 % COHb, compared to 0.5% at that same COHb level associated with air quality adjusted to just meet the current standard.

- Results for the five air quality scenarios are further analyzed in the Policy Assessment to inform consideration of the level of public health protection that might be provided by alternative standard levels associated with different combinations of averaging time and form.
- Results generated in the current assessment for the air quality conditions just meeting the current NAAQS were compared with estimates from the assessment conducted in 2000 (Johnson et al., 2000) for similar conditions in the Denver and Los Angeles study areas (section 6.3). The two assessments employed similar approaches, similar, although not identical air quality data for this scenario, and they used different exposure models (APEX vs. pNEM). Results were similar for the 1.5% and 2% COHb level for the simulated Los Angeles study area population and somewhat different for the Denver study area population. For example, the two assessments' Los Angeles estimates of population percentages with highest daily maximum end-of hour COHb at or above these COHb levels were similar and within about 10% of one another. For the Denver simulated study populations, however, the estimates for these two COHb levels were about 3 and 8 times greater, respectively, in the current assessment when compared with that estimated in the prior assessment.

6.5 REFERENCES

Graham SE and McCurdy T. (2004). Developing meaningful cohorts for human exposure models. *J Expos Anal Environ Epidemiol*. 14(1):23-43.

Johnson T, Mihlan G, LaPointe J, Fletcher K, Capel J. (2000). Estimation of Carbon Monoxide Exposures and Associated Carboxyhemoglobin Levels for Residents of Denver and Los Angeles Using pNEM/CO (Version 2.1). Report prepared by ICF Consulting and TRJ Environmental, Inc., under EPA Contract No. 68-D6-0064. U.S. Environmental Protection Agency, Research Triangle Park, North Carolina. Available at: http://www.epa.gov/ttn/fera/human_related.html. June 2000.

Rodes C, Sheldon L, Whitaker D, Clayton A, Fitzgerald K, Flanagan J, DiGenova F, Hering S, Frazier C. (1998). Measuring Concentrations of Selected Air Pollutants Inside California Vehicles. Final Report. Prepared by Research Triangle Institute under Contract No. 95-339. California Air Resources Board. Sacramento, California.

Shikiya D, Liu C, Kahn M, Juarros J, Barcikowski W. (1989). In-Vehicle Air Toxics Characterization Study in the South Coast Air Basin. Office of Planning and Rules, South Coast Air Quality Management District. October 1989.

7 VARIABILITY ANALYSIS AND UNCERTAINTY CHARACTERIZATION

An important issue associated with any population exposure or risk assessment is the characterization of variability and uncertainty. *Variability* refers to the inherent heterogeneity in a population or variable of interest (e.g., residential air exchange rates). The degree of variability cannot be reduced through further research, only better characterized with additional measurement. *Uncertainty* refers to the lack of knowledge regarding the values of model input variables (i.e., *parameter uncertainty*), the physical systems or relationships used (i.e., use of input variables to estimate exposure or risk or *model uncertainty*), and in specifying the scenario that is consistent with purpose of the assessment (i.e., *scenario uncertainty*). Uncertainty is, ideally, reduced to the maximum extent possible through improved measurement of key parameters and iterative model refinement. The approaches used to assess variability and to characterize uncertainty in this REA are discussed in the following two sections. Each section also contains a concise summary of the identified components contributing to uncertainty and how each source may affect the estimated exposures.

7.1 ANALYSIS OF VARIABILITY

The purpose for addressing variability in this REA is to ensure that the estimates of exposure and risk reflect the variability of ambient CO concentrations, population characteristics, associated CO exposure and dose, and potential health risk across the study area and for the simulated at-risk populations. In this CO REA, there are several algorithms that account for variability of input data when generating the number of estimated benchmark exceedances or health risk outputs. For example, variability may arise from differences in the population residing within census tracts (e.g., age distribution) and the activities that may affect population exposure to CO and the resulting dose (e.g., time spent inside vehicles, performing moderate or greater exertion level activities outdoors). A complete range of potential exposure levels and associated risk estimates can be generated when appropriately addressing variability in exposure and risk assessments; note however that the range of values obtained would be within the constraints of the input parameters, algorithms, or modeling system used, not necessarily the complete range of the true exposure or risk values.

Where possible, staff identified and incorporated the observed variability in input data sets to estimate model parameters within the exposure and dose assessment rather than employing standard default assumptions and/or using point estimates to describe model inputs. The details regarding variability distributions used in data inputs are described in chapter 5. To the extent possible given the data available for the assessment, staff accounted for variability within the exposure and dose modeling. APEX has been designed to account for variability in

some of the input data, including the physiological variables that are important inputs to determining ventilation rates and COHb levels. As a result, APEX addresses much of the variability in factors that affect human exposure and dose. Important sources of the variability accounted for in this analysis are summarized in Table 7-1.

Table 7-1. Summary of how variability was incorporated into the assessment.

Component	Variability Source	Comment
Simulated Individuals	Population data	Individuals are randomly sampled from US census tracts used in model domains, by age (single years) and gender (US Census Bureau, 2007).
	Commuting data	Individuals are probabilistically assigned ambient concentrations originating from either their home or work tract based on US Census derived commuter data (US Census Bureau, 2007).
	Activity patterns	Data diaries are randomly selected from CHAD master (35,000 diaries) using six diary pools stratified by two day-types (weekday, weekend) and three temperature ranges (< 55.0 °F, between 55.0 and 83.9°F, and ≥84.0 °F). The CHAD diaries capture real locations that people visit and the activities they perform, ranging from 1 minute to 1 hour in duration (US EPA, 2002).
	Longitudinal profiles	A sequence of diaries is linked together for each individual that preserves both the inter- and intra-personal variability in human activities (Glen et al., 2008).
	Coronary heart disease (CHD) prevalence	CHD prevalence is stratified by four age groups (18-44, 45-64, 65-74, and 75+) and both genders (CDC, 2009)
Ambient Input	Measured ambient CO concentrations	Temporal: 1-hour CO for an entire year predicted using ambient monitoring data. Spatial: Four monitors were used to represent ambient conditions in Denver; ten monitors used in Los Angeles; each monitor was assigned a 10 km zone of influence.
	Meteorological data	Spatial: Local surface NWS stations used. Temporal: 1-hour NWS temperature data for each year.
Microenvironmental Approach	Microenvironments	Eight total microenvironments were represented, including those expected to be associated with high exposure concentrations (i.e., in-vehicle and near-road). This results in differential exposure estimates for each individual (and event) when spending time within each microenvironment.
	Proximity factors	In the current APEX approach, microenvironmental concentrations were estimated using proximity factors to adjust the outdoor CO concentrations. All proximity factors were represented by lognormal distributions whose values are randomly selected for every individual exposure event.
	Mass balance model	For the indoor microenvironments, using a mass balance model accounts for CO concentrations occurring during a previous hour (and of ambient origin) to calculate current indoor CO concentrations.

Component	Variability Source	Comment
	Air exchange rates	Several lognormal distributions are sampled based on five daily mean temperature ranges, two regions, and location specific A/C prevalence rates.
Physiological Factors Relevant to Ventilation Rate and Estimation of COHb Levels	Resting metabolic rate	Regression equations for three age-group (18-29, 30-59, and 60+) by two genders were used with body mass as the independent variable (Johnson et al., 2000).
	Metabolic equivalents by activity (METS)	Values randomly sampled from distributions developed for specific activities (some age-specific) (McCurdy, 2000; US EPA, 2002).
	Oxygen uptake per unit of energy expended	Values randomly sampled from a uniform distribution (Johnson et al., 2000).
	Weight (body mass)	Randomly selected from population-weighted lognormal distributions with age- and gender-specific geometric mean (GM) and geometric standard deviation (GSD) derived from data from the National Health and Nutrition Examination Survey (NHANES), for the years 1999-2004 (Isaacs and Smith (2005) in Appendix A).
	Height	Values randomly sampled from distribution based on equations developed for each gender developed by Johnson (1998) using height and weight data from Brainard and Burmaster (1992) (see Appendix B for details).
	Blood volume	Values determined according to gender using equations developed from Allen et al. (1956) (see Appendix B for details).
	Hemoglobin content of the blood	Values randomly selected from distributions developed by gender and age categories based on NHANES study (see Isaacs and Smith (2005) in Appendix A).
	Pulmonary CO diffusion rate	Values selected according to gender, height, and age based on equations adapted from Salorinne (1976) (see Appendix B for details).
	Endogenous CO production rate	Values randomly selected from lognormal distributions according to equations specific to age, gender, and menstrual phase (data obtained from eight independent studies; see Appendix B for details).

7.2 CHARACTERIZATION OF UNCERTAINTY

While it may be possible to capture a range of exposure or risk values by accounting for variability inherent to influential factors, the true exposure or risk for any given individual within a study area is largely unknown. To characterize health risks, exposure and risk assessors commonly use an iterative process of gathering data, developing models, and estimating exposures and risks, given the goals of the assessment, scale of the assessment performed, and limitations of the input data available. However, significant uncertainty often remains and emphasis is then placed on characterizing the nature of that uncertainty and its impact on exposure and risk estimates.

We have used such an iterative process in characterizing the uncertainty associated with the approach and data used in developing this final CO REA. Following a review of the draft REA's by CASAC and the public, a few sources of uncertainty were identified as important in improving the approach used to estimate exposure and dose. These included spatial representation of the monitors used, the number of microenvironments and approach used to estimate exposure, and representation of the at-risk population, among a few others (e.g., Brain and Samet, 2010a). Major approach modifications and analyses conducted throughout the evaluation of this final assessment included the following:

- Expanding the number of monitors used to better address spatial variability in ambient CO concentrations;
- Increasing the number of microenvironments modeled from two to eight;
- Using distributions of proximity factors to estimate all microenvironmental concentrations rather than simple point estimates;
- Expanding analysis of historical trends in ambient CO concentrations at individual monitors;
- Including two simulated at-risk populations based on prevalence rates for CHD and all types of heart disease (including estimates of undiagnosed CHD prevalence);
- Evaluating endogenous CO production and the ambient contribution to individual and population COHb levels;
- Identifying the specific microenvironments that contribute to low- and high-level exposures;
- Estimating the percent of simulated at-risk persons experiencing multiple occurrences per year at or above selected COHb levels;
- Evaluating the distribution of microenvironmental factors used to estimate exposure concentrations, and;
- Performing sensitivity analyses including
    - Evaluating the impact of additional monitoring data on estimated exposures and COHb levels;

- Evaluating the impact of varying undiagnosed prevalence rates by gender to estimated population COHb levels, and;
- Evaluating the impact of using alternative hemoglobin content distributions to represent a hypothetical population with anemia.

These additional analyses and approaches used are not without their own uncertainties, and following this iterative process, these uncertainties also need to be characterized. This characterization of uncertainty can include either qualitative or quantitative evaluations, or a combination of both. The approach can also be tiered; that is, the analysis can begin with a simple qualitative uncertainty characterization and then progress to a complex probabilistic uncertainty analysis. This second level of analysis may be appropriate when a lower tier analysis indicates there is a high degree of uncertainty for certain identified sources, the sources of uncertainty are highly influential variables in estimating the exposure and risk, and sufficient information and other resources are available to conduct a quantitative uncertainty assessment. This is not to suggest that quantitative uncertainty analyses should always be performed in all exposure and risk assessments. The decision regarding the type of uncertainty characterization performed is also informed by the intended scope and purpose of the assessment, whether the selected analysis will provide additional information to the overall decision regarding health protection, whether sufficient data are available to conduct a complex quantitative analysis, and whether time and resources are available for higher tier characterizations (US EPA, 2004; WHO, 2008).

The primary purpose of the uncertainty characterization approach selected in this CO REA is to identify and compare the relative impact that important sources of uncertainty may have on the estimated potential health effect endpoints. The approach used to characterize uncertainty was adapted from guidelines outlining how to conduct a qualitative uncertainty characterization (WHO, 2008) and applied in the most recent NO_2 (US EPA, 2008) and SO_2 NAAQS reviews (US EPA, 2009). While it may be considered ideal to follow a tiered approach in the REA to quantitatively characterize all identified uncertainties, staff selected the mainly qualitative approach given the extremely limited data available to inform probabilistic analyses.

The qualitative approach used in this REA varies from that of WHO (2008) in that a greater focus was placed on evaluating the direction and the magnitude[1] of the uncertainty; that is, qualitatively rating how the source of uncertainty, in the presence of alternative information, may affect the estimated exposures and health risk results. In addition and consistent with the WHO (2008) guidance, staff discuss the uncertainty in the knowledge base (e.g., the accuracy of the data used, acknowledgement of data gaps) and decisions made where possible (e.g., selection

[1] This is synonymous with the "level of uncertainty" discussed in WHO (2008), section 5.1.2.2.

of particular model forms), although qualitative ratings were assigned only to uncertainty regarding the knowledge base.

First, staff identified the key aspects of the assessment approach that may contribute to uncertainty in the exposure and risk estimates and provided the rationale for their inclusion. Then, staff characterized the magnitude and direction of the influence on the assessment results for each of these identified sources of uncertainty. Consistent with the WHO (2008) guidance, staff subjectively scaled the overall impact of the uncertainty by considering the degree of uncertainty as implied by the relationship between the source of uncertainty and the exposure concentrations and COHb levels.

Where the magnitude of uncertainty was rated *low*, it was judged that large changes within the source of uncertainty would have only a small effect on the exposure results. For example, a statistical procedure was used to substitute missing ambient concentrations in each ambient data set. Staff compared the air quality distributions and found negligible differences between the substituted data set and the one with missing values (e.g., Tables 5-13 through 5-16). There is still uncertainty in the approach used, since there may be alternative methods available. However, staff judged that the quantitative comparison of the data sets indicates that there would likely be little influence on exposure estimates by the data substitution procedure.

A magnitude designation of *medium* implies that a change within the source of uncertainty would likely have a moderate (or proportional) effect on the results. For example, the magnitude of uncertainty associated with using the historical data to represent a hypothetical future scenario was rated as *low-medium*. While we do not have information regarding how the ambient CO concentration distribution might look in the future, we do know however what the distribution might look like based on historical trends and the primary emission sources. If these trends in observed concentrations and emissions remain consistent in the future, then the magnitude of the impact to estimated exposures in this assessment would be judged as likely *low* or having negligible impact on the exposure and dose estimates. However, if there are entirely new emission sources, the magnitude of influence might be greater. When adjusting air quality in each location to simulate the various exposure scenarios, staff observed mainly proportional differences (e.g., a factor of two or three) in the estimated exposure and dose levels. Assuming that these types of ambient concentration adjustments could reflect the addition of a new source in each area carries its own uncertainties; however, based on this information, staff also judged the magnitude of influence in using the historical air quality data to represent a hypothetical future scenario as *medium*. A characterization of *high* implies that a small change in the source would have a large affect on results, potentially an order of magnitude or more. This rating would be used where the model was extremely sensitive to the identified source of uncertainty.

In addition to characterizing the magnitude of uncertainty, staff also included the direction of influence, indicating how the source of uncertainty was judged to affect estimated

exposures or risk estimates; either the estimated values were likely *over*- or *under-estimated*. In the instance where the component of uncertainty can affect the assessment endpoint in either direction, the influence was judged as *both*. Staff characterized the direction of influence as *unknown* when there was no evidence available to judge the directional nature of uncertainty associated with the particular source. Staff also subjectively scaled the knowledge-base uncertainty associated with each identified source using a three level scale: *low* indicated significant confidence in the data used and its applicability to the assessment endpoints, *medium* implied that there were some limitations regarding consistency and completeness of the data used or scientific evidence presented, and *high* indicated the extent of the knowledge base was extremely limited.

The output of the uncertainty characterization was a summary describing, for each identified source of uncertainty, the magnitude of the impact and the direction of influence the uncertainty may have on the exposure and risk characterization results. We identified sixteen sources of uncertainty associated with this approach for modeling CO population exposure and dose and associated potential health risk, each summarized in Table 7-2. Section 7.2.1 describes the sources more fully and provides support for the ratings ultimately selected by staff, while section 7.2.2 includes model sensitivity analyses referenced in section 7.2.1. As mentioned in earlier chapters, given the significant time constraints of this review, results of the characterization are provided in this document without substantial interpretation. Rather, interpretative discussion of these results, including further consideration of public health implications, is provided in the Policy Assessment.

Table 7-2. Characterization of key uncertainties in the assessment.

Sources of Uncertainty		Influence of Uncertainty on Exposure/Dose Estimates		Knowledge-base Uncertainty
Category	**Element**	**Direction**	**Magnitude**	
Ambient Monitoring Concentrations	Database Quality	Over	Low	Low
	Missing Data Substitution Method	Under	Low	Low
	Zero Concentration Frequency	Under	Low	Low
	Temporal Representation	Both	Low	Medium
	Spatial Representation	Both	Low – Medium	Medium
Adjustment of Air Quality to Simulate Just Meeting the Current and Potential Alternative Standards	Historical Data Used	Unknown	Low – Medium	Medium
	Proportional Approach Used	Both	Low	Low
APEX Input Data and Algorithms	Population Database	Both	Low	Low
	Activity Pattern Database	Unknown	Low – Medium	Medium
	Longitudinal Profile Algorithm	Both	Low – Medium	Medium
	Meteorological Data	Both	Low	Low
	Microenvironmental Algorithm and Input Data	Unknown	Medium	Medium
	Commuting Algorithm	Both	Low	Low
	At-Risk Prevalence Rates	Both	Low	Medium
	Physiological Variables	Unknown	Low – Medium	Medium
Potential Health Effect Benchmark Levels	Simulated At-Risk Populations [a]	Unknown	Low	Medium

Notes:
[a] This entry focuses on the uncertainty associated with the benchmark levels in their application to estimated COHb levels for the simulated at-risk populations (i.e., individuals with diagnosed HD or CHD combined with an estimate of undiagnosed CHD). With regard to other potentially susceptible populations (as described in section 2.4 above), we additionally note the lack of studies that describe COHb levels and health effects that might be expected as a result of short-term elevations in CO exposure in those populations.

7.2.1 Considerations in Characterizing Sources of Uncertainty

Staff considerations in reaching the judgments summarized in Table 7-2 above are noted below in order of the presentation in Table 7-2.

7.2.1.1 Ambient Monitoring Concentrations

Five elements of uncertainty were identified regarding the ambient monitoring concentrations used to estimate at-risk population exposures and COHb levels. These include the following elements: database quality, the method used to substitute for missing ambient concentrations, use of reported zero ambient concentrations, and the temporal and spatial representation of the monitors used as input to the exposure model.

Database Quality

All ambient CO measurements available in AQS are quality-assured. There may be a limited number of poor-quality, high concentration data within the ambient concentration data sets, potentially influencing the number of benchmark dose-level exceedances. Note also that any uncertainty regarding low level concentrations at or near the monitoring detection limit is unlikely to influence high COHb levels, the levels of which are of greatest interest in this assessment. Based on this, we judge there to be potential for overestimation in the number and percent of persons at or above a given COHb level, though the magnitude of this potential overestimation would be low. The source of ambient monitoring data used in the analyses, EPA's Air Quality System, is of high quality. There is no other source of ambient monitoring data as comprehensive. In addition, the data are being used in a manner consistent with one of the defined objectives of ambient monitoring. Therefore, we judge uncertainty associated with the knowledge base as low.

Missing Data Substitution Method

There were very few missing hourly concentration values when considering the years of ambient monitoring data used in this assessment. This is because we first screened all available monitoring data for a minimum of 75% completeness regarding hours/day and days/year for all four quarters within each year. In meeting the completeness criteria, they are (by definition), valid and appropriate for the purposes of this assessment. In Denver, the amount of missing hourly data ranged from a low of 0.7% to a high of 2.3% of the potentially reportable concentrations for a year (mean = 1.3%) (Tables 5-7 and 5-8). There was a greater percentage of missing values in the Los Angeles ambient monitoring data set, with an average of about 5.4% of the possible reportable concentrations for a year (minimum = 4.4%; maximum = 8.4%) (Tables 5-9 and 5-10). Therefore, both sets of data were well within the bounds set by the completeness criteria.

The method used to substitute for missing concentrations is informed by the measurements available within and among each of the monitors. A variety of standard techniques were used to fill missing values depending on the nature of the data gaps, including the development of linear regression models and interpolation between two points, with each method considering important factors that may influence concentration such as time-of-day, day-of-week, or month-of-year. While a number of alternative methods might be available, it is likely that the distribution of estimated concentrations would be similar to those generated here given that most of these potential alternative data substitution methods are also informed by the existing measurement data. Note also that there were negligible differences between the air quality distributions when comparing the before-substitution and after-substitution data sets (section 5.7.2).

Assuming there is an equal probability of missing either low or high concentration hourly values, and that substituted data are limited by the bounds of the data substitution algorithm (i.e., as defined by limits in the measurement data), there still may be a few instances where missing high concentration data would not be appropriately estimated. If this were the case, the selected substitution method would lead to an underestimation in exposure concentrations and COHb levels experienced by the simulated at-risk populations. This also assumes that the substitution of missing low-level concentration data with potentially higher concentrations (though still within the bounds of the algorithm) does not affect exposure and COHb results of interest. Very few data values were substituted with respect to the number of measured values available in each location.

Zero Concentration Frequency

The ambient monitoring data contain reported values equivalent to zero ppm, indicating that the monitor was in operation, though concentrations were below a quantitative detection limit. The minimum reported concentration in both study areas was 0.1 ppm, though reported detection limits for many of the instruments are typically 0.5 ppm (section 3.1.2). This indicates that reported concentrations between 0.1 and 0.5 ppm were quantified, though likely having greater uncertainty in their assigned values compared with other reported concentrations > 0.5 ppm. There is a possibility that exposures and associated COHb levels are underestimated because a reported zero value may represent a non-zero concentration less than 0.1 ppm.

Staff elected to use the reported monitoring data as a zero concentration rather than substitute the zero concentrations with some other value. In Denver, there were very few instances where a zero concentration was reported for either monitoring year of data (Table 7-3). Given the limited occurrence of zero concentrations in Denver, it is highly unlikely that a data substitution method employed to assign non-zero concentrations of less than 0.1 ppm would change the number or percent of persons exposed or experiencing %COHb above levels of

interest in this REA. There were, however, a greater number of instances where a zero ppm monitoring concentration was reported in Los Angeles (Table 7-3). Staff judge that it would also be of little consequence if all of these values were substituted with a non-zero concentration less than or equal to 0.1 ppm, given that the COHb levels of interest are driven exclusively by upper percentile ambient and microenvironmental exposure concentrations (For example, see Appendix B.6).

Table 7-3. Frequency of CO concentrations reported as zero in Denver and Los Angeles ambient monitoring data.

	Frequency of Reported Zero CO Concentrations			
	Denver Ambient Monitoring Data			
	1995		2006	
Monitor ID	n	%	n	%
0310002	3	0.0	3	0.0
0310013	0	0.0	154	1.8
0310014	1	0.0	139	1.6
0590002	0	0.0	143	1.6
	Los Angeles Monitoring Data			
	1997		2006	
Monitor ID	n	%	n	%
0370113	980	11.2	6	0.1
0371002	81	0.9	95	1.1
0371103	126	1.4	236	2.7
0371201	393	4.5	3	0.0
0371301	74	0.8	1	0.0
0372005	430	4.9	307	3.5
0374002	206	2.4	41	0.5
0590001	7	0.1	290	3.3
0591003	908	10.4	1288	14.7
0595001	61	0.7	2	0.0

Temporal Representation

As described above (section 7.2.1.2), staff used hourly ambient monitoring data that met completeness criteria largely defined by temporal attributes (hours per day, days per year). The hourly ambient CO concentrations are used to estimate event-level exposure concentrations that can range from 1 minute to 1 hour in duration. The relationships used to estimate these exposure concentrations are commonly derived from hourly measurements, thus are generally consistent with how the ambient monitor data are being used in this REA. In addition, the microenvironmental algorithm employed a factor that adjusts for temporal differences in outdoor concentrations with respect to that measured at an ambient monitor (section 4.4.4.3). Therefore,

staff judges the hourly ambient monitoring data of appropriate time resolution when modeling an individual's maximum end-of-hour COHb level. Further, given the observed individual doses in response to highly variable ambient/exposure concentrations (see Figure B-2 in Appendix B.6), staff judges that there would likely be low impact to the estimated percent of persons experiencing elevated COHb levels with improved temporal representation (e.g., minute-by-minute concentrations). Staff judges that there is a medium level of uncertainty in the knowledge base regarding the temporal representation. This is because much of the data used to derive the temporal adjustment factors are based on ambient, microenvironmental, and personal exposure measurements conducted in the 1980's, although it is likely that while CO concentrations have changed dramatically, the relationships among the measurements remain constant.

Spatial Representation

In evaluating the uncertainty associated with representation of the spatial variability in ambient CO concentrations in this REA, we have considered the impact of the improvements made in representing spatial variability in ambient CO levels throughout each study area for this REA as compared with the simplified approach used in the first draft CO REA.

Before considering the impact improving spatial representation of monitoring concentrations had on dose estimates, we first considered the spatial variability in the air quality data used for the study areas. Analysis of the full set of monitoring data indicates spatial variability in monitoring concentrations across each area is relatively limited, particularly when considering more recent years (Tables 3-1 through 3-6). This could indicate that ambient monitored concentrations do not vary greatly across the study area or that the study area monitors are sited in locations that measure similar (though still temporally variable) CO concentration levels. Note also that the microenvironmental algorithm we used in this assessment to estimate outdoor microenvironmental concentrations has an adjustment factor to address spatial variability in ambient concentrations expected to occur when modeling human exposures (section 4.4.4.3). Based on this limited analysis of air quality data from the existing ambient monitoring network and observed relationships between monitor and outdoor concentrations, it is possible that there would be a low magnitude of influence on estimated COHb levels in the presence of an alternative or supplemental monitoring network.

Staff also considered the impact on dose estimates of using the full monitoring data set to represent the spatial variability in each study area, as compared to a more limited approach such as what was done for the first draft REA, in which a single high concentration ambient monitor was used to represent the ambient concentrations across a larger study area (see section 7.2.2.1).

Based on these sensitivity results, staff judged improving spatial representativeness of the monitoring network to potentially have a medium magnitude of impact on the estimated

exposures and COHb levels of interest if the existing monitoring network does not adequately represent high ambient concentrations to which people might be exposed. We note that the limited, single monitor, approach described here assigned the highest monitor to all monitor locations, which illustrated a potential impact associated with representation of higher ambient concentrations. Conversely, a similar hypothetical scenario could be constructed to investigate the potential impact associated with representation of lower ambient concentrations. Such a comparison might find a similar, medium, magnitude of influence to the estimated number and percent of persons at or above COHb levels (albeit lower COHb levels experienced by the at-risk population compared with simulations that employed all monitors).

In considering uncertainty in the knowledge base, we note that each ambient monitor comprising the existing monitoring network has specific objectives and monitoring scale that may not appropriately capture the true spatial variability in CO concentrations. In the absence of 1) a monitoring network designed to better measure spatial variability in CO concentrations, 2) performing air quality modeling to estimate fine scale spatial and temporal variability in CO concentrations, and 3) analysis of additional monitoring data that can potentially indicate spatial concentration gradients, staff judge the uncertainty in the knowledge base as medium.

7.2.1.2 Adjustment of Air Quality to Simulate Just Meeting the Current and Potential Alternative Standards

Two elements of uncertainty were identified regarding the ambient monitoring concentrations used to estimate at-risk population exposures and COHb levels. These include the use of historical data to represent the hypothetical air quality scenarios (with adjustment) and the proportional approach that was used for adjustment.

Historical Data Used

Even though the historical data represent air quality conditions that have existed in the past, the conditions simulated using these data are hypothetical scenarios. There is uncertainty in how the temporal and spatial distribution of CO concentrations represented by these historical data might reflect the scenarios being simulated with these data given the air quality conditions that affect ambient concentration levels. More specifically, there is uncertainty regarding how influential factors such as emission levels per vehicle, vehicular traffic, and meteorology associated with the historical monitoring data set might influence air quality conditions in future situations which the simulated scenarios have been designed to represent.

We have noted differences between the two study areas in the percent of simulated populations estimated to experience a daily maximum end-of-hour COHb level at or above 2.0% COHb level when considering conditions just meeting the current standard (e.g., Tables 6-18 and 6-19). In these simulations involving adjusted historical hourly concentrations, there are a

greater number of high 1-hour concentrations (e.g., above 8 ppm) in Denver (Tables 5-18 and 5-19) as compared to the Los Angeles study area. It is evident that ambient concentrations at the upper percentiles of the distribution likely have a strong influence on the number and percent of persons experiencing the higher COHb levels. Whether these conditions that existed at the time the Denver data were collected are appropriate to the modeled hypothetical scenario is largely unknown. However, based on observed trends in air quality over time (Figures 3-4 and 3-5) and the results generated using the adjusted ambient concentrations, staff judges that, at most, the magnitude of potential influence to the estimated COHb levels in using these historical data could be a medium level. It is possible that these historical patterns can serve as a reasonable basis for predicting future air quality scenarios, though these patterns would not account for the influence of a new CO emission source(s). Therefore, staff judges the magnitude of the knowledge-base uncertainty as medium.

Proportional Approach Used

The magnitude of the adjustment applied to historical ambient concentration data was wide ranging across the air quality scenarios. For example, in Denver, to simulate conditions just meeting the current standard, 0.989 was the adjustment applied to the 1995 ambient monitoring data. In comparison, in adjusting the 1997 ambient monitoring data to just meet a 2nd highest 8-hour average CO concentration of 9.4 in Los Angeles, a greater adjustment to the data was needed (i.e., a factor of 0.627). However, in comparing recent and historical ambient CO concentrations for several ambient monitors in Los Angeles (Figure 3-4) and Denver (Figure 3-5), a strong proportional relationship is present when comparing the recent and historic CO concentrations. In general, the regression slopes and intercepts were similar for each of the monitors used to represent the air quality within each study area, indicating a similarity in the rate of change in concentration occurring at the monitors. This finding suggests there are likely similar sources affecting each of the monitors and that their associated source emissions have also changed at a similar rate over time.

The use of a proportional approach to simulate alternative air quality scenarios is not uncommon. A similar proportional adjustment approach was judged adequate in simulating air quality conditions just meeting the 8-hour CO NAAQS in prior assessments (US EPA, 1992; Johnson et al., 2000). A proportional approach was also used in evaluating exposure scenarios associated with just meeting the current and several alternative standards in the most recent NO_2 and SO_2 NAAQS reviews (US EPA, 2008; US EPA, 2009).

In addition, the simulations involving Los Angeles data indicate little difference in the percentage of persons estimated to experience daily maximum end-of-hour COHb at or above selected COHb levels between simulations using the historical data adjusted downwards to conditions similar to *as is* air quality and simulations using the 2006 as is air quality. This is

shown in Table 7-4 where COHb population estimates are presented for *as is* conditions (denoted by the asterisk) and contrasted to results for simulations of potential alternative standards that result in similar air quality conditions. As indicated by the presentation in Table 7-4, the *as is* conditions in Los Angeles can be considered to just meet several potential alternative standard of different form and level. For example, the 2nd highest non-overlapping 8-hour concentration at the design monitor in Los Angeles was equal to 5.6 ppm (i.e., consistent with air quality just meeting an 8-hour standard with a form of 2nd highest and level of 5.6; see Table 5-12). Table 7-4 indicates, based on this Los Angeles analysis, that whether using *as is* air quality, or historical air quality adjusted to a level similar to *as is* air quality, the estimated percent of persons at or above selected COHb levels are similar, thus indicating the lack of a strong or unrealistic influence of the air quality adjustment procedure on the results.

Table 7-4. Percentage of simulated at-risk CHD population in Los Angeles with highest daily maximum end-of-hour COHb levels at or above indicated COHb level considering potential alternative standards.

Form	Level (ppm)	≥ 2.0 % COHb	≥ 1.75 % COHb	≥ 1.5 % COHb
Second Highest Non-overlapping 8-hour Concentration	**5.7**	< 0.1	0.3	0.9
	5.6*	< 0.1	0.5	1.6
	5.4	< 0.1	0.2	0.7
99th Percentile of 8-hour Daily Maximum Concentration	**5.7**	0.1	0.4	1.4
	5.1*	< 0.1	0.5	1.6
	5.0	< 0.1	0.3	0.9
Second Highest 1-hour concentration	**8.2***	< 0.1	0.5	1.6
	8.1	0.1	0.4	1.4
99th percentile of 1-hour Daily Maximum Concentration	**8.0**	0.1	0.4	1.4
	7.4*	< 0.1	0.5	1.6
	7.1	< 0.1	0.3	0.9

Notes:
* Asterisk indicates simulation used *as is* (2006) air quality.

7.2.1.3 APEX Input Data and Algorithms

Eight elements of uncertainty were identified regarding the APEX input data and algorithms used to simulate population activity. These include the population and activity pattern databases, the longitudinal profile algorithm, meteorological data, microenvironmental algorithm and input data, commuting algorithm, at-risk prevalence rates and physiological variables.

Population Database

Population data (tract population density, age/gender distributions) are from the US Census Bureau, a reliable and quality-assured source. Data used are specifically for census tracts modeled in Denver and Los Angeles. Staff assumed any remaining uncertainties in the database would have negligible influence on exposure and %COHb results.

Activity Pattern Database

Data are actual records of the time spent in specific locations while performing specific activities. While not specific to a particular study area, the activity patterns of a population are generally well represented by the mainly population-based and nationally-representative survey data. There is, however, uncertainty in how well the CHAD data represent the intended simulated at-risk population, given that there may be local geographic attributes that influence a person's exposure that are not accounted for by CHAD. For example, in each study area it was observed that the in-vehicle microenvironment contributed greatly to concentrations at or above 3-6 ppm (Figures 6-1 through 6-4). This indicates that in-vehicle exposures are likely important determinants in upper level exposures and, thus, the distribution of time spent commuting may be an important influential factor.

To evaluate how well the CHAD data represented persons residing within each study area regarding commute times, we obtained information on travel time to work for workers ages 16 years[2] and over specific to Denver County, Colorado and Los Angeles, CA (US Census Bureau, 2009, Table P31). We next isolated persons in CHAD that were ≥18 years of age and spent at least one minute in a motor vehicle between 6 am and 9 am. The distributions of commute times associated with these data are illustrated in Figure 7-1 (see Appendix E, Table E-1 for the details). This comparison indicates that the available CHAD diaries[3] reasonably represent typical commute times in both the urban locations modeled in this assessment. Not surprisingly, the percentage of CHAD diaries containing longer duration commute times (> 40 minutes) are more representative of Los Angeles than Denver, likely a function of the number of CHAD diaries from that geographic area (Table 4-1).

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[2] This is how these data are reported by the US Census. We assumed that the distribution of commute times for persons aged 18 years or older in Los Angeles and Denver counties would be similar to this.

[3] Note, however, that this CHAD distribution is developed from an un-weighted sample of all possible diaries that could be used in each study area. The actual diaries used, their frequency of use, and associated distribution of commute times may be different from that presented in Figure 7-1. To obtain this information is not a trivial computational undertaking and would involve generating the necessary data in the APEX *daily* output file (which was not done here).

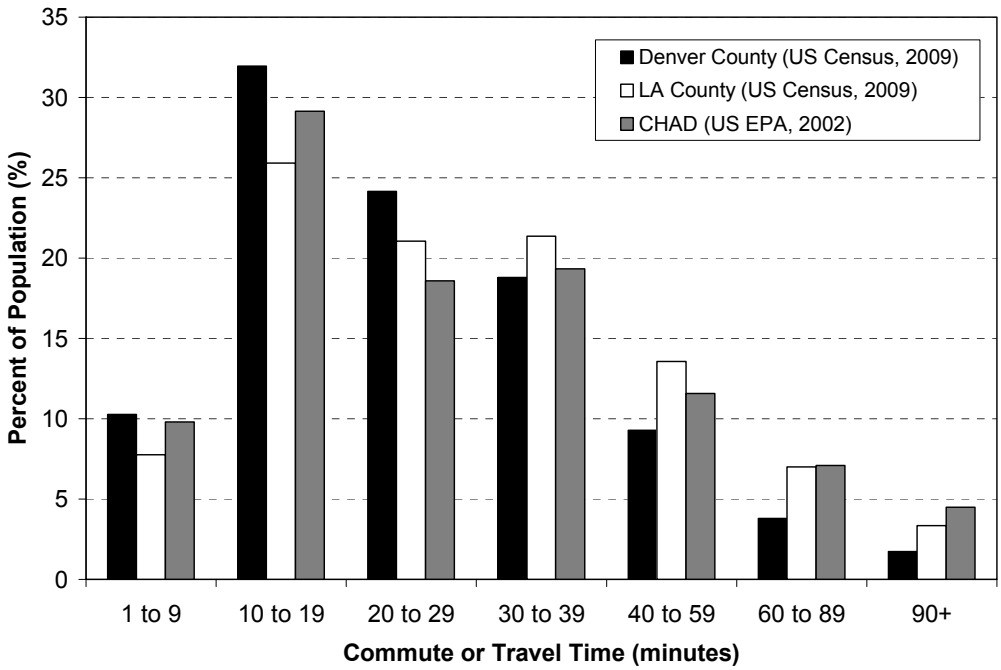

Figure 7-1. Comparison of commute and travel times for persons residing in Denver and Los Angeles counties to those persons surveyed in CHAD.

We also recognize that the health status of an individual may affect their time-location-activity patterns, and hence their estimated exposure and dose levels. This could include factors such as time spent in certain locations as well as exertion levels attained by simulated individuals. CHAD is comprised of data from individuals that have, or do not have, an identified health condition[4] and are assumed to represent the activities of persons with normal health status as well as those with certain health conditions that may not significantly affect general activity patterns. While some of the diary days are potentially reflective of the simulated at-risk population, the majority of the diaries may be from persons identified as having a normal health status. Thus, if there are differences in activities performed and locations visited that depend on health status, there would be uncertainty in the representation of the simulated at-risk population activity patterns modeled in this CO REA by the CHAD diaries.

A statistical analysis was performed on a subset of the CHAD data where persons were specifically asked whether they had angina (see Appendix F of CO REA and Johnson et al., 2000, for details). Activity patterns for persons with angina were compared to those for

[4] Of the approximately 35,000 diary days within the CHAD master file, about 65% contain information on whether the person was identified as asthmatic (or not) or whether the person was identified as having a heart or lung condition (or not). The remaining 35% have unknown health status (i.e., the health status was not requested in the original survey questionnaire).

individuals not having angina using selected exertion level metrics and time spent outdoors or inside vehicles. The percentages of time spent outdoors or in a vehicle were generally not statistically significantly different between angina and non-angina subjects. While there were statistically significant differences in the exertion level attained between angina and non-angina subjects,[5] actual differences were generally numerically small compared to the mean values. The differences in activity and exertion level between angina and non-angina subjects, although statistically significant, were judged not large enough to severely impact the validity of APEX (or pNEM/CO) modeling results that do not adjust for an angina/non-angina difference in activity patterns.

In characterizing the knowledge base uncertainty, we note that the CHAD time-location activity diaries used are the most comprehensive source of such data and realistically represent where individuals are located and what they are doing. Features of an individual's activity pattern are well represented, adjustments are made to represent the population distribution in a specific area (using age and gender), and temperature is used to link CHAD diaries with the simulated individuals residing in a specific area. In addition, the CHAD data are from a reliable and quality-assured source (US EPA, 2002) and have recently incorporated several thousand new diary days (see Table 4-1). However, we judge the knowledge-base uncertainty as medium given the overall limited number of diary days available to represent the large simulated at-risk populations residing within each study area.

Longitudinal Profile Algorithm

Much of this assessment focused on persons having at least one exposure or dose above a selected level; therefore, the potential magnitude of influence from the longitudinal profile algorithm would be considered low. However, when considering multi-day exposures, staff judges the magnitude of potential influence to COHb levels could range upwards to a medium level. In developing the longitudinal method, the evaluation indicated that both the *D* and *A* statistics are reasonably reproduced for the population (Glen et al., 2008). The approach was also compared with two other independent methods used for constructing longitudinal activity patterns (see Appendix B, Attachment 4 of US EPA, 2009). This particular comparison indicated that, depending on the longitudinal profile method selected, the number of persons experiencing multiple exposure events at or above a selected level could differ by about 15 to 50%.[6] Note however, long-term diary profiles (i.e., monthly, annual) do not exist for a

[5] Note there was a very large sample size for the non-angina subjects.

[6] The comparison used simulated persons in Atlanta and evaluated the number of persons experiencing three or more ozone 8-hour average exposures at or above 0.07 ppm concomitant with moderate or greater exertion.

population, though a few persons surveyed have longitudinal diary profiles (Table 4-1). Therefore, the knowledge-base uncertainty is judged by staff as medium.

Meteorological Data

Data are from the National Weather Service, a well-known and quality-assured source. The daily maximum temperatures are used when selecting appropriate CHAD diaries to simulate the at-risk population. The temperature bin ranges that were used (see section 5.5.3) are wide such that any erroneous temperatures that do exist within the data set would likely have limited impact to estimated exposure and dose results. Daily mean temperatures are used when selecting air exchange rates (section 5.9.4). Given the overlap of the AER distributions and the wide temperature ranges used to categorize them, it is also likely that there is limited impact by erroneous temperature data that may exist. Therefore, staff judges uncertainty regarding meteorological data and its potential magnitude of influence on COHb levels as low.

Microenvironmental Algorithm and Input Data

In this REA, the number of microenvironments selected captures the likely locations persons spend time and where CO exposures would occur. Using distributions of proximity factors derived from measurement data in Denver and applied to estimate microenvironmental concentrations is judged by staff to be a reasonable approach. However, the extent to which these Denver study data reflect similar relationships in Los Angeles likely has greater uncertainty. Additionally, the Denver measurement data were collected in the 1980's; therefore, there is also uncertainty as to how these data might reflect relationships observed for other years modeled in this assessment (i.e., 2006). However, the distributions of microenvironmental concentrations (Tables 6-8 and 6-11) and the effective microenvironmental-to-ambient concentration ratios (e.g., Tables 6-9 and 6-12), in particular those used to estimate high-exposure microenvironments, were found comparable to other measurement data and relationships available (albeit limited in number) and generally support the algorithm and distributions applied in this assessment.

Commuting Algorithm

In this REA, the commuting algorithm within APEX was implemented. Use of this algorithm better represents individual exposures across each modeling domain. The data are derived from the US Census, a well-known and quality-assured source. The data are used in addressing home-to-work travel, certainly within the bounds of the objectives associated with the original data collection; therefore, staff judged the knowledge-base uncertainty as low.

While there may be some uncertainties associated with the application of the database (see US EPA, 2009), they are limited in the potential magnitude of influence they might have on estimated exposures and COHb levels. For example, although several of the APEX microenvironments account for time spent in travel, the travel is assumed to always occur in

basically a composite of the home- and work-tracts. No other provision is made for the possibility of passing through other census tracts during travel. This could contribute to either over- or under-estimating exposure concentrations, dependent on the number and identity of tracts the simulated individual would actually traverse and the spatial variability of the concentration across different tracts. Given that most persons would likely experience ambient concentrations from within their home air district (i.e., encompassing all tracts within a 10 km radius of the monitor location), tracts existing between home and work tracts for these persons would not have a different assigned ambient concentration. In addition, the commuting route (i.e., which roads individuals are traveling on during the commute) is not accounted for. From a practical perspective though, if staff was to consider multi-tract commuting, further complexity would need to be added to the modeling while also requiring additional input data that are not readily available (e.g., commuting route data for simulated individuals). These model adjustments would come with a number of additional uncertainties and would require additional time and resources not available for the assessment.

At-risk Prevalence Rates

Data are from the Centers for Disease Control, a well-known and quality-assured source. Though prevalence data are not specific for each region, the national prevalence data were stratified by selected age-groups and gender. Staff used gender-specific ratios and applied them to all age groups uniformly even though there may be uncertainty in the accuracy of the prevalence estimates for specific age and gender groups. In addition, potentially undiagnosed individuals with CHD were included to expand the total CHD population considered. This was based on several assumptions including using 1990 estimates of the population with undiagnosed IHD. The percent of the population with undiagnosed CHD (i.e., 43.8%) was applied to the diagnosed CHD prevalence, without any difference between genders. In comments on the second draft REA, it was suggested that women with undiagnosed heart disease may be underrepresented by this approach. In the limited time available, extant literature regarding this topic were reviewed with regard to the suitability for developing an improved estimate of the undiagnosed prevalence rate. Relevant data that could be used to generate new undiagnosed prevalence rates and provide a greater degree of confidence than what was used in this assessment were not identified.

We recognize there is uncertainty associated with the undiagnosed prevalence rate used. To evaluate the potential impact the prevalence rate might have on the estimated COHb levels, we performed simulations using alternative values for undiagnosed CHD prevalence rates. These analyses are described in section 7.2.2.2 below. The COHb results generated from this sensitivity analysis, as well as when using different prevalence rates to estimate COHb levels for the HD population, had little impact to the percent of persons at or above the selected COHb

levels. Only the total number of persons was affected by using the alternative prevalence rates. This suggests that, if new data were uncovered with improved representation of either the diagnosed or undiagnosed prevalence rates, there would be little change to the percent of persons at or above selected COHb levels. Therefore, staff judges the magnitude of influence to COHb as low for the estimated percent of persons at or above selected levels. The prevalence rates do have a medium level of influence to the estimated number of persons at or above selected COHb levels, though the observed impact was proportional across the range of selected COHb levels.

Physiological Variables

Many of the parameters used to estimate the physiological attributes of the simulated at-risk population were developed from healthy individuals; there were no adjustments made to account for a particular health condition. While the ISA notes some variability in some parameters in individuals with specific health conditions that might affect CO uptake and elimination, most of the identified health conditions that could affect the physiological variables used in the CFK model may not necessarily be associated with the simulated at-risk populations, i.e., HD or CHD individuals. In addition, there is uncertainty in some of the parameter values used in the COHb algorithm due to the age of source publications cited (e.g., dating back to the mid 20th century) or uncertainty as to their representativeness. As an example, alveolar ventilation is represented in the simulations as a single point estimate of 19.63 and applied directly to activity-specific oxygen consumption rates. This was based on an analysis by Joumard et al. (1981), of data generated by Galetti (1959), which did not include measurements made at elevated exertion levels, although theoretically one would expect there to be a nonlinear relationship between V_A and VO_2 given the non-linear relationship of dead space volume (V_D) to tidal volume (V_T) with increasing breathing rate.[7] Thus, the point estimate of 19.63 used may not adequately represent the V_A to VO_2 relationship at higher ventilation rates. We note however that most of the upper level exposure concentrations in this assessment are associated with time spent inside vehicles, where it is expected that the exertion level and breathing rate would be at a relatively low level. Therefore, it may be that the point estimate is appropriately used for these activities and the estimated maximum end-of-hour COHb associated with the in-vehicle microenvironment may not be adversely affected. As described in this example, it is possible that most of the data and or relationships still remain appropriate in modeling the current population; however, in the absence of conducting a comprehensive review and comparing the historical data to recent measurements, staff judges the knowledge base uncertainty as medium.

[7] Dead space volume (V_D) will remain relatively constant, increasing only slightly with increasing ventilation rate. Tidal volume (V_T) consistently increases with increasing ventilation rate. Alveolar ventilation (V_A) will approach that of total ventilation (V_E) at higher ventilation rates, given that $V_A = V_E (1-V_D/V_T)$. Note also, V_E is not linear with respect to VO_2 (see Graham and McCurdy, 2005).

The potential influence of another physiological parameter – hemoglobin content – was evaluated in response to comments received on earlier drafts of this document. These analyses are described in section 7.2.2.3 below.

7.2.1.4 Potential Health Effect Benchmark Levels for the Simulated At-risk Populations

The potential health effect benchmark levels for considering the COHb estimates for the simulated at-risk populations[8] in this REA were identified (in section 2.6) based on data from a well-conducted multi-center controlled human exposure study demonstrate cardiovascular effects in subjects with moderate to severe coronary artery disease at study mean COHb levels as low as 2.0-2.4% of which were increased from a baseline mean of 0.6-0.7% as a result of short (~1hour) experimentally controlled increases in CO exposures (study mean of 117 ppm CO). No laboratory study has been specifically designed to evaluate the effect of experimentally increased exposure to CO resulting in an increase in COHb levels to a study mean below 2.0%. However, based on analysis of individual study subject responses at baseline and at the two increased COHb levels, study authors concluded that each increase in COHb produced further changes in the study response metric, without evidence of a measurable threshold effect. There is no established "no adverse effect level" and, thus, there is greater uncertainty concerning the lowest benchmark level identified (i.e., 1.5%). There is also uncertainty about whether individuals with the most severe CHD are adequately represented. Additionally the COHb levels estimated in this assessment result from CO exposure concentrations much lower than the experimental exposure concentrations used to increase study subject COHb levels to the study targets (e.g., 2.0%) and with which the responses were associated. Given that the evidence supporting the choice of benchmark levels is based on controlled human exposure data, staff judged the influence of this uncertainty on the risk characterization as being low.

7.2.2 Sensitivity Analyses

This section describes sensitivity analyses referenced in section 7.2.1 with regard to three sources of uncertainty in the assessment, one in the category of ambient monitoring concentrations and two in the category of APEX input data and algorithms.

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[8] Discussion here focuses on the uncertainty associated with benchmark levels in their application to estimated COHb levels for the simulated at-risk populations (i.e., individuals with diagnosed HD or CHD combined with an estimate of undiagnosed CHD). With regard to other potentially susceptible populations (as described in section 2.4 above), we additionally note the lack of studies that describe COHb levels and health effects that might be expected as a result of short-term elevations in CO exposure in those populations.

7.2.2.1 Spatial Representation

We performed sensitivity analyses to illustrate the quantitative impact of the improvements made by better representing the spatial variability in ambient CO concentrations. Of particular interest was how expanding the number of monitors used in this REA for both study areas compared with the simplified approach used in the first draft CO REA. In the analysis shown here, however, the more spatially limited approach applied all hourly concentrations from the single design monitor to all monitoring locations defined for each study area to ensure comparable modeling domains.[9] Four model simulations for the HD population are shown: two air quality conditions (*as is* and just meeting the current 8-hour standard) in each of the two study areas (Denver and Los Angeles). The results for the more spatially-limited approach (single monitor) might be considered to provide an upper bound estimate of COHb levels for this modeling domain, given that the design monitor represents the highest measured concentrations in each study area and that there are restricted opportunities for persons to experience ambient CO concentrations lower than that of the design monitor.

As shown in Tables 7-5 through 7-8, the use of multiple monitors (versus using the design monitor alone) to represent the air quality input to the exposure model results in a lower number and percent of persons at or above a given COHb level. In general, there were larger differences in the number and percent of persons at or above the higher COHb levels (i.e., ≥ 1.75% COHb). A similar pattern was observed when comparing air quality scenarios within each study area, although expanding spatial variability in ambient monitoring concentrations had a greater impact on the number of persons at or above selected COHb levels in the Los Angeles study area (Tables 7-6 and 7-8). This is likely the result of the Los Angeles study area, which is larger, having generally greater spatial variability in ambient monitoring concentrations (i.e., from ten monitors) when compared with that provided by the four monitors representing air quality in the Denver study area. The spatial heterogeneity in ambient concentrations in the Los Angeles study area allowed simulated persons to experience a wider range of ambient concentrations when compared with the simulated persons Denver. As a result of the limited spatial heterogeneity in Denver ambient concentrations (given that only four monitors were selected, their close proximity to one another, and having similar concentration levels), a lesser difference in the percent of persons at or above selected COHb levels was observed when using the design monitor to represent all ambient concentrations in the model domain. This difference

[9] In the first draft CO REA, the design monitor in each study area was used to represent air quality for all census tracts within a 20 km radius of the monitor. In this current investigation, the 10 km radii for the 4 monitor locations in Denver, and 10 monitor locations in Los Angeles were retained to define the respective exposure modeling domains. All of these monitoring locations (and hence the air quality districts) used the CO concentrations from the single design monitor for each respective study area (080310002 in Denver and 060371301 in Los Angeles).

in spatial variability between the two study areas may also play a role in the study area differences observed for the estimated percent of persons at or above the selected COHb levels when using air quality just meeting the current standard (e.g., Table 6-18 and 6-19). This is because a greater proportion of the simulated persons will experience generally similar exposure levels in Denver (and at higher exposure concentrations, note Tables 6-7 and 6-9) than compared with simulated persons in Los Angeles (Tables 6-10 and 6-12).

Table 7-5. Comparison of highest estimated daily maximum end-of-hour COHb levels for Denver HD population for two model simulations – all monitor concentrations versus the design monitor concentrations – as is air quality.

COHB Level (%)	Number of HD Persons		Percent of HD Persons		
	All Monitors[a]	Design Monitor only[b]	All Monitors[a]	Design Monitor only[b]	Ratio[c]
≥ 0.0	85,926	85,926	100	100	1.0
≥ 1.0	17,807	25,125	20.7	29.2	1.4
≥ 1.5	1,074	1,715	1.2	2.0	1.6
≥ 1.75	234	444	0.3	0.5	1.9
≥ 2.0	12	99	< 0.1	0.1	8.3
≥ 2.5	0	0	0	0	-
≥ 3.0	0	0	0	0	-
≥ 4.0	0	0	0	0	-

Notes:
[a] Each monitor site used ambient concentrations from that site (dose results from Table 6-15).
[b] Each monitor site used ambient concentrations from design site (080310002).
[c] Ratio = (value for design site scenario) / (value for all sites scenario).

Table 7-6. Comparison of highest estimated daily maximum end-of-hour COHb levels for Los Angeles HD population for two model simulations – all monitor concentrations versus the design monitor concentrations – *as is* air quality.

COHB Level (%)	Number of HD Persons		Percent of HD Persons		
	All Monitors[a]	Design Monitor only[b]	All Monitors[a]	Design Monitor only[b]	Ratio[c]
≥ 0.0	630,807	630,807	100	100	1.0
≥ 1.0	165,880	406,020	26.3	64.4	2.4
≥ 1.5	9,834	61,816	1.6	9.8	6.3
≥ 1.75	3,011	22,378	0.5	3.5	7.4
≥ 2.0	502	7,526	< 0.1	1.2	15.0
≥ 2.5	0	401	0	< 0.1	-
≥ 3.0	0	0	0	0	-
≥ 4.0	0	0	0	0	-

Notes:
[a] Each monitor site used ambient concentrations from that site (dose results from Table 6-16).
[b] Each monitor site used ambient concentrations from design site (060371301).
[c] Ratio = (value for design site scenario) / (value for all sites scenario).

Table 7-7. Comparison of highest estimated daily maximum end-of-hour COHb levels for Denver HD population for two model simulations – all monitor concentrations versus the design monitor concentrations – air quality just meeting the current 8-hour standard.

COHB Level (%)	Number of HD Persons		Percent of HD Persons		
	All Monitors[a]	Design Monitor only[b]	All Monitors[a]	Design Monitor only[b]	Ratio[c]
≥ 0.0	85,926	85,926	100	100	1.0
≥ 1.0	71,710	81,743	83.5	95.1	1.1
≥ 1.5	21,028	38,206	24.5	44.5	1.8
≥ 1.75	9,502	19,276	11.1	22.4	2.0
≥ 2.0	3,826	9,329	4.5	10.9	2.4
≥ 2.5	802	2,295	0.9	2.7	2.9
≥ 3.0	222	592	0.3	0.7	2.7
≥ 4.0	25	74	< 0.1	< 0.1	3.0

Notes:
[a] Each monitor site used ambient concentrations from that site (dose results from Table 6-18).
[b] Each monitor site used ambient concentrations from design site (080310002).
[c] Ratio = (value for design site scenario) / (value for all sites scenario).

Table 7-8. Comparison of highest estimated daily maximum end-of-hour COHb levels for Los Angeles HD population for two model simulations – all monitor concentrations versus the design monitor concentrations – air quality just meeting the current 8-hour standard.

COHB Level (%)	Number of HD Persons		Percent of HD Persons		
	All Monitors[a]	Design Monitor[b]	All Monitors[a]	Design Monitor[b]	Ratio[c]
≥ 0.0	630,807	630,807	100	100	1.0
≥ 1.0	260,612	558,955	41.3	88.6	2.1
≥ 1.5	31,410	168,289	5.0	26.7	5.4
≥ 1.75	10,537	68,941	1.7	10.9	6.5
≥ 2.0	3,613	29,302	0.6	4.6	8.1
≥ 2.5	401	4,817	< 0.1	0.8	12.0
≥ 3.0	100	602	< 0.1	< 0.1	6.0
≥ 4.0	0	0	0	0	-

Notes:
[a] Each monitor site used ambient concentrations from that site (dose results from Table 6-19).
[b] Each monitor site used ambient concentrations from design site (060371301).
[c] Ratio = (value for design site scenario) / (value for all sites scenario).

7.2.2.2 At-risk Prevalence Rates

To evaluate the potential impact that the prevalence rate used for undiagnosed CHD might have on the estimated COHb levels, we performed simulations using alternative values for undiagnosed CHD prevalence rates. The alternative values were based on assuming that the total CHD prevalence (diagnosed and undiagnosed combined) for females equaled that of the males, in effect representing a greater proportion of undiagnosed CHD for females (Table 7-9). Two air quality scenarios were considered in Denver; *as is* air quality and air quality adjusted to just meet the current standard. All standard model settings previously described for these scenarios were retained.

Table 7-9. Estimated alternative prevalence rates for CHD, stratified by age and gender.

Age range	Prevalence rate (fraction) for coronary heart disease					
	Males[a]			Females		
	Diagnosed	Undiagnosed	Total	Diagnosed[a]	Undiagnosed[b]	Total
18 to 44	0.012	0.005	0.017	0.007	0.010	0.017
45 to 64	0.088	0.038	0.127	0.050	0.077	0.127
65 to 74	0.244	0.107	0.351	0.138	0.213	0.351
75+	0.310	0.135	0.446	0.175	0.271	0.446

Notes:
[a] Values obtained from Table 5-6.
[b] Generated assuming total CHD prevalence for females was equal to that of males.

The outputs generated from these new simulations were compared with output from the previous simulations that applied an undiagnosed CHD uniformly to the two genders (termed *base-CHD*). As expected, there are a greater number of persons at or above selected COHb levels for both air quality scenarios due to the expansion of the simulated at-risk population (Tables 7-10 and 7-11). However, there is little observed difference in the percentage of CHD population at or above the selected COHb levels.

Interestingly, this was the same outcome when we expanded the simulated at-risk population to include all persons with diagnosed heart disease (HD) along with undiagnosed CHD. That is, the percentage of the HD population estimated to experience COHb at or above selected levels was nearly identical to that estimated for the CHD population (e.g., Tables 6-18 and 6-19). Note that these three at-risk population simulations not only contain differing total prevalence of a particular health condition, but contain variable prevalence when comparing across age groups and the two genders. The variation in the prevalence rates used have only resulted in differences in the number of persons exposed, indicating that if additional prevalence

rates were available that varied across age groups and the two genders, there may be little impact to the percentage of persons at or above selected COHb levels.

Table 7-10. Comparison of the portion of the simulated CHD population in the Denver study area estimated to experience a daily maximum end-of-hour COHb at or above specified levels using base and alternative undiagnosed CHD prevalence rates – *as is* air quality.

COHb Level (%)	CHD persons			
	Base Prevalence[a,b,c]		Alternative Prevalence[a,d]	
	Number	Percent	Number	Percent
≥ 0.0	53,656	100	71,093	100
≥ 1.0	10,773	20.1	15,512	21.8
≥ 1.5	654	1.2	963	1.4
≥ 1.75	111	0.2	185	0.3
≥ 2.0	12	< 0.1	12	< 0.1
≥ 2.5	0	0	0	0

Notes:
Unadjusted ambient concentrations from four monitors in 2006 were used to represent the *As Is* air quality scenario.
[a] Includes persons with diagnosed coronary heart disease, angina pectoris, and heart attack (CDC, 2009).
[b] Includes estimate of persons with undiagnosed ischemia developed by EPA (see section 5.5.2.1).
[C] Dose results obtained from Table 6-15.
[d] Effectively, a hypothetical undiagnosed CHD prevalence was used to generate an equivalent total CHD prevalence for both genders. See Table 7-9.

Table 7-11. Comparison of the portion of the simulated CHD population in the Denver study area estimated to experience a daily maximum end-of-hour COHb at or above specified levels using base and alternative undiagnosed CHD prevalence rates – air quality just meeting the current standard.

COHb Level (%)	CHD persons			
	Base Prevalence[a,b,c]		Alternative Prevalence[a,d]	
	Number	Percent	Number	Percent
≥ 0.0	53,656	100	71,093	100
≥ 1.0	44,166	82.3	58,851	82.8
≥ 1.5	12,563	23.4	16,721	23.5
≥ 1.75	5,800	10.8	7,663	10.8
≥ 2.0	2,258	4.2	2,999	4.2
≥ 2.5	444	0.8	580	0.8
≥ 3.0	111	0.2	148	0.2
≥ 3.5	62	0.1	62	< 0.1
≥ 4.0	12	< 0.1	12	< 0.1

Adjusted ambient concentrations from four monitors in 1995 were used to represent the air quality just meeting the current 8-hour standard.
[a] Includes persons with diagnosed coronary heart disease, angina pectoris, and heart attack (CDC, 2009).
[b] Includes estimate of persons with undiagnosed ischemia developed by EPA (see section 5.5.2.1).
[C] Dose results obtained from Table 6-18.
[d] Effectively, a hypothetical undiagnosed CHD prevalence was used to generate an equivalent total CHD prevalence for both genders. See Table 7-9.

7.2.2.3 Physiological Variables

Sensitivity analyses performed on one potentially influential physiological variable – hemoglobin content - is described here. This physiological variable was identified and evaluated in response to a comment suggesting that the some of the physiological variables used in the simulations may not necessarily be adequately representing the at-risk populations or subgroups having characteristics that may contribute to increased susceptibility. One variable identified within the CFK module that could have an impact on estimated COHb levels, and for which data were available to evaluate variation among population subgroups, is an individual's hemoglobin content. For any simulated individual, the model currently samples from age- and gender-stratified distributions developed from the 1999-2004 NHANES (see Appendices A and B). These NHANES data are population-based; as such, represent a collection of individuals that may be based on population age, gender, and race groupings. In addition, persons having been diagnosed with anemia are represented in these data, although in a small fraction. Nevertheless,

hemoglobin content estimates in this REA are drawn from a sample that includes persons with anemia.

To evaluate the influence of hemoglobin on dose estimates, we obtained the most recent data available from NHANES (2005-2008), combined these data with the previously used data set (NHANES 1999-2004), and evaluated whether alternative distributions could be developed based on influential factors such as race and health condition. Descriptive statistics were generated using the hemoglobin content (Hb) of four data groups: African-Americans, pregnant women, persons identified using WHO et al. (2001) guidelines as potentially having anemia (Table 7-12),[10] and all other persons.

Table 7-12. Hemoglobin levels below which anemia is present in a population (from WHO et al., 2001).

Age or gender group	Hb threshold (g/dl)
Children (0.5–5.0 yrs)	11.0
Children (5–12 yrs)	11.5
Children (12–15 yrs)	12.0
Women, non-pregnant (>15yrs)	12.0
Women, pregnant	11.0
Men (>15yrs)	13.0

The hemoglobin data for the four groups, as represented by normal distributions, are provided in Table 7-13. Kolgomorov-Smirnov (KS) tests were performed using the SAS procedure NPAR1WAY to test for differences between the subgroups and dataset comprised of all other persons. All of these tests were significant ($p<0.0001$), indicating that the Hb distributions were different for the compared groups. In knowing that the group of persons with anemia contained the lowest values for hemoglobin content, we decided that this group would be used to develop an alternative distribution for evaluating the effect it has on estimated COHb levels.

Rather than identify anemic persons using the WHO (2001) thresholds and develop distributions from these samples, we elected to apply the WHO (2001) thresholds to the existing hemoglobin distributions when sampling for that variable within APEX. This way the original population distribution shape is preserved, though truncated at the portion of the distribution of interest to represent an anemic person's hemoglobin content. A model simulation was performed

[10] While there were persons that responded to a question asking whether they were being treated for anemia, we judged that these persons might not best represent the anemic population based on the medical intervention. The WHO et al. (2001) thresholds used here are given in Table 7-12.

as described previously, using the Denver study area, the CHD at-risk population, and air quality just meeting the current standard.

The COHb levels experienced by this new simulated population (i.e., CHD persons with anemic hemoglobin) were compared with the corresponding results generated when sampling for hemoglobin content from the full distribution (base hemoglobin) (Table 7-14). Using the anemic hemoglobin distribution resulted in a greater number of persons and hence a greater percent of persons at or above selected COHb levels when compared with the base hemoglobin simulation. The difference between results from the two simulations was not large when considering differences in the percentage points, with the smallest differences observed at the upper COHb levels. As far as the magnitude of the difference expressed as a percent increase in persons, there was a 50 – 100% increase in the percent of persons at or above selected COHb levels when considering this hypothetical anemic CHD population. This indicates that it is possible that the number and percent of persons estimated to experience %COHb at or above selected benchmarks may be underestimated when considering certain physiological attributes such as hemoglobin content, but the overall magnitude of the effect is dependent on the benchmark level considered. A quantitative characterization is not possible at this time due to the lack of readily available information on the percent of HD or CHD population with anemia and regarding the extent to which persons with anemia might have been included in the CAD/COHb clinical studies.

Table 7-13. Descriptive statistics of blood hemoglobin content measured in various groups (from NHANES 1999-2008).

Group	Blood Hemoglobin Content (g/dL)				
	N	mean	stdev	min	max
African-American	10,171	13.4	1.5	5.8	18.5
Anemia	2,853	11.3	1.0	5.8	12.9
Pregnant	659	12.5	1.1	8.6	16.4
All Other Persons	41,985	14.2	1.5	5.8	19.7

Table 7-14. Comparison of the portion of the simulated CHD population in the Denver study area estimated to experience a daily maximum end-of-hour COHb at or above specified levels when sampling from the base and anemic hemoglobin content distributions – air quality just meeting the current standard.

COHb Levels (%)	CHD Persons[a,b]			
	Base Hemoglobin[c]		Anemic Hemoglobin[d]	
	Number	Percent	Number	Percent
0.0	53,656	100	53,656	100
1.0	44,166	82.3	46,918	87.4
1.5	12,563	23.4	15,845	29.5
1.75	5,800	10.8	7,639	14.2
2.0	2,258	4.2	3,344	6.2
2.5	444	0.8	827	1.5
3.0	111	0.2	197	0.4
3.5	62	0.1	74	0.1
4.0	12	< 0.1	25	< 0.1

Notes:
Adjusted ambient concentrations from four monitors in 1995 were used to represent the air quality just meeting the current 8-hour standard.
[a] Includes persons with diagnosed coronary heart disease, angina pectoris, and heart attack (CDC, 2009).
[b] Includes estimate of persons with undiagnosed ischemia developed by EPA (see section 5.5.2.1).
[c] Used hemoglobin distributions defined in Appendix A for general population. Dose results were obtained from Table 6-18.
[d] Used hemoglobin distributions defined in Appendix A for general population, only truncated the distributions by upper limits defined in Table 7-13.

7.3 KEY OBSERVATIONS

Based on an overall qualitative judgment of the identified sources of uncertainty in the assessment approach, selections made regarding input data, and algorithms used, and their characterization as to direction and magnitude of influence on exposures and doses, staff consider the exposure and dose estimates to be reasonable for the simulated population the assessment is intended to represent (i.e., the CHD or HD population residing within the urban core of each study area). This is because:

- Only three sources of uncertainty were associated with a potential directional influence - data base quality (overestimation), missing data substitution (underestimation), and zero concentration frequency (underestimation) - and all were judged to have a low magnitude of influence on estimated exposures and doses.
- Thirteen of the identified sources of uncertainty were judged by staff to have either bidirectional influence (eight sources) or unknown direction (five sources):
  - One source of uncertainty (i.e., microenvironmental algorithm and data inputs) was judged as having a potentially medium magnitude of influence on exposure and dose estimates.
  - Five of the remaining twelve sources (i.e., spatial representation, historical data used, activity pattern database, longitudinal profile algorithm, physiological factors) were judged as having low to medium magnitude of influence, the level of which varied based on whether an identified condition existed.
  - Ten of the sources were judged to have a low magnitude of influence on estimated exposures and doses (i.e., database quality, missing data substitution method, zero concentration frequency, proportional approach used, population database, meteorological data, commuting database and algorithm, at-risk population prevalence rates, and benchmark levels for the simulated at-risk population).

There was a wide-ranging level of uncertainty in the knowledge base for the identified sources:

- Nine sources were judged by staff as having medium knowledge-base uncertainty including: spatial and temporal representation, historical data used, activity pattern database, longitudinal profile algorithm, microenvironmental algorithm and input data, at-risk population prevalence rates, physiological factors, and the benchmark levels for the simulated at-risk population.
- The knowledge-base uncertainty was judged as low for four of the identified sources having either unknown or bidirectional influence. This included the proportional approach used in adjusting air quality conditions, the population database, meteorological data, and commuting data.

- The knowledge-base uncertainty was also judged as low for the three sources identified above as being associated with either under- or overestimating exposures, i.e., the data base quality, missing data substitution, and zero concentration frequency.

The ratings of the knowledge-base uncertainty can indicate the need for additional data or analyses to better characterize the uncertainty. When combined with the potential magnitude of influence associated with each identified source, a prioritization can be given to the higher rated influential sources. Based on the results of this uncertainty characterization, staff judges that seven sources (i.e., the spatial and temporal representation of ambient monitoring data, historical data used, activity pattern database, longitudinal profile algorithm, microenvironmental algorithm and input data, and physiological factors) remain as the most important uncertainties in this assessment.

7.4 REFERENCES

Allen TH, Peng MT, Chen KP, Huang TF, Chang C, Fang HS. (1956). Prediction of blood volume and adiposity in man from body weight and cube of height. *Metabolism*. 5:328-345.

Brain JD and Samet JM. (2010a). Letter from Drs. JD Brain and JM Samet to Administrator Lisa Jackson. Re: Review of the Risk and Exposure Assessment to Support the Review of the Carbon Monoxide (CO) Primary National Ambient Air Quality Standards: First External Review Draft. CASAC-10-006. February 12, 2010.

Brain JD and Samet JM. (2010b). Letter from Drs. JD Brain and JM Samet to Administrator Lisa Jackson. Re: Review of the Risk and Exposure Assessment to Support the Review of the Carbon Monoxide (CO) Primary National Ambient Air Quality Standards: Second External Review Draft. EPA-CASAC-10-012. May 19, 2010.

Brainard J and Burmaster D. (1992). Bivariate distributions for height and weight of men and women in the United States. *Risk Analysis*. 12(2):267-275.

CDC. (2009). Summary Health Statistics for U.S. Adults: National Health Interview Survey, 2007. Series 10, Number 240. U.S. Department of Health and Human Services, Hyattsville, MD, May 2009.

Galetti PM. (1959). Respiratory exchanges during muscular effort. *Helv Physiol Acta*. 17:34-61.

Graham SE and McCurdy T. (2005). Revised ventilation rate (VE) equations for use in inhalation-oriented exposure models. Report no. EPA/600/X-05/008. Report is found within Appendix A of US EPA (2009). Metabolically Derived Human Ventilation Rates: A Revised Approach Based Upon Oxygen Consumption Rates (Final Report). Report no. EPA/600/R-06/129F. Appendix D contains "Response to peer-review comments on Appendix A", prepared by S. Graham (US EPA). Available at: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=202543.

Glen G, Smith L, Isaacs K, McCurdy T, Langstaff J. (2008). A new method of longitudinal diary assembly for human exposure modeling. *J Expos Sci Environ Epidemiol*. 18:299-311.

Issacs K and Smith L. (2005). New Values for Physiological Parameters for the Exposure Model Input File Physiology.txt. Technical memorandum to Tom McCurdy, NERL WA10. December 20, 2005. Provided in Appendix A of the CO REA.

Johnson T. (1998). Memo No. 5: Equations for Converting Weight to Height Proposed for the 1998 Version of pNEM/CO. Memorandum Submitted to U.S. Environmental Protection Agency. TRJ Environmental, Inc., 713 Shadylawn Road, Chapel Hill, North Carolina 27514.

Johnson T, Mihlan G, LaPointe J, Fletcher K, Capel J. (2000). Estimation of Carbon Monoxide Exposures and Associated Carboxyhemoglobin Levels for Residents of Denver and Los Angeles Using pNEM/CO (Version 2.1). Report prepared by ICF Consulting and TRJ Environmental, Inc., under EPA Contract No. 68-D6-0064. U.S. Environmental Protection Agency, Research Triangle Park, North Carolina. Available at: http://www.epa.gov/ttn/fera/human_related.html. June 2000.

Joumard R, Chiron M, Vidon R, Maurin M, Rouzioux JM. (1981). Mathematical models of the uptake of carbon monoxide on hemoglobin at low carbon monoxide levels. *Environ Health Persp*. 41:277-289.

McCurdy T. (2000). Conceptual basis for multi-route intake dose modeling using an energy expenditure approach. *J Expos Anal Environ Epidemiol*. 10:1-12.

SAIC. (2001). Technical Peer Review of "Estimation of Carbon Monoxide Exposures and Associated Carboxyhemoglobin Levels for Residents of Denver and Los Angeles Using pNEM/CO (version 2.1)" Prepared by Science Applications International Corporation under EPA Contract No. 68-D-98-113. Available at: http://www.epa.gov/ttn/fera/human_related.html.

Salorinne Y. (1976). Single-breath pulmonary diffusing capacity. *Scand J Resp Diseases*. Supplementum 96.

US Census Bureau. (2007). Employment Status: 2000- Supplemental Tables. Available at: http://www.census.gov/population/www/cen2000/phc-t28.html.

US Census Bureau. (2009). American Fact Finder. Census Summary File 3 (SF3) – custom tables. Available at: www.factfinder.census.gov.

US EPA. (1992). Review of the National Ambient Air Quality Standards for Carbon Monoxide: Assessment of Scientific and Technical Information. Office of Air Quality Planning and Standards Staff Paper. Report no. EPA/452/R-92-004.

US EPA. (2002). EPA's Consolidated Human Activities Database. Available at: http://www.epa.gov/chad/.

US EPA. (2004). An Examination of EPA Risk Assessment Principles and Practices. Staff Paper prepared by the US EPA Risk Assessment Task Force. Report no. EPA/100/B-04/001. Available at: http://www.epa.gov/OSA/pdfs/ratf-final.pdf.

US EPA. (2008). Risk and Exposure Assessment to Support the Review of the NO_2 Primary National Ambient Air Quality Standard. Report no. EPA-452/R-08-008a. November 2008. Available at: http://www.epa.gov/ttn/naaqs/standards/nox/data/20081121_NO2_REA_final.pdf.

US EPA. (2009). Risk and Exposure Assessment to Support the Review of the SO_2 Primary National Ambient Air Quality Standard. Report no. EPA-452/R-09-007. August 2009. Available athttp://www.epa.gov/ttn/naaqs/standards/so2/data/200908SO2REAFinalReport.pdf.

WHO, UNICEF, UNU. (2001). Iron Deficiency Anaemia: Prevention, Assessment and Control. Report of a joint WHO/UNICEF/UNU consultation. World Health Organization, Geneva.

WHO. (2008). Harmonization Project Document No. 6. Part 1: Guidance document on characterizing and communicating uncertainty in exposure assessment. Available at: http://www.who.int/ipcs/methods/harmonization/areas/exposure/en/.

8 SUMMARY OF KEY OBSERVATIONS

This document describes the quantitative human exposure assessment and risk characterization being conducted to inform the U.S. Environmental Protection Agency's (EPA's) current review of the National Ambient Air Quality Standards (NAAQS) for carbon monoxide (CO). An assessment of ambient CO exposure/dose was developed in an earlier phase of this review in the late 1990s. The design of this REA builds upon recommendations from CASAC, information presented in the final ISA, as well as comments made by the public. Presented together below are the key observations made in each of the chapters.

Conceptual Overview: Assessing Ambient Carbon Monoxide Exposure and Risk

- Carbon monoxide in ambient air is formed primarily by the incomplete combustion of carbon-containing fuels and photochemical reactions in the atmosphere, with on-road mobile sources representing significant sources of CO to ambient air.
- Microenvironments influenced by on-road mobile sources are important contributors to ambient CO exposures, particularly in urban areas. Where present, other (nonambient) CO sources can also be important influences on total CO exposure and on the impact of ambient CO exposure on COHb levels.
- The formation of COHb is a key step in the elicitation of various health effects by CO. Further, COHb level is commonly used in exposure assessment and is considered the best biomarker for evaluating CO exposure and potential for health effects of concern.
- An individual's COHb levels reflect their endogenous CO production, as well as CO taken into the body during exposure to ambient and nonambient CO sources. CO uptake into the bloodstream during exposure is influenced by a number of variables including internal levels of CO and COHb, such that net uptake may be lower or negligible in instances where a preceding exposure has been substantially higher than the current one. Thus, the magnitude of the change in COHb level in response to ambient CO exposure may decrease with the presence of concurrent or preceding nonambient CO exposure.
- Individuals with CHD are the population with greatest susceptibility to short-term exposure to CO, and the population for which the current evidence indicates health effects occurring at the lowest exposures. The evidence further indicates a potential for other underlying cardiovascular conditions, particularly other types of heart disease, to contribute susceptibility to CO effects. Other populations potentially at risk include those with diseases such as chronic obstructive pulmonary disease (COPD), anemia, or diabetes, and those in prenatal or elderly life stages.
- Cardiovascular effects are the category of health effects for which the evidence is strongest and indicative of a likely causal relationship with relevant short-term CO exposures, particularly for people with CHD. Other endpoints for which the evidence

is suggestive of causal relationships include effects on the central nervous system, reproduction and prenatal development, and the respiratory system.

- The specific cardiovascular effects occurring at the lowest COHb levels studied in CHD patients are reduced time to exercise-induced angina and other markers of myocardial ischemia, in particular, specific changes to the ST-segment of an electrocardiogram.
- Risk is characterized in this REA through evaluation of COHb estimated in simulations involving ambient CO exposures experienced by two target populations: (1) individuals with CHD (including undiagnosed CHD persons) and (2) individuals with HD, including CHD (diagnosed and undiagnosed).
- Two types of COHb estimates are considered for the two target populations: (1) daily maximum end-of-hour COHb levels and (2) ambient contribution to daily maximum end-of-hour COHb levels (i.e., the change in COHb associated with ambient CO exposure alone).
- Results from simulations are reported in terms of percent of the simulated at-risk population expected to experience daily maximum end-of-hour COHb levels (or ambient CO contribution to daily maximum end-of-hour COHb levels) at or above a series of levels that range as low as 1%. These results are interpreted in the Policy Assessment document in light of potential health effects benchmarks.
    - For daily maximum end-of-hour COHb levels (absolute), these benchmarks range from 1.5%, which is below the lowest study mean COHb level resulting from experimental CO exposure in controlled human exposures of subjects with CAD, up to 3.0%, a level within the range associated with effects in those studies. For ambient contribution to daily maximum end-of-hour COHb levels, the comparison benchmarks include the range from 1.4% up to 2.4%, which are the COHb increments associated with effects in those studies.
- Beyond the at-risk populations and myocardial ischemia-related effects that are the focus of this quantitative REA, the current evidence regarding other potentially susceptible populations and other health effects associated with CO exposures is discussed and considered with regard to the review of the CO NAAQS in the Policy Assessment.

<u>Air Quality Considerations</u>

- Mobile sources (i.e., gasoline powered vehicles) are the primary contributor to CO emissions, particularly in urban areas due to greater vehicle and roadway densities.
- Recent (2005-2007) ambient CO concentrations across the US are lower than those reported in the previous CO NAAQS review and are also well below the current CO NAAQS levels. Further, a large proportion of the reported concentrations are below the conventional instrument lower detectable limit of 1 ppm.
- The currently available information for CO monitors indicates that siting of microscale and middle scale monitors in the current network is primarily associated with roads having moderate traffic density (<100,000 AADT), however, factors other than

reported AADT (e.g., orientation with regard to dense urban roadway networks) can contribute to sites reporting higher CO concentrations.

- Ambient CO concentrations are highest at monitors sited closest to roadways (i.e., microscale and middle scale monitors) and exhibit a diurnal variation linked to the typical commute times of day, with peak concentrations generally observed during early morning and late afternoon during weekdays.
- Policy relevant background (PRB) concentrations across the US are generally less than 0.2 ppm, far below that of interest in this REA with regard to ambient CO exposures.
- Historical trends in ambient monitoring data indicate that at individual sites, ambient concentrations have generally decreased in a proportional manner. This comparison included air quality distributions with concentrations at or above the current 8-hour standard and those reflecting current (*as is*) conditions.
- The temporal variability in selected upper percentile ambient concentrations (e.g., 99th percentile 1-hour daily maximum) at individual monitors in Denver and Los Angeles is relatively small across a three-year monitoring period, particularly when considering recent air quality. Much of the within-monitor temporal variability is due to a trend in decreasing concentration from year-to-year.
- There is greater spatial variability in selected upper percentile ambient concentrations (e.g., 99th percentile 1-hour daily maximum) at ten selected monitoring sites in Los Angeles when compared with four selected monitoring sites Denver, particularly when considering the recent air quality.

<u>Overview of Approach Used for Estimating Co Exposure and COHb Dose Levels</u>

- APEX, an EPA human exposure and dose model, has a long history of use in estimating exposure and dose for many of the criteria pollutants including CO, O_3, SO_2, and NO_2. Over time, EPA has improved and developed new model algorithms, incorporated newer available input data and parameter distributions, as well as performed several model evaluations, sensitivity analyses, and uncertainty characterizations for the above pollutants. Based on this analysis, APEX was judged to be an appropriate model to use for assessing CO exposure and dose.

<u>Application of APEX4.3 in this Assessment</u>

- Two exposure model domains (Denver and Los Angeles study areas) were defined by overlaying ambient monitor locations having 10 km radii with US census tract population data. Monitors selected comprised the bulk of the urban core in each location, where ambient monitoring data exist.
- Two simulated at-risk subpopulations were identified by combining the census tract-specific age and gender population distributions with HD and CHD prevalence rates, each also stratified by age and gender. In using this approach, staff can represent the variability that exists in the simulated at-risk HD and CHD subpopulations that reside in each census tract and within each study area.
    - Both simulated at-risk subpopulations include an estimate of persons with undiagnosed CHD.

- To represent spatial variability in ambient concentrations in Denver, a total of four monitors were used; in Los Angeles, the total number of monitors was ten. Temporal variability was represented by use of hourly ambient concentrations in each study area.
- The exposure and dose model simulations included 8 microenvironments in each location to represent the expected variability in microenvironmental CO concentrations.
- All indoor microenvironments were modeled using a mass balance model to represent temporal variability in indoor CO concentrations with respect to the outdoor CO concentration variability. In addition, distributions of microenvironmental factors were used for all microenvironments rather than point estimates. Using distributions of microenvironmental factors will better represent both spatial and temporal variability in estimated microenvironmental CO concentrations.
- Additional analyses using output from individual-level simulations were performed to provide information on the microenvironments most influential to population exposure at different exposure levels. This included an analysis of the effective ratios of microenvironment to ambient concentrations and the contribution of ambient CO exposure to total COHb level estimates. The smaller sample sizes generated for these analyses were found to be representative of the larger simulations employed for estimating exposure and dose in the different air quality exposure scenarios.

<u>Simulated Exposure and COHb Dose Results</u>

- Ambient CO exposures and resulting COHb levels in the blood of two simulated at-risk populations in the Los Angeles and Denver study areas were estimated considering five air quality scenarios: *as is* air quality, air quality adjusted to simulate *just meeting* the current 8-hour CO NAAQS, and air quality adjusted to just meet three potential alternative standards.
- The two at-risk populations simulated were: (1) persons with diagnosed CHD, including those estimated to have undiagnosed CHD, and (2) the larger group of persons with any type of HD including those estimated to have undiagnosed CHD. While the number of persons and person-days at or above selected COHb levels differed between the two populations, reflecting their differing size, the percentage of each population's persons and person-days were similar.
- The relative contribution of various microenvironments to exposure concentrations was generally similar between the two study areas. When considering *as is* air quality, indoor microenvironments contributed mostly to low level exposures (at or above 1 ppm and 2 ppm), comprising between 40 – 80% of the time spent at those exposure levels, while time spent inside vehicles contributed to most exposures at or above 3 ppm (70 – 100%). In comparison, when considering air quality just meeting the current standard, the percent contribution from indoor microenvironments was generally higher for low level exposures (about 65 – 85% of exposure concentrations at or above 1 ppm and 2 ppm), though again higher level exposures were dominated by the contributions from inside-vehicle microenvironments.

- The relationship between the two study areas with regard to estimated distribution of maximum end-of-hour COHb levels differed with the different air quality scenarios. Under *as is* air quality conditions, the simulated at-risk populations in the Los Angeles study area were estimated to experience a slightly higher distribution of maximum end-of-hour COHb levels than the Denver populations. Under conditions of air quality adjusted from historical air quality data to just meet the current or alternative standards, however, appreciably larger percentages of the Denver populations were estimated to experience COHb at or above specific levels than the Los Angeles populations.
- For *as is* air quality conditions, the highest daily maximum end-of-hour COHb estimated to be experienced over the course of the simulated year was below 1.5% for more than 98% of the at-risk populations simulated in each study area; it was below 2% COHb for more than 99.9% of these simulated populations. A lower percentage of the simulated at-risk populations in Denver were estimated to experience daily maximum end-of hour COHB below these benchmarks than were the populations in Los Angeles.
    - Under *as is* air quality conditions, the highest incremental contribution of ambient CO exposure to maximum end-of-hour COHb levels estimated in the simulated populations was 1.7% COHb, and more than 99% of both study area populations were estimated to have ambient CO contributions to COHb below 1.4%. As with estimates of total COHb (i.e., COHb from endogenous CO production and ambient exposure together), a larger percentage of the Los Angeles population was estimated to experience the higher ambient contributions to maximum end-of-hour COHb compared to the Denver population. For example, the percentage of the population estimated to experience ambient contributions to COHb at or above COHb levels above 1.0% was approximately 2 to 3 times as high in Los Angeles than in Denver.
- For simulations of air quality adjusted to just meet the current 8-hour standard of 9 ppm, the highest estimated daily maximum end-of-hour COHb over the course of the simulated year was below 1.5% for 95% of both simulated at-risk populations in the Los Angeles study area, and was below 2% COHb for 99.4% of these populations. In contrast, the percentage of the simulated at-risk populations in the Denver study area estimated to experience daily maximum end-of-hour COHb levels that did not exceed 1.5% was about 80%. The percentage of the Denver populations with their highest estimated daily maximum end-of-hour COHb below 2% was approximately 95%.
    - As with estimates of total COHb (i.e., COHb from endogenous CO production and ambient exposure together), the percentage of the simulated population estimated to experience the higher ambient contributions to maximum end-of hour COHb was appreciably greater in Denver as compared to Los Angeles. While estimated ambient CO contributions to daily maximum end-of-hour COHb were below 1.4% for nearly 98% of the Los Angeles simulated population, the corresponding percentage of the Denver population was about 87%.
- In addition to the simulations for *as is* and just meeting the current 8-hour standard air quality conditions, three simulations of air quality just meeting potential alternative

standards were performed. The alternatives comprise different combinations of form, averaging time and level which were expected to achieve somewhat similar exposure and dose results. The combinations that were selected were based on consideration of exposure and dose results obtained for the *as is* air quality conditions and the higher just meeting the current 8-hour standard conditions. The combinations of form, averaging time and level that were simulated include: (1) a second-highest 8-hour average of 5 ppm, (2) a 99th percentile daily maximum 8-hour average of 5.0 ppm, and (3) a 99th percentile daily maximum 1-hour average of 8.0 ppm.

  - These three simulations generated generally similar percentages of the at-risk populations estimated to be exposed at selected concentrations and experience maximum end-of hour COHb levels at or above selected levels. Each of these three simulations generated fewer persons and a lower percent of the at-risk populations at or above selected COHb levels than did simulations for air quality adjusted to just meet the current 8-hour standard. For example, about 1% or less of the Denver populations had a highest daily maximum end-of-hour COHb at or above the 2.0% COHb level in the alternative standards' simulations as compared to approximately 4.2% in simulations of air quality just meeting the current standard. When considering the potential alternative standards in Los Angeles, generally fewer than 0.1% of the simulated at-risk populations were estimated to experience a maximum end-of-hour COHb level at or above 2.0 % COHb, compared to 0.5% at that same COHb level associated with air quality adjusted to just meet the current standard.

- Results for the five air quality scenarios are further analyzed in the Policy Assessment to inform consideration of the level of public health protection that might be provided by alternative standard levels associated with different combinations of averaging time and form.

- Results generated in the current assessment for the air quality conditions just meeting the current NAAQS were compared with estimates from the assessment conducted in 2000 (Johnson et al., 2000) for similar conditions in the Denver and Los Angeles study areas (section 6.3). The two assessments employed similar approaches, similar, although not identical air quality data for this scenario, and they used different exposure models (APEX vs. pNEM). Results were similar for the 1.5% and 2% COHb level for the simulated Los Angeles study area population and somewhat different for the Denver study area population. For example, the two assessments' Los Angeles estimates of population percentages with highest daily maximum end-of hour COHb at or above these COHb levels were similar and within about 10% of one another. For the Denver simulated study populations, however, the estimates for these two COHb levels were about 3 and 8 times greater, respectively, in the current assessment when compared with that estimated in the prior assessment.

Variability Analysis and Uncertainty Characterization

- Based on an overall qualitative judgment of the identified sources of uncertainty in the assessment approach, selections made regarding input data, and algorithms used, and their characterization as to direction and magnitude of influence on exposures and doses, staff consider the exposure and dose estimates to be reasonable for the simulated population the assessment is intended to represent (i.e., the CHD or HD population residing within the urban core of each study area). This is because:
    - Only three sources of uncertainty were associated with a potential directional influence - data base quality (overestimation), missing data substitution (underestimation), and zero concentration frequency (underestimation) - and all were judged to have a low magnitude of influence on estimated exposures and doses.
    - Thirteen of the identified sources of uncertainty were judged by staff to have either bidirectional influence (eight sources) or unknown direction(five sources):
        - One source of uncertainty (i.e., microenvironmental algorithm and data inputs) was judged as having a potentially medium magnitude of influence on exposure and dose estimates.
        - Five of the remaining twelve sources (i.e., spatial representation, historical data used, activity pattern database, longitudinal profile algorithm, physiological factors) were judged as having low to medium magnitude of influence, the level of which varied based on whether an identified condition existed.
        - Ten of the sources were judged to have a low magnitude of influence on estimated exposures and doses (i.e., database quality, missing data substitution method, zero concentration frequency, proportional approach used, population database, meteorological data, commuting database and algorithm, at-risk population prevalence rates, and benchmark levels for the simulated at-risk population).
- There was a wide-ranging level of uncertainty in the knowledge base for the identified sources:
    - Nine sources were judged by staff as having medium knowledge-base uncertainty including: spatial and temporal representation, historical data used, activity pattern database, longitudinal profile algorithm, microenvironmental algorithm and input data, at-risk population prevalence rates, physiological factors, and the benchmark levels for the simulated at-risk populations.
    - The knowledge-base uncertainty was judged as low for four of the identified sources having either unknown or bidirectional influence. This included the proportional approach used in adjusting air quality conditions, the population database, meteorological data, and commuting data.

    - The knowledge-base uncertainty was also judged as low for the three sources identified above as being associated with either under- or overestimating exposures, i.e., the data base quality, missing data substitution, and zero concentration frequency.

- The ratings of the knowledge-base uncertainty can indicate the need for additional data or analyses to better characterize the uncertainty. When combined with the potential magnitude of influence associated with each identified source, a prioritization can be given to the higher rated influential sources. Based on the results of this uncertainty characterization, staff judges that seven sources (i.e., the spatial and temporal representation of ambient monitoring data, historical data used, activity pattern database, longitudinal profile algorithm, microenvironmental algorithm and input data, and physiological factors) remain as the most important uncertainties in this assessment.

APPENDICES

Appendix A

Technical Memorandum on Updates To APEX Physiology.Txt File (Isaacs And Smith, 2005)

The following contains a technical memo provided by Isaacs and Smith (2005) in its original format. Staff included page numbers and performed some minor formatting to text and table headers for the purposes of inclusion into the CO REA appendices.

TECHNICAL MEMORANDUM

TO: Tom McCurdy, WA-COR, NERL WA 10
FROM: Kristin Isaacs and Luther Smith, Alion Science and Technology
DATE: December 20, 2005
SUBJECT: New Values for Physiological Parameters for the Exposure Model Input File Physiology.txt.

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1. INTRODUCTION

The purpose of this memo is to present an updated version of the physiological parameters input file (Physiology.txt) for the APEX model. Portions of this file are also used as input for SHEDS-PM and SHEDS-AirToxics.

The physiology file contains age- and gender-based information for several physiological parameters used in human exposure modeling. This information includes distributional shapes and parameters for all age and gender cohorts from age 0 to 100 years for normalized maximal oxygen uptake (nvo2max), body mass, resting metabolic rate (RMR), and blood hemoglobin content. In addition, a parameter called blood volume factor (BVF), which is a cohort-dependent parameter in the equation for blood volume as a function of body mass, is present in the file as well.

New age- and gender-dependent distributions were developed based the best available physiological data from the literature. In this report, a summary of the current state of the physiology file is presented, followed by the derivation of new physiological data for body mass, normalized vo2max, and hemoglobin content. Portions of the SAS code used for analysis are included (Appendices A-C), as is the new Physiology.txt file (Appendix D). The final appendix (Appendix E) contains tables of all the derived physiological parameters.

2. EVALUATION OF THE CURRENT PHYSIOLOGY FILE DATA

The physiology.txt file was originally generated for the PNEM model by T. Johnson. It was last updated 6/11/1998, as documented in the report *User's Guide: Software for Estimating Ventilation (Respiration) Rates for Use in Dosimetry Models*, (T. Johnson and J. Capel). In that report, the original references for the data in the file were provided. An evaluation of the data in the file was included in a previous memo to the WA-COR under this work assignment. A summary of those findings is repeated here.

2.1 2.1 NORMALIZED MAXIMAL OXYGEN UPTAKE (NVO2MAX).

The nvo2max data were derived from a number of sources. The data for males, especially, were pieced together from a variety of studies (a total of 6), leading to discontinuities in the distributional parameters. However, in each age and gender cohort, the distributions parameters were derived from a single published study. Additionally, much of the nvo2max data is quite old. The data for males at age 20 and at 28-69 came

from a study from 1960 [1]. Data for males aged 0-8 and 16-19, and females 0-19 came from a figure in a textbook from 1977 [2], which in turn was based on limited earlier data. An additional issue with the 1977 data is (according to the report mentioned above) that values for certain ages (very young or elderly) were acquired by simple tangential extrapolation of the data in the figure.

In addition, in some cases it was not clear how the parameters were derived from the referenced studies. For example, Heil et al. [3] was referenced as the source of the values for females aged 66-100. However, an examination of that study provided no clues as to how the values were actually determined. As far as can be determined, in no place did the authors break down the means and SDs of their data into groups separated by both gender and age simultaneously.

2.2 BODY MASS.

The current body mass data were derived from an in-depth analysis [4, 5] of the second CDC National Health and Nutrition Examination Survey (NHANES II) body mass data [6]. The data were relatively comprehensive, and the methods used to generate the lognormal distributions were sound. However, the NHANES II data were compiled for the years 1976-1980, so an analysis of more recent data is necessary to accurately account for changes in human activity patterns in adults and especially children.

2.3 RESTING METABOLIC RATE.

Not included for evaluation, per discussion with WA-COR.

2.4 HEMOGLOBIN CONTENT AND BLOOD VOLUME FACTOR.

The original references for the hemoglobin content or blood volume factor values given in the current physiology.txt file could not be identified. Therefore, their validity could not be evaluated and it was desirable that new statistics be calculated.

2.5 SUMMARY OF FINDINGS

- In some cases, especially for nvo2max, the data are unnecessarily and confusingly disjointed across ages.
- It is also unclear how some of the nvo2max values were derived from the referenced studies.
- With the exception of the Schofield equations for the BM/RMR regression, parameter distributions at each age and gender cohort were derived from data from a single study.

- Many of the studies used are very old (ex. 1960, 1977).
- Some the data is of questionable validity (for example, the extrapolation of a textbook figure is used), although it may have been the best available at the time of the compilation of the file.
- The original source of the hemoglobin content and blood volume factor data could not be identified.
- Given these conclusions, we recommended a full review and update of the current physiology.txt file data. Specifically, we recommended that where possible, new distributions or equations should be developed based on thorough, compiled data from appropriate studies.

3. DERIVATION OF NEW DISTRIBUTIONS FOR BODY MASS

3.1 THE NHANES BODY MASS DATASET.

New body mass distributions were generated from data from the National Health and Nutrition Examination Survey (NHANES). This survey is an ongoing study carried out by the National Center for Health Statistics of the Centers for Disease Control. EPA recognizes the utility of this dataset in characterizing the American population for risk assessment and policy support purposes [7].

Older NHANES data (for the years 1976-1980) have been used previously to develop population estimates of body mass distributions [4,5]. The current Physiology.txt file body mass distributions are based on this work. However, the analysis presented here is based on the most recent NHANES data, for the years 1999-2004 [8].

Demographic (Demo) and Body Measurement (BMX) datasets for each of the NHANES studies were downloaded from the NHANES website. The files were downloaded as SAS xpt datasets. The downloaded files were as follows:

1999-2000	**2001-2002**	**2003-2004**
BMX.xpt	BMX_b_r.xpt	BMX_c.xpt
Demo.xpt	Demo_b.xpt	Demo_c.xpt

The Demographic datasets contained the age and gender values for each survey participant, while the Body Measurement datasets contained the body weights for each subject. The combined dataset comprised 31,126 individuals. This resulted in approximately 400-500 persons in each age 0-18 year cohort, and approximately 80-150 persons in each age 19-85 year cohort (the NHANES studies more heavily sampled children).

3.2 CALCULATION OF THE NEW SAMPLING WEIGHTS FOR THE COMBINED NHANES DATASET.

In the analysis of the NHANES data, sampling weights must be used to ensure that the data are weighted to appropriately represent the national population. Sampling weights for the combined NHANES body mass dataset were derived as recommended by the documentation provided with the most recent NHANES release [9]. Specifically, the sampling weight for each subject was calculated as:

$$w_{combined} = \frac{1}{3} w_{2003-2004} \tag{1}$$

$$w_{combined} = \frac{2}{3} w_{1999-2002} \tag{2}$$

where $w_{combined}$ is the sampling weight for the combined dataset, $w_{2003\text{-}2004}$ is the weight for the subjects in the most recent study, and $w_{1999\text{-}2002}$ is the weight for subjects in combined 4-year (1999-2000 and 2001-2002) NHANES dataset. (Both weights are provided with the appropriate NHANES release. The combined 1999-2002 weight, which is not a simply half of that for the corresponding 2-year periods, was explicitly calculated for researcher use by CDC since the two 2-year periods use different census data.)

By using the sampling weights, once can consider any 2-year NHANES dataset or any combination of datasets as a nationally representative sample.

3.3 FITTING THE BODY MASS DATA.

In the current physiology file, body mass is modeled as a two-parameter lognormal distribution. The NHANES body mass data were fit to several types of distributions (including normal, beta, and three-parameter lognormal distributions). It was determined that overall, the distribution that provided the best combination of good behavior over ages and good fit to the data was a two-parameter lognormal distribution.

The data were fit to the lognormal distributions using the SAS PROC UNIVARIATE procedure. The FREQ option of the procedure was used to apply the sampling weights. The SAS code used to generate the body mass distributions is provided in Appendix A.

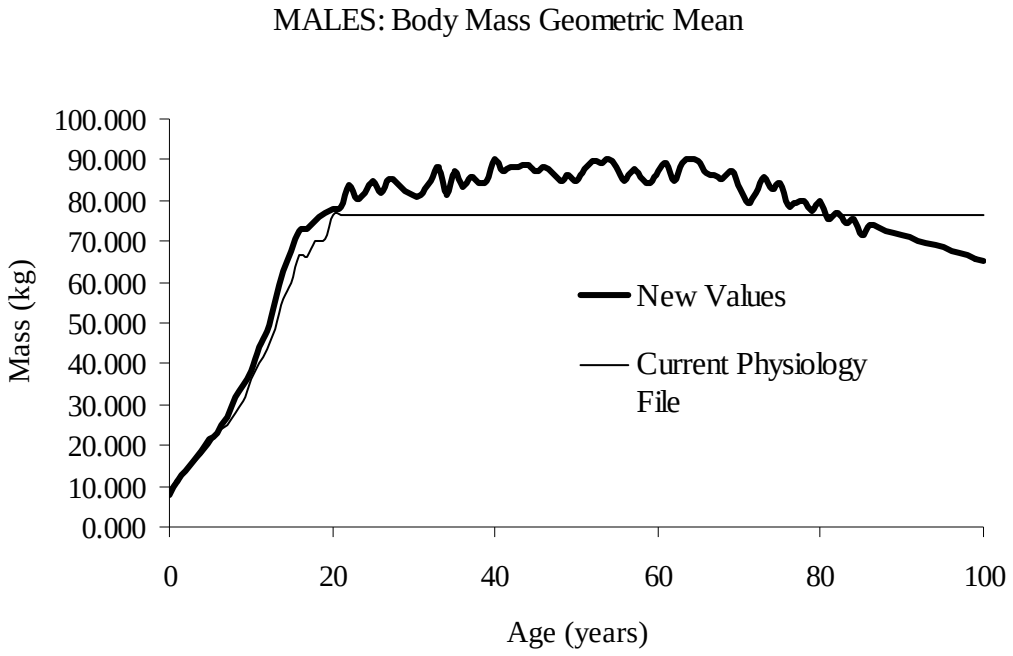
As the NHANES 1999-2003 studies only covered persons up to age 85, linear forecasts were made for ages 86-100, as based on the data for ages 60 and greater.

3.4 Body Mass Results.

Geometric means and standard deviations (SD) for the best-fit lognormal distributions for body mass are given in Figures 1 and 2. The means behaved fairly smoothly across ages. Note that for children age 0-18, the values of the new fits are similar, but slightly higher than those in the current Physiology.txt file, which were derived from earlier NHANES studies. The new means also capture the trend towards decreasing body weight in older persons that was previously neglected in the Physiology.txt file.

The maximum and minimum values for the distributions are presented in Figures 3 and 4. The minimums and maximums were calculated as the 1st and 99th percentile of the raw body mass data for the cohort. (Note that these values differ from the 1st and 99th percentiles of the fitted lognormals.) While the minimum value is consistent with the current Physiology.txt (which was based on earlier NHANES studies), the new cohort maximums are generally higher than before.

The behavior of several of the body mass parameters (especially the SD) is fairly noisy, especially for adults. This is most likely due to the smaller number of samples for adults as compared to children. Therefore, it may desirable to use age-grouped data or running averages over years in these age ranges. While the attached prepared Physiology.txt file uses the “raw” parameters, smoothed results using 5-year running averages are provided in the attached data tables (Appendix E, plots not shown). These could be used at the direction of EPA; changing the “official” release Physiology.txt file would be trivial.



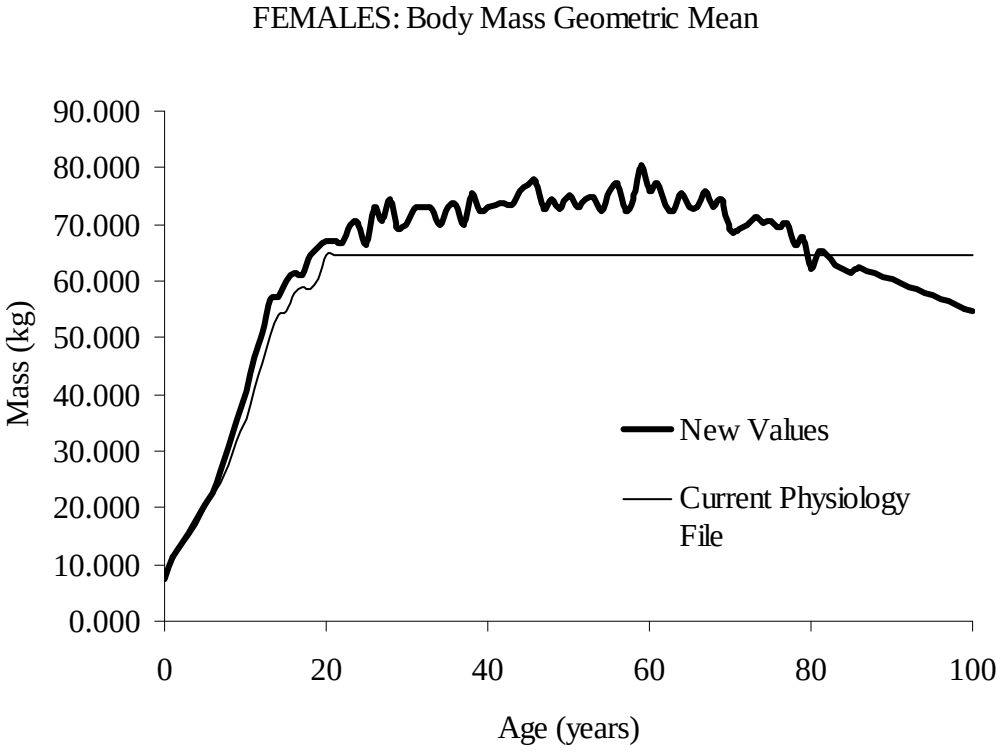
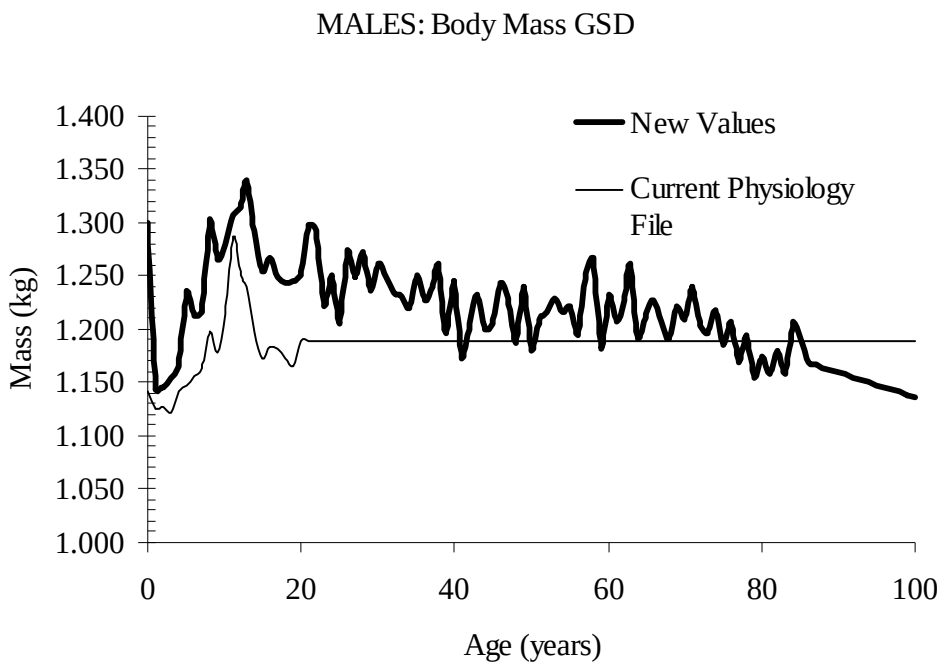


Figure 1. Geometric Means for the Best-fit Lognormal Distributions for Body Mass as a Function of Age, Derived from NHANES 1999-2004 Study Data.



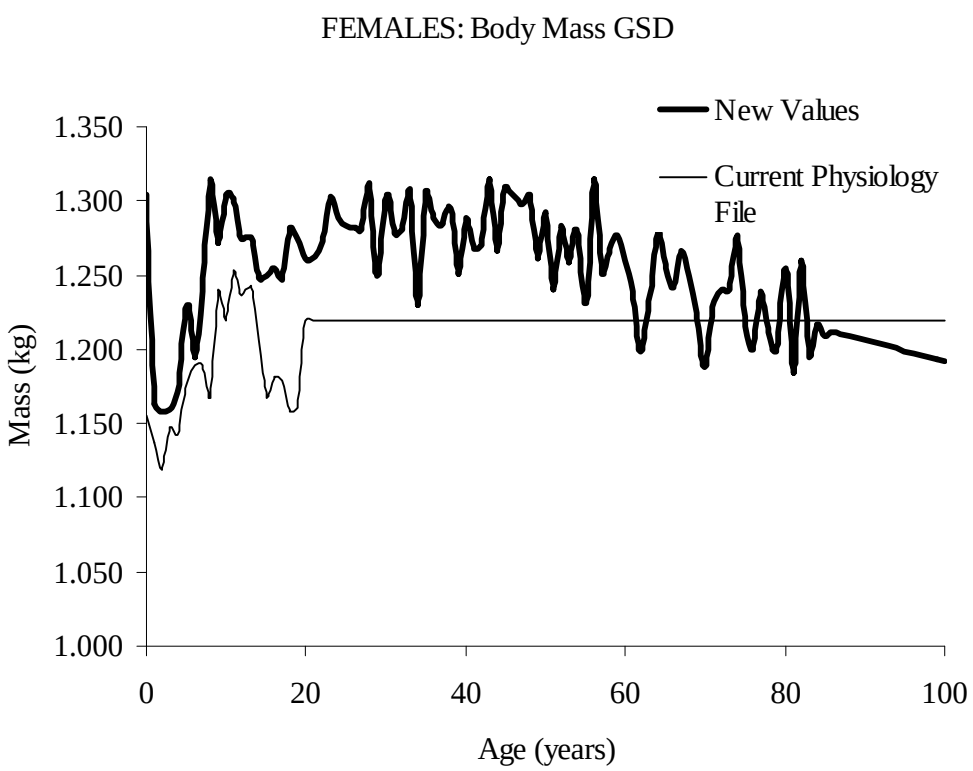
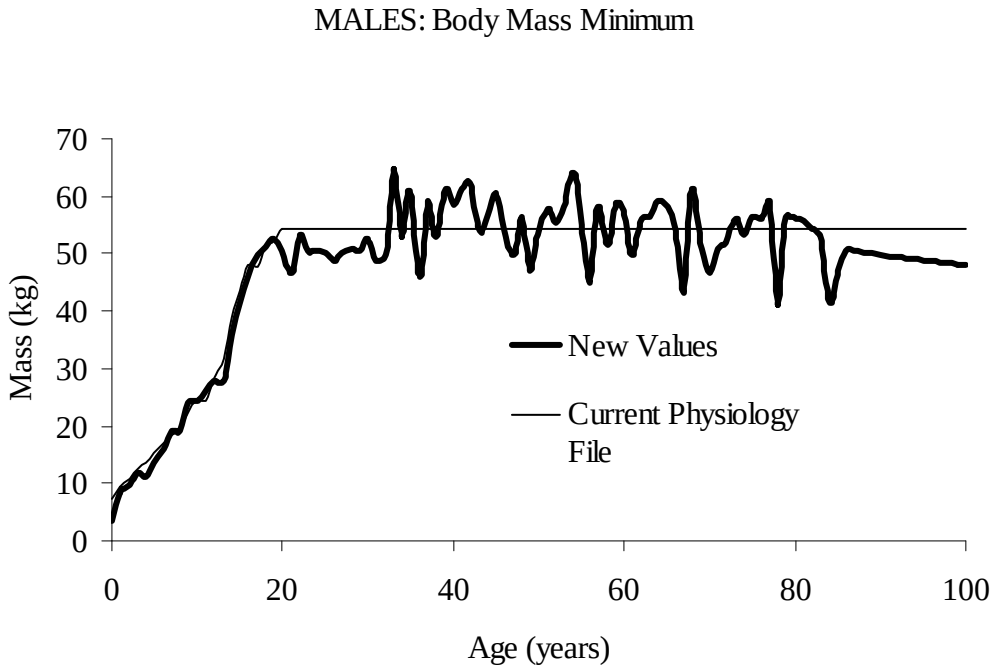


Figure 2. Geometric Standard Deviations for the Best-fit Lognormal Distributions for Body Mass as a Function of Age, Derived from NHANES 1999-2004 Study Data.



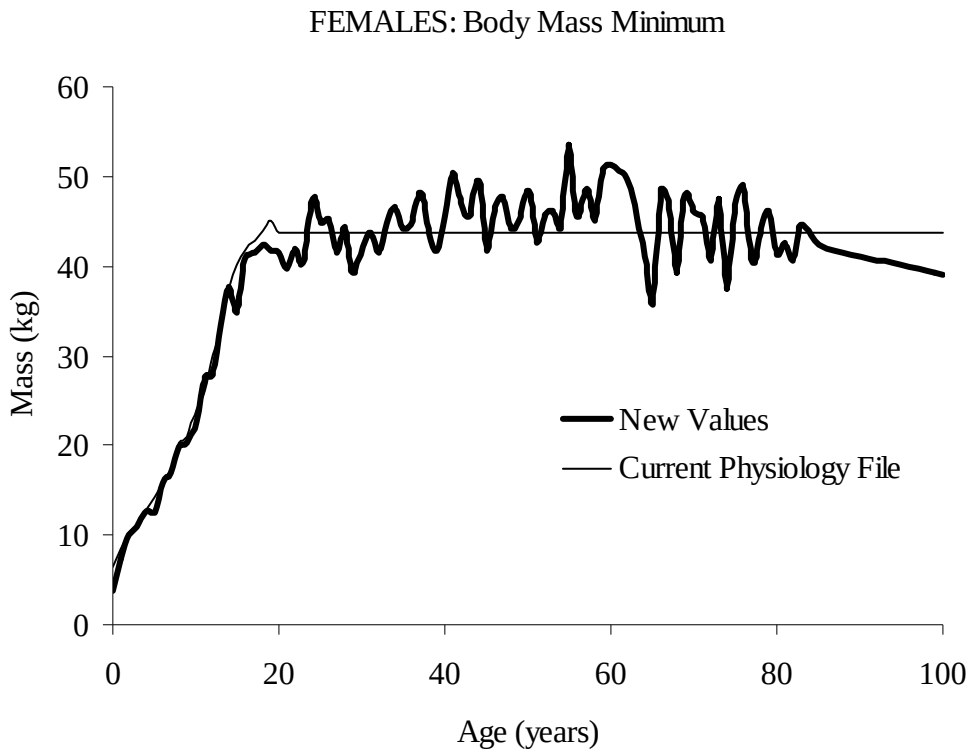
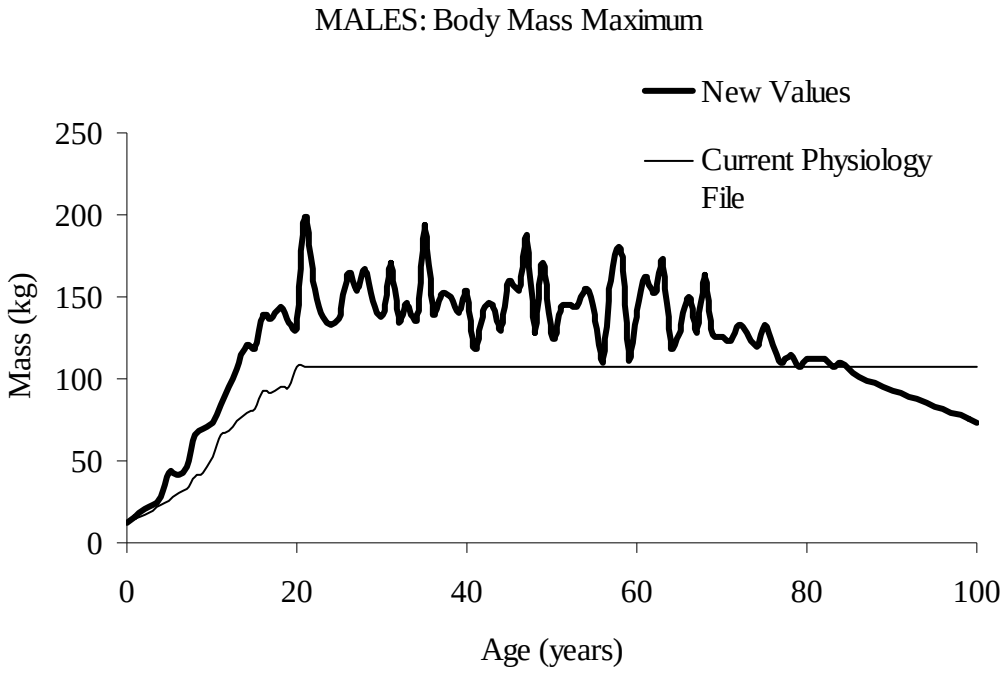


Figure 3. Minimums (1st Percentile) for Body Mass as a Function of Age, Derived from NHANES 1999-2004 Study Data.



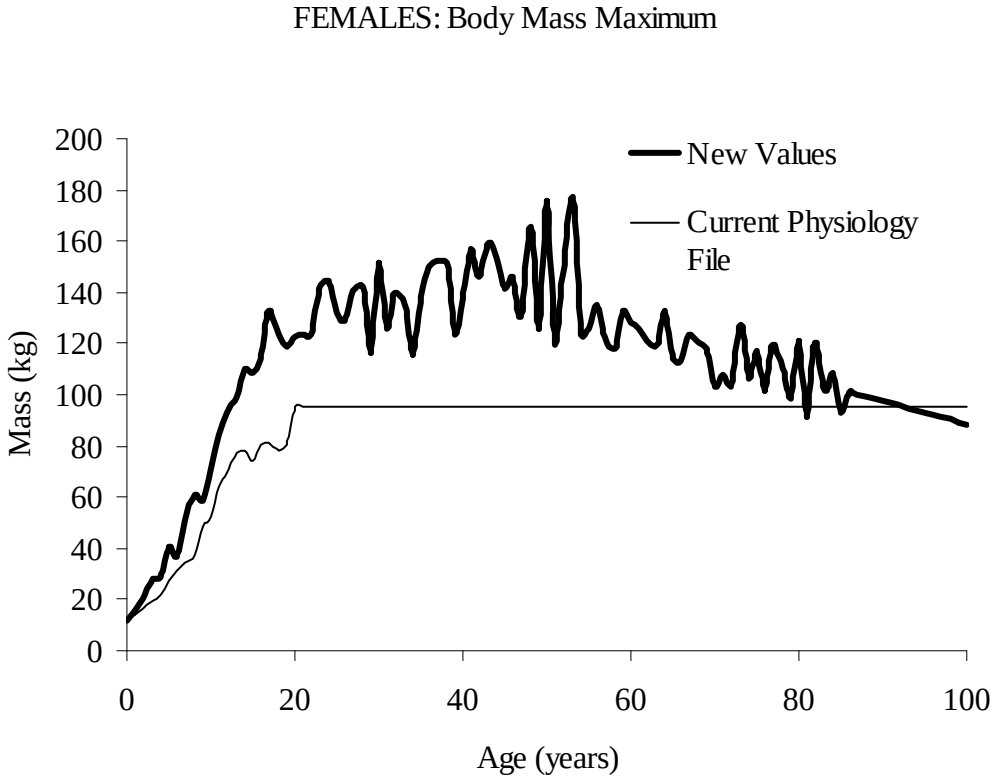


Figure 4. Maximums (99th Percentile) for Body Mass as a Function of Age, Derived from NHANES 1999-2004 Study Data.

4. DERIVATION OF NEW DISTRIBUTIONS FOR NORMALIZED VO2MAX

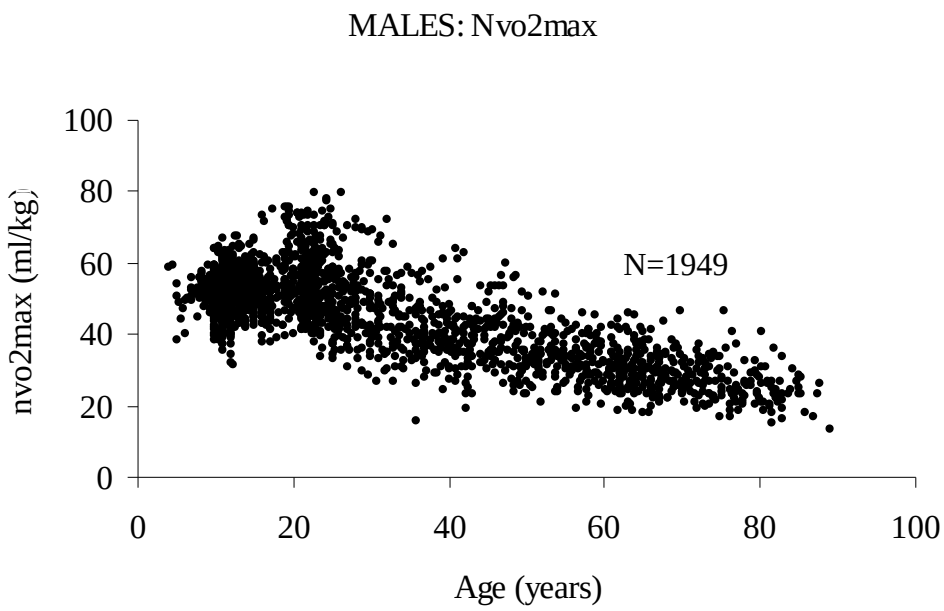
2.2 4.1 THE NVO2MAX DATA

The NHANES studies do report data for vo2max in individuals. However, the NHANES vo2max values are estimated values, i.e. they are not measured directly. Such estimated values are not appropriate for use in this context (as per discussion with the WA-COR). Therefore, nvo2max distributional shapes were determined from a large database of experimental and literature vo2max measurements for different age/gender cohorts.

A PubMed-based literature search located a number of studies in which vo2max was directly measured. In addition, a large number of scientific papers (~350) reporting vo2max were also provided to Alion by the WA-COR. All the studies were evaluated for use by determining if: 1) any normalized vo2max data for individuals were reported or 2) any group means for narrow age-gender cohorts were reported. Studies in which the studied age group was very broad or contained both males and females were discarded. Also discarded were any studies in which vo2max was not normalized by body mass, or for which no age data were reported. Data for ill or highly-trained individuals were not used; however, studies in which subjects underwent mild or moderate exercise training were included. Two large databases, one of individual vo2max data and one of grouped means and SDs, were constructed from the valid studies.

The database of individual data comprised age versus nvo2max data for 1949 men and 1558 women. The data were pulled from either tables or graphs in 20 published studies [11-30]. Additional raw experimental data were provided by the WA-COR [31]. In the case of the graphical data, the original source was digitized and the data points were pulled from the digital figure using graphics software. (This was accomplished by calibrating the pixels of the digitized image with the range of age and nvo2max values.) The individual nvo2max data for males and females are shown in Figure 5.

The grouped mean and SD data were derived from 136 studies [32-167]. These data comprised approximately 550 means and SDs for different age/gender cohorts. Single age/gender cohort means and SD values for the Adams data [31] were also included in this dataset. Only data for subject groups having an age SD of less than approximately 2-3 years were considered. The grouped mean values for men and women are shown in Figure 6, while the group SD values are shown in Figure 7.



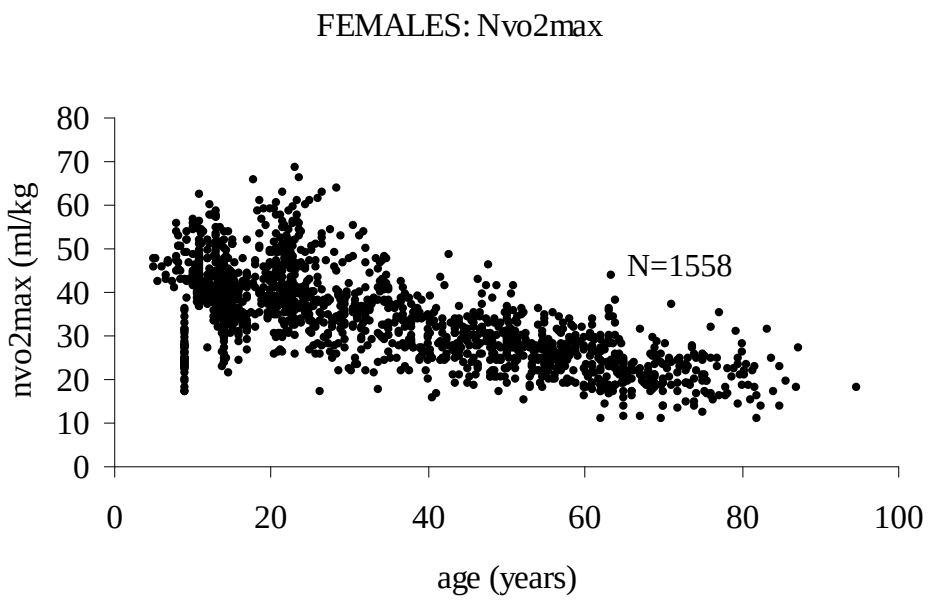
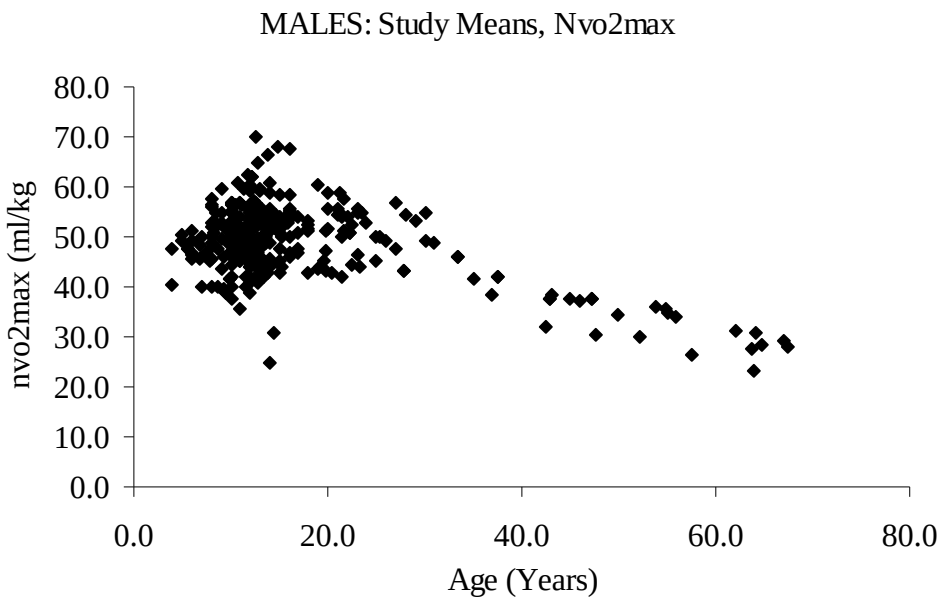


Figure 5. Individual Nvo2max Measurements for Males and Females, Derived from Literature Studies and Experimental Measurements.



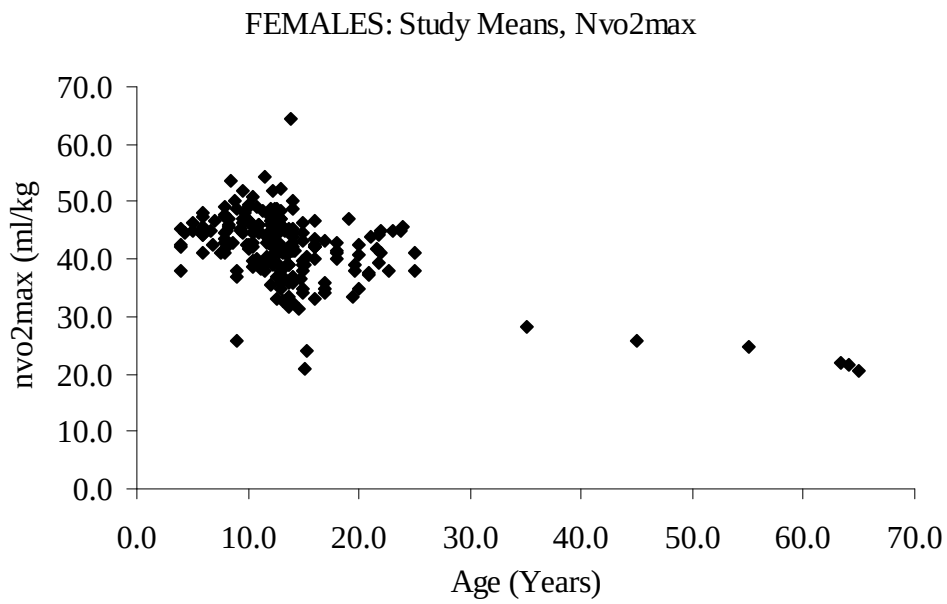
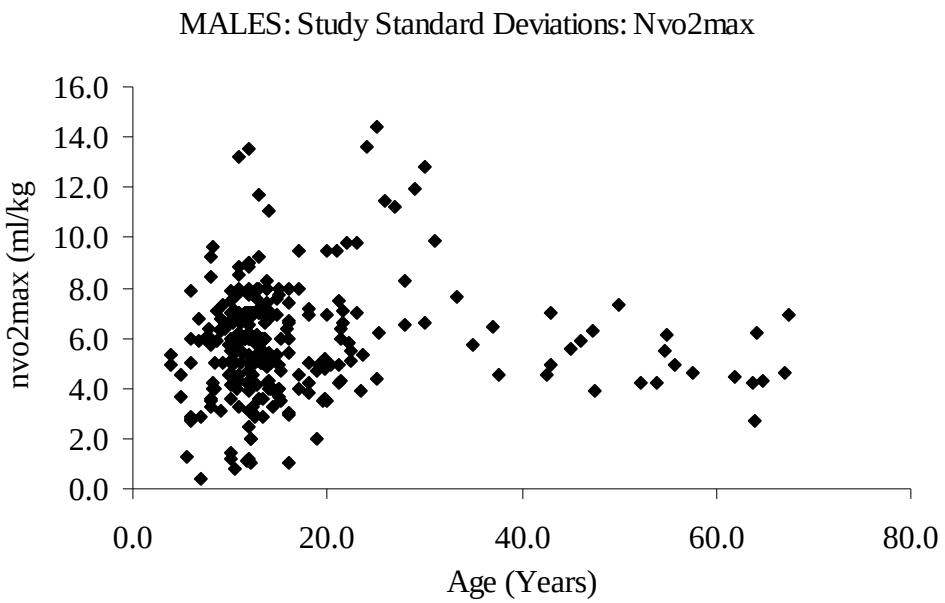


Figure 6. Grouped Mean Nvo2max Measurements for Males and Females, Derived from Literature Studies.



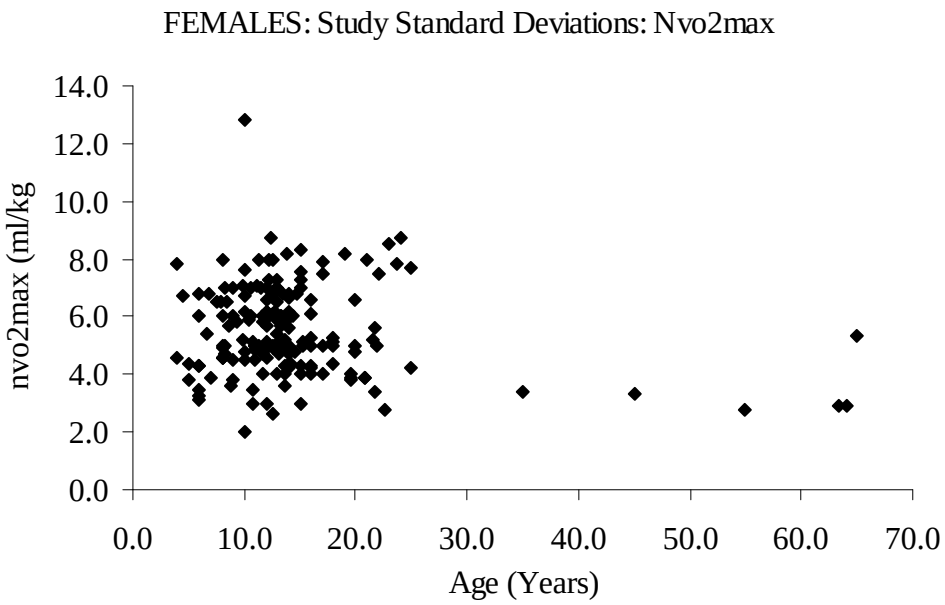


Figure 7. Nvo2max Standard Deviations for Males and Females, Derived from Literature Studies.

4.2 Determining the NVo2max Distributions

Both the grouped mean and the individual datasets were evaluated for use in deriving the nvo2max parameters.

The group means and SD were combined into single age/gender cohort values. The combined means were calculated as mean of the group means, weighted by the number of subjects. The group SD were calculated by transforming each group SD to a group variance, calculating the mean variance (weighted by the number of subjects in each study) and retransforming the variances to SDs. The combined group means and SDs are given in Figures 8 and 9.

The combined group means were fairly well-behaved across age and gender cohorts (see Figure 8), while the SD data (Figure 9) were noisier. These data may be appropriate for use in the Physiology.txt file; however, it was noted that the group mean data, while plentiful for children, were not very well represented in the adult (30+ years) age range (especially for women). This is mainly due to the fact that very few investigators use narrow age cohorts when studying adults, rather, it was far more common for broader age groups to be used. These data were not included in the grouped mean analysis, as the mean nvo2max for a broad age group cannot be assumed valid for the cohort represented by the study age mean. Therefore, we opted to use the database of individual nvo2max measurements to develop new distributions for the Physiology.txt file.

The individual nvo2max data were fit to several types of distributions (including normal, beta, and lognormal distributions). It was determined that the normal distribution fit the data best. The parameters (means and standard deviations) of the best-fit distributions were obtained using the SAS PROC UNIVARIATE procedure. The SAS code used to fit the data is given in Appendix B.

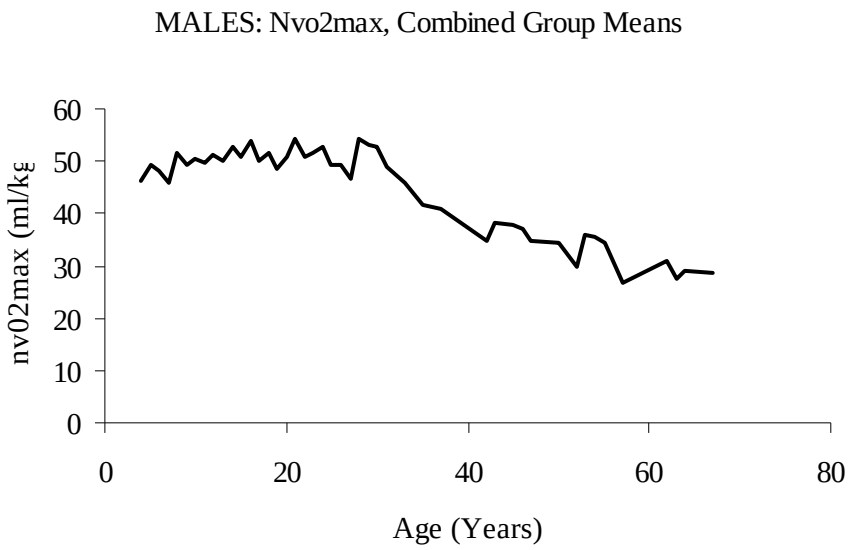
Both raw and smoothed nvo2max fits were calculated. Calculating 5-year running averages did not smooth the data considerably. Therefore, the smoothed fits were determined by choosing a best-fit functional form for the nv02max data. The data were fit to functions as follows:

Mean (Age 0-20): Linear function
Mean (Age 21-100): Parabolic function
SD (Age 0-26): Linear function
SD (Age 27-100): Parabolic function

Fitting the data in this manner also allowed for all age/gender cohorts to be represented. Since only cohorts having N>10 were fit to distributions, there were some cohorts for which no parameters were calculated. The raw and smoothed fits for means are given in Figure 10; analogous data for SD is given in Figure 11. The raw nvo2max parameters were not as clean across ages as the body mass data (probably due to the much smaller sample size), and thus the smoothed fits were selected for use in the attached Physiology.txt file. As with body mass, the raw fits may be used at the direction of EPA.

The results for the nvo2max means were in fact quite close to those in the current file. However, the values exhibited much more consistent behavior across ages, and the values for elderly persons were lower than previously. The SD values were also in the same range as the current values, yet they no longer demonstrate nonsensical discontinuities across ages.

The minimum and maximum nvo2max values were assumed to be the 1st and 99th percentile of the best-fit lognormal distribution. (**Note**: this is different from the method used for estimating the body mass limits. In that case, the samples were large enough that the percentiles of the raw data were appropriate for use as minimum and maximum. As the nvo2max data cohorts had much smaller N than the NHANES studies, the raw percentiles were less appropriate.) The maximum and minimum values are shown in Figures 12 and 13.



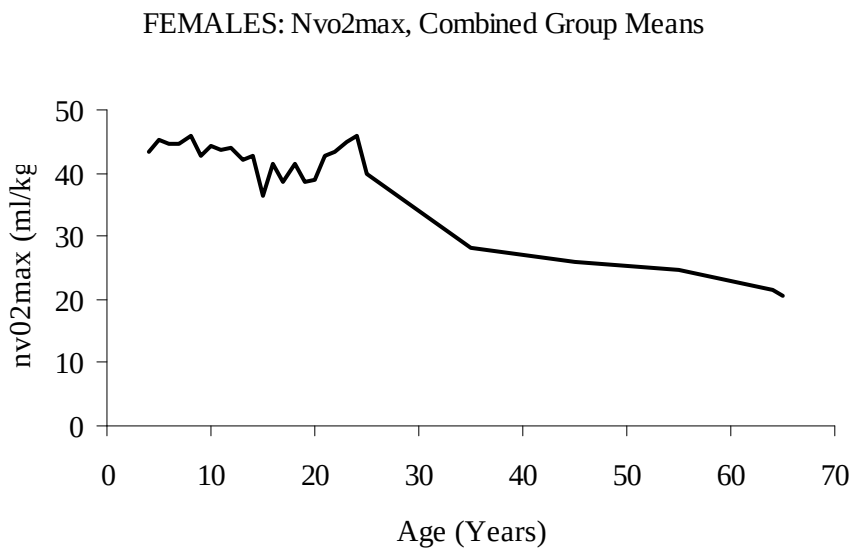
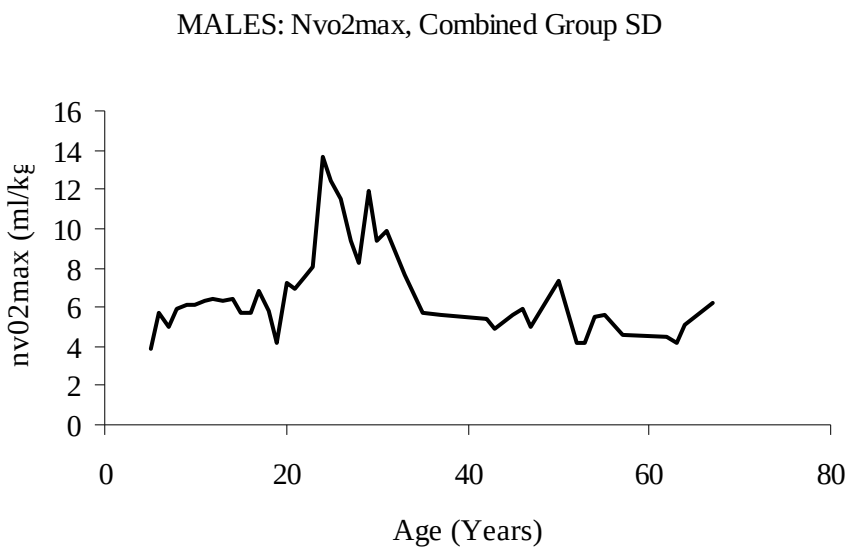


Figure 8. Combined Nvo2max Group Means for Males and Females



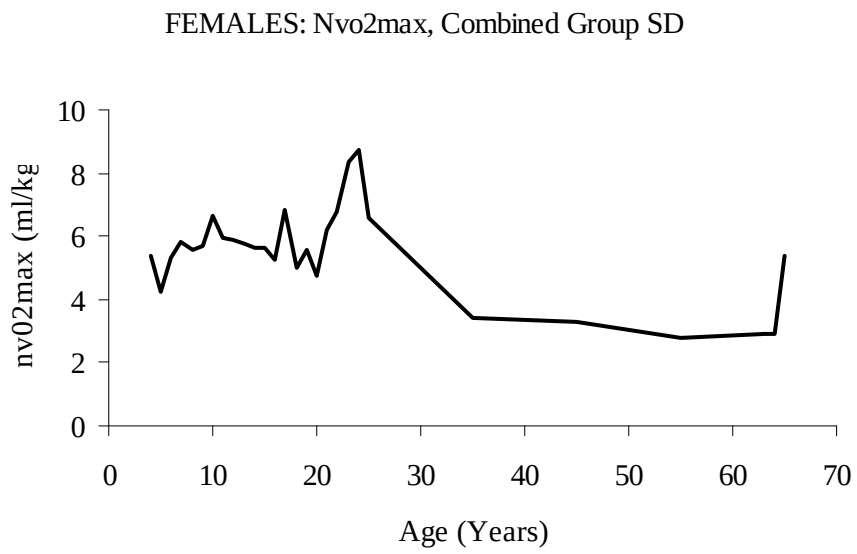
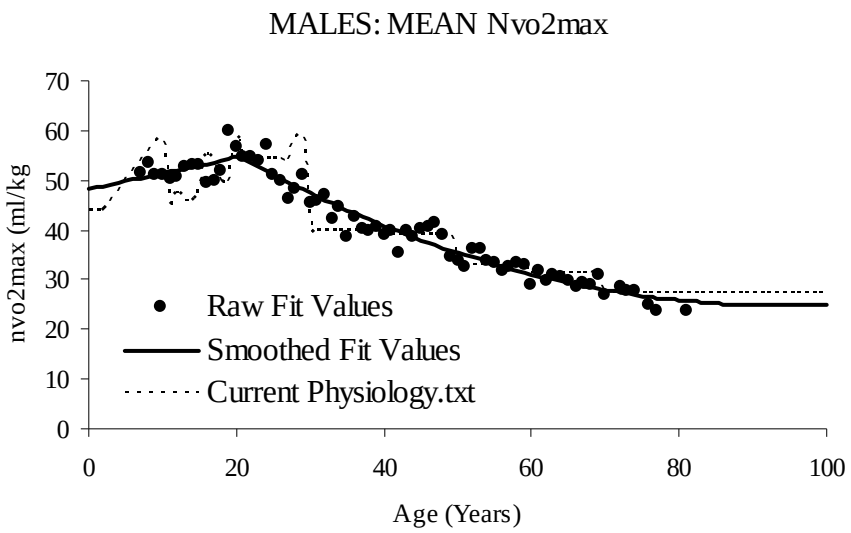


Figure 9. Combined Nvo2max Group Standard Deviations.



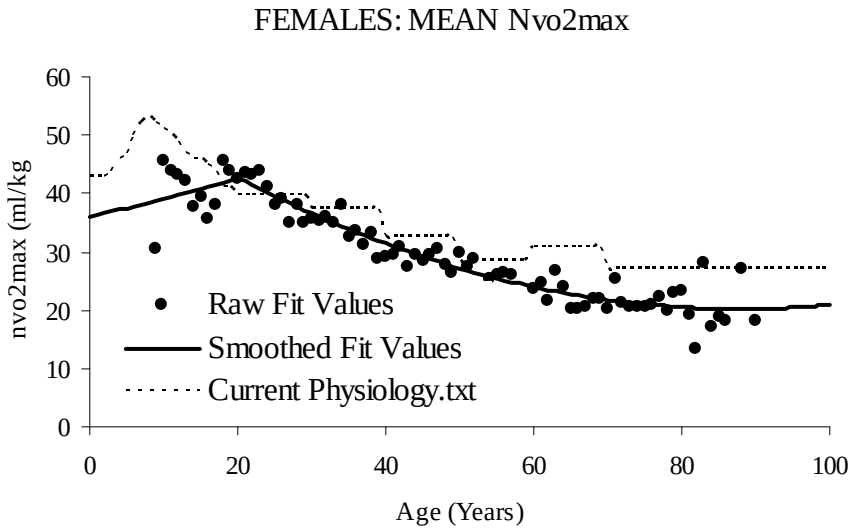
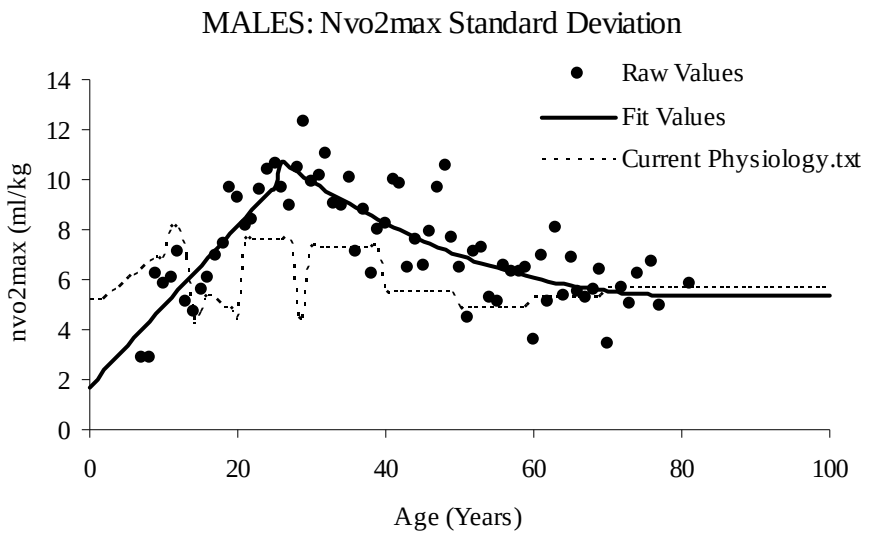


Figure 10. Nvo2max Normal Distribution Fits: Raw Fit Means and Smoothed Fits.



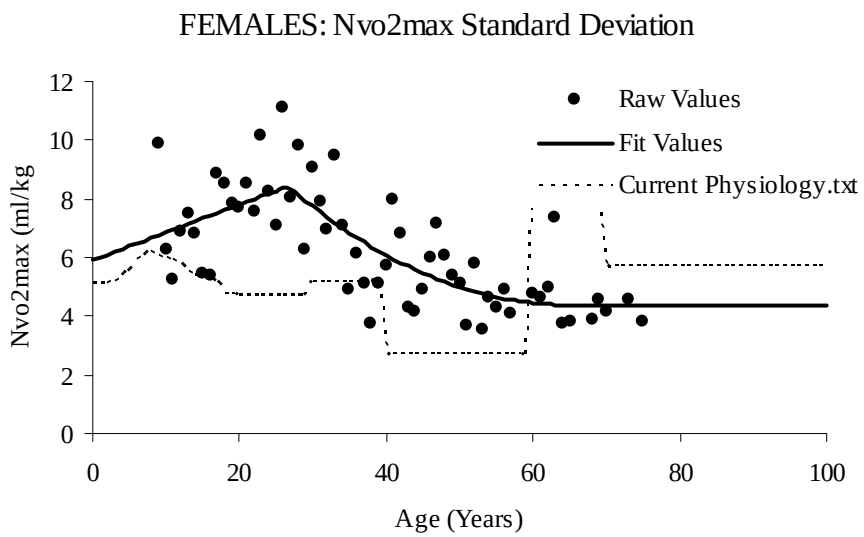
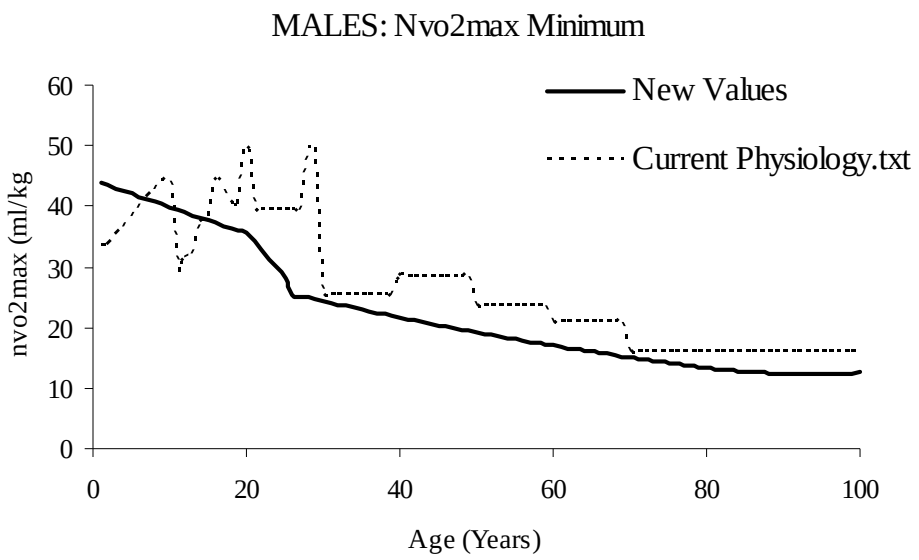


Figure 11. Nvo2max Normal Distribution Fits: Raw Fit Standard Deviations and Smoothed Fits.



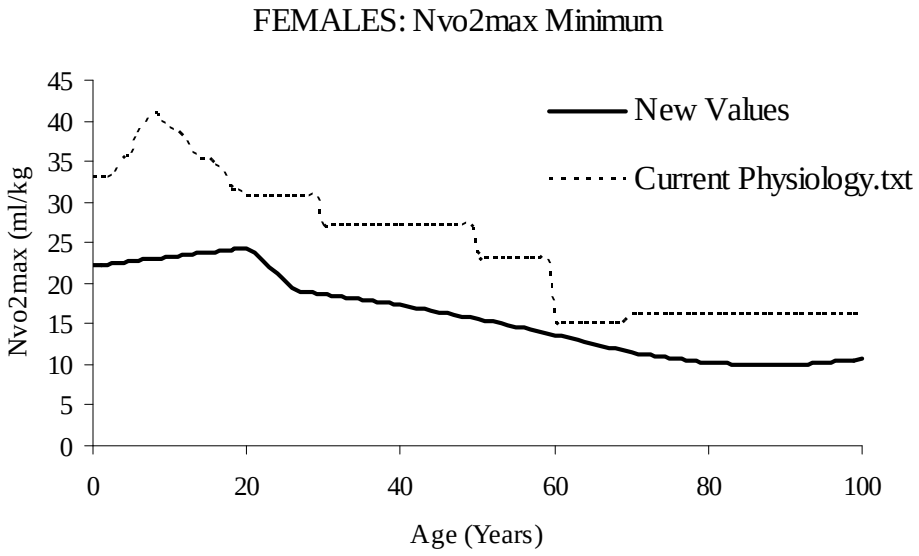
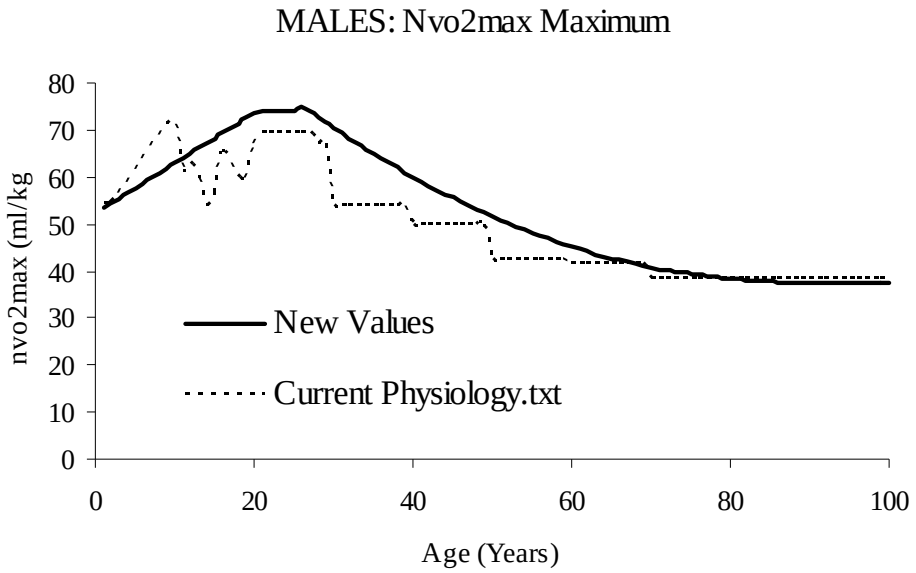


Figure 12. Nvo2max Minimums. 1st Percentile of the Best-fit Normal Distribution.



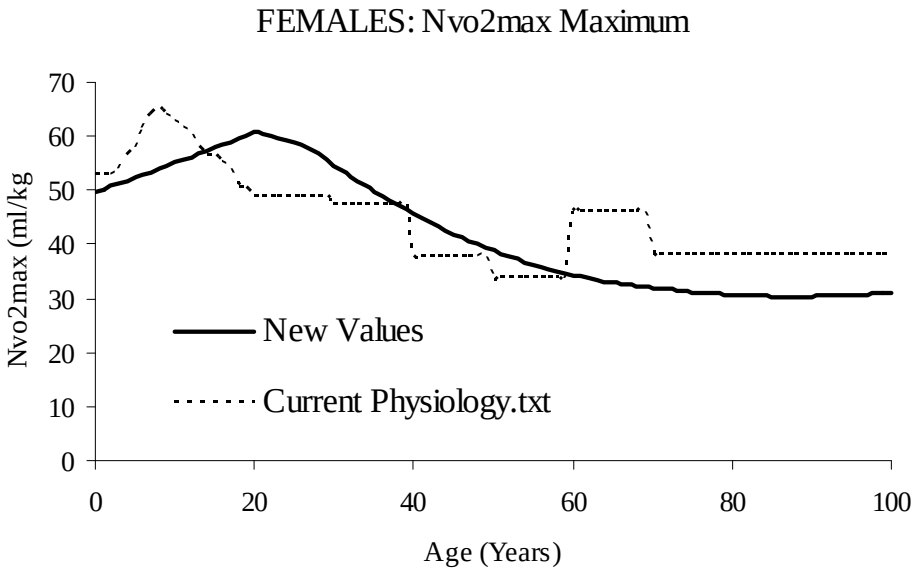


Figure 13. Nvo2max Maximums. 99th Percentile of the Best-fit Normal Distribution.

5. DERIVATION OF NEW DISTRIBUTIONS FOR HEMOGLOBIN CONTENT (HEMOGLOBIN DENSITY)

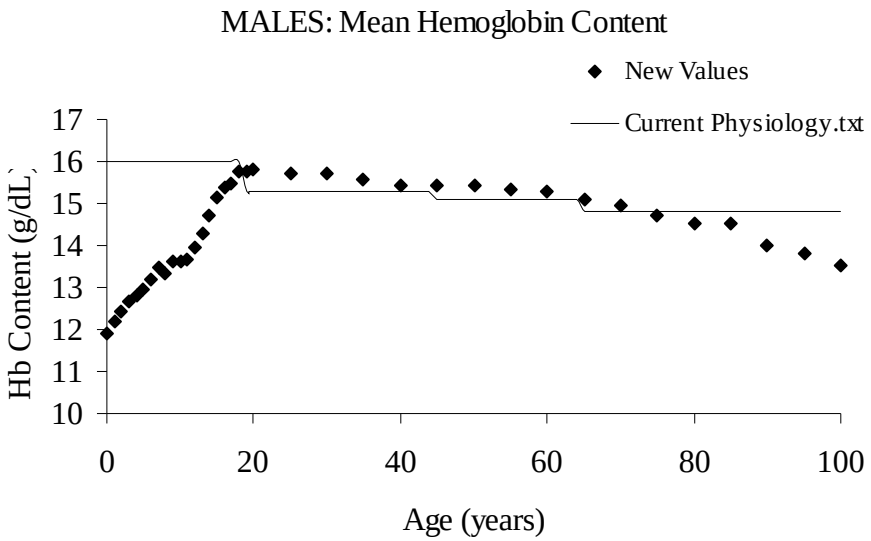
The new hemoglobin content values were derived from the combined NHANES 1999-2000 and 2001-2002 datasets. As of December 2005, hemoglobin data had not yet been released for the 2003-2004 study. The age data was provided in the Demographic datasets (Demo.xpt and Demo_b.xpt, previously downloaded for the body mass analysis) for the two survey periods, while hemoglobin content (in g/dL) was provided in the Laboratory #25 (Complete Blood Count) datasets (lab25.xpt and l25_b.xpt, which were downloaded for this analysis). The dataset comprised 20,321 individuals; appropriate sample weights were used for the combined 4-year (1999-2002) dataset as provided with the NHANES 2001-2002 data release. Similarly to the body mass data, the hemoglobin content values were analyzed in SAS. The age and hemoglobin datasets were merged and fit to normal distributions using the SAS PROC UNIVARIATE procedure. The FREQ option of the procedure was used to apply the sampling weights. The SAS code in provided in the Appendix C.

Hemoglobin content statistics were estimated for single-year age and gender cohorts for ages 1-19, as the behavior of the means were smooth in this age range. For persons 20 and over, the data were grouped in 5-year cohorts (20-24, 25-29, etc.) No blood count data were available for subjects under 1 year of age or greater than 90. The age 0 mean values were obtained by a linear regression of ages 1-20 (males) or 1 to 11 (females) back to age 0. These were the ages for which the hemoglobin content demonstrated an increase with age. The 91-95 and 96-100 mean values were obtained by a linear regression of the 61-65 and older age groups. As the standard deviations did not appear to behave as smoothly with age as did the mean values, the age 0 value was assumed equal to the age 1 value, and the age 91-95 and 96-100 value was assumed equal to the age 90-94 value.

The resulting means and standard deviations for the best-for normal distributions for hemoglobin content are given in Figures 14 and 15**.** The current hemoglobin content values are shown for comparison.

The main conclusions that can be made is that the current Physiology.txt input file overestimates mean hemoglobin content in children and in older persons. The standard deviation values in the current physiology.txt file are fairly close to those found in this analysis. The new values are not very smooth over ages; EPA may elect to continue to use the current values. It should be noted that the original reference for the current hemoglobin statistics is unknown.

Note: In the current implementation of APEX, the hemoglobin content statistics affect only the CO dose algorithm calculations.



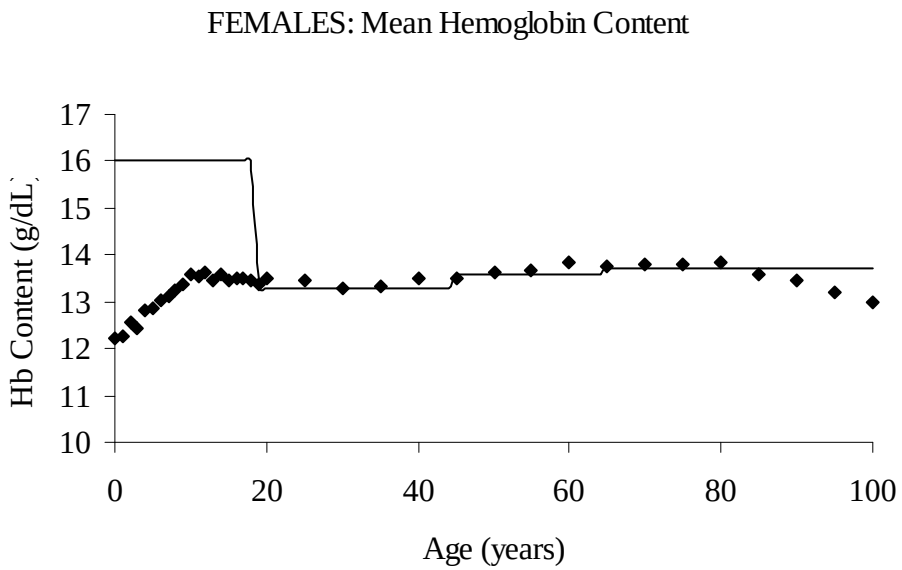
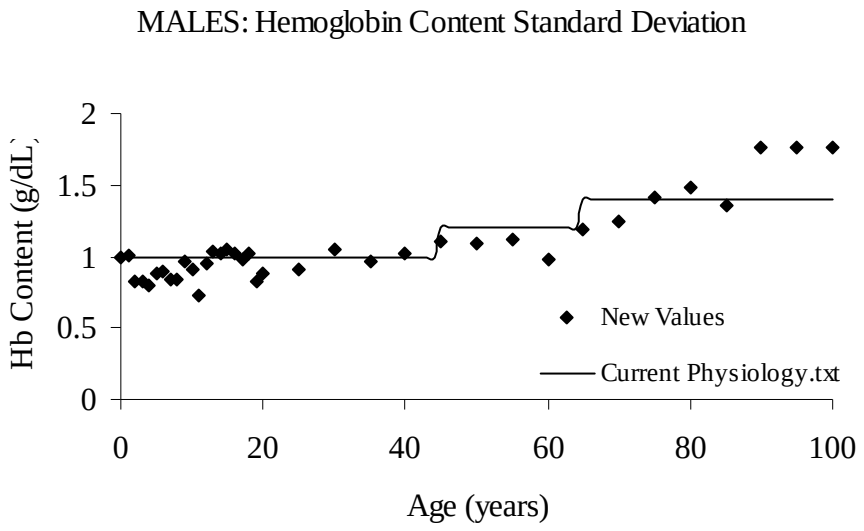


Figure 14. Mean Values of Hemoglobin Content as Derived from the 1999-2002 NHANES Dataset, with Comparison to Current Physiology.txt Values



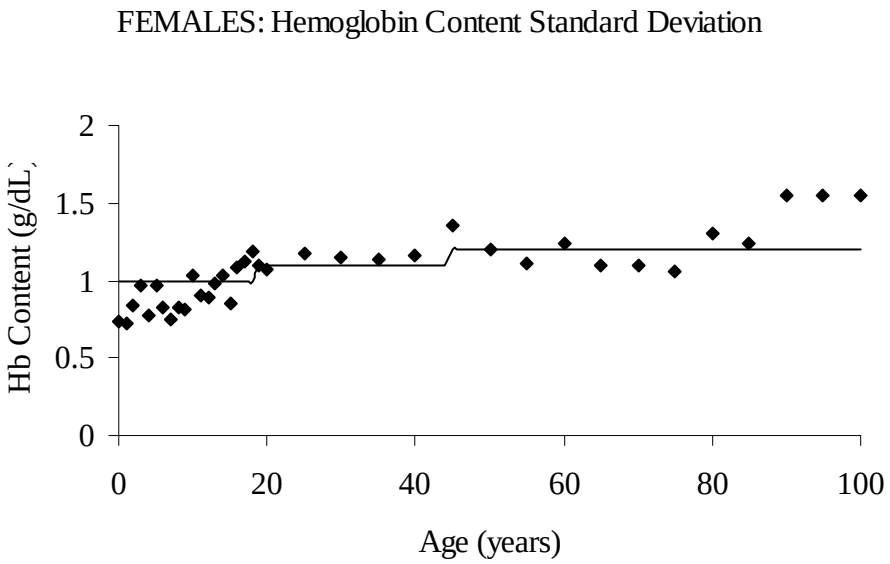


Figure 15. Values of Hemoglobin Content Standard Deviation as Derived from the 1999-2002 NHANES Dataset, with Comparison to Current Physiology.txt Values

6. BLOOD VOLUME AS A FUNCTION OF HEIGHT AND WEIGHT

In APEX, blood volume is estimated as a function of height and weight by the following equation:

$$V_{blood} = BVF*Weight + K*Height^3 - 30$$

where V_{blood} is the blood volume (ml), Weight is in pounds, and height is in inches. BVF is the blood volume factor that is read in from the physiology file, and K is a gender-dependent constant (0.00683 for males, 0.00678 for females). This is a modification of Allen's equation [168] to include the age/gender dependent BVF and adjusted for the given units.

As previously mentioned, the data upon which the BVF values in the physiology file were based could not be identified. The available documentation for pNEM documents a non-age-dependent use of these equations.

In addition, no appropriate data were found for deriving new estimates for the BVF variable as a function of age and gender for use with the Allen equations. It should be noted however, that these equations were modified by Nadler [169]. These equations seem to be used somewhat more often than the originals in the literature.

In addition, other (more recent) equations exist for estimation of blood volume from height and weight specifically in children [170,171] or body surface area [172]. In particular, Linderkamp et al. [170] derived prediction equations for blood volume as a function of a number of physiological parameters for children in three different age groups. It is recommended that further analysis of this study and others be undertaken.

However, inclusion of new blood volume equations in APEX would require changes beyond the current physiology file (i.e. other, more intensive, code changes would be needed). Thus, at the present time, no specific improvements to the current BVF values in the physiology file can be made.

REFERENCES

1. Astrand, I. 1960. Aerobic work capacity in men and women with special reference to age. Acta. Phys. Scand. 49: Suppl. 169.
2. Astrand, PO and Rodhal K. 1977. Textbook of Work Physiology. 2nd addition, McGraw-Hill, NY.
3. Heil DP, Freedson PS, Ahlquist LE, Price J, and Rippe JM. 1995. Nonexercise regression models to estimate peak oxygen consumption. Med. Sci. Sports Exer 27:599-606.
4. Brainard J and Burmaster D. 1992. Bivariate distributions for height and weight of men and women in the United States. Risk Analysis, 12(2):267-275.
5. Burmaster DE and Crouch E. 1997. Lognormal distributions of body weight as a function of age for males and females in the United States, 1976-1980. Risk Analysis, 17(4): 499-505.
6. Centers for Disease Control and Prevention (CDC). National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey Data. Hyattsville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 1976-1980. <http://www.cdc.gov/nchs/nhanes.htm>.
7. U.S. Environmental Protection Agency (EPA). (2003) Handbook for use of data from the national health and nutrition examination surveys (NHANES). National Center for Environmental Assessment, Washington, DC: EPA/600/R-02/044. Available from: National Technical Information Service, Springfield, VA, and <http://www.epa.gov/ncea>.
8. Centers for Disease Control and Prevention (CDC). National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey Data. Hyattsville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 1999-2004. <http://www.cdc.gov/nchs/nhanes.htm>.
9. Center for Disease Control. National Center For Health Statistics. The National Health and Nutriation Examination Survey (NHANES). *Analytic and Reporting Guidelines*. December 2005. Available online at www.cdc.gov.
10. Andersen KL, Ilmarinen J, Rutenfranz J, Ottmann W, Berndt I, Kylian H. Leisure time sport activities and maximal aerobic power during late adolescence. Eur J Appl Physiol 1984; 52: 431-6.
11. Armstrong N, Kirby BJ, McManus AM, Welsman JR. Aerobic fitness of prepubescent children. Ann Hum Biol. 1995 Sep-Oct;22(5):427-41.
12. Armstrong N, Welsman JR. Assessment and interpretation of aerobic fitness in children and adolescents.Exerc Sport Sci Rev. 1994;22:435-76.
13. Astrand I. Aerobic work capacity in men and women with special reference to age. Acta Physiol Scand. 1960;49(Suppl 169):1-92.
14. Eliakim A, Scheett T, Allmendinger N, Brasel JA, Cooper DM. Training, muscle volume, and energy expenditure in nonobese American girls. J Appl Physiol. 2001 Jan;90(1):35-44.

15. Falgairette, G. 1989. Evolution de la puissance maximal aerobie de l'enfance a l'age adulte: influence de l'activite physique et al. sportive. Revue Des Sciences et al. Techniques en Activites Physiques et al. Sportives. 10:43-58.
16. Fleg JL, Lakatta EG. Role of muscle loss in the age-associated reduction in VO2 max. J Appl Physiol. 1988 Sep;65(3):1147-51.
17. Ghesquiere J, Reybrouck T, Faulkner JA, Cattaert A, Fagard R, Amery A. Anaerobic threshold for long-term exercise and maximal exercise performance. Ann Clin Res. 1982;14 Suppl 34:37-41.
18. Kamon E, Pandolf KB. Maximal aerobic power during laddermill climbing, uphill running, and cycling. J Appl Physiol. 1972 Apr;32(4):467-73.
19. Katch VL, Park MW. Minute-by-minute oxygen requirement and work efficiency for constant-load exercise of increasing duration. Res Q. 1975 Mar;46(1):38-47.
20. McMiken DF. Oxygen deficit and repayment in submaximal exercise. Eur J Appl Physiol Occup Physiol. 1976 Jun 21;35(2):127-36.
21. Nevill A, Rowland T, Goff D, Martel L, Ferrone L. Scaling or normalising maximum oxygen uptake to predict 1-mile run time in boys. Eur J Appl Physiol. 2004 Jul;92(3):285-8. Epub 2004 Apr 9.
22. Pivarnik JM, Fulton JE, Taylor WC, Snider SA. Aerobic capacity in black adolescent girls. Res Q Exerc Sport. 1993 Jun;64(2):202-7.
23. Posner JD, Gorman KM, Klein HS, Cline CJ. Ventilatory threshold: measurement and variation with age. J Appl Physiol. 1987 Oct;63(4):1519-25.
24. Reybrouck T, Heigenhauser GF, Faulkner JA. Limitations to maximum oxygen uptake in arms, leg, and combined arm-leg ergometry. J Appl Physiol. 1975 May;38(5):774-9.
25. Ribisl PM, Kachadorian WA. Maximal oxygen intake prediction in young and middle-aged males. J Sports Med Phys Fitness. 1969 Mar;9(1):17-22.
26. Schiller BC, Casas YG, Desouza CA, Seals DR. Maximal aerobic capacity across age in healthy Hispanic and Caucasian women. J Appl Physiol. 2001 Sep;91(3):1048-54.
27. Seals DR, Hagberg JM, Hurley BF, Ehsani AA, Holloszy JO. Endurance training in older men and women. I. Cardiovascular responses to exercise. J Appl Physiol. 1984 Oct;57(4):1024-9.
28. Sheel A, Seddon N, Knight A, McKenzie DC, R Warburton DE. Physiological responses to indoor rock-climbing and their relationship to maximal cycle ergometry. Med Sci Sports Exerc. 2003 Jul;35(7):1225-31.
29. Talbot LA, Metter EJ, Fleg JL. Leisure-time physical activities and their relationship to cardiorespiratory fitness in healthy men and women 18-95 years old. Med Sci Sports Exerc. 2000 Feb;32(2):417-25.
30. Tanaka H, Desouza CA, Jones PP, Stevenson ET, Davy KP, Seals DR. Greater rate of decline in maximal aerobic capacity with age in physically active vs. sedentary healthy women. J Appl Physiol. 1997 Dec;83(6):1947-53.
31. Adams. Personal Communication – T. McCurdy EPA.
32. Ahmad F, Kavey RE, Kveselis DA, Gaum WE, Smith FC. Responses of non-obese white children to treadmill exercise. J Pediatr. 2001 Aug;139(2):284-90.
33. Andersen KL, Hermansen L. Aerobic work capacity in middle-aged Norwegian men. J Appl Physiol. 1965 May;20(3):432-6.

34. Andersen KL, Ilmarinen J, Rutenfranz J, Ottmann W, Berndt I, Kylian H, Ruppel M. Leisure time sport activities and maximal aerobic power during late adolescence. Eur J Appl Physiol Occup Physiol. 1984;52(4):431-6.
35. Andersen KL, Seliger V, Rutenfranz J, Mocellin R. Physical performance capacity of children in Norway. Part I. Population parameters in a rural inland community with regard to maximal aerobic power. Eur J Appl Physiol Occup Physiol. 1974;33(3):177-95.
36. Armstrong N and Welsman J. Daily physical activity estimated from continuous heart rate monitoring and laboratory indices of aerobic fitness in pre-adolescent children. (abs.) Res Q Exer Sport 64:A-24, 1993.
37. Armstrong N, Balding J, Gentle P, Kirby B. Estimation of coronary risk factors in British schoolchildren: a preliminary report. Br J Sports Med. 1990 Mar;24(1):61-6.
38. Armstrong N, Balding J, Gentle P, Kirby B. Patterns of physical activity among 11 to 16 year old British children. BMJ. 1990 Jul 28;301(6745):203-5.
39. Armstrong N, Bray S. Physical activity patterns defined by continuous heart rate monitoring. Arch Dis Child. 1991 Feb;66(2):245-7.
40. Armstrong N, Davies B, Heal M. The specificity of energy utilisation by trained and untrained adolescent boys. Br J Sports Med. 1983 Sep;17(3):193-9.
41. Armstrong N, Kirby BJ, McManus AM, Welsman JR. Aerobic fitness of prepubescent children. Ann Hum Biol. 1995 Sep-Oct;22(5):427-41. Erratum in: Ann Hum Biol 1996 Mar-Apr;23(2):188.
42. Armstrong N, Welsman JR, Kirby BJ. Submaximal exercise and maturation in 12-year-olds. J Sports Sci. 1999 Feb;17(2):107-14.
43. Armstrong N, Welsman JR, Kirby BJ. Peak oxygen uptake and maturation in 12-yr olds. Med Sci Sports Exerc. 1998 Jan;30(1):165-9.
44. Armstrong N, Williams J, Balding J, Gentle P, Kirby B. The peak oxygen uptake of British children with reference to age, sex and sexual maturity. Eur J Appl Physiol Occup Physiol. 1991;62(5):369-75.
45. Atomi Y, Fukunaga T, Yamamoto Y, Hatta H. Lactate threshold and vo2max of trained and untrained boys relative to muscle mass and composition. In: Rutenfranz J, Mocellin R, Klimt F, eds. children and exercise XII. International series on sport sciences, Vol 16. Champaign, IL: Human Kinetics, 1986:227-232.
46. Atomi Y, Iwaoka K, Hatta H, Miyashita M, Yamamoto Y. Daily physical activity levels in preadolescent boys related to VO2max and lactate threshold. Eur J Appl Physiol Occup Physiol. 1986;55(2):156-61.
47. Bailey, D.A., Ross, W.D., Mirwald, R.L. and Weese, C. Size dissociation of maximal aerobic power during growth in boys. Medicine in Sport 1978; 11: 140-151.
48. Bale P. Pre- and post-adolescents' physiological response to exercise. Br J Sports Med. 1981 Dec;15(4):246-9.
49. Bar-Or O, Skinner JS, Bergsteinova V, Shearburn C, Royer D, Bell W, Haas J, Buskirk ER. Maximal aerobic capacity of 6--15 year-old girls and boys with subnormal intelligence quotients. Acta Paediatr Scand Suppl. 1971;217:108-13.
50. Becker DM, Vaccaro P. Anaerobic threshold alterations caused by endurance training in young children. J Sports Med Phys Fitness. 1983 Dec;23(4):445-9.

51. Binkhorst 1984 (Ref??) From T. McCurdy spreadsheet, dated Nov 15, 2000.
52. Binkhorst RA, Saris WHM, Noordeloos AM, et al. Maximal oxygen consumption of children (6 to 18 years) predicted from maximal and submaximal values in treadmill and bicycle tests. In: Rutenfranz J, Mocellin R, Klimt F, eds. children and exercise XII. International series on sport sciences, Vol 16. Champaign, IL: Human Kinetics, 1986:227-232.
53. Boileau RA, Bonen A, Heyward VH, Massey BH. Maximal aerobic capacity on the treadmill and bicycle ergometer of boys 11-14 years of age. J Sports Med Phys Fitness. 1977 Jun;17(2):153-62.
54. Bonen A, Heyward VH, Cureton KJ, Boileau RA, Massey BH. Prediction of maximal oxygen uptake in boys, ages 7-15 years. Med Sci Sports. 1979 Spring;11(1):24-9.
55. Brown, J.D., A.D. Mahon and D.M. Plank. Attainment of maximal exercise criteria in boys and men. Journal of Sports Medicine and Physical Fitness, 42: 135-140, 2002.
56. Buskirk E, Taylor HL. Maximal oxygen intake and its relation to body composition, with special reference to chronic physical activity and obesity. J Appl Physiol. 1957 Jul;11(1):72-8.
57. Chausow 1984 (Ref??) In T. McCurdy spreadsheet, dated Nov 15, 2000.
58. Cooper DM, Berry C, Lamarra N, Wasserman K. Kinetics of oxygen uptake and heart rate at onset of exercise in children. J Appl Physiol. 1985 Jul;59(1):211-7.
59. Cooper DM, Weiler-Ravell D, Whipp BJ, Wasserman K. Aerobic parameters of exercise as a function of body size during growth in children.J Appl Physiol. 1984 Mar;56(3):628-34.
60. Cumming GR, Borysyk LM. Criteria for maximum oxygen uptake in men over 40 in a population survey. Med Sci Sports. 1972 Spring;4(1):18-22.
61. Cumming GR, Everatt D, Hastman L. Bruce treadmill test in children: normal values in a clinic population. Am J Cardiol. 1978 Jan;41(1):69-75.
62. Cumming GR, Goulding D, Baggley G. Failure of school physical education to improve cardiorespiratory fitness. Can Med Assoc J. 1969 Jul 26;101(2):69-73.
63. Cunningham DA, Paterson DH, Blimkie CJ, Donner AP. Development of cardiorespiratory function in circumpubertal boys: a longitudinal study. J Appl Physiol. 1984 Feb;56(2):302-7.
64. Cunningham DA, Stapleton JJ, MacDonald IC, Paterson DH. Daily energy expenditure of young boys as related to maximal aerobic power. Can J Appl Sport Sci. 1981 Dec;6(4):207-11.
65. Cunningham DA, Telford P, Swart GT. The cardiopulmonary capacities of young hockey players: age 10. Med Sci Sports. 1976 Spring;8(1):23-5.
66. Cunningham DA, van Waterschoot BM, Paterson DH, Lefcoe M, Sangal SP. Reliability and reproducibility of maximal oxygen uptake measurement in children. Med Sci Sports. 1977 Summer;9(2):104-8.
67. Cureton KJ, Sloniger MA, Black DM, McCormack WP, Rowe DA. Metabolic determinants of the age-related improvement in one-mile run/walk performance in youth. Med Sci Sports Exerc. 1997 Feb;29(2):259-67.

68. Cureton KJ, Sloniger MA, O'Bannon JP, Black DM, McCormack WP. A generalized equation for prediction of VO2peak from 1-mile run/walk performance. Med Sci Sports Exerc. 1995 Mar;27(3):445-51.
69. Davies CT. Limitations to the prediction of maximum oxygen intake from cardiac frequency measurements. J Appl Physiol. 1968 May;24(5):700-6.
70. Davies CT. Metabolic cost of exercise and physical performance in children with some observations on external loading. Eur J Appl Physiol Occup Physiol. 1980;45(2-3):95-102.
71. Dehn MM, Bruce RA. Longitudinal variations in maximal oxygen intake with age and activity. J Appl Physiol. 1972 Dec;33(6):805-7.
72. Docherty D, Wenger HA, Collis ML. The effects of resistance training on aerobic and anaerobic power of young boys.Med Sci Sports Exerc. 1987 Aug;19(4):389-92.
73. Eiberg S, Hasselstrom H, Gronfeldt V, Froberg K, Svensson J, Andersen LB. Maximum oxygen uptake and objectively measured physical activity in Danish children 6-7 years of age: the Copenhagen school child intervention study. Br J Sports Med. 2005 Oct;39(10):725-30.
74. Eisenman PA, Golding LA. Comparison of effects of training on Vo2max in girls and young women. Med Sci Sports. 1975 Summer;7(2):136-8.
75. Fawkner S, Armstrong N. Modeling the vo2 kinetic response to moderate intensity exercise in children. Acta Kinesiol Universit Tartu 7:80-84, 2002.
76. Fox EL, Bartels RL, Billings CE, O'Brien R, Bason RM, Mathews DK. Frequency and duration of interval training programs and changes in aerobic power. J Appl Physiol 1975; 38:481-84
77. Fredriksen PM, Ingjer F, Nystad W, Thaulow E. A comparison of VO2(peak) between patients with congenital heart disease and healthy subjects, all aged 8-17 years. Eur J Appl Physiol Occup Physiol. 1999 Oct;80(5):409-16.
78. Gastin PB, Costill DL, Lawson DL, Krzeminski K, McConell GK. Accumulated oxygen deficit during supramaximal all-out and constant intensity exercise. Med Sci Sports Exerc. 1995 Feb;27(2):255-63.
79. George JD. Alternative approach to maximal exercise testing and VO2 max prediction in college students. Res Q Exerc Sport. 1996 Dec;67(4):452-7.
80. Gilliam TB, Sady S, Thorland WG, Weltman AL. Comparison of peak performance measures in children ages 6 to 8, 9 to 10, and 11 to 13 years. Res Q. 1977 Dec;48(4):695-702.
81. Gilliam, T. & Freedson, P. Effects of a twelve-week school physical fitness program on peak VO2, body composition, and blood lipids in 7 to 9 year old children. Int J of Sports Med 1980;1:73-78.
82. Gutin B, Barbeau P, Owens S, Lemmon CR, Bauman M, Allison J, Kang HS, Litaker MS. Effects of exercise intensity on cardiovascular fitness, total body composition, and visceral adiposity of obese adolescents. Am J Clin Nutr. 2002 May;75(5):818-26.
83. Hansen, H. S., K. Froberk, J. R. Nielsen, and N. Hyldebrandt. A new approach to assessing maximal aerobic power in children: the Odense School Child Study. Euro. J. Appl. Physiol. 58: 618-624, 1989.

84. Harms C, Cordain L, Stager J, Sockler J, and Harris M. Body fat mass affects postexercise metabolism in males of similar lean body mass. Med Exer Nutr Health 4:33-39, 1995.
85. Hebestreit H, Bar-Or O, McKinty C, Riddell M, Zehr P. Climate-related corrections for improved estimation of energy expenditure from heart rate in children. J Appl Physiol. 1995 Jul;79(1):47-54.
86. Hebestreit H, Kriemler S, Hughson RL, Bar-Or O. Kinetics of oxygen uptake at the onset of exercise in boys and men. J Appl Physiol. 1998 Nov;85(5):1833-41.
87. Hebestreit H, Mimura K, Bar-Or O. Recovery of muscle power after high-intensity short-term exercise: comparing boys and men. J Appl Physiol. 1993 Jun;74(6):2875-80.
88. Hermansen L, Andersen KL. Aerobic work capacity in young Norwegian men and women. J Appl Physiol. 1965 May;20(3):425-31.
89. Hossack KF, Bruce RA. Maximal cardiac function in sedentary normal men and women: comparison of age-related changes. J Appl Physiol. 1982 Oct;53(4):799-804.
90. Humphrey LD, Falls HB. Circulatory and metabolic responses of young women at HR = 180 and HR = max. Res Q. 1975 Dec;46(4):498-504.
91. Hunt B. R, George J.D., Vehrs P.R., Fisher A. G., Fellingham G. W. (2000), Validity of a submaximal 1-mile track jog test in predicting VO2max in fit teenagers. Pediatric exercise science 12(1):80-90.
92. Ikai M, Kitagawa K. Maximum oxygen uptake of Japanese related to sex and age. Med Sci Sports. 1972 Fall;4(3):127-31.
93. Kaminsky L, and Whaley M. Effect of interval-type exercise on excess postexercise oxygen consumption in obese and normal-weight women. Med Exer Nutr Health 2:106-111, 1993.
94. Kaminsky LA, Wehrli KW, Mahon AD, Robbins GC, Powers DL, Whaley MH. Evaluation of a shallow water running test for the estimation of peak aerobic power. Med Sci Sports Exerc. 1993 Nov;25(11):1287-92.
95. Kanaley JA, Boileau RA. The onset of the anaerobic threshold at three stages of physical maturity. J Sports Med Phys Fitness. 1988 Dec;28(4):367-74.
96. Katch FI, McArdle WD, Pechar GS. Relationship of maximal leg force and leg composition to treadmill and bicycle ergometer maximum oxygen uptake. Med Sci Sports. 1974 Spring;6(1):38-43.
97. Kemper H and Vershuur R. Maximal aerobic power in 13 and 14 year old teenagers in relation to biologic age. Int J Sports Med. 2:97-100, 1981.
98. Koch G, Eriksson BO. Effect of physical training on pulmonary ventilation and gas exchange during submaximal and maximal work in boys aged 11 to 13 years. Scand J Clin Lab Invest. 1973 Jan;31(1):87-94.
99. Kohrt WM, Malley MT, Coggan AR, Spina RJ, Ogawa T, Ehsani AA, Bourey RE, Martin WH 3rd, Holloszy JO. Effects of gender, age, and fitness level on response of VO2max to training in 60-71 yr olds. J Appl Physiol. 1991 Nov;71(5):2004-11.
100. Krahenbuhl GS, Pangrazi RP, Burkett LN, Schneider MJ, Petersen G. Field estimation of VO2 max in children eight years of age. Med Sci Sports. 1977 Spring;9(1):37-40.

101. Krahenbuhl GS, Pangrazi RP, Petersen GW, Burkett LN, Schneider MJ. Field testing of cardiorespiratory fitness in primary school children. Med Sci Sports. 1978 Fall;10(3):208-13.
102. Krahenbuhl GS, Pangrazi RP. Characteristics associated with running performance in young boys. Med Sci Sports Exerc. 1983;15(6):486-90.
103. Loftin M, Strikmiller P, Warren B, Myers L, Schroth L, Pittman J, Harsha D, and Sothern M. Comparison and relationship of Vo2peak and physical activity patterns in elementary and high school females. Ped Exer Sci. 10:153-163, 1998.
104. Macek M and Vavra J. The adjustment of oxygen uptake at the onset of exercise: a comparison between prepubertal boys and young adults. In J Sports Med 1:70-72, 1980.
105. Macek M, Vavra J, Novosadova J. Prolonged exercise in prepubertal boys. I. Cardiovascular and metabolic adjustment. Eur J Appl Physiol Occup Physiol. 1976 Sep 23;35(4):291-8.
106. Macek M, Vavra J. Cardiopulmonary and metabolic changes during exercise in children 6-14 years old. J Appl Physiol. 1971 Feb;30(2):200-4.
107. Mahler DA, Mejia-Alfaro R, Ward J, Baird JC. Continuous measurement of breathlessness during exercise: validity, reliability, and responsiveness. J Appl Physiol. 2001 Jun;90(6):2188-96.
108. Mahon AD, Anderson CS, Hipp MJ, Hunt KA. Heart rate recovery from submaximal exercise in boys and girls. Med Sci Sports Exerc. 2003 Dec;35(12):2093-7.
109. Mahon AD, Gay JA, Stolen KQ. Differentiated ratings of perceived exertion at ventilatory threshold in children and adults. Eur J Appl Physiol Occup Physiol. 1998 Jul;78(2):115-20.
110. Mahon AD, Vaccaro P. Ventilatory threshold and VO2max changes in children following endurance training. Med Sci Sports Exerc. 1989 Aug;21(4):425-31.
111. Mahon, A.D., C.C. Cheatham, K.Q. Kelsey, and J.D. Brown. Plasma fibrinogen, physical activity and aerobic fitness in children. In: Children and Exercise XIX: 19th International Seminar on Paediatric Work Physiology, N. Armstrong, B. Kirby, and J. Wellsman, Editors. London: Chapman & Hall Ltd., 1997. rs. London: Chapman & Hall Ltd., 997
112. Maksud MG, Coutts KD, Hamilton LH. Oxygen uptake, ventilation, and heart rate. Study in Negro children during strenuous exercise. Arch Environ Health. 1971 Jul;23(1):23-8.
113. Mandigout S, Lecoq AM, Courteix D, Guenon P, Obert P. Effect of gender in response to an aerobic training programme in prepubertal children. Acta Paediatr. 2001 Jan;90(1):9-15.
114. Massicotte DR, Macnab RB. Cardiorespiratory adaptations to training at specified intensities in children. Med Sci Sports. 1974 Winter;6(4):242-6.
115. Matsui H, Miyashita M, Miura M, Kobayashi K, Hoshikawa T. Maximum oxygen intake and its relationship to body weight of Japanese adolescents.Med Sci Sports. 1972 Spring;4(1):27-32.
116. McArdle WD and Magel JR. Physical work capacity and maximum oxygen uptake in treadmill and bicycle exercise. Med Sci Sports 2: 118-126, 1971 McCardle et al. 1972

117. McDonough JR, Kusumi F, Bruce RA. Variations in maximal oxygen intake with physical activity in middle-aged men. Circulation. 1970 May;41(5):743-51.
118. McManus AM, Armstrong N, Williams CA. Effect of training on the aerobic power and anaerobic performance of prepubertal girls. Acta Paediatr. 1997 May;86(5):456-9.
119. McMurray RG, Guion WK, Ainsworth BE, Harrell JS. Predicting aerobic power in children. A comparison of two methods. J Sports Med Phys Fitness. 1998 Sep;38(3):227-33.
120. Mercier J, Varray A, Ramonatxo M, Mercier B, Prefaut C. Influence of anthropometric characteristics on changes in maximal exercise ventilation and breathing pattern during growth in boys. Eur J Appl Physiol Occup Physiol. 1991;63(3-4):235-41.
121. Murray TD, Walker JL, Jackson AS, Morrow JR Jr, Eldridge JA, Rainey DL. Validation of a 20-minute steady-state jog as an estimate of peak oxygen uptake in adolescents. Res Q Exerc Sport. 1993 Mar;64(1):75-82.
122. Nakagawa A, Ishiko T. Assessment of aerobic capacity with special reference to sex and age of junior and senior highschool students in Japan.
123. Palgi Y, Gutin B, Young J, Alejandro D. Physiologic and anthropometric factors underlying endurance performance in children. Int J Sports Med. 1984 Apr;5(2):67-73.
124. Paterson DH, Cunningham DA, Bumstead LA. Recovery O2 and blood lactic acid: longitudinal analysis in boys aged 11 to 15 years. Eur J Appl Physiol Occup Physiol. 1986;55(1):93-9.
125. Paterson DH, Cunningham DA, Donner A. The effect of different treadmill speeds on the variability of VO2 max in children. Eur J Appl Physiol Occup Physiol. 1981;47(2):113-22.
126. Paterson DH, McLellan TM, Stella RS, Cunningham DA. Longitudinal study of ventilation threshold and maximal O2 uptake in athletic boys. J Appl Physiol. 1987 May;62(5):2051-7.
127. Petzl DH, Haber P, Schuster E, Popow C, Haschke F. Reliability of estimation of maximum performance capacity on the basis of submaximum ergometric stress tests in children 10-14 years old. Eur J Pediatr. 1988 Feb;147(2):174-8.
128. Pivarnik JM, Bray MS, Hergenroeder AC, Hill RB, Wong WW. Ethnicity affects aerobic fitness in US adolescent girls. Med Sci Sports Exerc. 1995 Dec;27(12):1635-8.
129. Pivarnik JM, Dwyer MC, Lauderdale MA. The reliability of aerobic capacity (VO2max) testing in adolescent girls. Res Q Exerc Sport. 1996 Sep;67(3):345-8.
130. Pivarnik, J.M., W.C. Taylor, and S.S. Cummings. Longitudinal assessment of aerobic fitness in middle-school African American girls. Pediatr Exerc Sci 10: 21-27, 1998.
131. Reybrouck T, Ghesquiere J, Weymans M, Amery A. Ventilatory threshold measurement to evaluate maximal endurance performance. Int J Sports Med. 1986 Feb;7(1):26-9.
132. Rivera-Brown, A.M. and Frontera, W.R. Achievement of plateau and reliability of VO2max in active adolescents: Effects of testing ergometer. Ped. Exer. Sci., 10:164-175, 1998.

133. Rivera-Brown, A.M., Alvarez ,A., Rodríguez-Santana, J., Benetti, P. Anaerobic power and achievement of VO2 plateau in pre-pubertal boys. Int. J. Sports Med. 22:111-115, 2001.
134. Rivera-Brown, AM, Rivera, MA, Frontera, WR (1992) Applicability of criteria for VO2max in active children Pediatr Exerc Sci 4,331-339.
135. Rogers DM, Olson BL, Wilmore JH. Scaling for the VO2-to-body size relationship among children and adults. J Appl Physiol. 1995 Sep;79(3):958-67.
136. Rogers, DM, Turley, KR, Kujawa, KI, Harper, KM, Wilmore, J. (1995) Allometric scaling factors for oxygen uptake during exercise in children Pediatr Exerc Sci 7,12-25.
137. Rowland T, Kline G, Goff D, Martel L, and Ferrone L. Physiological determinants of maximal aerobic power in healthy 12-year-old boys. Ped Exer Sci 11:317-326, 1999.
138. Rowland TW, Green GM. Physiological responses to treadmill exercise in females: adult-child differences. Med Sci Sports Exerc. 1988 Oct;20(5):474-8.
139. Rowland TW, Martel L, Vanderburgh P, Manos T, Charkoudian N. The influence of short-term aerobic training on blood lipids in healthy 10-12 year old children. Int J Sports Med. 1996 Oct;17(7):487-92.
140. Rowland, T, Miller K, Vanderburgh P, Goff D, Martel L, and Ferrone L. Cardiovascular fitness in premenarcheal girls and young women. Int J Sports Med 20: 1-5, 1999.
141. Rutenfranz J, Macek M, Lange Andersen K, Bell RD, Vavra J, Radvansky J, Klimmer F, Kylian H. The relationship between changing body height and growth related changes in maximal aerobic power. Eur J Appl Physiol Occup Physiol. 1990;60(4):282-7.
142. Sady, S. Transient oxygen uptake and heart rate responses at the onset of relative endurance exercise in prepubertal boys and adult men. Int. J. Sports Med. 2: 240-244, 1981.
143. Sargent 1985 (Ref??) From T. McCurdy spreadsheet, dated Nov 15, 2000.
144. Saris WH, Noordeloos AM, Ringnalda BEM, et al. Binkhorst RA, Kemper HCG, Saris WHM, editors. Children and Exercise XI. Champaign: Human Kinetics Publisher; 1985; Reference values for aerobic power of healthy 4- to 18-year-old Dutch children: Preliminary results. p. 151-60.
145. Savage MP, Petratis MM, Thomson WH, Berg K, Smith JL, Sady SP. Exercise training effects on serum lipids of prepubescent boys and adult men. Med Sci Sports Exerc. 1986 Apr;18(2):197-204.
146. Shuleva K, Hunter G, Hester D, Dunaway D. Exercise oxygen uptake in 2 to 6 year olds. Ped Exer Sci 2:130-139, 1990.
147. Sobolova V, Seliger V, Grussova D, Machovcova J, Zelenka V. The influence of age and sports training in swimming on physical fitness. Acta Paediatr Scand Suppl. 1971;217:63-7.
148. Spurr, G.B. & Reina, J.C. (1990). Daily pattern of %VO2 max and heart rates in normal and undernourished school children. Med. Sci. Sports Exerc. 22:643-652.
149. Stewart KJ, Gutin B. Effects of physical training on cardiorespiratory fitness in children. Res Q. 1976 Mar;47(1):110-20.

150. Stoedefalke K, Armstrong N, Kirby BJ, Welsman JR. Effect of training on peak oxygen uptake and blood lipids in 13 to 14-year-old girls. Acta Paediatr. 2000 Nov;89(11):1290-4.
151. Sundberg S, Elovainio R. Cardiorespiratory function in competitive endurance runners aged 12-16 years compared with ordinary boys. Acta Paediatr Scand. 1982 Nov;71(6):987-92.
152. Sunnegardh J, Bratteby LE. Maximal oxygen uptake, anthropometry and physical activity in a randomly selected sample of 8 and 13 year old children in Sweden. Eur J Appl Physiol Occup Physiol. 1987;56(3):266-72.
153. Tolfrey K, Campbell IG, Batterham AM. Exercise training induced alterations in prepubertal children's lipid-lipoprotein profile. Med Sci Sports Exerc. 1998 Dec;30(12):1684-92.
154. W Bell (1997) Aerobic fitness and fat patterning in adolescent boys. In: Children and Exercise (Eds N Armstrong, B Kirby, J Welsman) pp 63-68. London: E & F Spon.
155. W.D. McArdle et al. (1972) Reliability and interrelationships between maximal oxygen uptake, physical work capacity and step test scores in college women. Medicine and Science in Sports, Vol 4, p182-186.
156. Washington RL, van Gundy JC, Cohen C, Sondheimer HM, Wolfe RR. Normal aerobic and anaerobic exercise data for North American school-age children. J Pediatr. 1988 Feb;112(2):223-33.
157. Welsman JR, Armstrong N, Nevill AM, Winter EM, Kirby BJ. Scaling peak VO2 for differences in body size. Med Sci Sports Exerc. 1996 Feb;28(2):259-65.
158. Welsman JR, Armstrong N, Withers S. Responses of young girls to two modes of aerobic training. Br J Sports Med. 1997 Jun;31(2):139-42.
159. Welsman JR, Armstrong N. Daily physical activity and blood lactate indices of aerobic fitness in children. Br J Sports Med. 1992 Dec;26(4):228-32.
160. Williams CA, Armstrong N, Powell J. Aerobic responses of prepubertal boys to two modes of training. Br J Sports Med. 2000 Jun;34(3):168-73.
161. Williford HN, Blessing DL, Duey WJ, Barksdale JM, Wang N, Olson MS, Teel S. Exercise training in black adolescents: changes in blood lipids and Vo2max. Ethn Dis. 1996 Autumn;6(3-4):279-85.
162. Wilmore JH, Sigerseth PO. Physical work capacity of young girls, 7-13 years of age. J Appl Physiol. 1967 May;22(5):923-8.
163. Yamaji K, Miyashita M, Shephard RJ. Relationship between heart rate and relative oxygen intake in male subjects aged 10 to 27 years. J Hum Ergol (Tokyo). 1978 Sep;7(1):29-39.
164. Yoshizawa S, Ishizaki T, and Honda H. Aerobic power and endurance running in young children. In: Rutenfranz J, Mocellin R, Klimt F, eds. children and exercise XII. International series on sport sciences, Vol 16. Champaign, IL: Human Kinetics, 1986:227-232.
165. Yoshizawa S, Honda H, Nakamura N. Effects of an 18-month endurance run program on maximal aerobic power in 4- to 6- year old girls. Pediatr Exer Sci 9:33-43, 1997.

166. Yoshizawa S, Honda H, Urushibara M, Nakamura N. Effects of endurance run on circulorespiratory system in young children. J Hum Ergol (Tokyo). 1990 Jun;19(1):41-52.
167. Yoshizawa S, Ishizaki T, Honda H. Physical fitness of children aged 5 and 6 years. J Hum Ergol (Tokyo). 1977 Sep;6(1):41-51.
168. Allen TH, Peng MT, et al. Prediction of blood volume and adiposity in man from body weight and cube of height. Metabolism. 1956; 5: 328.
169. Nadler SB, Hidalgo JU, Bloch T. Prediction of blood volume in normal human adults. Surgery. 1962;51:224-232.
170. Linderkamp O, Versmold HT, et al. Estimation and prediction of blood volume in infants and children. Europ J Pediat. 1977; 125: 227-234.
171. Cropp GJA. Changes in blood and plasma volumes during growth. J Pediatrics. 1971; 78: 220-229.
172. Smetannikov Y, Hopkins D. Intraoperative bleeding: A mathematical model for minimizing hemoglobin loss. Transfusion. 1996; 36: 832-835.

Appendix A. SAS Code for Estimating the Body Mass Distributions

```
/* This program calculates lognormal distributions for BM from the NHANES 1999-2004 Data

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Distributions are derived from raw body mass and age data downloaded from the CDC site at
http://www.cdc.gov/nchs/about/major/nhanes/

The data are stored in the downloaded datasets:

1999-2000 (SAS export files)
BMX.xpt (NHANES Body Measurement Data, contains body wt in kg)
Demo.xpt  (NHAMES Demographic Data, contains age in years or months)

2001-2002 (SAS export files)
BMX_b_r.xpt (NHANES Body Measurement Data, contains body wt in kg)
Demo_b.xpt  (NHAMES Demographic Data, contains age in years or months)

2003-2004 (SAS export files)
BMX_c.xpt (NHANES Body Measurement Data, contains body wt in kg)
Demo_c.xpt  (NHAMES Demographic Data, contains age in years or months)

*/

* Merge the Body Measurement and Demographics datasets;

Data weight;
   merge Demo Demo_b Demo_c Bmx Bmx_b_r Bmx_c;
   by SEQN;
   mass=BMXWT;
   gen=RIAGENDR;
   ageyrs=RIDAGEYR;
   agemonths=RIDAGEEX;
   wt = (2/3)*WTMEC4YR;
   if (SEQN>21004) THEN wt=(1/3)*WTMEC2YR;
   if agemonths<12 and agemonths>0 THEN ageyrs=0;
   keep SEQN mass gen ageyrs agemonths wt;
run;

proc sort data=weight;
   by gen ageyrs;
run;

Proc univariate data=weight;
by gen ageyrs;
var mass;
freq wt;
histogram mass / lognormal;

run;
```

Appendix B. SAS Code for Estimating the Normalized Vo2max Distributions

```
/*********************************************************************/
/*   This is a program to fit the  V02Max (Adams and others) data to different
distributional shapes.

Adams experimental data provided in Excel form by Stephen Graham and Tom McCurdy, EPA

Other data collected by Alion Science and Tech.

This work was performed for WA 10, APEX/SHEDS Physiology File Update

K. K. Isaacs October 2005

Alion Science and Technology
/*********************************************************************/;

*load datasets;

Data   alldata ;
  infile  'H:\kki-05-PHYSIOLOGY_10\NVO2MAX\vo2max.csv' DLM="," END=eof;
  input    age nvo2max gender;
  output alldata;

proc sort data=alldata;
by gender age;
run;

Proc univariate data=alldata;
by gender age;
var nvo2max;
histogram nvo2max / normal;
output out=outputdata1 N=samplesize mean=Mean
        std=StdDeviation ProbN=NormalFit;
run;

Proc export data=outputdata1 outfile="H:\kki-05-PHYSIOLOGY_10\Alldata_vo2max.csv"
replace;
run;
```

Appendix C. SAS Code for Estimating the Hemoglobin Content Data

```
/* This program calculates best fit normal distributions for hemoglobin content
from the NHANES 1999-2000 and 2001-2002 datasets.

Alion Science and Technology
K K Isaacs 12/2005

Distributions are derived from hemoglobin content and age data downloaded from the CDC
site at
http://www.cdc.gov/nchs/about/major/nhanes/nhanes99-00.htm
and
http://www.cdc.gov/nchs/about/major/nhanes/nhanes01-02.htm

The data are stored in the downloaded datasets:

1999-2000
lab25.xpt (NHANES Lab dataset #25)
Demo.xpt  (NHANES Demographic Data, contains age in years or months)

2001-2002
l25_b.xpt (NHANES Lab dataset #25)
Demo_b.xpt  (NHANES Demographic Data, contains age in years or months)
*/

*Data are read into SAS by loading the xpt files.

* Merge the Laboratory and Demographics datasets;

Data Hb;
   merge Demo Lab25 Demo_b L25_b;
   by SEQN;                          * Sample number;
   Hb=LBXHGB;                        * Hb content g/dL;
   gen=RIAGENDR;                     * Gender;
   ageyrs=RIDAGEYR;                  * Age in years;
   agemonths=RIDAGEEX;               * Age in months;
   wt = WTMEC4YR;                    * 4-year sample weights;
   if agemonths<12 and agemonths>0 THEN ageyrs=0;    * Age 0;
   if ageyrs>20 then ageyrs=(floor(ageyrs/5)+1)*5;   * Bin in 5-year incs;
   keep SEQN Hb gen ageyrs agemonths wt;
run;

proc sort data=Hb;
   by gen ageyrs;
run;

Proc univariate data=Hb;
by gen ageyrs;
var Hb;
req wt;                              * Apply sample weights;
histogram Hb / normal;               * Fit to Normal;
output out=outputs N=samplesize mean=Mean
        std=StdDeviation ProbN=NormalFit;
run;

Proc export data=outputs outfile="H:\kki-05-PHYSIOLOGY_10\Hemoglobin\HbFitswt.csv"
replace;
run;
```

Appendix D. The New Physiology.Txt File

Note: The values contained in the file conform to the current APEX read formats. That is, the number of decimal places for each parameter is dictated by the APEX code. It is likely that this will change in the future, at which point more significant digits could be added to the Physiology.txt file.

Males age 0-100, then females age 0-100 (last revised 12-20-05)
NVO2max distribution

Age	Source	Distr	Mean	SD	Lower	Upper	Assumptions
0	NA	Normal	48.3	1.7	44.3	52.2	
1	NA	Normal	48.6	2.0	43.8	53.3	
2	NA	Normal	48.9	2.4	43.4	54.4	
3	NA	Normal	49.2	2.7	43.0	55.4	
4	NA	Normal	49.5	3.0	42.5	56.5	
5	NA	Normal	49.8	3.3	42.1	57.6	
6	NA	Normal	50.1	3.7	41.6	58.6	
7	NA	Normal	50.4	4.0	41.2	59.7	
8	NA	Normal	50.8	4.3	40.8	60.8	
9	NA	Normal	51.1	4.6	40.3	61.8	
10	NA	Normal	51.4	5.0	39.9	62.9	
11	NA	Normal	51.7	5.3	39.4	64.0	
12	NA	Normal	52.0	5.6	39.0	65.0	
13	NA	Normal	52.3	5.9	38.6	66.1	
14	NA	Normal	52.6	6.2	38.1	67.2	
15	NA	Normal	53.0	6.6	37.7	68.2	
16	NA	Normal	53.3	6.9	37.3	69.3	
17	NA	Normal	53.6	7.2	36.8	70.4	
18	NA	Normal	53.9	7.5	36.4	71.4	
19	NA	Normal	54.2	7.9	35.9	72.5	
20	NA	Normal	54.5	8.2	35.5	73.6	
21	NA	Normal	54.2	8.5	34.5	74.0	
22	NA	Normal	53.4	8.8	32.9	74.0	
23	NA	Normal	52.6	9.2	31.4	73.9	
24	NA	Normal	51.8	9.5	29.8	73.9	
25	NA	Normal	51.1	9.8	28.3	73.9	
26	NA	Normal	50.3	10.7	25.5	75.2	
27	NA	Normal	49.6	10.5	25.2	74.0	
28	NA	Normal	48.8	10.3	24.9	72.8	
29	NA	Normal	48.1	10.1	24.6	71.6	
30	NA	Normal	47.4	9.9	24.3	70.4	
31	NA	Normal	46.7	9.7	24.0	69.3	
32	NA	Normal	46.0	9.6	23.8	68.2	
33	NA	Normal	45.3	9.4	23.5	67.1	
34	NA	Normal	44.6	9.2	23.2	66.0	
35	NA	Normal	44.0	9.0	23.0	65.0	
36	NA	Normal	43.3	8.9	22.7	64.0	
37	NA	Normal	42.7	8.7	22.4	62.9	
38	NA	Normal	42.1	8.6	22.2	61.9	
39	NA	Normal	41.4	7.3	25.5	54.1	
40	NA	Normal	40.8	5.5	28.4	50.0	
41	NA	Normal	40.2	5.5	28.4	50.0	
42	NA	Normal	39.7	5.5	28.4	50.0	
43	NA	Normal	39.1	5.5	28.4	50.0	
44	NA	Normal	38.5	5.5	28.4	50.0	
45	NA	Normal	38.0	5.5	28.4	50.0	
46	NA	Normal	37.4	5.5	28.4	50.0	
47	NA	Normal	36.9	5.5	28.4	50.0	
48	NA	Normal	36.4	5.5	28.4	50.0	
49	NA	Normal	35.9	5.5	28.4	50.0	
50	NA	Normal	35.4	4.9	23.5	42.7	
51	NA	Normal	34.9	4.9	23.5	42.7	
52	NA	Normal	34.5	4.9	23.5	42.7	
53	NA	Normal	34.0	4.9	23.5	42.7	
54	NA	Normal	33.6	4.9	23.5	42.7	
55	NA	Normal	33.1	4.9	23.5	42.7	
56	NA	Normal	32.7	4.9	23.5	42.7	
57	NA	Normal	32.3	4.9	23.5	42.7	
58	NA	Normal	31.9	4.9	23.5	42.7	

59	NA	Normal	31.5	4.9	23.5	42.7
60	NA	Normal	31.1	5.3	21.0	41.8
61	NA	Normal	30.7	5.3	21.0	41.8
62	NA	Normal	30.4	5.3	21.0	41.8
63	NA	Normal	30.0	5.3	21.0	41.8
64	NA	Normal	29.7	5.3	21.0	41.8
65	NA	Normal	29.4	5.3	21.0	41.8
66	NA	Normal	29.1	5.3	21.0	41.8
67	NA	Normal	28.8	5.3	21.0	41.8
68	NA	Normal	28.5	5.3	21.0	41.8
69	NA	Normal	28.2	5.3	21.0	41.8
70	NA	Normal	27.9	5.7	16.1	38.3
71	NA	Normal	27.7	5.7	16.1	38.3
72	NA	Normal	27.4	5.7	16.1	38.3
73	NA	Normal	27.2	5.7	16.1	38.3
74	NA	Normal	27.0	5.7	16.1	38.3
75	NA	Normal	26.7	5.7	16.1	38.3
76	NA	Normal	26.5	5.7	16.1	38.3
77	NA	Normal	26.4	5.7	16.1	38.3
78	NA	Normal	26.2	5.7	16.1	38.3
79	NA	Normal	26.0	5.7	16.1	38.3
80	NA	Normal	25.8	5.7	16.1	38.3
81	NA	Normal	25.7	5.7	16.1	38.3
82	NA	Normal	25.6	5.7	16.1	38.3
83	NA	Normal	25.4	5.7	16.1	38.3
84	NA	Normal	25.3	5.7	16.1	38.3
85	NA	Normal	25.2	5.7	16.1	38.3
86	NA	Normal	25.1	5.7	16.1	38.3
87	NA	Normal	25.1	5.7	16.1	38.3
88	NA	Normal	25.0	5.7	16.1	38.3
89	NA	Normal	24.9	5.7	16.1	38.3
90	NA	Normal	24.9	5.7	16.1	38.3
91	NA	Normal	24.9	5.7	16.1	38.3
92	NA	Normal	24.8	5.7	16.1	38.3
93	NA	Normal	24.8	5.7	16.1	38.3
94	NA	Normal	24.8	5.7	16.1	38.3
95	NA	Normal	24.8	5.7	16.1	38.3
96	NA	Normal	24.9	5.7	16.1	38.3
97	NA	Normal	24.9	5.7	16.1	38.3
98	NA	Normal	25.0	5.7	16.1	38.3
99	NA	Normal	25.0	5.7	16.1	38.3
100	NA	Normal	25.1	5.7	16.1	38.3
0	NA	Normal	35.9	5.9	22.2	49.6
1	NA	Normal	36.2	6.0	22.3	50.2
2	NA	Normal	36.5	6.1	22.4	50.7
3	NA	Normal	36.9	6.2	22.5	51.3
4	NA	Normal	37.2	6.3	22.6	51.8
5	NA	Normal	37.5	6.4	22.7	52.4
6	NA	Normal	37.9	6.5	22.8	52.9
7	NA	Normal	38.2	6.6	22.9	53.5
8	NA	Normal	38.5	6.7	23.0	54.0
9	NA	Normal	38.9	6.8	23.1	54.6
10	NA	Normal	39.2	6.9	23.3	55.1
11	NA	Normal	39.5	7.0	23.4	55.7
12	NA	Normal	39.9	7.0	23.5	56.2
13	NA	Normal	40.2	7.1	23.6	56.8
14	NA	Normal	40.5	7.2	23.7	57.3
15	NA	Normal	40.9	7.3	23.8	57.9
16	NA	Normal	41.2	7.4	23.9	58.5
17	NA	Normal	41.5	7.5	24.0	59.0
18	NA	Normal	41.8	7.6	24.1	59.6
19	NA	Normal	42.2	7.7	24.2	60.1
20	NA	Normal	42.5	7.8	24.4	60.7
21	NA	Normal	42.1	7.9	23.7	60.5
22	NA	Normal	41.5	8.0	22.9	60.1
23	NA	Normal	40.8	8.1	22.0	59.6
24	NA	Normal	40.2	8.2	21.1	59.2
25	NA	Normal	39.6	8.3	20.3	58.8
26	NA	Normal	39.0	8.4	19.5	58.4
27	NA	Normal	38.4	8.4	18.9	57.8
28	NA	Normal	37.8	8.1	18.8	56.7
29	NA	Normal	37.2	7.9	18.7	55.6
30	NA	Normal	36.6	7.7	18.6	54.6
31	NA	Normal	36.0	7.6	18.5	53.6
32	NA	Normal	35.5	7.4	18.4	52.6
33	NA	Normal	34.9	7.2	18.2	51.7
34	NA	Normal	34.4	7.0	18.1	50.7
35	NA	Normal	33.9	6.8	18.0	49.8
36	NA	Normal	33.4	6.7	17.8	48.9
37	NA	Normal	32.9	6.5	17.7	48.0
38	NA	Normal	32.4	6.4	17.6	47.2

39	NA	Normal	31.9	6.2	17.4	46.4
40	NA	Normal	31.4	6.1	17.3	45.6
41	NA	Normal	31.0	6.0	17.1	44.8
42	NA	Normal	30.5	5.8	17.0	44.0
43	NA	Normal	30.1	5.7	16.8	43.3
44	NA	Normal	29.6	5.6	16.6	42.6
45	NA	Normal	29.2	5.5	16.5	41.9
46	NA	Normal	28.8	5.4	16.3	41.2
47	NA	Normal	28.4	5.3	16.1	40.6
48	NA	Normal	28.0	5.2	16.0	40.0
49	NA	Normal	27.6	5.1	15.8	39.4
50	NA	Normal	27.2	5.0	15.6	38.8
51	NA	Normal	26.8	4.9	15.4	38.3
52	NA	Normal	26.5	4.8	15.2	37.7
53	NA	Normal	26.1	4.8	15.1	37.2
54	NA	Normal	25.8	4.7	14.9	36.7
55	NA	Normal	25.5	4.7	14.7	36.3
56	NA	Normal	25.2	4.6	14.5	35.9
57	NA	Normal	24.9	4.6	14.3	35.4
58	NA	Normal	24.6	4.5	14.1	35.1
59	NA	Normal	24.3	4.5	13.9	34.7
60	NA	Normal	24.0	4.5	13.6	34.3
61	NA	Normal	23.7	4.4	13.4	34.0
62	NA	Normal	23.5	4.4	13.2	33.7
63	NA	Normal	23.2	4.4	13.0	33.4
64	NA	Normal	23.0	4.4	12.8	33.2
65	NA	Normal	22.7	4.4	12.5	33.0
66	NA	Normal	22.5	4.4	12.3	32.7
67	NA	Normal	22.3	4.4	12.1	32.5
68	NA	Normal	22.1	4.4	11.9	32.3
69	NA	Normal	21.9	4.4	11.7	32.1
70	NA	Normal	21.7	4.4	11.5	32.0
71	NA	Normal	21.6	4.4	11.4	31.8
72	NA	Normal	21.4	4.4	11.2	31.6
73	NA	Normal	21.3	4.4	11.1	31.5
74	NA	Normal	21.1	4.4	10.9	31.3
75	NA	Normal	21.0	4.4	10.8	31.2
76	NA	Normal	20.9	4.4	10.7	31.1
77	NA	Normal	20.8	4.4	10.6	31.0
78	NA	Normal	20.7	4.4	10.4	30.9
79	NA	Normal	20.6	4.4	10.4	30.8
80	NA	Normal	20.5	4.4	10.3	30.7
81	NA	Normal	20.4	4.4	10.2	30.6
82	NA	Normal	20.3	4.4	10.1	30.6
83	NA	Normal	20.3	4.4	10.1	30.5
84	NA	Normal	20.3	4.4	10.0	30.5
85	NA	Normal	20.2	4.4	10.0	30.4
86	NA	Normal	20.2	4.4	10.0	30.4
87	NA	Normal	20.2	4.4	10.0	30.4
88	NA	Normal	20.2	4.4	10.0	30.4
89	NA	Normal	20.2	4.4	10.0	30.4
90	NA	Normal	20.2	4.4	10.0	30.4
91	NA	Normal	20.2	4.4	10.0	30.4
92	NA	Normal	20.3	4.4	10.1	30.5
93	NA	Normal	20.3	4.4	10.1	30.5
94	NA	Normal	20.4	4.4	10.2	30.6
95	NA	Normal	20.4	4.4	10.2	30.6
96	NA	Normal	20.5	4.4	10.3	30.7
97	NA	Normal	20.6	4.4	10.4	30.8
98	NA	Normal	20.7	4.4	10.5	30.9
99	NA	Normal	20.8	4.4	10.6	31.0
100	NA	Normal	20.9	4.4	10.7	31.1

Males age 0-100, then females age 0-100 (last revised 12-20-05)

Body mass distribution, kg

Age	Source	Distr	GM	GSD	Lower	Upper	Assumptions
0	CDC	LN	7.8	1.301	3.6	11.8	
1	CDC	LN	11.4	1.143	8.2	16.1	
2	CDC	LN	13.9	1.146	9.8	20.9	
3	CDC	LN	16.0	1.154	11.7	23.7	
4	CDC	LN	18.5	1.165	11.1	28.1	
5	CDC	LN	21.6	1.234	13.7	42.4	
6	CDC	LN	23.1	1.213	16.1	41.1	
7	CDC	LN	27.1	1.216	19.3	46.8	
8	CDC	LN	31.7	1.302	19.1	66.2	
9	CDC	LN	34.7	1.265	24.0	69.9	
10	CDC	LN	38.3	1.280	24.3	72.9	
11	CDC	LN	44.1	1.308	26.2	83.8	
12	CDC	LN	48.0	1.315	27.7	94.8	
13	CDC	LN	55.4	1.340	27.7	106.6	
14	CDC	LN	62.8	1.293	35.7	121.0	
15	CDC	LN	67.7	1.255	41.5	117.9	

16	CDC	LN	72.5	1.267	45.8	139.1
17	CDC	LN	73.1	1.248	49.9	136.6
18	CDC	LN	75.1	1.243	51.2	144.2
19	CDC	LN	77.2	1.245	52.6	134.5
20	CDC	LN	78.0	1.250	50.5	130.0
21	CDC	LN	78.2	1.297	46.8	199.2
22	CDC	LN	83.8	1.292	53.3	155.4
23	CDC	LN	80.6	1.222	50.5	137.6
24	CDC	LN	81.7	1.251	50.6	132.6
25	CDC	LN	84.8	1.206	50.2	136.1
26	CDC	LN	81.8	1.273	48.9	164.5
27	CDC	LN	85.2	1.249	50.0	153.9
28	CDC	LN	84.3	1.272	51.0	167.2
29	CDC	LN	82.1	1.236	50.6	147.2
30	CDC	LN	81.6	1.262	52.5	139.0
31	CDC	LN	81.3	1.249	48.8	170.6
32	CDC	LN	84.7	1.235	49.7	135.8
33	CDC	LN	88.2	1.231	64.8	146.3
34	CDC	LN	81.2	1.221	53.1	136.9
35	CDC	LN	87.2	1.251	61.0	193.3
36	CDC	LN	83.4	1.228	45.8	140.5
37	CDC	LN	85.8	1.241	59.3	150.9
38	CDC	LN	84.1	1.260	52.8	149.7
39	CDC	LN	84.6	1.196	61.2	140.6
40	CDC	LN	90.1	1.246	58.5	154.0
41	CDC	LN	87.4	1.173	61.3	117.7
42	CDC	LN	88.3	1.205	62.2	144.0
43	CDC	LN	88.4	1.233	54.0	145.3
44	CDC	LN	88.5	1.200	56.6	128.9
45	CDC	LN	87.1	1.205	60.6	160.2
46	CDC	LN	88.2	1.243	54.2	154.3
47	CDC	LN	86.5	1.229	49.9	188.3
48	CDC	LN	84.8	1.186	56.3	128.3
49	CDC	LN	86.2	1.240	47.0	171.3
50	CDC	LN	84.7	1.179	53.4	124.4
51	CDC	LN	88.0	1.208	57.9	143.6
52	CDC	LN	89.9	1.216	55.2	144.9
53	CDC	LN	89.0	1.228	58.2	143.3
54	CDC	LN	90.1	1.216	64.1	155.2
55	CDC	LN	88.3	1.222	55.1	138.6
56	CDC	LN	84.8	1.195	45.0	110.3
57	CDC	LN	87.5	1.253	58.3	160.0
58	CDC	LN	85.1	1.266	51.6	179.0
59	CDC	LN	84.2	1.182	58.7	112.4
60	CDC	LN	87.0	1.232	57.3	141.7
61	CDC	LN	89.0	1.207	49.9	162.8
62	CDC	LN	84.8	1.228	56.0	152.1
63	CDC	LN	89.1	1.262	56.3	171.6
64	CDC	LN	90.0	1.193	59.1	119.0
65	CDC	LN	89.9	1.215	58.1	126.3
66	CDC	LN	86.8	1.228	54.0	150.1
67	CDC	LN	86.2	1.207	43.1	127.5
68	CDC	LN	85.2	1.191	61.2	163.2
69	CDC	LN	87.1	1.222	50.7	127.2
70	CDC	LN	82.8	1.210	46.5	125.5
71	CDC	LN	79.6	1.240	51.0	122.8
72	CDC	LN	82.0	1.204	51.9	132.7
73	CDC	LN	85.6	1.196	56.2	128.3
74	CDC	LN	83.0	1.217	53.3	120.0
75	CDC	LN	84.5	1.185	56.5	133.5
76	CDC	LN	78.7	1.207	55.9	121.1
77	CDC	LN	79.4	1.170	58.7	109.3
78	CDC	LN	79.9	1.195	41.1	115.1
79	CDC	LN	77.6	1.155	56.4	107.8
80	CDC	LN	79.9	1.174	56.0	111.9
81	CDC	LN	75.4	1.157	55.8	111.9
82	CDC	LN	76.8	1.180	54.4	111.8
83	CDC	LN	74.6	1.158	53.2	107.0
84	CDC	LN	75.3	1.205	41.5	109.5
85	CDC	LN	71.8	1.191	46.9	105.8
86	CDC	LN	74.0	1.170	50.6	101.1
87	CDC	LN	73.4	1.170	50.4	99.1
88	CDC	LN	72.7	1.160	50.2	97.2
89	CDC	LN	72.1	1.160	50.0	95.2
90	CDC	LN	71.5	1.160	49.8	93.2
91	CDC	LN	70.9	1.160	49.6	91.3
92	CDC	LN	70.3	1.160	49.4	89.3
93	CDC	LN	69.6	1.150	49.3	87.4
94	CDC	LN	69.0	1.150	49.1	85.4
95	CDC	LN	68.4	1.150	48.9	83.4
96	CDC	LN	67.8	1.150	48.7	81.5

97	CDC	LN	67.1	1.140	48.5	79.5
98	CDC	LN	66.5	1.140	48.3	77.6
99	CDC	LN	65.9	1.140	48.1	75.6
100	CDC	LN	65.3	1.140	47.9	73.6
0	CDC	LN	7.4	1.304	3.7	12.1
1	CDC	LN	11.1	1.163	7.4	15.3
2	CDC	LN	13.3	1.158	10.1	20.4
3	CDC	LN	15.6	1.160	11.0	27.9
4	CDC	LN	18.0	1.171	12.8	29.1
5	CDC	LN	20.4	1.229	12.6	40.4
6	CDC	LN	22.5	1.194	15.9	36.7
7	CDC	LN	26.5	1.239	16.9	51.0
8	CDC	LN	30.5	1.315	19.8	60.8
9	CDC	LN	35.2	1.271	20.3	58.6
10	CDC	LN	40.6	1.304	22.7	71.2
11	CDC	LN	46.6	1.302	27.7	84.6
12	CDC	LN	50.7	1.274	27.8	93.3
13	CDC	LN	56.6	1.275	33.4	99.5
14	CDC	LN	57.2	1.248	37.7	110.0
15	CDC	LN	60.1	1.249	34.9	108.4
16	CDC	LN	61.6	1.255	40.9	113.8
17	CDC	LN	61.2	1.248	41.5	133.1
18	CDC	LN	64.6	1.281	42.4	123.6
19	CDC	LN	66.2	1.274	41.6	118.5
20	CDC	LN	67.0	1.262	41.5	122.6
21	CDC	LN	67.2	1.262	39.7	123.7
22	CDC	LN	66.8	1.273	42.0	123.5
23	CDC	LN	69.7	1.304	40.3	143.0
24	CDC	LN	70.3	1.289	47.5	144.5
25	CDC	LN	66.3	1.283	44.8	131.8
26	CDC	LN	73.0	1.281	45.3	128.9
27	CDC	LN	70.6	1.281	41.4	140.9
28	CDC	LN	74.4	1.312	44.3	142.1
29	CDC	LN	69.1	1.250	39.3	116.3
30	CDC	LN	70.6	1.305	42.1	151.5
31	CDC	LN	73.0	1.278	43.7	125.9
32	CDC	LN	72.9	1.281	41.5	139.7
33	CDC	LN	72.7	1.307	44.9	135.2
34	CDC	LN	69.8	1.230	46.6	115.3
35	CDC	LN	73.0	1.306	44.2	138.4
36	CDC	LN	73.5	1.289	44.6	150.1
37	CDC	LN	70.0	1.284	48.1	152.1
38	CDC	LN	75.6	1.295	43.7	151.7
39	CDC	LN	72.3	1.251	41.6	123.1
40	CDC	LN	72.9	1.289	45.5	137.4
41	CDC	LN	73.4	1.268	50.5	156.9
42	CDC	LN	73.7	1.270	47.1	146.1
43	CDC	LN	73.4	1.314	45.6	159.5
44	CDC	LN	75.7	1.266	49.5	153.0
45	CDC	LN	76.8	1.308	41.6	141.5
46	CDC	LN	77.5	1.304	46.6	145.8
47	CDC	LN	72.8	1.298	47.8	130.6
48	CDC	LN	74.6	1.303	44.2	166.0
49	CDC	LN	72.8	1.261	45.1	125.5
50	CDC	LN	75.2	1.292	48.4	175.7
51	CDC	LN	72.9	1.240	42.5	120.2
52	CDC	LN	74.5	1.283	45.7	146.6
53	CDC	LN	74.7	1.259	46.2	176.6
54	CDC	LN	72.4	1.281	44.3	123.1
55	CDC	LN	76.0	1.231	53.6	125.6
56	CDC	LN	77.3	1.315	45.6	134.9
57	CDC	LN	72.4	1.252	48.6	122.6
58	CDC	LN	74.5	1.267	45.0	117.7
59	CDC	LN	80.6	1.277	50.9	133.0
60	CDC	LN	75.8	1.260	51.3	128.3
61	CDC	LN	77.1	1.240	50.7	125.6
62	CDC	LN	73.3	1.198	49.7	121.1
63	CDC	LN	72.3	1.238	46.9	119.9
64	CDC	LN	75.4	1.281	41.1	132.5
65	CDC	LN	72.9	1.254	35.9	113.7
66	CDC	LN	73.1	1.242	48.4	113.3
67	CDC	LN	75.8	1.266	47.2	123.8
68	CDC	LN	73.2	1.250	39.3	120.7
69	CDC	LN	74.4	1.225	48.0	118.0
70	CDC	LN	69.0	1.188	45.9	102.8
71	CDC	LN	69.1	1.232	45.5	108.1
72	CDC	LN	69.9	1.240	40.7	103.8
73	CDC	LN	71.4	1.240	47.4	127.6
74	CDC	LN	70.4	1.277	37.4	106.4
75	CDC	LN	70.5	1.216	46.8	117.4
76	CDC	LN	69.5	1.199	48.8	101.7

77	CDC	LN	70.1	1.240	40.3	119.8
78	CDC	LN	66.4	1.211	44.1	109.8
79	CDC	LN	67.8	1.200	46.2	98.4
80	CDC	LN	62.2	1.255	41.2	121.4
81	CDC	LN	65.4	1.184	42.7	91.4
82	CDC	LN	64.8	1.260	40.6	120.0
83	CDC	LN	62.9	1.196	44.7	101.2
84	CDC	LN	62.2	1.216	43.5	108.4
85	CDC	LN	61.5	1.209	42.3	93.2
86	CDC	LN	62.4	1.210	41.9	101.2
87	CDC	LN	61.8	1.210	41.7	100.3
88	CDC	LN	61.3	1.210	41.5	99.4
89	CDC	LN	60.7	1.210	41.3	98.4
90	CDC	LN	60.2	1.210	41.1	97.5
91	CDC	LN	59.6	1.200	40.9	96.6
92	CDC	LN	59.1	1.200	40.7	95.7
93	CDC	LN	58.5	1.200	40.5	94.8
94	CDC	LN	58.0	1.200	40.3	93.9
95	CDC	LN	57.4	1.200	40.1	93.0
96	CDC	LN	56.9	1.200	39.9	92.1
97	CDC	LN	56.3	1.200	39.7	91.2
98	CDC	LN	55.8	1.190	39.5	90.3
99	CDC	LN	55.2	1.190	39.3	89.4
100	CDC	LN	54.7	1.190	39.1	88.5

Males age 0-100 then females age 0-100 (last revised 6-11-98)

Regression equation Estimate for RMR

Age	Source	DV	IV	Slope	Interc	SE	Units	med. wgt
0	R47g	BMR	BM	0.244	-0.127	0.290	MJ/day	2.1
1	R47g	BMR	BM	0.244	-0.127	0.290	MJ/day	2.7
2	R47g	BMR	BM	0.244	-0.127	0.280	MJ/day	3.2
3	R47h	BMR	BM	0.095	2.110	0.280	MJ/day	3.6
4	R47h	BMR	BM	0.095	2.110	0.280	MJ/day	3.8
5	R47h	BMR	BM	0.095	2.110	0.280	MJ/day	4.0
6	R47h	BMR	BM	0.095	2.110	0.280	MJ/day	4.3
7	R47h	BMR	BM	0.095	2.110	0.280	MJ/day	4.5
8	R47h	BMR	BM	0.095	2.110	0.280	MJ/day	4.8
9	R47h	BMR	BM	0.095	2.110	0.280	MJ/day	5.0
10	R47i	BMR	BM	0.074	2.754	0.440	MJ/day	5.4
11	R47i	BMR	BM	0.074	2.754	0.440	MJ/day	5.7
12	R47i	BMR	BM	0.074	2.754	0.440	MJ/day	6.0
13	R47i	BMR	BM	0.074	2.754	0.440	MJ/day	6.3
14	R47i	BMR	BM	0.074	2.754	0.440	MJ/day	6.9
15	R47i	BMR	BM	0.074	2.754	0.440	MJ/day	7.2
16	R47i	BMR	BM	0.074	2.754	0.440	MJ/day	7.7
17	R47i	BMR	BM	0.074	2.754	0.440	MJ/day	7.6
18	R47j	BMR	BM	0.063	2.896	0.640	MJ/day	7.3
19	R47j	BMR	BM	0.063	2.896	0.640	MJ/day	7.4
20	R47j	BMR	BM	0.063	2.896	0.640	MJ/day	7.7
21	R47j	BMR	BM	0.063	2.896	0.640	MJ/day	7.7
22	R47j	BMR	BM	0.063	2.896	0.640	MJ/day	7.7
23	R47j	BMR	BM	0.063	2.896	0.640	MJ/day	7.7
24	R47j	BMR	BM	0.063	2.896	0.640	MJ/day	7.7
25	R47j	BMR	BM	0.063	2.896	0.640	MJ/day	7.7
26	R47j	BMR	BM	0.063	2.896	0.640	MJ/day	7.7
27	R47j	BMR	BM	0.063	2.896	0.640	MJ/day	7.7
28	R47j	BMR	BM	0.063	2.896	0.640	MJ/day	7.7
29	R47j	BMR	BM	0.063	2.896	0.640	MJ/day	7.7
30	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
31	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
32	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
33	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
34	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
35	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
36	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
37	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
38	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
39	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
40	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
41	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
42	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
43	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
44	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
45	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
46	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
47	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
48	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
49	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
50	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
51	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
52	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
53	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3

54	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
55	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
56	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
57	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
58	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
59	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
60	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
61	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
62	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
63	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
64	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
65	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
66	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
67	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
68	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
69	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
70	R47k	BMR	BM	0.048	3.653	0.700	MJ/day	7.3
71	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
72	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
73	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
74	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
75	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
76	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
77	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
78	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
79	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
80	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
81	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
82	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
83	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
84	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
85	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
86	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
87	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
88	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
89	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
90	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
91	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
92	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
93	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
94	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
95	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
96	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
97	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
98	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
99	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
100	R47l	BMR	BM	0.049	2.459	0.690	MJ/day	6.2
0	R47a	BMR	BM	0.244	-0.130	0.250	MJ/day	2.0
1	R47a	BMR	BM	0.244	-0.130	0.250	MJ/day	2.5
2	R47a	BMR	BM	0.244	-0.130	0.250	MJ/day	3.0
3	R47b	BMR	BM	0.085	2.033	0.290	MJ/day	3.3
4	R47b	BMR	BM	0.085	2.033	0.290	MJ/day	3.5
5	R47b	BMR	BM	0.085	2.033	0.290	MJ/day	3.7
6	R47b	BMR	BM	0.085	2.033	0.290	MJ/day	3.9
7	R47b	BMR	BM	0.085	2.033	0.290	MJ/day	4.1
8	R47b	BMR	BM	0.085	2.033	0.290	MJ/day	4.4
9	R47b	BMR	BM	0.085	2.033	0.290	MJ/day	4.7
10	R47c	BMR	BM	0.056	2.898	0.470	MJ/day	4.9
11	R47c	BMR	BM	0.056	2.898	0.470	MJ/day	5.2
12	R47c	BMR	BM	0.056	2.898	0.470	MJ/day	5.5
13	R47c	BMR	BM	0.056	2.898	0.470	MJ/day	5.7
14	R47c	BMR	BM	0.056	2.898	0.470	MJ/day	5.9
15	R47c	BMR	BM	0.056	2.898	0.470	MJ/day	6.0
16	R47c	BMR	BM	0.056	2.898	0.470	MJ/day	6.1
17	R47c	BMR	BM	0.056	2.898	0.470	MJ/day	6.2
18	R47d	BMR	BM	0.062	2.036	0.500	MJ/day	5.7
19	R47d	BMR	BM	0.062	2.036	0.500	MJ/day	5.8
20	R47d	BMR	BM	0.062	2.036	0.500	MJ/day	6.0
21	R47d	BMR	BM	0.062	2.036	0.500	MJ/day	6.0
22	R47d	BMR	BM	0.062	2.036	0.500	MJ/day	6.0
23	R47d	BMR	BM	0.062	2.036	0.500	MJ/day	6.0
24	R47d	BMR	BM	0.062	2.036	0.500	MJ/day	6.0
25	R47d	BMR	BM	0.062	2.036	0.500	MJ/day	6.0
26	R47d	BMR	BM	0.062	2.036	0.500	MJ/day	6.0
27	R47d	BMR	BM	0.062	2.036	0.500	MJ/day	6.0
28	R47d	BMR	BM	0.062	2.036	0.500	MJ/day	6.0
29	R47d	BMR	BM	0.062	2.036	0.500	MJ/day	6.0
30	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
31	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
32	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
33	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7

34	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
35	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
36	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
37	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
38	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
39	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
40	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
41	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
42	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
43	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
44	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
45	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
46	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
47	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
48	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
49	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
50	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
51	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
52	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
53	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
54	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
55	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
56	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
57	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
58	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
59	R47e	BMR	BM	0.034	3.538	0.470	MJ/day	5.7
60	R47e	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
61	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
62	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
63	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
64	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
65	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
66	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
67	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
68	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
69	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
70	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
71	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
72	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
73	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
74	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
75	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
76	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
77	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
78	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
79	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
80	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
81	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
82	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
83	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
84	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
85	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
86	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
87	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
88	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
89	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
90	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
91	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
92	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
93	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
94	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
95	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
96	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
97	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
98	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
99	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2
100	R47f	BMR	BM	0.038	2.755	0.450	MJ/day	5.2

Males age 0-100 then females age 0-100 (HG last revised 12-20-05)
Blood Volume factor and Hemoglobin content

Age	BLDFAC	HGMN	HGSTD
0	17.0	11.9	1.0
1	17.0	12.2	1.0
2	17.0	12.4	0.8
3	17.0	12.7	0.8
4	17.0	12.8	0.8
5	17.0	13.0	0.9
6	17.0	13.2	0.9
7	17.0	13.5	0.8
8	17.0	13.4	0.8
9	17.0	13.6	1.0
10	17.0	13.6	0.9

11	17.0	13.7	0.7
12	17.0	14.0	1.0
13	17.0	14.3	1.0
14	17.0	14.7	1.0
15	17.0	15.1	1.0
16	17.0	15.4	1.0
17	17.0	15.5	1.0
18	17.0	15.7	1.0
19	20.4	15.8	0.8
20	20.4	15.8	0.9
21	20.4	15.7	0.9
22	20.4	15.7	0.9
23	20.4	15.7	0.9
24	20.4	15.7	0.9
25	20.4	15.7	0.9
26	20.4	15.7	1.0
27	20.4	15.7	1.0
28	20.4	15.7	1.0
29	20.4	15.7	1.0
30	20.4	15.7	1.0
31	20.4	15.6	1.0
32	20.4	15.6	1.0
33	20.4	15.6	1.0
34	20.4	15.6	1.0
35	20.4	15.6	1.0
36	20.4	15.4	1.0
37	20.4	15.4	1.0
38	20.4	15.4	1.0
39	20.4	15.4	1.0
40	20.4	15.4	1.0
41	20.4	15.4	1.1
42	20.4	15.4	1.1
43	20.4	15.4	1.1
44	20.4	15.4	1.1
45	20.4	15.4	1.1
46	20.4	15.4	1.1
47	20.4	15.4	1.1
48	20.4	15.4	1.1
49	20.4	15.4	1.1
50	20.4	15.4	1.1
51	20.4	15.3	1.1
52	20.4	15.3	1.1
53	20.4	15.3	1.1
54	20.4	15.3	1.1
55	20.4	15.3	1.1
56	20.4	15.3	1.0
57	20.4	15.3	1.0
58	20.4	15.3	1.0
59	20.4	15.3	1.0
60	20.4	15.3	1.0
61	20.4	15.1	1.2
62	20.4	15.1	1.2
63	20.4	15.1	1.2
64	20.4	15.1	1.2
65	20.4	15.1	1.2
66	20.4	15.0	1.2
67	20.4	15.0	1.2
68	20.4	15.0	1.2
69	20.4	15.0	1.2
70	20.4	15.0	1.2
71	20.4	14.7	1.4
72	20.4	14.7	1.4
73	20.4	14.7	1.4
74	20.4	14.7	1.4
75	20.4	14.7	1.4
76	20.4	14.5	1.5
77	20.4	14.5	1.5
78	20.4	14.5	1.5
79	20.4	14.5	1.5
80	20.4	14.5	1.5
81	20.4	14.5	1.4
82	20.4	14.5	1.4
83	20.4	14.5	1.4
84	20.4	14.5	1.4
85	20.4	14.5	1.4
86	20.4	14.0	1.8
87	20.4	14.0	1.8
88	20.4	14.0	1.8
89	20.4	14.0	1.8
90	20.4	14.0	1.8
91	20.4	13.8	1.8

92	20.4	13.8	1.8
93	20.4	13.8	1.8
94	20.4	13.8	1.8
95	20.4	13.8	1.8
96	20.4	13.5	1.8
97	20.4	13.5	1.8
98	20.4	13.5	1.8
99	20.4	13.5	1.8
100	20.4	13.5	1.8
0	17.0	12.2	0.7
1	17.0	12.3	0.7
2	17.0	12.6	0.8
3	17.0	12.5	1.0
4	17.0	12.8	0.8
5	17.0	12.9	1.0
6	17.0	13.0	0.8
7	17.0	13.1	0.8
8	17.0	13.3	0.8
9	17.0	13.4	0.8
10	17.0	13.6	1.0
11	17.0	13.5	0.9
12	17.0	13.6	0.9
13	17.0	13.5	1.0
14	17.0	13.6	1.0
15	17.0	13.5	0.9
16	17.0	13.5	1.1
17	17.0	13.5	1.1
18	17.0	13.5	1.2
19	14.6	13.4	1.1
20	14.6	13.5	1.1
21	14.6	13.5	1.2
22	14.6	13.5	1.2
23	14.6	13.5	1.2
24	14.6	13.5	1.2
25	14.6	13.5	1.2
26	14.6	13.3	1.1
27	14.6	13.3	1.1
28	14.6	13.3	1.1
29	14.6	13.3	1.1
30	14.6	13.3	1.1
31	14.6	13.3	1.1
32	14.6	13.3	1.1
33	14.6	13.3	1.1
34	14.6	13.3	1.1
35	14.6	13.3	1.1
36	14.6	13.5	1.2
37	14.6	13.5	1.2
38	14.6	13.5	1.2
39	14.6	13.5	1.2
40	14.6	13.5	1.2
41	14.6	13.5	1.3
42	14.6	13.5	1.3
43	14.6	13.5	1.3
44	14.6	13.5	1.3
45	14.6	13.5	1.3
46	14.6	13.6	1.2
47	14.6	13.6	1.2
48	14.6	13.6	1.2
49	14.6	13.6	1.2
50	14.6	13.6	1.2
51	14.6	13.7	1.1
52	14.6	13.7	1.1
53	14.6	13.7	1.1
54	14.6	13.7	1.1
55	14.6	13.7	1.1
56	14.6	13.8	1.2
57	14.6	13.8	1.2
58	14.6	13.8	1.2
59	14.6	13.8	1.2
60	14.6	13.8	1.2
61	14.6	13.8	1.1
62	14.6	13.8	1.1
63	14.6	13.8	1.1
64	14.6	13.8	1.1
65	14.6	13.8	1.1
66	14.6	13.8	1.1
67	14.6	13.8	1.1
68	14.6	13.8	1.1
69	14.6	13.8	1.1
70	14.6	13.8	1.1
71	14.6	13.8	1.1

72	14.6	13.8	1.1
73	14.6	13.8	1.1
74	14.6	13.8	1.1
75	14.6	13.8	1.1
76	14.6	13.8	1.3
77	14.6	13.8	1.3
78	14.6	13.8	1.3
79	14.6	13.8	1.3
80	14.6	13.8	1.3
81	14.6	13.6	1.2
82	14.6	13.6	1.2
83	14.6	13.6	1.2
84	14.6	13.6	1.2
85	14.6	13.6	1.2
86	14.6	13.4	1.6
87	14.6	13.4	1.6
88	14.6	13.4	1.6
89	14.6	13.4	1.6
90	14.6	13.4	1.6
91	14.6	13.2	1.6
92	14.6	13.2	1.6
93	14.6	13.2	1.6
94	14.6	13.2	1.6
95	14.6	13.2	1.6
96	14.6	13.0	1.6
97	14.6	13.0	1.6
98	14.6	13.0	1.6
99	14.6	13.0	1.6
100	14.6	13.0	1.6

Appendix E. All Derived Physiological Parameters

Table 1. Nv02max Values for Males: Raw and Smoothed Fits.

	MALES					
Age	MEAN Raw Fit Values	MEAN Smoothed Fit Values	SD Raw Fit Values	SD Smoothed Fit Values	MIN (1st Pctl)	MAX (99th Pctl)
0.00		48.25		1.71	44.26	52.24
1.00		48.56		2.04	43.82	53.30
2.00		48.88		2.36	43.39	54.37
3.00		49.19		2.68	42.95	55.43
4.00		49.50		3.01	42.51	56.50
5.00		49.82		3.33	42.07	57.56
6.00		50.13		3.65	41.63	58.63
7.00	51.37	50.44	2.86	3.98	41.19	59.70
8.00	53.46	50.76	2.86	4.30	40.76	60.76
9.00	51.10	51.07	6.26	4.62	40.32	61.83
10.00	51.28	51.39	5.87	4.95	39.88	62.89
11.00	50.13	51.70	6.04	5.27	39.44	63.96
12.00	50.70	52.01	7.13	5.59	39.00	65.02
13.00	52.74	52.33	5.13	5.92	38.56	66.09
14.00	52.93	52.64	4.72	6.24	38.13	67.16
15.00	53.18	52.95	5.57	6.56	37.69	68.22
16.00	49.46	53.27	6.06	6.89	37.25	69.29
17.00	49.77	53.58	6.93	7.21	36.81	70.35
18.00	51.98	53.90	7.48	7.53	36.37	71.42
19.00	59.88	54.21	9.65	7.86	35.93	72.48
20.00	56.80	54.52	9.31	8.18	35.50	73.55
21.00	54.60	54.23	8.17	8.50	34.45	74.01
22.00	54.61	53.42	8.40	8.83	32.89	73.95
23.00	53.76	52.63	9.60	9.15	31.35	73.91
24.00	57.23	51.84	10.44	9.47	29.81	73.88
25.00	50.90	51.07	10.63	9.80	28.29	73.86
26.00	50.06	50.31	9.66	10.69	25.45	75.17
27.00	46.38	49.56	8.95	10.49	25.16	73.96
28.00	48.32	48.82	10.47	10.29	24.88	72.77
29.00	51.02	48.10	12.31	10.10	24.60	71.59
30.00	45.59	47.38	9.91	9.92	24.32	70.44
31.00	45.86	46.67	10.14	9.73	24.04	69.31
32.00	46.90	45.98	11.03	9.55	23.76	68.20
33.00	42.08	45.30	9.08	9.38	23.49	67.10
34.00	44.48	44.63	8.95	9.20	23.22	66.03
35.00	38.63	43.97	10.10	9.03	22.95	64.98
36.00	42.63	43.32	7.11	8.87	22.69	63.95
37.00	40.41	42.68	8.81	8.71	22.42	62.94
38.00	39.70	42.05	6.22	8.55	22.16	61.94
39.00	40.62	41.44	8.01	8.40	21.90	60.97
40.00	39.02	40.83	8.28	8.25	21.64	60.02

	MALES					
Age	MEAN Raw Fit Values	MEAN Smoothed Fit Values	SD Raw Fit Values	SD Smoothed Fit Values	MIN (1st Pctl)	MAX (99th Pctl)
41.00	39.72	40.24	9.96	8.10	21.39	59.09
42.00	35.58	39.66	9.85	7.96	21.14	58.18
43.00	39.98	39.09	6.46	7.82	20.89	57.28
44.00	38.65	38.53	7.60	7.69	20.64	56.41
45.00	40.15	37.98	6.59	7.56	20.40	55.56
46.00	40.67	37.44	7.89	7.43	20.16	54.73
47.00	41.51	36.92	9.68	7.31	19.91	53.92
48.00	38.92	36.40	10.52	7.19	19.68	53.12
49.00	34.65	35.90	7.68	7.07	19.44	52.35
50.00	33.85	35.41	6.49	6.96	19.21	51.60
51.00	32.52	34.92	4.51	6.86	18.98	50.87
52.00	36.31	34.45	7.08	6.75	18.75	50.16
53.00	36.23	34.00	7.31	6.65	18.52	49.47
54.00	33.91	33.55	5.29	6.56	18.30	48.79
55.00	33.40	33.11	5.08	6.46	18.08	48.14
56.00	31.68	32.69	6.52	6.37	17.86	47.51
57.00	32.47	32.27	6.33	6.29	17.64	46.90
58.00	33.24	31.87	6.32	6.21	17.43	46.31
59.00	33.05	31.48	6.45	6.13	17.22	45.74
60.00	29.02	31.10	3.59	6.06	17.01	45.19
61.00	31.68	30.73	6.95	5.99	16.80	44.66
62.00	29.72	30.37	5.09	5.92	16.60	44.14
63.00	30.90	30.02	8.06	5.86	16.40	43.65
64.00	30.65	29.69	5.32	5.80	16.20	43.18
65.00	29.86	29.36	6.90	5.75	16.00	42.73
66.00	28.60	29.05	5.51	5.70	15.80	42.30
67.00	29.47	28.75	5.25	5.65	15.61	41.89
68.00	28.95	28.46	5.63	5.61	15.42	41.50
69.00	31.13	28.18	6.43	5.57	15.23	41.13
70.00	27.12	27.91	3.44	5.53	15.05	40.78
71.00		27.65		5.50	14.86	40.45
72.00	28.56	27.41	5.71	5.47	14.68	40.13
73.00	27.62	27.17	5.03	5.45	14.50	39.84
74.00	27.84	26.95	6.27	5.43	14.33	39.57
75.00		26.74		5.41	14.15	39.32
76.00	25.05	26.54	6.68	5.40	13.98	39.09
77.00	23.74	26.35	4.99	5.39	13.81	38.88
78.00		26.17		5.38	13.65	38.69
79.00		26.00		5.38	13.48	38.52
80.00		25.84		5.39	13.32	38.37
81.00	23.68	25.70	5.88	5.39	13.17	38.22
82.00		25.57		5.39	13.04	38.09
83.00		25.44		5.39	12.92	37.97
84.00		25.33		5.39	12.81	37.86
85.00		25.23		5.39	12.70	37.76
86.00		25.14		5.39	12.62	37.67

Age	MALES MEAN Raw Fit Values	MEAN Smoothed Fit Values	SD Raw Fit Values	SD Smoothed Fit Values	MIN (1st Pctl)	MAX (99th Pctl)
87.00		25.06		5.39	12.54	37.59
88.00		25.00		5.39	12.47	37.52
89.00		24.94		5.39	12.42	37.47
90.00		24.90		5.39	12.37	37.42
91.00		24.86		5.39	12.34	37.39
92.00		24.84		5.39	12.32	37.37
93.00		24.83		5.39	12.31	37.36
94.00		24.83		5.39	12.31	37.36
95.00		24.84		5.39	12.32	37.37
96.00		24.87		5.39	12.34	37.39
97.00		24.90		5.39	12.37	37.43
98.00		24.95		5.39	12.42	37.47
99.00		25.00		5.39	12.48	37.53
100.00		25.07		5.39	12.54	37.60

Table 2. Nv02max Values for Females: Raw and Smoothed Fits

Age	FEMALES MEAN Raw Fit Values	MEAN Smoothed Fit Values	SD Raw Fit Values	SD Smoothed Fit Values	MIN (1st Pctl)	MAX (99th Pctl)
0.00		35.88		5.90	22.15	49.61
1.00		36.21		6.00	22.26	50.17
2.00		36.54		6.09	22.37	50.72
3.00		36.87		6.19	22.48	51.27
4.00		37.20		6.28	22.59	51.82
5.00		37.54		6.38	22.70	52.37
6.00		37.87		6.47	22.81	52.93
7.00		38.20		6.57	22.92	53.48
8.00		38.53		6.66	23.03	54.03
9.00	30.56	38.86	9.90	6.76	23.14	54.58
10.00	45.53	39.19	6.27	6.85	23.25	55.13
11.00	43.88	39.52	5.26	6.95	23.36	55.69
12.00	43.03	39.85	6.88	7.04	23.47	56.24
13.00	42.00	40.18	7.48	7.14	23.58	56.79
14.00	37.57	40.51	6.79	7.23	23.69	57.34
15.00	39.57	40.85	5.43	7.33	23.80	57.89
16.00	35.51	41.18	5.36	7.42	23.91	58.45
17.00	38.22	41.51	8.86	7.52	24.02	59.00
18.00	45.67	41.84	8.53	7.61	24.13	59.55
19.00	43.87	42.17	7.83	7.71	24.24	60.10

	FEMALES					
Age	MEAN Raw Fit Values	MEAN Smoothed Fit Values	SD Raw Fit Values	SD Smoothed Fit Values	MIN (1st Pctl)	MAX (99th Pctl)
20.00	42.52	42.50	7.69	7.80	24.35	60.65
21.00	43.45	42.10	8.51	7.90	23.73	60.48
22.00	43.22	41.45	7.59	7.99	22.86	60.05
23.00	43.87	40.81	10.13	8.09	21.99	59.63
24.00	41.14	40.18	8.22	8.18	21.14	59.22
25.00	38.20	39.56	7.09	8.28	20.30	58.82
26.00	38.98	38.95	11.12	8.37	19.47	58.43
27.00	34.94	38.35	8.02	8.35	18.93	57.76
28.00	38.08	37.75	9.80	8.14	18.82	56.69
29.00	35.13	37.17	6.30	7.94	18.71	55.64
30.00	35.79	36.60	9.10	7.74	18.59	54.61
31.00	35.22	36.04	7.89	7.55	18.47	53.60
32.00	36.06	35.48	6.93	7.37	18.35	52.62
33.00	34.95	34.94	9.51	7.19	18.23	51.66
34.00	38.13	34.41	7.08	7.01	18.10	50.72
35.00	32.63	33.88	4.88	6.84	17.97	49.80
36.00	33.59	33.37	6.17	6.68	17.83	48.91
37.00	31.11	32.87	5.13	6.52	17.70	48.04
38.00	33.12	32.37	3.76	6.37	17.55	47.19
39.00	28.80	31.89	5.14	6.22	17.41	46.37
40.00	29.06	31.42	5.74	6.08	17.26	45.57
41.00	29.54	30.95	8.00	5.95	17.11	44.79
42.00	30.90	30.50	6.82	5.82	16.96	44.03
43.00	27.60	30.05	4.32	5.70	16.80	43.30
44.00	29.33	29.62	4.17	5.58	16.64	42.59
45.00	28.53	29.19	4.90	5.47	16.48	41.90
46.00	29.41	28.78	6.00	5.36	16.31	41.24
47.00	30.49	28.37	7.15	5.26	16.14	40.60
48.00	27.92	27.97	6.05	5.16	15.97	39.98
49.00	26.48	27.59	5.36	5.07	15.79	39.38
50.00	29.80	27.21	5.13	4.99	15.61	38.81
51.00	27.49	26.84	3.66	4.91	15.43	38.26
52.00	28.95	26.49	5.83	4.83	15.24	37.73
53.00	23.77	26.14	3.56	4.77	15.06	37.23
54.00	25.34	25.80	4.61	4.70	14.86	36.74
55.00	26.05	25.48	4.29	4.65	14.67	36.29
56.00	26.30	25.16	4.91	4.60	14.47	35.85
57.00	26.06	24.85	4.07	4.55	14.27	35.44
58.00		24.55		4.51	14.06	35.05
59.00		24.27		4.48	13.85	34.68
60.00	23.67	23.99	4.81	4.45	13.64	34.33
61.00	24.70	23.72	4.65	4.43	13.43	34.01
62.00	21.63	23.46	4.99	4.41	13.21	33.71
63.00	26.64	23.21	7.38	4.40	12.99	33.44
64.00	23.84	22.97	3.77	4.39	12.76	33.18

	FEMALES					
Age	MEAN Raw Fit Values	MEAN Smoothed Fit Values	SD Raw Fit Values	SD Smoothed Fit Values	MIN (1st Pctl)	MAX (99th Pctl)
65.00	20.26	22.74	3.83	4.39	12.53	32.95
66.00	20.38	22.52		4.39	12.31	32.73
67.00	20.49	22.31		4.39	12.10	32.52
68.00	22.05	22.11	3.90	4.39	11.90	32.32
69.00	21.92	21.92	4.56	4.39	11.71	32.13
70.00	20.38	21.74	4.15	4.39	11.53	31.95
71.00	25.30	21.57		4.39	11.36	31.78
72.00	21.21	21.41		4.39	11.20	31.62
73.00	20.46	21.26	4.59	4.39	11.05	31.47
74.00	20.63	21.12		4.39	10.91	31.33
75.00	20.60	20.99	3.80	4.39	10.78	31.20
76.00	20.91	20.87		4.39	10.66	31.08
77.00	22.27	20.76		4.39	10.55	30.97
78.00	19.93	20.65		4.39	10.44	30.86
79.00	22.80	20.56		4.39	10.35	30.77
80.00	23.19	20.48		4.39	10.27	30.69
81.00	19.29	20.41		4.39	10.20	30.62
82.00	13.44	20.34		4.39	10.13	30.55
83.00	28.03	20.29		4.39	10.08	30.50
84.00	17.00	20.25		4.39	10.04	30.46
85.00	18.69	20.21		4.39	10.00	30.42
86.00	18.18	20.19		4.39	9.98	30.40
87.00		20.18		4.39	9.97	30.39
88.00	27.15	20.17		4.39	9.96	30.38
89.00		20.18		4.39	9.97	30.39
90.00	18.18	20.20		4.39	9.98	30.41
91.00		20.22		4.39	10.01	30.43
92.00		20.26		4.39	10.05	30.47
93.00		20.30		4.39	10.09	30.51
94.00		20.36		4.39	10.15	30.57
95.00		20.42		4.39	10.21	30.63
96.00		20.50		4.39	10.28	30.71
97.00		20.58		4.39	10.37	30.79
98.00		20.67		4.39	10.46	30.88
99.00		20.78		4.39	10.57	30.99
100.00		20.89		4.39	10.68	31.10

Table 3. Body Mass Raw Fits.

	MALES				FEMALES			
Age	Geometric Mean	GSD	Min	Max	Geometric Mean	GSD	Min	Max
0.00	7.767	1.301	3.6	11.8	7.429	1.304	3.7	12.1
1.00	11.440	1.143	8.2	16.1	11.119	1.163	7.4	15.3
2.00	13.932	1.146	9.8	20.9	13.258	1.158	10.1	20.4
3.00	15.967	1.154	11.7	23.7	15.587	1.160	11	27.9
4.00	18.475	1.165	11.1	28.1	18.005	1.171	12.8	29.1
5.00	21.618	1.234	13.7	42.4	20.353	1.229	12.6	40.4
6.00	23.142	1.213	16.1	41.1	22.454	1.194	15.9	36.7
7.00	27.072	1.216	19.3	46.8	26.483	1.239	16.9	51
8.00	31.651	1.302	19.1	66.2	30.534	1.315	19.8	60.8
9.00	34.656	1.265	24	69.9	35.235	1.271	20.3	58.6
10.00	38.329	1.280	24.3	72.9	40.550	1.304	22.7	71.2
11.00	44.149	1.308	26.2	83.8	46.579	1.302	27.7	84.6
12.00	47.988	1.315	27.7	94.8	50.673	1.274	27.8	93.3
13.00	55.364	1.340	27.7	106.6	56.649	1.275	33.4	99.5
14.00	62.832	1.293	35.7	121	57.214	1.248	37.7	110
15.00	67.650	1.255	41.5	117.9	60.091	1.249	34.9	108.4
16.00	72.460	1.267	45.8	139.1	61.582	1.255	40.9	113.8
17.00	73.081	1.248	49.9	136.6	61.229	1.248	41.5	133.1
18.00	75.060	1.243	51.2	144.2	64.591	1.281	42.4	123.6
19.00	77.182	1.245	52.6	134.5	66.156	1.274	41.6	118.5
20.00	77.952	1.250	50.5	130	66.981	1.262	41.5	122.6
21.00	78.239	1.297	46.8	199.2	67.218	1.262	39.7	123.7
22.00	83.845	1.292	53.3	155.4	66.823	1.273	42	123.5
23.00	80.607	1.222	50.5	137.6	69.721	1.304	40.3	143
24.00	81.706	1.251	50.6	132.6	70.284	1.289	47.5	144.5
25.00	84.818	1.206	50.2	136.1	66.300	1.283	44.8	131.8
26.00	81.812	1.273	48.9	164.5	72.973	1.281	45.3	128.9
27.00	85.166	1.249	50	153.9	70.604	1.281	41.4	140.9
28.00	84.321	1.272	51	167.2	74.363	1.312	44.3	142.1
29.00	82.144	1.236	50.6	147.2	69.110	1.250	39.3	116.3
30.00	81.581	1.262	52.5	139	70.616	1.305	42.1	151.5
31.00	81.275	1.249	48.8	170.6	73.039	1.278	43.7	125.9
32.00	84.715	1.235	49.7	135.8	72.938	1.281	41.5	139.7
33.00	88.188	1.231	64.8	146.3	72.710	1.307	44.9	135.2
34.00	81.163	1.221	53.1	136.9	69.773	1.230	46.6	115.3
35.00	87.192	1.251	61	193.3	73.044	1.306	44.2	138.4
36.00	83.404	1.228	45.8	140.5	73.547	1.289	44.6	150.1
37.00	85.759	1.241	59.3	150.9	70.019	1.284	48.1	152.1
38.00	84.132	1.260	52.8	149.7	75.587	1.295	43.7	151.7
39.00	84.611	1.196	61.2	140.6	72.295	1.251	41.6	123.1
40.00	90.071	1.246	58.5	154	72.888	1.289	45.5	137.4
41.00	87.425	1.173	61.3	117.7	73.363	1.268	50.5	156.9
42.00	88.290	1.205	62.2	144	73.697	1.270	47.1	146.1
43.00	88.423	1.233	54	145.3	73.438	1.314	45.6	159.5

Age	MALES Geometric Mean	GSD	Min	Max	FEMALES Geometric Mean	GSD	Min	Max
44.00	88.528	1.200	56.6	128.9	75.742	1.266	49.5	153
45.00	87.102	1.205	60.6	160.2	76.795	1.308	41.6	141.5
46.00	88.157	1.243	54.2	154.3	77.544	1.304	46.6	145.8
47.00	86.547	1.229	49.9	188.3	72.849	1.298	47.8	130.6
48.00	84.793	1.186	56.3	128.3	74.646	1.303	44.2	166
49.00	86.235	1.240	47	171.3	72.844	1.261	45.1	125.54
50.00	84.659	1.179	53.4	124.4	75.217	1.292	48.4	175.7
51.00	87.975	1.208	57.9	143.6	72.941	1.240	42.5	120.2
52.00	89.886	1.216	55.2	144.9	74.472	1.283	45.7	146.6
53.00	89.012	1.228	58.2	143.3	74.733	1.259	46.2	176.6
54.00	90.098	1.216	64.1	155.2	72.413	1.281	44.3	123.1
55.00	88.268	1.222	55.1	138.6	75.951	1.231	53.6	125.6
56.00	84.796	1.195	45	110.3	77.322	1.315	45.6	134.9
57.00	87.501	1.253	58.3	160	72.378	1.252	48.6	122.6
58.00	85.116	1.266	51.6	179	74.548	1.267	45	117.7
59.00	84.190	1.182	58.7	112.4	80.638	1.277	50.9	133
60.00	87.044	1.232	57.3	141.7	75.777	1.260	51.3	128.3
61.00	89.007	1.207	49.9	162.8	77.121	1.240	50.7	125.6
62.00	84.788	1.228	56.04	152.1	73.347	1.198	49.7	121.1
63.00	89.137	1.262	56.3	171.6	72.308	1.238	46.9	119.9
64.00	89.974	1.193	59.1	119	75.440	1.281	41.1	132.5
65.00	89.891	1.215	58.1	126.3	72.910	1.254	35.9	113.7
66.00	86.814	1.228	54	150.1	73.101	1.242	48.4	113.3
67.00	86.207	1.207	43.1	127.5	75.835	1.266	47.2	123.8
68.00	85.172	1.191	61.2	163.2	73.207	1.250	39.3	120.7
69.00	87.116	1.222	50.7	127.2	74.368	1.225	48	118
70.00	82.775	1.210	46.5	125.5	68.977	1.188	45.9	102.8
71.00	79.630	1.240	51	122.8	69.083	1.232	45.5	108.1
72.00	82.011	1.204	51.9	132.7	69.898	1.240	40.7	103.8
73.00	85.590	1.196	56.2	128.3	71.360	1.240	47.4	127.6
74.00	83.001	1.217	53.3	120	70.410	1.277	37.4	106.4
75.00	84.465	1.185	56.5	133.5	70.526	1.216	46.8	117.4
76.00	78.733	1.207	55.9	121.1	69.549	1.199	48.8	101.7
77.00	79.376	1.170	58.7	109.3	70.128	1.240	40.3	119.8
78.00	79.909	1.195	41.1	115.1	66.375	1.211	44.1	109.8
79.00	77.629	1.155	56.4	107.8	67.780	1.200	46.2	98.4
80.00	79.866	1.174	56	111.9	62.214	1.255	41.2	121.4
81.00	75.405	1.157	55.8	111.9	65.397	1.184	42.7	91.4
82.00	76.798	1.180	54.4	111.8	64.755	1.260	40.6	120
83.00	74.611	1.158	53.2	107	62.886	1.196	44.7	101.2
84.00	75.325	1.205	41.5	109.5	62.215	1.216	43.5	108.4
85.00	71.776	1.191	46.9	105.8	61.453	1.209	42.3	93.2
86.00	73.986494	1.17	50.57	101.07	62.400356	1.21	41.85	101.16
87.00	73.364276	1.17	50.38	99.113	61.847614	1.21	41.66	100.26
88.00	72.742058	1.16	50.19	97.154	61.294872	1.21	41.47	99.351
89.00	72.11984	1.16	50	95.194	60.74213	1.21	41.27	98.445

Age	MALES Geometric Mean	GSD	Min	Max	FEMALES Geometric Mean	GSD	Min	Max
90.00	71.497622	1.16	49.81	93.235	60.189388	1.21	41.08	97.538
91.00	70.875404	1.16	49.62	91.276	59.636646	1.2	40.88	96.632
92.00	70.253186	1.16	49.44	89.317	59.083904	1.2	40.69	95.726
93.00	69.630968	1.15	49.25	87.358	58.531162	1.2	40.49	94.82
94.00	69.00875	1.15	49.06	85.399	57.97842	1.2	40.3	93.914
95.00	68.386532	1.15	48.87	83.44	57.425678	1.2	40.1	93.008
96.00	67.764314	1.15	48.68	81.481	56.872936	1.2	39.91	92.102
97.00	67.142096	1.14	48.49	79.522	56.320194	1.2	39.71	91.195
98.00	66.519878	1.14	48.3	77.563	55.767452	1.19	39.52	90.289
99.00	65.89766	1.14	48.11	75.604	55.21471	1.19	39.32	89.383
100.00	65.275442	1.14	47.92	73.645	54.661968	1.19	39.13	88.477

**Dark shading (age 86+) designates linear forecast.

Table 4. Body Mass Smoothed Fits (5-Year Running Averages).

Age	MALES Geometric Mean	GSD	Min	Max	FEMALES Geometric Mean	GSD	Min	Max
0.00	7.767209794	1.300901	3.6	11.8	7.428916349	1.304229	3.7	12.1
1.00	11.44008024	1.143324	8.2	16.1	11.11947416	1.162608	7.4	15.3
2.00	13.93227373	1.145566	9.8	20.9	13.25797158	1.158434	10.1	20.4
3.00	15.96664726	1.153689	11.7	23.7	15.58684049	1.159883	11	27.9
4.00	18.47458493	1.164972	11.1	28.1	18.00506307	1.17108	12.8	29.1
5.00	21.61756114	1.233822	13.7	42.4	20.35285099	1.229237	12.6	40.4
6.00	23.14243627	1.213499	16.1	41.1	22.45431948	1.194119	15.9	36.7
7.00	27.07246068	1.215834	19.3	46.8	26.48323788	1.23892	16.9	51
8.00	31.6505017	1.301873	19.1	66.2	30.53391399	1.315137	19.8	60.8
9.00	34.65600448	1.265317	24	69.9	35.23472141	1.271364	20.3	58.6
10.00	38.32939135	1.279707	24.3	72.9	40.54996835	1.303997	22.7	71.2
11.00	44.14863459	1.30753	26.2	83.8	46.57910267	1.302182	27.7	84.6
12.00	47.98795299	1.314848	27.7	94.8	50.67329267	1.273946	27.8	93.3
13.00	55.36374737	1.33952	27.7	106.6	56.64881107	1.275455	33.4	99.5
14.00	62.83159173	1.292533	35.7	121	57.21362103	1.24795	37.7	110
15.00	67.65031426	1.254999	41.5	117.9	60.09135575	1.24897	34.9	108.4
16.00	72.45980541	1.267468	45.8	139.1	61.58214656	1.255162	40.9	113.8
17.00	73.08089659	1.248405	49.9	136.6	61.22931022	1.248057	41.5	133.1
18.00	75.06031573	1.243204	51.2	144.2	64.59054256	1.281298	42.4	123.6
19.00	77.18236513	1.244928	52.6	134.5	66.15556407	1.274083	41.6	118.5
20.00	77.95205826	1.250326	50.5	130	66.98146906	1.261822	41.5	122.6
21.00	78.45564692	1.265585	50.88	152.66	66.35375002	1.270386	41.44	122.38
22.00	79.56489519	1.261251	50.74	151.34	67.37976393	1.274844	41.02	126.26

Age	MALES Geometric Mean	GSD	Min	Max	FEMALES Geometric Mean	GSD	Min	Max
23.00	80.46958232	1.262527	50.34	150.96	68.20537834	1.277813	42.2	131.46
24.00	81.84267254	1.253588	50.28	152.18	68.06901959	1.282127	42.86	133.3
25.00	82.55729313	1.248802	50.7	145.24	69.21992781	1.285979	43.98	134.34
26.00	82.82151847	1.240222	50.04	144.94	69.97607936	1.287735	43.86	137.82
27.00	83.56439112	1.250399	50.14	150.86	70.90453453	1.289413	44.66	137.64
28.00	83.65195203	1.247428	50.14	153.78	70.66975978	1.28161	43.02	132
29.00	83.00459482	1.258753	50.6	154.36	71.53295767	1.285847	42.48	135.94
30.00	82.89721864	1.253937	50.58	155.58	71.54621552	1.285108	42.16	135.34
31.00	82.80701235	1.251132	50.52	151.96	72.01313142	1.28495	42.18	135.1
32.00	83.58034187	1.242848	53.28	147.78	71.6826276	1.283915	42.3	133.72
33.00	83.38418057	1.239735	53.78	145.72	71.81523165	1.280002	43.76	133.52
34.00	84.50647805	1.237533	55.48	156.58	72.30094254	1.280205	44.18	130.9
35.00	84.9321819	1.233184	54.88	150.56	72.40264379	1.282492	44.36	135.74
36.00	85.14102649	1.234298	56.8	153.58	71.81884258	1.283151	45.68	138.22
37.00	84.32994666	1.240177	54.4	154.26	72.3941641	1.280709	45.44	141.52
38.00	85.01958212	1.235131	56.02	155	72.89859355	1.284821	44.44	143.08
39.00	85.59524544	1.233983	55.52	147.14	72.86733489	1.281407	44.7	142.88
40.00	86.39949423	1.223065	58.62	142.58	72.830387	1.277165	45.88	144.24
41.00	86.90564401	1.215924	59.2	141.2	73.56585153	1.274483	45.68	143.04
42.00	87.76379051	1.210495	59.44	140.32	73.13604869	1.278433	46.06	144.6
43.00	88.54719729	1.211458	58.52	137.98	73.82543503	1.281514	47.64	150.58
44.00	87.95342484	1.203416	58.94	139.22	74.60684165	1.285327	46.86	151.4
45.00	88.09985934	1.217379	57.52	146.54	75.44302619	1.292445	46.08	149.18
46.00	87.751282	1.222211	55.06	155.4	75.27348935	1.29795	46.22	146.08
47.00	87.02523405	1.212835	55.52	152	75.51517243	1.295658	45.94	147.38
48.00	86.56661258	1.220669	53.6	160.48	74.93569966	1.29459	45.06	141.888
49.00	86.07815707	1.215489	52.16	153.32	74.62001355	1.291492	46.42	148.728
50.00	86.04175058	1.208607	52.9	151.18	73.69947055	1.278764	45.6	143.608
51.00	86.70964624	1.206031	53.96	142.5	74.02400492	1.27574	45.18	146.808
52.00	87.55345712	1.2144	54.34	145.5	74.04127315	1.266893	45.58	148.928
53.00	88.32616726	1.209663	57.76	142.28	73.95491798	1.270898	45.42	148.44
54.00	89.04784314	1.218268	58.1	145.12	74.10188224	1.25873	46.46	138.42
55.00	88.4120991	1.215526	55.52	138.46	74.97813364	1.273724	47.08	141.36
56.00	87.93495739	1.222906	56.14	141.48	74.55937637	1.267547	47.66	136.56
57.00	87.15584772	1.230391	54.82	148.62	74.52242942	1.269258	47.42	124.78
58.00	85.97418819	1.223617	53.74	140.06	76.16748501	1.268509	48.74	126.76
59.00	85.72952642	1.22558	54.18	140.68	76.13252691	1.274205	48.28	127.3
60.00	86.57173577	1.228074	55.16	151.18	76.09221736	1.259138	49.3	125.44
61.00	86.0292098	1.222944	54.708	149.6	76.28599922	1.248419	49.52	125.14
62.00	86.83331368	1.22222	55.648	148.12	75.83796229	1.242552	49.9	125.58
63.00	87.99005122	1.224363	55.728	149.44	74.79845832	1.243365	47.94	125.48
64.00	88.55927286	1.220869	55.888	146.36	74.22522224	1.242246	44.86	122.56
65.00	88.12051692	1.225034	56.708	143.82	73.42130739	1.242692	44.4	120.1
66.00	88.40439667	1.220898	54.12	138.9	73.91902253	1.256261	43.9	120.64
67.00	87.61146369	1.206714	55.1	137.22	74.09892054	1.258602	42.38	120.8
68.00	87.03986775	1.212565	53.42	138.86	73.88448789	1.247351	43.76	117.9

	MALES				FEMALES			
Age	Geometric Mean	GSD	Min	Max	Geometric Mean	GSD	Min	Max
69.00	85.61667034	1.211601	51.1	138.7	73.09783811	1.234088	45.76	115.72
70.00	84.17987726	1.213949	50.5	133.24	72.29417333	1.23216	45.18	114.68
71.00	83.34052655	1.213444	52.26	134.28	71.10679374	1.227009	43.88	110.68
72.00	83.42413149	1.214423	51.26	127.3	70.73734313	1.225132	45.5	112.06
73.00	82.60108145	1.213508	51.78	125.86	69.94568967	1.235452	43.38	109.74
74.00	82.93914453	1.208433	53.78	127.46	70.25540111	1.241	43.56	112.66
75.00	82.75981666	1.201809	54.76	127.12	70.34868617	1.23444	44.22	111.38
76.00	82.23282472	1.19492	56.12	122.44	70.39465694	1.234265	44.14	114.58
77.00	81.09670348	1.194698	53.1	119.8	69.39757689	1.228511	43.48	111.02
78.00	80.02242628	1.182282	53.72	117.36	68.87151054	1.213229	45.24	109.42
79.00	79.10265965	1.180128	53.62	113.04	67.20924709	1.221048	44.12	110.22
80.00	78.43698141	1.170309	53.6	111.2	66.37891246	1.217987	42.9	108.16
81.00	77.92142176	1.17229	52.74	111.7	65.30424541	1.222093	42.96	108.2
82.00	76.86173441	1.164819	55.16	110.08	64.60647334	1.219074	43.08	106.48
83.00	76.40090269	1.174796	52.18	110.42	63.49351577	1.22226	42.54	108.48
84.00	74.7828307	1.17822	50.36	109.2	63.34131978	1.213219	42.76	102.84
85.00	74.4992137	1.180574	49.31362	107.0343	62.74189138	1.218822	42.59095	104.7926
86.00	73.81250877	1.177977	48.50949	104.4969	62.16041309	1.208932	42.80295	100.844
87.00	73.43871959	1.179377	47.90759	102.5276	61.84223228	1.211505	42.15598	100.4742
88.00	72.79767378	1.170756	49.60794	99.66646	61.5476723	1.209819	41.71005	98.48308
89.00	72.74205786	1.164535	50.19052	97.15354	61.29487188	1.209189	41.46516	99.35077
90.00	72.11983988	1.162177	50.00172	95.19446	60.74212987	1.207753	41.27036	98.44462
91.00	71.4976219	1.159818	49.81292	93.23538	60.18938785	1.206317	41.07556	97.53846
92.00	70.87540393	1.157459	49.62412	91.27631	59.63664584	1.20488	40.88075	96.63231
93.00	70.25318595	1.1551	49.43532	89.31723	59.08390383	1.203444	40.68595	95.72615
94.00	69.63096798	1.152742	49.24652	87.35815	58.53116181	1.202008	40.49115	94.82
95.00	69.00875	1.150383	49.05772	85.39908	57.9784198	1.200571	40.29634	93.91385
96.00	68.38653203	1.148024	48.86892	83.44	57.42567778	1.199135	40.10154	93.00769
97.00	67.76431405	1.145665	48.68012	81.48092	56.87293577	1.197699	39.90674	92.10154
98.00	67.14209607	1.143307	48.49132	79.52185	56.32019375	1.196263	39.71193	91.19538
99.00	66.5198781	1.140948	48.30252	77.56277	55.76745174	1.194826	39.51713	90.28923
100.00	66.20876911	1.139769	48.20812	76.58323	55.49108073	1.194108	39.41973	89.83615

Table 5. Hemoglobin Content.

	MALES		FEMALES	
Age	MEAN	STD	MEAN	STD
0	11.927	0.993545	12.209	0.729499905
1	12.20959	1.013091	12.27307	0.719158646
2	12.42075	0.823171	12.55018	0.843436666
3	12.69015	0.83159	12.4519	0.965868504
4	12.8006	0.80152	12.83442	0.773409545
5	12.95822	0.878515	12.87154	0.969254536
6	13.19574	0.893008	13.01866	0.828912341
7	13.46198	0.836639	13.09899	0.754370806
8	13.35161	0.833121	13.25291	0.826349227
9	13.59742	0.971019	13.36671	0.808377267
10	13.63062	0.906785	13.58919	1.034306588
11	13.66	0.726155	13.52681	0.90041802
12	13.9727	0.955869	13.6273	0.884271668
13	14.28293	1.036749	13.46986	0.97623121
14	14.70654	1.020254	13.58878	1.034527514
15	15.13583	1.04546	13.47154	0.856131982
16	15.36442	1.021623	13.50562	1.088863466
17	15.45945	0.979296	13.49842	1.117860417
18	15.7487	1.02514	13.46091	1.18250671
19	15.76812	0.831813	13.35445	1.090493585
20	15.79371	0.880956	13.5016	1.072791517
25	15.71703	0.91072	13.47168	1.170602542
30	15.70837	1.045808	13.2967	1.145254677
35	15.55635	0.959964	13.34583	1.134192006
40	15.43525	1.021741	13.4881	1.163867696
45	15.44038	1.105939	13.48617	1.348669176
50	15.41492	1.096952	13.61113	1.193756618
55	15.31983	1.123792	13.67737	1.106237392
60	15.27653	0.97796	13.83717	1.237714453
65	15.07274	1.192645	13.76529	1.093354796
70	14.96193	1.24457	13.81911	1.093565513
75	14.72786	1.418355	13.79013	1.056812752
80	14.51	1.476879	13.84426	1.30818261
85	14.52915	1.352814	13.57546	1.238910845
90	13.97647	1.757686	13.43767	1.552685662
95	13.801	1.757686	13.2085	1.552685662
100	13.534	1.757686	13.005	1.552685662

Appendix B

COHb Module for APEX4.3

This appendix describes the probabilistic carboxyhemoglobin (COHb) module used in the current APEX4.3 model. The approach described here is based primarily on the COHb module originally described by Biller and Richmond (1982) and contained within two reports (Johnson et al., 1992; Johnson et al., 2000) and used in EPA probabilistic NAAQS exposure model for CO (pNEM/CO), a predecessor of APEX4.3. This appendix also describes the principal changes made to the COHb module when it was incorporated into APEX4.3, including a change in the method used to solve the Coburn-Forster-Kane (CFK) equation (Coburn et al., 1965). Lastly, section B.6 summarizes outputs that were generated in performing event-level model simulations.

B.1 Base Physiological Model for Computing COHb Levels

Using time/activity data obtained from various diary studies, APEX constructs a composite diary for each simulated person in the specified population at risk. The composite diary consists of a sequence of events spanning the specified period of the exposure assessment (typically one calendar year). Each event is defined by a start time, a duration, a geographic location, a microenvironment, and an activity. Using various algorithms described in Section 4 of the Quantitative Risk and Exposure Assessment for Carbon Monoxide (CO REA), APEX4.3 provides estimates of CO concentration and alveolar ventilation rate for each event in the composite diary. APEX4.3 then uses these data, together with estimates of various physiological parameters specific to the simulated individual, to estimate the percent COHb in the blood (%COHb) as an average %COHb value over the duration of each exposure event and as an instantaneous %COHb level at the end of each event.

The %COHb calculation is based on the solution to the non-linear CFK equation, previously described in Appendix E of Johnson et al. (2000). The CFK model describes the rate of change of COHb blood levels as a function of the following quantities:

1. Inspired CO pressure
2. COHb level
3. Oxyhemoglobin (O_2Hb) level
4. Hemoglobin (Hb) content of blood
5. Blood volume
6. Alveolar ventilation rate
7. Endogenous CO production rate
8. Mean pulmonary capillary oxygen pressure
9. Pulmonary diffusion rate of CO
10. Haldane coefficient (M)
11. Barometric pressure
12. Vapor pressure of water at body temperature (i.e., 47 torr).

If all of the listed quantities except COHb level are constant over some time interval, the CFK equation has a linear form over the interval and is readily integrated. The solution to the linear form gives reasonably accurate results for lower levels of COHb. However, CO and oxygen compete for the available hemoglobin and are, therefore, not independent of each other. If this dependency is taken into account, the resulting differential equation is no longer linear. Peterson and Stewart (1975) proposed a heuristic approach to account for this dependency which assumed the linear form and then adjusted the O_2Hb level iteratively based on the assumption of a linear relationship between COHb and O_2Hb. This approach was used in the COHb module of the original CO-NEM exposure model (Biller and Richmond, 1982; Johnson and Paul, 1983).

Alternatively, it is possible to determine COHb at any time by numerical integration of the nonlinear CFK equation (e.g., by use of the Runge-Kutta method) if one assumes a particular relationship between COHb and O_2Hb. Muller and Barton (1987) demonstrated that assuming a linear relationship between COHb and O_2Hb leads to a form of the CFK equation equivalent to the Michaelis-Menten kinetic model which can be analytically integrated. However, the analytical solution in this case cannot be solved explicitly for COHb. Muller and Barton (1987) demonstrated a binary search method for determining the COHb value.

The COHb module used in pNEM/CO employed a linear relationship between COHb and O_2Hb which was consistent with the basic assumptions of the CFK model. The approach differed from the linear forms used by other modelers in that the Muller and Barton (1987) solution was employed. However, instead of the simple binary search described by Muller and Barton (1987), a combination of the binary search and Newton-Raphson root-finding methods was used to solve for COHb (Press et al., 1986). Using the Muller and Barton (1987) solution increased computation time compared to the Peterson and Stewart (1975) method but was shown to be faster than fourth-order Runge-Kutta numerical integration.

APEX4.3 employs a different approach in which the CFK equation is solved using a fourth-order Taylor's series expansion with subintervals. This method, first incorporated in Version 3 of APEX, is described in Section B.2 of this appendix. A more detailed description can be found in the Programmer's Guide for the APEX3 model (Glen, 2002).

B.2 CFK Model for Estimation of Carboxyhemoglobin

Table B-1 defines the variables which appear in the equations of this section. Coburn, Forster, and Kane (1965) derived the following differential equation governing COHb levels in the blood upon exposure to CO.

$$\frac{d[COHb]}{dt} = \frac{\dot{V}_{co}}{V_b} + \frac{P_{Ico}}{BV_b} - \frac{\overline{P}_{CO_2}[COHb]}{MBV_b[O_2Hb]} \qquad \text{(Eq. B-1)}$$

where,

$$B = \frac{1}{D_{Lco}} + \frac{P_B - P_{H_2O}}{\dot{V}_A} \qquad \text{(Eq. B-2)}$$

Table B-1. Definitions of CFK model variables.

Variable	Definition	Units
t	Time from start of an exposure event	minutes
[COHb]	Concentration of carboxyhemoglobin (COHb) in blood at time t	ml CO per ml blood at STPD
$[O_2Hb]$	Concentration of oxyhemoglobin (O_2Hb) in blood at time t	ml O_2 per ml blood at STPD
[RHb]	Concentration of reduced hemoglobin in blood	equivalent ml CO per ml of blood at STPD
$[COHb]_0$	[COHb] at t = 0	ml CO per ml blood at STPD
$[THb]_0$	[RHb] + [COHb] + $[O_2Hb]$	
%[COHb]	[COHb] expressed as percent of $[RHb]_0$	%
$\%[O_2Hb]$	$[O_2Hb]$ expressed as percent of $[RHb]_0$	%
$\%[COHb]_0$	[COHb] at t = 0	%
$\%[COHB]_\infty$	[COHb] at t = ∞	%
$P_{I_{CO}}$	Pressure of inspired CO in air saturated with water vapor at body temperature	torr
$\overline{P}_{C_{CO}}$	Mean pulmonary capillary CO pressure	torr
$\overline{P}_{C_{O_2}}$	Mean pulmonary capillary O_2 pressure	torr
P_B	Barometric pressure	torr
P_{H_2O}	Vapor pressure of water at body temperature, or 47	torr
$\dot{V}_A$	Alveolar ventilation rate	ml/min STPD
$\dot{V}_{CO}$	Endogenous CO production rate	ml/min STPD
$D_{L_{CO}}$	Pulmonary CO diffusion rate	ml/min/torr, STPD
M	Haldane coefficient	
k	Equilibrium constant for reaction O_2 + RHb = O_2Hb	
V_b	Blood volume	ml
Hb	Total hemoglobin in blood	g/100ml
%MetHb	Methemoglobin as weight percent of Hb	%

Notes:
[1] Standard Temperature Pressure, and Dry (STPD)

If the only quantity in equation (B-1) that varies with time is [COHb], the CFK equation is linear and can be readily integrated. However, since oxygen (O_2) and CO compete for the available Hb, [COHb] and [O_2Hb] must be related. Increasing [COHb] will result in decreasing [O_2Hb]. Thus the CFK equation is not linear and requires the relationship between the two quantities to be known if it is to be accurately integrated over a wide range of COHb levels.

Various linear relationships between [COHb] and [O_2Hb] have been used (see Marcus, 1980; McCartney, 1990; Muller and Barton, 1987; and Tikuisis et al., 1987). A relationship not previously used follows directly from the basic assumptions of the CFK model. The CFK model employs the Haldane coefficient, which is the equilibrium constant associated with the following reaction representing the replacement of O_2 in O_2Hb by CO:

$$CO + O_2Hb \leftrightarrow O_2 + COHb \qquad \text{(Eq. B-3)}$$

Equation B-4, the Haldane relationship, applies approximately at equilibrium conditions:

$$\frac{\overline{P}c_{O_2}[COHb]}{\overline{P}c_{CO}[O_2Hb]} = M \qquad \text{(Eq. B-4)}$$

The Haldane coefficient, M, is the chemical equilibrium constant for reaction (B-3). The above reaction can also be viewed as the difference between two competing chemical reactions:

$$CO + RHb \leftrightarrow COHb \qquad \text{(Eq. B-5)}$$

$$O_2 + RHb \leftrightarrow O_2Hb \qquad \text{(Eq. B-6)}$$

Subtracting (B-6) from (B-5) yields (B-3). If (B-3) is in equilibrium, then (B-5) and (B-6) are in equilibrium. If *k* represents the equilibrium constant for (B-6) then:

$$\frac{[O_2Hb]}{\overline{P}c_{O_2}[RHb]} = k \qquad \text{(Eq. B-7)}$$

It is known that an individual breathing air free of CO for an extended period will have about 97% of their reactive Hb bound with oxygen (O_2Hb) and the remainder (3%) as the reduced form (RHb). It is also known that at one atmosphere barometric pressure, the mean pulmonary capillary oxygen pressure is approximately 100 torr. Substituting into (B-7) yields 0.32 as the approximate value of *k* at body temperature. From mass balance considerations:

$$[O_2Hb] + [COHb] + [RHb] = [THb]_O \qquad \text{(Eq. B-8)}$$

Eliminating [RHb] between (B-7) and (B-8) and solving for [O_2Hb] yields:

$$[O_2Hb] = \frac{k\overline{P}c_{O_2}}{1 + k\overline{P}c_{O_2}}([THb]_0 - [COHb]) \qquad \text{(Eq. B-9)}$$

This equation represents the aforementioned linear form of the CFK equation. It has the same form as a relationship given by McCartney (1990), but replaces the constant in the McCartney equation by the term in (B-9) involving the mean pulmonary capillary oxygen pressure and the equilibrium constant *k*. Substituting (B-9) into (B-1) yields a CFK equation free of $[O_2Hb]$ and fully consistent with Coburn, Forster, and Kane's original derivation.

$$\frac{d[COHb]}{dt} = \frac{\dot{V}_{CO}}{\dot{V}_b} + \frac{P_{I_{CO}}}{BV_b} - \frac{[COHb]}{[THb]_O - [COHb]} \times \frac{1 + k\overline{P}c_{O_2}}{kMBV_b} \qquad \text{(Eq. B-10)}$$

In working with the CFK model it is convenient to express COHb as a percent of $[RHb]_0$. Multiplying (B-10) by 100 and dividing by $[RHb]_0$ yields the expression

$$\frac{d\%[COHb]}{dt} = \frac{100}{[THb]_O}\left(\frac{\dot{V}_{CO}}{V_b} + \frac{P_{I_{CO}}}{BV_b}\right) - \frac{\%[COHb]}{100 - \%[COHb]} \times \frac{100(1 + k\overline{P}_{CO_2})}{k[RHb]_O MBV_b} \qquad \text{(Eq. B-11)}$$

Equation (B-11) can be written in the form suggested by Muller and Barton (1987):

$$\frac{d\%[COHb]}{dt} = C_O - C_1 \frac{\%[COHb]}{100 - \%[COHb]} \qquad \text{(Eq. B-12)}$$

where,

$$C_O = \frac{100}{[THb]_O}\left(\frac{\dot{V}_{CO}}{V_b} + \frac{P_{I_{CO}}}{BV_b}\right) \qquad \text{(Eq. B-13)}$$

$$C_1 = \frac{100(1 + k\overline{P}_{CO_2})}{k[THb]_O MBV_b} \qquad \text{(Eq. B-14)}$$

Given values for the atmospheric pressure and the physiological variables in equations (B-12) through (B-14), the value of %[COHb] at time *t* can be found by numerical integration using such techniques as the fourth-order Runge-Kutta method (Press et al., 1986). Muller and Barton (1987) demonstrated that an equation of the form of (B-12) is equivalent to a Michaelis-Menten kinetics model which can be integrated. The integration yields:

$$-(C_O + C_1)t + \%[COHb]_t - \%[COHb]_O - (100 - \%[COHb]_\infty)\ln\frac{(\%[COHb]_\infty - \%[COHb]_t)}{\%[COHb]_\infty - \%[COHb]_O} = 0 \qquad \text{(Eq. B-15)}$$

The equation for $\%[COHb]_\infty$ is obtained by setting equation (B-12) equal to zero and solving for %[COHb], which is now equal to $\%[COHb]_\infty$:

$$\%[COHb]_\infty = \frac{100C_O}{(C_O + C_1)} \qquad \text{(Eq. B-16)}$$

Equation (B-15) cannot be solved explicitly for %[COHb]. Muller and Barton (1987) suggest the binary search method as one way to find the value of %[COHb]. Press et al. (1986) contend a combination of the binary search and Newton-Raphson methods is faster on average. Consequently, the pNEM/CO version of the COHb module used a combination of the binary search and Newton-Raphson root finding methods to solve for COHb (Press et al., 1986). Using the Muller and Barton (1987) solution increased the computation time when compared with the Peterson and Stewart (1975) method, however it was still shown to be faster than the fourth-order Runge-Kutta numerical integration.

The current version of APEX (APEX4.3) employs an alternative approach in which the CFK equation is solved using a fourth-order Taylor's series expansion with subintervals. This method, first incorporated in Version 3 of APEX, is described in detail in the Programmer's Guide for the APEX3 Model by Glen (2002). This reference also includes the results of various tests conducted on 10 candidate methods for solving the CFK equation. The selected method (fourth-order Taylor series with subintervals) was chosen because of its simplicity, fast execution speed, and ability to produce relatively accurate estimates of %COHb at both low and high levels of CO exposure. Additional information concerning the %COHb calculation method and its theoretical basis can be found in Section 10.2 of US EPA (2008a).

In developing the fourth-order Taylor Series expansion approach, Glen (2002) began by defining *N(t)* as the %COHb level in the blood at time *t*, a quantity that is mathematically restricted to range between 0 and 100 (percent). *N(t)* satisfies the following differential equation:

$$N`(t) = C_0 - C_1 N(t) / (100 - N(t)) \qquad \text{(Eq. B-17)}$$

where C_0 and C_1 are constants (at least over the duration of one event) that depend on physical and physiological parameters and on the CO concentration in the air. Equation (B-17) is equivalent to (B-12) above, except that (B-12) uses the symbol %[COHb] instead of N(t).

The task of expanding *N(t)* in a Taylor's series becomes simpler if the following new variables are defined:

$$D_0 = 1 - N(0) / 100 \qquad \text{(Eq. B-18)}$$

$$A_0 = C_0 / (C_0 + C_1) \qquad \text{(Eq. B-19)}$$

$$A_1 = C_1 / (C_0 + C_1) \qquad \text{(Eq. B-20)}$$

$$D = D_0 - A_1 \qquad \text{(Eq. B-21)}$$

$$z = (C_0 + C_1)\, t / (100 \times D_0^2) \qquad \text{(Eq. B-22)}$$

The *z* variable is a re-scaled time variable that is dimensionless. It is used as the independent variable for the Taylor's series expansion. In equations expressed as functions of *z* rather than *t*, any primes will indicate the derivatives with respect to *z*.

Expressing (B-17) as a function of *z* yields the expression

$$N`(z) = 100\ D_0^2\ A_0 - 100\ D_0^2\ A_1\ N(z) / (\ 100 - N(z)\ ) \qquad \text{(Eq. B-23)}$$

The Taylor's series about the origin (z = 0) for N(z) is given by

$$N(z) = N(0) + N`(0)\ z + N``(0)\ z^2 / 2 + N```(0)\ z^3 / 6 + N^{iv}(0)\ z^4 / 24 + ... \qquad \text{(Eq. B-24)}$$

Through a series of algebraic substitutions, Glen (2002) shows that the Taylor series expansion of N(z) truncated to the fourth order can be represented by

$$T4(z) = T3(z) - 100\ A_1\ D_0\ D\ \ (A_1^{\ 2} - 8\ D\ A_1 + 6\ D^2)\ \ z^4 / 24 \qquad \text{(Eq. B-25)}$$

where

$$T3(z) = N(0) + 100\ D_0\ D\ z - 100\ A_1\ D_0\ D\ z^2 / 2 + 100\ A_1\ D_0\ D\ (A_1 - 2D)\ z^3 / 6 \qquad \text{(Eq. B-26)}$$

Tests showed that the fourth-order Taylor series expansion (B-25) provided greater accuracy than the third-order expansion for *z* values close to one. Glen (2002) found that *z* values below one generally correspond to N(0) values or %COHb below forty to fifty percent for one-hour exposure events.

The *z* value for a given event depends on the event duration, the initial %COHb level N(0), and on the physiological parameters, and can be directly evaluated at the start of each event. For events with a *z* value above some threshold, it is possible to improve the performance of (B-25) by dividing the event into smaller events ("subintervals"), each with a shorter duration and hence smaller *z* value. As the subinterval duration decreases, accuracy increases at the expense of program execution time. APEX4.3 enables the user to select a limit on *z* which in turn determines the number of subintervals to be used in applying the fourth-order Taylor expansion. Glen (2002) recommends that the limit on *z* be set at 0.4 or 0.5.

B.3 Application of the COHb Model in APEX4.3

<u>Description of APEX4.3 for CO</u>

APEX4.3 follows the daily activities over an extended period of a finite set of simulated individuals residing within a given geographic area. The period may be a single season or a calendar year. Each simulated individual is defined by a set of general demographic characteristics that includes age, gender, and body weight. The values of these factors are used to derive values for blood volume, menstrual phase, endogenous CO production rate, and other factors required by the COHb module (see Section B.4). The exposure of each individual is represented by a continuous sequence of exposure events which span the time period of interest. Each exposure event represents a time interval of 60 minutes or less during which the individual resides in a single environment and engages in a single activity. To permit calculation of hourly average exposures, exposure events are not permitted to fall in more than one clock hour. Consequently, the passage from one exposure event to the next is indicated by a change in microenvironment, activity, or clock hour. Algorithms within APEX4.3 calculate an average CO

concentration for each exposure event according to the time, district, and microenvironment specified for the event. As the exposure events for a simulated individual are contiguous, the model can combine these concentrations to generate output distributions of one-hour and running eight-hour exposures for each individual. The exposures calculated for the simulated individuals can then be population-weighted to produce exposure distributions for population groups of particular interest (e.g., people with coronary heart disease).

APEX4.3 constructs a year-long time/activity pattern for each simulated individual by sampling 24-hour activity patterns from the Consolidated Human Activity Data Base (CHAD) (McCurdy et al., 2000; US EPA, 2002), which is described in Section 4.4.3 of the CO REA. The sampling approach attempts to match the 24-hour activity patterns to the simulated individual and exposure period according to the demographic characteristics of the individual and the season, day type (weekday/weekend), and maximum temperature of each day in the specified exposure period.

The COHb Module

The COHb module in APEX4.3 currently employs the version of the CFK model represented by equations (B-12) through (B-14) to compute an average COHb value over the duration of each exposure event and an instantaneous COHb level at the end of each event. To perform these computations, the COHb module requires information on each of the quantities listed in the section describing the CFK model. In addition, the COHb level at the beginning of the exposure event must be known. This latter quantity is usually the COHb level computed at the end of the previous contiguous exposure event. To obtain the initial COHb at the start of the exposure period, the computation is started one day before the beginning of the period. The effect of the initial COHb value on the end value is negligible after about 15 hours. The program stores the calculated COHb values for each exposure event and outputs distributions of COHb levels by population group for averaging times ranging from one hour to one day.

Assignment of CFK Model Input Data for an Exposure Event

Section B.4 describes the equations and procedures used by the APEX4.3 COHb module to obtain the values of the input variables for equations (B-2) and (B-13) through (B-16). A brief overview is given here.

The actual inspired CO level can change significantly during an exposure event. The model supplies an average exposure concentration for the event, which is used as the CO input. The time constant for the change in COHb is sufficiently large that the use of concentrations based on averaging times up to one hour can be used in place of the instantaneous concentrations over the averaging time period with little loss of accuracy in estimating the COHb level at the end of the exposure event. Furthermore, applying the average concentrations to a contiguous sequence of exposure events does not cause an accumulation of error.

The COHb model presently used in APEX4.3 does not account for changing barometric pressure. It uses a constant barometric pressure calculated for each study area as a function of the average elevation of the area above sea level. The pressure at sea level is taken to be 760 torr.

The remaining input variables to the CFK model are all physiological parameters. While

the Haldane coefficient, the equilibrium constant k, and average pulmonary capillary oxygen pressure are treated as having the same constant values for all individuals, the remaining physiological input variables will vary among individuals. The next section describes the methods used to generate the various physiological input variables for each combination of individual and calendar day processed by APEX.

B.4 Computation of Input Data for the COHb Module

As discussed in the previous section and in Sections 4.4.5 and 4.4.7 of the CO REA, the algorithms used to estimate V_E and COHb require values for various physiological parameters such as body mass, blood volume, and pulmonary diffusion rate. Table B-2 provides a list and description of the principal parameters; additional parameters are listed and described in Chapter 5 of US EPA (2008a). An algorithm within APEX4.3 probabilistically generates a value for each parameter on the list (collectively referred to as a physiological profile) for each simulated individual. Figure B-1 is a flow diagram showing the process by which each physiological profile is generated. Each of the generated physiological profiles is internally consistent, in that the functional relationships among the various parameters are maintained. For example, blood volume is determined as a function of weight and height, where height is estimated as a function of weight. Weight in turn is selected from a distribution specific to gender and age.

For each simulated individual, APEX4.3 computes exposure for a contiguous sequence of exposure events spanning the total time period of the computation. This multi-day sequence of exposure events is determined by random sampling day-long event sequences from a set of pools of 24-hour activity patterns. An individual 24-hour pattern in one of these pools is referred to here as a unit exposure sequence (UES). Each pool consists of a collection of UESs that are specific to selected demographic characteristics of the individual (e.g., age and gender), season, day type (weekday/weekend), and maximum daily temperature.

A UES is a contiguous set of exposure events spanning 24 hours. Each event is characterized by start time, duration, home/work status, microenvironment, and activity. All exposure events are constrained to occur entirely within a clock hour. The CFK model within the COHb module is called for each exposure event. Each event requires the following data.

Time duration of event (minutes)
Inspired CO partial pressure averaged over the event (torr)
Percent COHb at the start of the event (%)
Alveolar ventilation rate (ml/min STPD)
Average pulmonary capillary oxygen pressure (torr)
Haldane Coefficient (unitless)
Equilibrium constant for the reaction of O_2
Atmospheric pressure (torr)
Blood volume (ml)
Total potential reduced hemoglobin content of blood (ml CO/ml STPD)
Pulmonary CO diffusion rate (ml/min/torr STPD)
Endogenous CO production rate (ml/min STPD)

Table B-2. Principal parameters included in the physiological profile for adults for applications of APEX4.3.

Parameter	Algorithm(s) Containing Parameter	Other Parameters Required for Calculating Parameter	Method Used to Estimate Parameter Value
Age	COHb Ventilation rate	Demographic group	Randomly selected from population-weighted distribution specific to demographic group
Gender	COHb Ventilation rate	Demographic group	Randomly selected from population-weighted distribution specific to demographic group
Body Weight	COHb Ventilation rate	Gender Age	Randomly selected from population-weighted lognormal distributions with age- and gender-specific geometric mean (GM) and geometric standard deviation (GSD) derived from data from the National Health and Nutrition Examination Survey (NHANES), for the years 1999-2004 (Isaacs and Smith, 2005)
Height	COHb	Weight Gender	Estimated using equations developed by Johnson (1998) using height and weight data provided by Brainard and Burmaster (1992). Males: height = 34.43 inches + (6.67)[ln(weight)] + (2.38 inches)(z) Females: height = 48.07 inches + (3.07)[ln(weight)] + (2.48 inches)(z) The z term is randomly selected from a unit normal [N(0,1)] distribution. Units: height (inches), weight (lbs).
Menstrual phase	COHb	Gender Age	If gender = female, menstrual phase was randomly assigned in alternating 14-day cycles according to the following age-specific probabilities. Age < 12 or >50: 100% premenstrual Age 12 through 50: 50% premenstrual, 50% postmenstrual.

Parameter	Algorithm(s) Containing Parameter	Other Parameters Required for Calculating Parameter	Method Used to Estimate Parameter Value
Blood volume	COHb	Gender Weight Height	Blood volume (V_b) was determined according to gender by the following equations developed from Allen et al. (1956) which were modified to accept the units used for height and weight. Males: $V_b = (20.4)(\text{weight}) + (0.00683)(H^3) - 30$ Females: $V_b = (14.6)(\text{weight}) + (0.00678)(H^3) - 30$ Units: blood volume (ml), weight (lbs), height (inches).
Hemoglobin content of the blood, Hb	COHb	Gender Age	Randomly selected from normal distribution with arithmetic mean (AM) and arithmetic standard deviation (ASD) determined by gender and age based on data obtained from the National Health and Nutrition Examination Survey (NHANES), for the years 1999-2004 (see Isaacs and Smith (2005) in the CO REA, Appendix A) Units: grams of Hb per deciliter of blood

Parameter	Algorithm(s) Containing Parameter	Other Parameters Required for Calculating Parameter	Method Used to Estimate Parameter Value
Pulmonary CO diffusion rate, $D_{L_{CO}}$	COHb	Gender Height Age	Pulmonary CO diffusion rate (DL) was determined according to gender, height, and age according to the following equations obtained from a paper by Salorinne (1976) and modified to conform to the units used in the COHb module. Males: $D_{L_{CO}}$ = (0.361)(height) - (0.232)(age) + 16.3 ml/min/torr Females: $D_{L_{CO}}$ = (0.556)(height) - (0.115)(age) - 5.97 ml/min/torr Units: $D_{L_{CO}}$ (ml/min/torr), height (inches), age (years). Given the alveolar ventilation rate for the exposure event the associated adjusted pulmonary diffusion rate is calculated as: $D_{L_{CO}}(Adjusted) = D_{L_{CO}}(Base) + 0.000845\dot{V}_A - 5.7$
Endogenous CO production rate	COHb	Gender Age Menstrual phase	Endogenous CO production rate was randomly selected from a lognormal distribution with geometric mean (GM) and geometric standard deviation (GSD) determined according to the following equations specific to age, gender, and menstrual phase groupings (see data in Table B-3). Males, 18+: GM = 0.473, GSD = 1.316 Females, 18+, premenstrual: GM = 0.497, GSD = 1.459 Females, 18+, postmenstrual: GM = 0.311, GSD = 1.459 Units: GM (ml/hr), GSD (dimensionless).

Parameter	Algorithm(s) Containing Parameter	Other Parameters Required for Calculating Parameter	Method Used to Estimate Parameter Value
Resting metabolic rate (RMR)	Ventilation rate	Gender Age Body Weight	See Section 4.4.5 of CO REA and Chapter 5 of US EPA (2008a).
Energy conversion factor (ECF)	Ventilation rate	Gender	See Section 4.4.5 of CO REA and Chapter 5 of US EPA (2008a).
NVO_{2max}	Ventilation rate	Gender Age	See Section 4.4.5 of CO REA and Chapter 5 of US EPA (2008a).
VO_{2max}	Ventilation rate	NVO_{2max} Body Weight	See Section 4.4.5 of CO REA and Chapter 5 of US EPA (2008a).

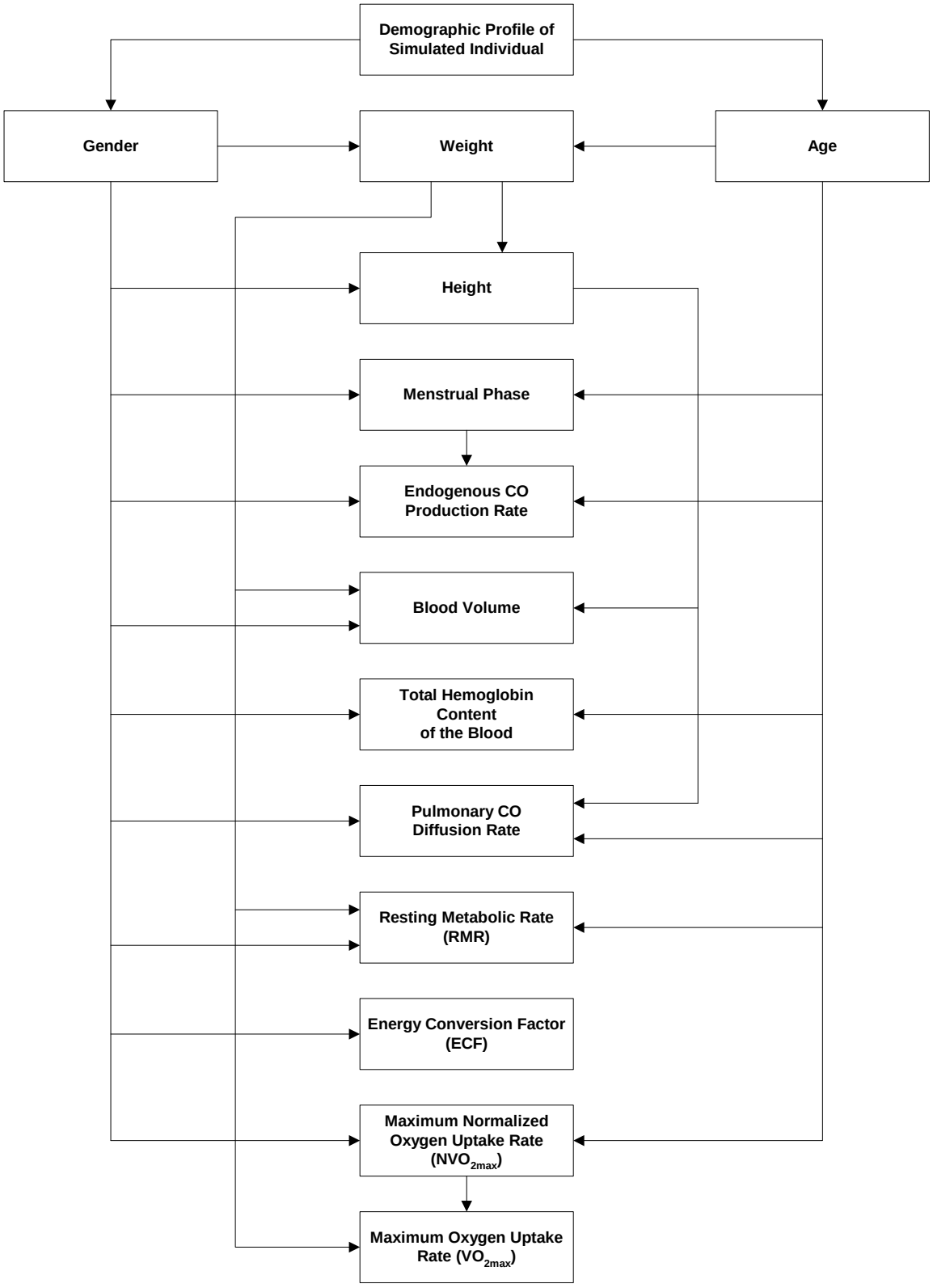

Figure B-1. Flow diagram for physiological profile generator. Input data is supplied at the start of the APEX4.3 computation.

Given these data as inputs, the module computes the percent COHb at the end of the exposure event. This value is used by the module as the initial percent COHb for the next contiguous exposure event. The module also computes the average percent COHb value for each exposure event. The main program retains these values and uses them to calculate percent COHb values for averaging times ranging from one hour to one day.

Some of the above data do not change during an APEX4.3 computer run and, therefore, need to be supplied to the computer program only once at the start. Some of the data vary with the individual and therefore need to be supplied at the beginning of each activity day. Other data tend to change with the exposure event and therefore need to be supplied for each new exposure event.

Barometric Pressure

A constant barometric pressure is assumed for the study area based on the average height above sea level:

$$P_B = 760 \times \exp(-0.0000386 \times Altitude) \qquad \text{(Eq. B-27)}$$

where altitude is the average height (in feet) of the study area above sea level (US EPA, 1978). The altitude was set at 5,183 feet for Denver and 328 feet for Los Angeles.

Average Pulmonary Capillary Oxygen Pressure

The equation employed is based on an approximation used by Peterson and Stewart (1975) in which 49 torr is subtracted from the partial pressure of inspired oxygen. This leads to the following approximate relationship:

$$\overline{P}c_{O_2} = 0.209(P_B - 47) - 49 \qquad \text{(Eq. B-28)}$$

where 0.209 is the mole fraction of O_2 in dry air and 47 is the vapor pressure of water at body temperature. This expression was used in an investigation of the CFK equation by Tikuisis et al. (1987). A value of 100 torr is commonly used since Equation (B-28) generates this value for a barometric pressure equivalent to 760 torr.

Haldane Coefficient

The value of 218 was used for the Haldane coefficient. While measured values in the range 210 to 270 have been reported in the extant literature, most researchers use values within the range of 210 to 240. In the early 1980's, the Clean Air Scientific Advisory Committee (CASAC) expressed the opinion to EPA (Friedlander, 1982) that the most careful work done in this area was that by Rodkey et al. (1969), who determined a value of 218. This value was selected for use in the COHb module of the earlier CO-NEM exposure model. Other researchers using values in the range 218 to 220 include Peterson and Stewart (1970), Marcus (1980), Collier and Goldsmith (1983), and Muller and Barton (1987). As the value 218 falls within the range currently used by researchers, we have elected to continue using this value in APEX4.3.

Equilibrium Constant for the Reaction of O_2 and RHb

This quantity was estimated in Section B.2 to have the value 0.32 based on the

observation that %[RHb] is about 3% in individuals breathing air which is free of CO and a value of 100 torr for $\overline{P}_{CO_2}$.

Total Reduced Hemoglobin in the Absence of O_2 and CO

The quantity $[THb]_0$ is expressed as equivalent milliliters of O_2 or CO at STPD per milliliter of blood. Total Hb blood levels are customarily expressed as grams per deciliter of blood. The total Hb level in the absence of COHb and O_2Hb would consist principally of RHb which can react with O_2 or CO and MetHb which cannot. Total Hb blood levels also tend to be higher in people living at higher altitudes. To relate $[THb]_0$ to Hb, it is therefore necessary to correct for the MetHb present, adjust for the effect of altitude, and convert to equivalent milliliters of CO at STPD. The later conversion is based on the observation that a gram of reduced Hb can react with a maximum of 1.39 ml of O_2 or CO at STPD. The application of these three factors yields the equation:

$$[RHb]_O = 1.39 \times Hb(100 - \%MetHb) \times \left(1 + \frac{HbAlt}{100}\right) \qquad \text{(Eq. B-29)}$$

where HbAlt is the percent increase in Hb due to exposure to altitude and is given by (US EPA, 1978):

$$HbAlt = 2.76e^{0.0001249\,Altitude}$$

Hb in equation (B-29) is a sea level value. Hb level in a human population is normally distributed with the mean Hb and standard deviation both dependent on gender and age class (see entry in Table B-2 for the distributions of Hb by age and gender). Given the hemoglobin content of the blood based on the distributions listed in Table B-2, $[THb]_0$ is calculated using equation (B-29). The weight percent MetHB, %MetHB, is taken to be 0.5% of the weight of Hb (Muller and Barton, 1987).

Determination of Weight

Body mass or weight (in kg) was determined by fitting lognormal distributions to data organized by age and gender from the National Health and Nutrition Examination Survey for the years 1999-2004 (Isaacs and Smith, 2005). Distribution parameters were estimated for single-year age cohorts for both genders for ages 0-85. As the NHANES 1999-2004 studies only covered persons up to age 85, linear forecasts for the parameters were made for ages 86-100, as based on the data for ages 60 and greater.

Determination of Height

The following equations were used to estimate height as a function of gender and weight. Equations B-30 and B-31 were derived by Johnson (1998) using height and weight data provided by Brainard and Burmaster (1992).

males: height = 34.43 inches + (6.67)[ln(weight)] + (2.38 inches)(z) (Eq. B-30)

females: height = 48.07 inches + (3.07)[ln(weight)] + (2.48 inches)(z) (Eq. B-31)

where the *z* term was randomly selected from a unit normal [N(0,1)] distribution.

Base Pulmonary Diffusion Rate of CO

A base lung diffusivity of CO for the individual is calculated as follows:

$$\text{Men:} \quad D_{L_{CO}} = 0.361 \times height - 0.232 \times age + 16.3 \qquad \text{(Eq. B-32)}$$

$$\text{Women:} \quad D_{L_{CO}} = 0.556 \times height - 0.115 \times age - 5.97 \qquad \text{(Eq. B-33)}$$

where height is in inches and age is in years.

The regression equations were obtained from a paper by Salorinne (1976) and modified to conform to the units used in the COHb module. The Salorinne data were obtained for non-exercising individuals. Tikuisis et al. (1992), working with eleven male subjects at various exercise levels, showed significant increase in lung diffusivity of CO with increasing alveolar ventilation rate. Regression analyses of data provided by Tikuisis et al. (1992) for the individual subjects in the study showed the relationship to be linear. From this relationship and the heights and ages of the subjects in the Tikuisis et al. (1992) study, it was determined that the Salorinne (1976) equations for male subjects correspond to an alveolar ventilation rate of 6.69 l/min STPD. In the absence of other data it is assumed that this same value applies to women. Thus, for each twenty-four hour period equations B-32 and B-33 are used to compute lung diffusion rates of CO for a base case alveolar ventilation rate of 6.69 1/min STPD. As will be seen, this value is adjusted to account for the actual ventilation rate experienced by the simulated individual during each individual exposure event.

Endogenous Rate of CO Production

The endogenous CO production rates taken from a number of sources show the rate to be distributed lognormally in the population (see Table B-3 for data and sources). The distribution is different for men and women. For a woman there is a further difference depending on whether she is in her premenstrual or postmenstrual phase. Table B-2 presents these distributions classified by class, gender, and menstrual phase.

For each male individual, APEX4.3 specifies a single value for endogenous CO production rate and uses it for all days of the year. For each female individual between 18 and 64 years of age, APEX4.3 specifies one value of endogenous CO production rate to represent premenstrual days and one value to represent postmenstrual days. Female individuals under 12 years and older than 50 are assumed to be premenstrual; consequently, APEX4.3 specifies a single value for endogenous CO production rate to be used for all days of the year. The specified values are randomly selected from the appropriate distributions presented in Table B-2. A random number, z, is sampled from the standardized normal distribution, N(0,1) to make each selection. The appropriate endogenous CO production rate is then obtained from:

$$\dot{V}_{CO} = 0.01667 \times (geom.mean) \times (geom.S.D.)^{z} \qquad \text{(Eq. B-34)}$$

The constant term converts ml/hr to ml/min.

A probabilistic algorithm within APEX4.3 assigns a menstrual phase to each day of the year for female individuals aged 12 to 50 years. The algorithm randomly assigns a number

between 1 and 28 to January 1. The number is increased by one for each successive day until number 28 is reached. The next day is numbered 1 and the 28-day numbering cycle is repeated until each day of the year has been assigned a number between 1 and 28. Days numbered 1 through 14 are identified as post-menstrual days; days numbered 15 through 28 are identified as pre-menstrual days.

Table B-3. Literature data used to derive lognormal distributions used to estimate endogenous CO production rate.

Reference	Gender	Menstrual Cycle (pre/post)	Endogenous CO Production Rate (ml/hr)							
Berk et al. (1974)	Male	NA	0.43	0.58	0.52	0.59	0.80	0.72		
Brouillard et al. (1975)	Male	NA	0.81	0.57	0.33	0.70				
Coburn et al. (1963)	Male	NA	0.35	0.40	0.39	0.43	0.35	0.51	0.42	0.57
			0.45							
Coltman and Dudley, (1969)	Male	NA	0.58	0.38	0.51	0.55	0.37	0.49	0.45	0.50
			0.33	0.45	0.36					
Delivoria-Papadoppulos et al. (1974)	Male	NA	0.46	0.26	0.60	0.45	0.39	0.40		
	Female	Pre	0.57	0.54	0.72	0.99	0.48	0.53	0.43	
		Post	0.23	0.51	0.34	0.41	0.26	0.16	0.30	
Luomanmaki and Coburn (1969)	Male	NA	0.38	0.42	0.41	0.54	0.38			
Lynch and Moede (1972)	Male	NA	0.40	0.81	0.26	0.65	0.55	0.62	0.44	
	Female	Pre	0.72	0.37	0.23	0.33	0.42	0.44	0.29	0.48
		Post	0.48	0.23	0.25	0.20	0.22	0.15	0.21	
Merke et al. (1975)	Female	Pre	0.64	0.86	0.35	0.52	0.80	0.54	0.68	0.28
	Female	Post	0.40	0.47	0.23	0.24	0.55	0.32	0.43	0.35
Werner and Lindahl (1980)	Male	NA	0.54	0.76	0.48	0.31	0.69	0.70	0.36	0.65

B.5 Input Data Supplied By APEX 4.3 with Each Exposure Event

Duration of Exposure Event

The duration of the exposure event in minutes is supplied by the main program to the COHb module.

Partial Pressure of Inspired Carbon Monoxide

The main program supplies the inspired CO concentration averaged over the duration of the exposure expressed as ppm. This quantity is converted to pressure via:

$$P_{I_{CO}} = (CO) \times (P_b - 47) \times 10^{-6} \qquad \text{(Eq. B-35)}$$

Initial Percent COHb Level at Start of Exposure Event

The program retains the percent COHb computed at the end of the previous exposure event and uses this value as the initial percent COHb for the present event. The starting COHb at the beginning of an activity day is the final COHb level at the end of the preceding activity day. This latter procedure is used for the first activity day of the overall computation since the program starts the day before the overall period covered by the APEX4.3 computation.

Alveolar Ventilation Rate

The main program supplies the COHb module with ventilation rate derived from the algorithm discussed in Section 4.4.5 of this report.

Adjusted Pulmonary Diffusion Rate of CO

Given the alveolar ventilation rate for the exposure event the associated adjusted pulmonary diffusion rate can be calculated from:

$$D_{L_{CO}}(Adjusted) = D_{L_{CO}}(Base) + 0.000845\dot{V}_A - 5.7 \qquad \text{(Eq. B-36)}$$

B.6 Analysis of Selected APEX COHb Outputs

This section provides analysis of APEX outputs by using the event-level APEX simulations. The APEX *events* and *hourly* output files can provide event-level and hourly-level exposure and dose profiles for all simulated individuals (US EPA, 2008a, 2008b). We generated the hourly time-series of dose for approximately 400 CHD simulated individuals, with the CHD population defined as described in section 5.5.1 of the CO REA.[1] Both the Los Angeles and Denver study areas were evaluated using two air quality scenarios: *as is* 2006 ambient air quality and historical[2] air quality adjusted to just meet the current 8-hour standard. Two model

[1] For each of these particular model runs, APEX generated the complete time-series of exposure and dose for 5,000 persons. Of the 5,000 persons simulated, APEX generated 438 CHD persons in Denver and 394 CHD persons in Los Angeles based on the NHIS CHD prevalence rates.

[2] 1997 ambient monitoring data was used in Los Angeles, 1995 data was used in Denver. An additional air quality/exposure scenario included air quality adjusted to just meet a 99th percentile 8-hour daily maximum of 5.0 ppm, though because these endogenous CO production runs were based on the same historical years of data in each

simulations were run for each scenario and study area; the first generated total COHb levels (i.e., COHb dose resulting from both ambient CO exposure and endogenous CO production) and the second simulation generated COHb levels with all exposure concentrations set to zero (i.e., to estimate COHb resulting from endogenous CO production alone). See CO REA chapters 4 and 5 for details regarding all other relevant APEX model simulation settings.

First, an analysis of the contribution of endogenous CO production to COHb levels is provided. This is followed by an analysis of the ambient concentration profile and dose time series for a few selected individuals. Finally, the total maximum end-of-hour COHb levels are evaluated with respect to the maximum COHb contribution from ambient exposure and maximum COHb contribution from endogenous CO production.

B.6.1 Contribution of Endogenous CO Production to COHb Level

We were interested in determining the relative contribution of endogenous CO production to an individual's total COHb level. In this first analysis, we generated the hourly time-series of dose for the approximately 400 CHD simulated individuals in the absence of CO exposure. When an APEX model simulation is performed with concentration input values equal to zero, endogenous CO production will be entirely responsible for the calculated COHb levels for each simulated person.

We note here that while the ambient CO concentration is set to zero for these runs, the temperature data associated with each simulation time period will affect the activity diaries sampled from CHAD used to construct each individual's longitudinal activity pattern profile. This will have a small impact on the estimated COHb doses due to, for example, differences in each simulated individual's ventilation rates that are linked to the activity pattern profile. Therefore, we expect there to be small differences in the contribution of endogenous CO production to COHb level when comparing the two exposure scenarios within each study area. Furthermore, we expect the contribution of endogenous COHb production to be greater in Denver when compared with that of simulated persons in Los Angeles, given the large differences in altitude between the two study areas.

First, we generated descriptive statistics for each individual's 8,760 hourly average COHb dose values resulting from endogenous CO production alone. Then annual means were calculated for each individual and used to generate a population distribution of annual means for each study area and air quality scenario. These population statistics are summarized in Table B-4. The annual average hourly COHb level for the population was 0.32% for the simulated CHD population in Denver and about 0.27% for the simulated CHD population in Los Angeles. There was variability in the population means as indicated by the range of individual annual mean values that extended from a low of about 0.11% COHb, to a high of about 1.1% COHb. Overall the population variability in annual average COHb, as measured by the coefficient of variability (COV), was about 42% for both study areas and for both exposure scenarios.

The variability in each individual's annual mean COHb, as measured by an average of each person's respective COV for the year, was also calculated and found generally consistent for each simulated individual, and when considering the two study areas and both exposure

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study area, the generated time-series data for the endogenous CO contribution would be identical. These exposure scenarios are described more fully in section 5.6 of the CO REA.

scenarios. On average, an individual's hourly COHb was estimated to vary by about 22-23% of their annual average hourly COHb. Note the standard deviation of the individual-based COVs equaled about 5%. When compared to the population variability statistics, it can be seen that there is greater inter-personal variability in the contribution of endogenous CO production to COHb levels than intra-personal variability. This finding is generally as expected, given the wide range of interpersonal attributes that might influence the COHb level including age, gender, body mass, blood hemoglobin content, endogenous CO production rate, etc., compared with the limited number of intra-personal attributes that might influence COHb level, such as alveolar ventilation rate. Note that this analysis does not include variability in COHb due to diseases and other medical conditions, some of which may increase or decrease the endogenous CO production rate (e.g., hemolytic anemia and infection) (ISA, Section 4.5).

B.6.2 Time-Series of COHb Levels In Individuals and Associated Ambient Concentrations

The time-series of hourly average COHb levels was plotted along with the hourly ambient CO concentration for three simulated CHD persons in Los Angeles. The purpose was to illustrate the variation in COHb levels occurring over time, with respect to endogenous CO production and ambient CO concentrations[3] (which of course would ultimately be related to ambient CO exposure). We purposefully selected these three simulated persons to represent a low, mid, and high level COHb time-series. A full week of data was extracted from the air quality scenario of just meeting the current standard and included the hours where the ambient CO concentration approached the 8-hour CO standard of 9.4 ppm. Note again that the *total COHb* in this analysis refers to the COHb dose resulting from both ambient CO exposure and endogenous CO production. The time-series for all three persons was for the 1-week period from December 17 through December 23 (Figure B-2), though the individuals have entirely different ambient CO concentration profiles and endogenous CO production rates, and therefore different total COHb levels over the time period of interest.

The person designated as 'low' had a mean total COHb dose level of about 0.6% across the time period, with hourly total COHb levels ranging from about 0.4 to 0.7% (Figure B-2, top). Hourly ambient CO concentrations used in calculating this person's exposure were generally low (i.e., less than 1 ppm) though, on occasion, ranged upwards to 4 ppm. This individual, while experiencing low total COHb levels across this time period, actually has a relatively high contribution from endogenous CO production (on average contributing to a COHb level of about 0.4 % over the 1-week period) with limited COHb contribution from ambient CO exposure (on average contributing to a COHb level of about 0.2%).

The person designated as 'mid' also had a mean COHb dose level of about 0.6% (Figure B-2, middle) though with greater variability in hourly COHb level when compared with the 'low' person. The COHb profile for the 'mid' person extended upwards to a peak COHb level of about 1.2% on several hourly excursions, largely in response to exposure to ambient CO concentrations. The estimated contribution to COHb levels resulting from endogenous CO production for the 'mid' person was within the lower range of the population average (Table B-4), having an average hourly COHb level from endogenous CO of less than 0.2% for this time period.

[3] This is the ambient concentration used as input to APEX, only adjusted for the air quality scenario. The 1997 Los Angeles monitoring data were adjusted by a factor of 0.627 to just meet the current 8-hour standard.

The response to ambient CO concentrations is more notable when observing the profile of the designated 'high' person (Figure B-2, bottom). On average, this person had a total COHb level of 1.0% across the illustrated 1-week period, though 1-hour total COHb levels peaked just above 2.9% following the upwards spiking of associated hourly ambient CO concentrations of between 10 and 12 ppm. Note that COHb levels resulting from endogenous CO production alone for this individual were similar to the population average (Table B-4), at about 0.3% COHb for this time period.

This analysis suggests that moderate to high total COHb levels result from ambient exposure rather than endogenous CO production, while individuals with lower total COHb levels have a greater contribution to total COHb from endogenous CO.

B.6.3 Evaluation of Maximum End-of-Hour COHb Levels with Respect to Contribution from Ambient CO Exposure and Endogenous CO Production

In this third analysis, we calculated three dose metrics using the event-level output files generated for the CHD population in each study area and for the two air quality scenarios: *as is* air quality and just meeting the current 8-hour standard. Consistent with the standard output generated for the CO REA, we generated a single maximum end-of-hour COHb level for each simulated CHD person, resulting from both ambient CO exposure and endogenous CO production (and termed total COHb in this document). Next, we used the COHb levels generated from APEX simulations employing zero exposure concentrations, to estimate a maximum COHb level resulting from endogenous CO production alone. And finally, the time-series of COHb levels resulting from endogenous CO production were subtracted from the time-series of total COHb (i.e., from endogenous production and ambient exposure), to estimate the maximum COHb level resulting from ambient CO exposure alone. In considering the results, we note that the focus is on ambient CO contribution to exposure, although in some cases, other CO sources can play a more important role in COHb levels (as described in section 2.3 of CO REA).

The percentiles of the distribution of each of these metrics were calculated in 0.5 percentile increments, the results of which are illustrated in Figure B-3. Selected percentiles of each distribution are provided in Table B-5. As noted above for the distribution of annual mean COHb levels resulting from endogenous CO production, the maximum contribution is nearly identical when comparing the air quality scenarios within the study areas. In general, over 98% of the simulated CHD population has a maximum end-of-hour COHb level resulting from endogenous CO production of less than 1.0%. There is a difference in the highest maximum end-of-hour COHb level contributed by endogenous CO production when comparing Denver to Los Angeles; the maximum extends upwards to a COHb level of about 1.5% in Denver, while in Los Angeles the highest maximum end-of-hour COHb level is about 1.0%.

The distribution of the maximum end-of-hour COHb levels resulting from ambient exposure alone is consistently higher than that resulting from endogenous CO production, indicating the relative importance of ambient CO exposure; however, it is not always the case that the maximum end-of-hour total COHb level occurred simultaneously with the maximum contribution from ambient exposure. About half of the time, this was the case (Table B-6), though it varied based on the study area and air quality scenario considered. Even when a person's maximum total COHb did not occur at the same time as the maximum ambient contribution, the ambient contribution, on average was between 51-66% of a person's maximum total COHb.

Table B-4. Descriptive statistics for annual average hourly COHb levels resulting from endogenous CO production alone and using an APEX simulated CHD population.

Study Area	Air Quality Scenario	CHD Population Annual Average Hourly COHb Levels (%)[a]										Individual Variability in Hourly COHb Levels (%)[b]	
		Mean	stdev	min	p1	p5	p50	p95	p99	max	COV	Mean of COVs	Stdev of COVs
Denver	As Is	0.315	0.132	0.121	0.136	0.161	0.285	0.573	0.799	1.074	42.1	20.2	5.2
	Current Standard	0.315	0.133	0.122	0.136	0.161	0.285	0.576	0.804	1.087	42.3	20.1	5.2
Los Angeles	As Is	0.268	0.111	0.095	0.105	0.139	0.246	0.506	0.675	0.695	41.5	22.8	5.6
	Current Standard	0.268	0.111	0.095	0.106	0.139	0.245	0.504	0.665	0.695	41.5	22.8	5.6

Notes:
[a] An annual hourly average COHb (i.e., the 8,760 hourly values) for each simulated individual was first calculated. Then the mean, standard deviation, and selected percentiles of this annual hourly average were calculated for the simulated population (i.e., 438 persons in Denver, 394 persons in Los Angeles).
[b] The COV (mean/standard deviation) was calculated for each individual using each person's 8,760 hourly values. Then the mean and standard deviation of these individual COVs was calculated for each simulated population

Table B-5. Selected percentiles of the maximum end-of-hour COHb levels using an APEX simulated CHD population, considering the maximum contribution from endogenous CO production, the maximum contribution from ambient CO exposure and the maximum total COHb level.

Study Area	Air Quality Scenario	Maximum End-of-Hour COHb Level (%)[a]								
		Endogenous Contribution			Ambient Contribution			Total		
		min	med	max	min	med	max	min	med	max
Denver	As Is	0.19	0.43	1.55	0.24	0.50	1.70	0.46	0.80	1.85
	Current Standard	0.19	0.43	1.54	0.43	0.94	2.74	0.64	1.21	2.95
Los Angeles	As Is	0.14	0.38	1.04	0.24	0.60	1.70	0.46	0.84	1.92
	Current Standard	0.14	0.37	1.04	0.30	0.72	2.77	0.48	0.97	3.04

Notes:
[a] Selected percentiles correspond to COHb levels in Figure B-3.

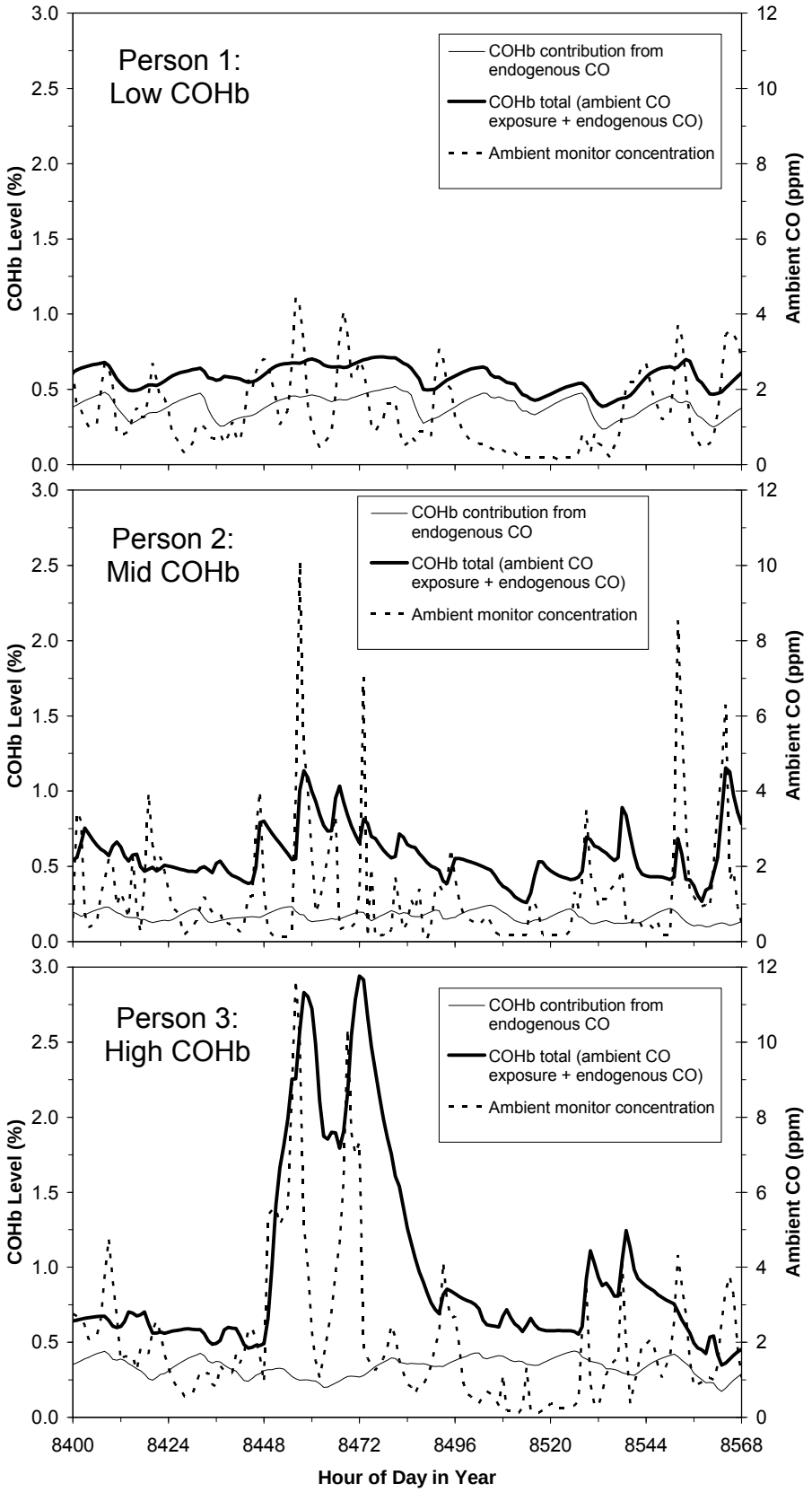

Figure B-2. Time-series profile of COHb levels and ambient CO for three simulated CHD persons in Los Angeles – air quality just meeting the current standard.

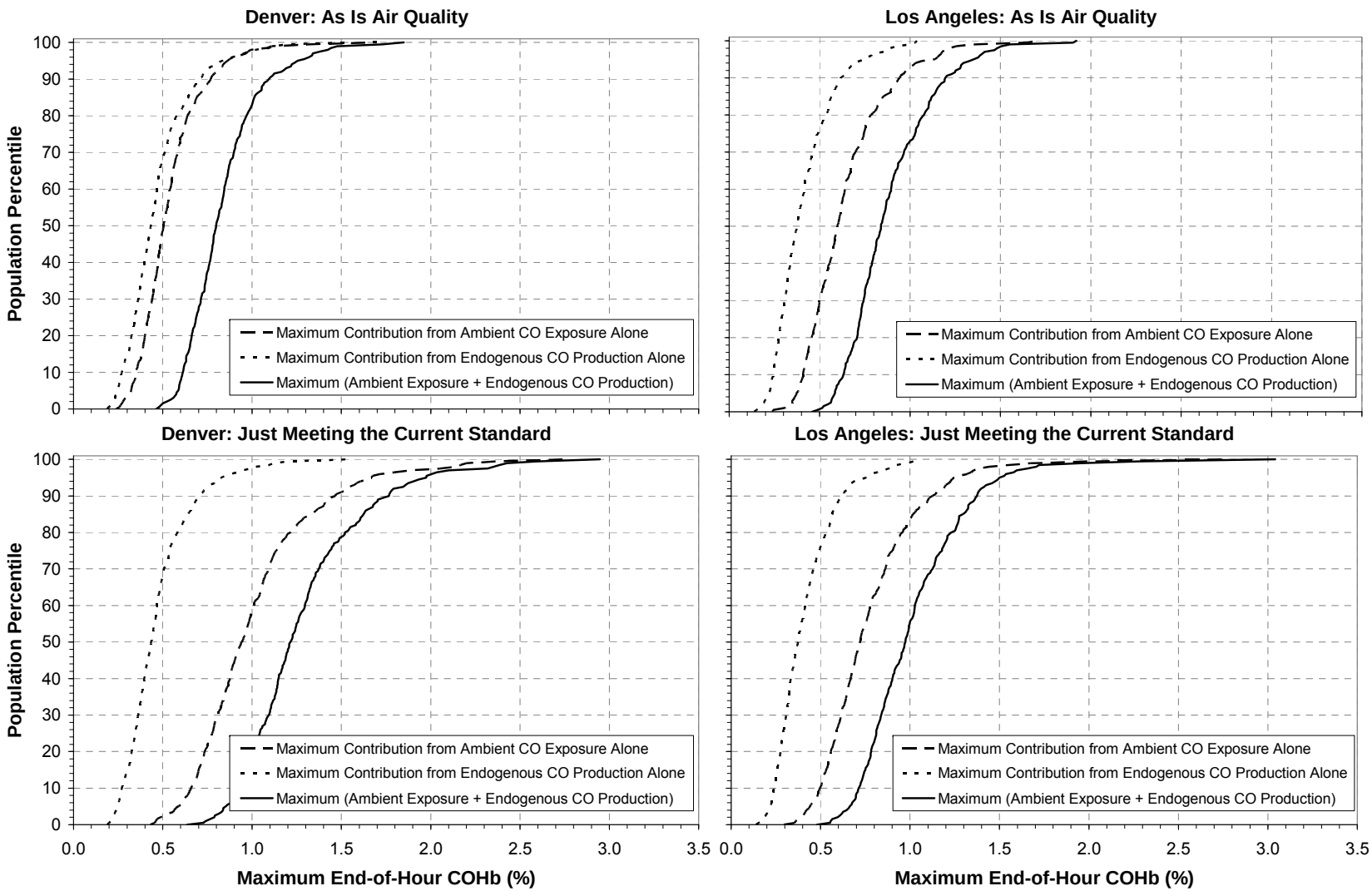

Figure B-3. Maximum end-of-hour COHb levels using an APEX simulated CHD population in Denver (left) and Los Angeles (right), considering *as is* air quality (top) and air quality adjusted to just meet the current 8-hour standard (bottom).

Table B-6. Evaluation of the ambient contribution occurring simultaneously with a CHD person's maximum total end-of-hour COHb in Denver and Los Angeles.

Study Area	Air Quality Scenario	Maximum Ambient COHb Contribution COHb Occurred Simultaneously with Maximum Total COHb	Persons		Percent of Ambient COHb Contribution to Maximum Total COHb[a]		
			(n)	(%)	min	mean	max
Denver	As Is	Yes	183	41.8	32.5	73.5	95.6
		No	255	58.2	7.5	50.6	86.2
	Current Standard	Yes	320	73.0	57.6	79.9	97.6
		No	118	27.9	23.4	65.9	89.9
Los Angeles	As Is	Yes	213	54.1	43.5	77.0	93.7
		No	181	45.2	20.1	57.7	90.1
	Current Standard	Yes	229	58.1	43.5	79.6	95.2
		No	165	41.9	26.2	63.6	90.5

Notes:
[a] The ambient COHb contribution that occurred at the same time as the persons maximum total COHb was used for this calculation.

Each simulated CHD person's maximum end-of-hour total COHb level was also plotted against their respective ambient contribution to that maximum COHb level. We separated each of the air quality scenarios, the study areas, and whether the maximum ambient contribution coincided with the maximum total COHb level or did not. The results of this analysis are illustrated in Figures B-4 and B-5 for Denver and Los Angeles, respectively.

As expected, strong linear relationships exist when the maximum ambient contribution occurred at the same time as the maximum total COHb level, regardless of air quality scenario or study area. The coefficient of determination (R^2 values) ranged from about 0.80 to 0.92, with linear regression slopes very close to unity, supporting the importance of the ambient contribution to these persons' maximum total COHb level. Regression intercepts were also similar to one another, ranging from a value about 0.21 to 0.31%, and generally approximate the average endogenous contribution to COHb.

Relatively weaker relationships were exhibited when the maximum total COHb level did not correspond with the maximum ambient contribution. The coefficient of determination ranged from about 0.11 to 0.48 with regression slopes ranging from 0.4 to 0.7. The relative greater importance of the endogenous contribution to COHb for these persons is indicated by the higher regression intercepts, estimated to range from about 0.51 to 0.65% COHb.

The most important message conveyed by these figures illustrating simulations for which exposure included only contribution from ambient CO sources is that for all simulated persons having a maximum end-of-hour COHb level at or above 2.0%, and for most persons having a maximum end-of-hour COHb level at or above 1.5%, the ambient contribution is a more important factor than endogenous CO production. This is indicated by the relatively few data points that greatly deviate from the bounded regression lines at or above these selected COHb levels, regardless of whether the maximum total COHb occurred at the same time as the maximum ambient contribution.

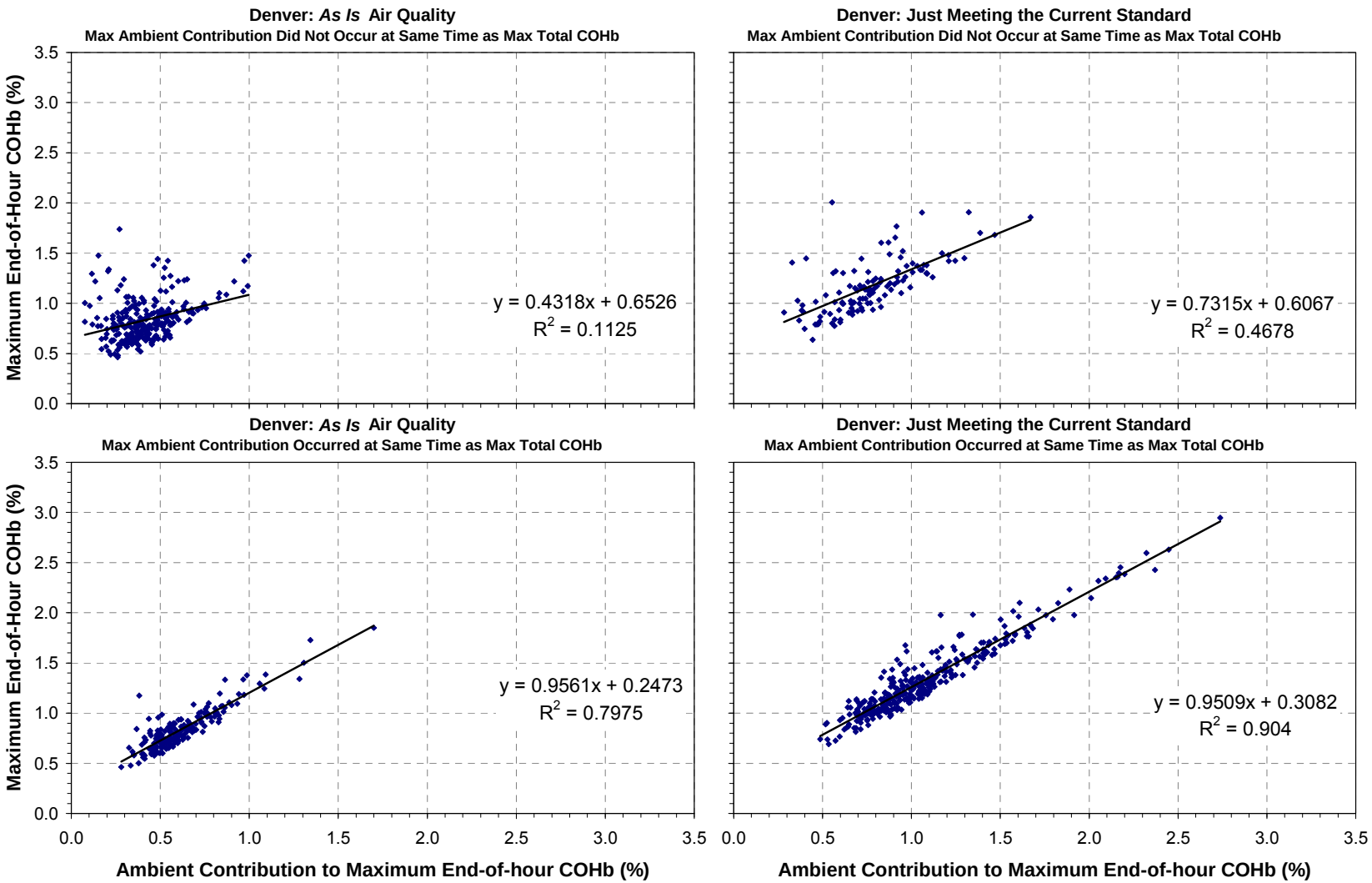

Figure B-4. Relationship between ambient contribution to COHb level and the corresponding maximum total end-of-hour COHb level in Denver. Air quality *as is* (left) and just meeting the current standard (right). Maximum ambient contribution did not occur with maximum total COHb (top) and maximum ambient contribution did occur with maximum total COHb (bottom).

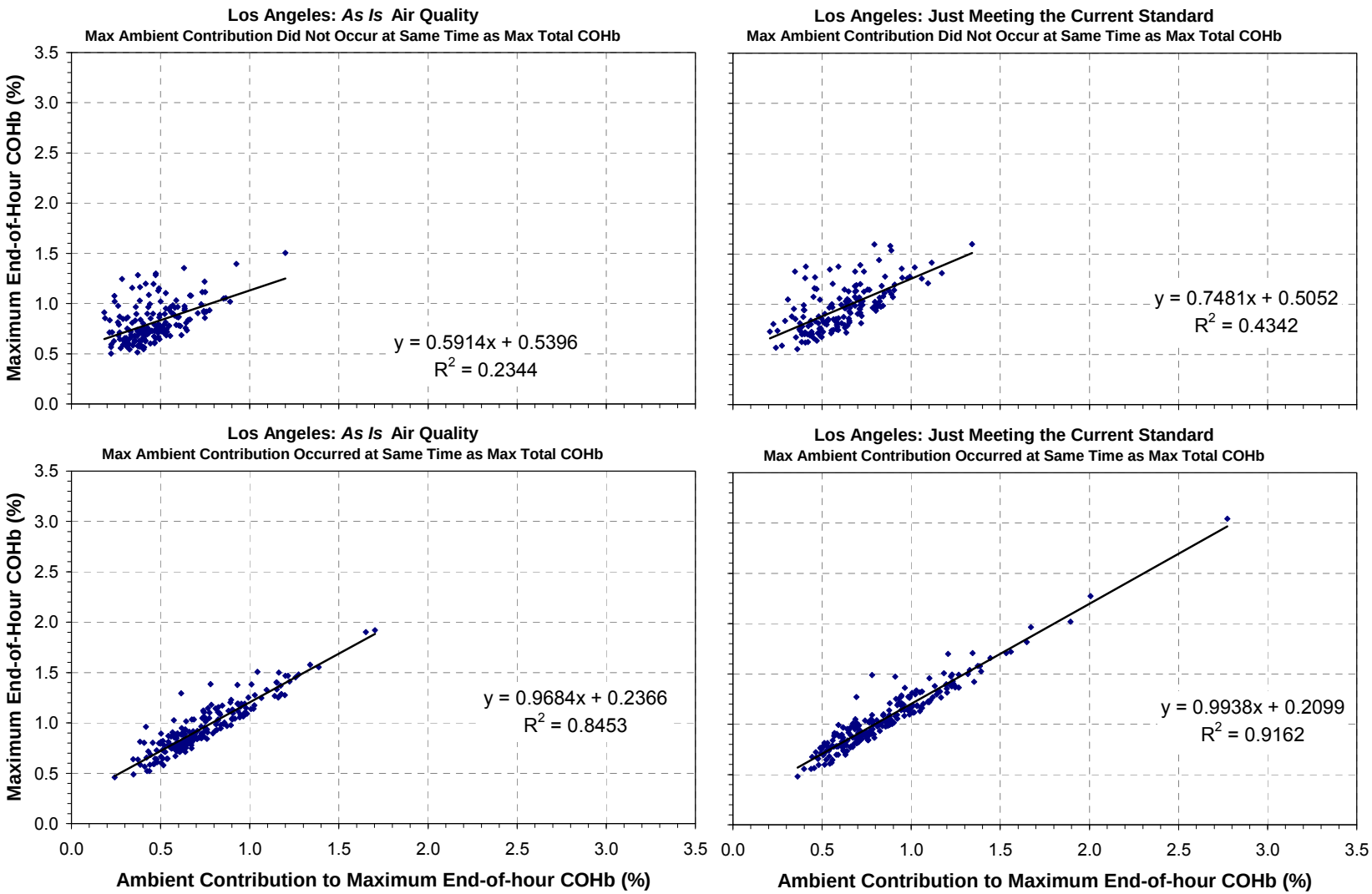

Figure B-5. Relationship between ambient contribution to COHb level and the corresponding maximum total end-of-hour COHb level in Los Angeles. Air quality *as is* (left) and just meeting the current standard (right). Maximum ambient contribution did not occur with maximum total COHb (top) and maximum ambient contribution did occur with maximum total COHb (bottom).

B.7 References

Allen TH, Peng MT, Chen KP, Huang TF, Chang C, Fang HS. (1956). Prediction of blood volume and adiposity in man from body weight and cube of height. *Metabolism*. 5:328-345.

Biller WF and Richmond HM. (1982). Sensitivity Analysis on Coburn Model Predictions of COHb Levels Associated with Alternative CO Standards. Report to Strategies and Air Standards Division of the Office of Air quality Planning and Standards, U.S. Environmental Protection Agency, Research Triangle Park, NC, November, 1982.

Brouillard RP, Contrad ME, Bensinger TA. (1975). Effect of blood in the gut on measurements of endogenous carbon monoxide production. *Blood*. 45:67-69.

Brainard J and Burmaster D. (1992). Bivariate distributions for height and weight of men and women in the United States. *Risk Analysis*. 12(2):267-275.

Berk PD, Rodkey FL, Blaschke TF, Collison HA, Waggoner JG. (1974). Comparison of plasma bilirubin turnover and carbon monoxide production in man. *J Lab Clin Med*. 83:29-37.

Coburn RF, Forster RE, Kane RB. (1965). Considerations of the physiology and variables that determine blood carboxyhemoglobin concentration in man. *J Clin Invest*. 44:1899-1910.

Coburn RF, Blakemore WS, Forster RE. (1963). Endogenous carbon monoxide production in man. *J Clin Invest.* 42:1172-1178.

Collier C and Goldsmith JR. (1983). Interactions of carbon monoxide and hemoglobin at high altitude. *Atmos Environ*. 17:723-728.

Coltman CA and Dudley III GM. 1969. The relationship between endogenous carbon monoxide and total heme mass in normal and abnormal subjects. *Am J Med Sci*. 258:374-385.

Delivoria-Papadoppulos M, Coburn RF, Forster RE. (1974). Cyclic variation of rate of carbon monoxide production in normal women. *J Appl Physiol*. 36:49-71.

Friedlander SK. (1982). Letter from the Clean Air Scientific Advisory Committee to US EPA Administrator. August 31, 1982.

Glen G. (2002). Programmer's Guide for the APEX3 Model. Prepared by ManTech Environmental Technology, Inc., for the U.S. Environmental Protection Agency, Research Triangle Park, NC. April 30.

Issacs K and Smith L. (2005). New Values for Physiological Parameters for the Exposure Model Input File Physiology.txt. Technical memorandum to Tom McCurdy, NERL WA10. December 20, 2005. Provided in Appendix A of the CO REA.

Johnson T and Paul RA. (1983). The NAAQS Model (NEM) Applied to Carbon Monoxide. Report no. EPA 450/5-83-003. U.S. Environmental Protection Agency, Research Triangle Park, NC.

Johnson T. (1998). Memo No. 5: Equations for Converting Weight to Height Proposed for the 1998 Version of pNEM/CO. Memorandum Submitted to U.S. Environmental Protection Agency. TRJ Environmental, Inc., 713 Shadylawn Road, Chapel Hill, North Carolina 27514.

Johnson T, Capel J, Olaguer E, Wijnberg L. (1992). Estimation of Carbon Monoxide Exposures and Associated Carboxyhemoglobin Levels in Denver Residents Using a Probabilistic Version of NEM. Prepared by TRJ Environmental, Inc., for the Office of Air Quality Planning and Standards, U.S. Environmental Protection Agency, Research Triangle Park, NC.

Johnson T, Mihlan G, LaPointe J, et al. (2000). Estimation of Carbon Monoxide Exposures and Associated Carboxyhemoglobin Levels in Residents of Denver and Los Angeles Using pNEM/CO (Version 2.1). Prepared by TRJ Environmental, Inc., for the Office of Air Quality Planning and Standards, U.S. Environmental Protection Agency, Research Triangle Park, NC.

Luomanmaki K and Coburn RF. (1969). Effects of metabolism and distribution of carbon monoxide on blood and body stores. *Am J Physiol*. 217(2):354-362.

Lynch SR and Moede AL. (1972). Variation in the rate of endogenous carbon monoxide production in normal human beings. *J Lab Clin Med*. 79:85-95.

Marcus AH. (1980). Mathematical models for carboxyhemoglobin. *Atmos Environ*. 14:841-844.

McCartney ML. (1990). Sensitivity analysis applied to Coburn-Forster-Kane models of carboxhemoglobin rormation. *Am Ind Hyg Assoc J*. 51(3):169-177.

McCurdy T, Glen G, Smith L, and Lakkadi Y. (2000). The National Exposure Research Laboratory's Consolidated Human Activity Database. *J Expos Anal and Environ Epidemiol*. 10:566-578.

Merke C, Cavallin-Stahl E, Lundh B. (1975). Carbon monoxide production and reticulocyte count in normal women: effect of contraceptive drugs and smoking. *Acta Med Scan*. 198:155-160.

Muller KE and Barton CN. (1987). A nonlinear version of the Coburn, Forster and Kane model of blood carboxyhemoglobin. *Atmos Environ*. 21:1963-1967.

Peterson JE and Stewart RD. (1970). Absorption and elimination of carbon monoxide by inactive young men. *Arch Environ Health*. 21:165-171.

Peterson JE and Stewart RD. (1975). Predicting the carboxhemoglobin levels resulting from carbon monoxide exposures. *J Appl Physiol*. 39:633-638.

Press WH, Flannery BP, Teukolsky SA, Vettering WT. (1986). Numerical Recipes: The Art of Scientific Computing. 1st edition. Cambridge University Press, Cambridge MA.

Rodkey FL, O'Neal JD, Collison HA. (1969). Oxygen and carbon monoxide equilibria of human adult hemoglobin at atmospheric and elevated pressure. *Blood*. 33:57-65.

Salorinne Y. (1976). Single-breath pulmonary diffusing capacity. *Scand J Resp Diseases*. Supplementum 96.

Tikuisis P, Madill HD, Gill BJ, Lewis WF, Cox KM, Kane DM. (1987). A critical analysis of the use of the CFK equation in predicting COHb formation. *Am Ind Hyg Assoc J*. 48(3):208-213.

Tikuisis P, Kane DM, McLellan TM, Buick F, Fairburn SM. (1992). Rate of formation of carboxyhemoglobin in exercising humans exposed to carbon monoxide. *J Appl Physiol*. 72(4):1311-1319.

US EPA. (1978). Altitude as a Factor in Air Pollution. Report no. EPA-600/9-78-015. U.S. Environmental Protection Agency, Research Triangle Park, NC.

US EPA. (2002). EPA's Consolidated Human Activities Database. Data and associated documentation available at: http://www.epa.gov/chad/.

US EPA. (2008a). Total Risk Integrated Methodology (TRIM) Air Pollutants Exposure Model Documentation (TRIM.Expo/APEX, Version 4.3). Volume 2: Technical Support Document. Report no. EPA-452/B-08-001b. Office of Air Quality Planning and Standards, U.S. Environmental Protection Agency, Research Triangle Park, NC. Available at: http://www.epa.gov/ttn/fera/human_apex.html.

US EPA. (2008b). Total Risk Integrated Methodology (TRIM) Air Pollutants Exposure Model Documentation (TRIM.Expo/APEX, Version 4.3). Volume 1: Users Guide. Report no. EPA-452/B-08-001a. Office of Air Quality Planning and Standards, U.S. Environmental Protection Agency, Research Triangle Park, NC. Available at: http://www.epa.gov/ttn/fera/human_apex.html.

Werner B and Lindahl J. (1980). Endogenous carbon monoxide production after bicycle exercise in healthy subjects and in patients with hereditary spherocytosis. *Scan J Lab Invest*. 40:319-324.

Appendix C

Isaacs et al. (2009) Reference Used in Developing D and A Statistics Input to APEX Model

The following presents a reformatted version of the Isaacs et al. (2009) presentation to allow for easier reading. The poster, included at the end of this Appendix in its entirety, was originally presented at the *American Time Use Research Conference*, June 25-26, 2009, University of Maryland, College Park, MD.

Statistical Properties of Longitudinal Time-Activity Data for Use in EPA Exposure Models

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ABSTRACT

Realistic simulation of longitudinal activity patterns is necessary for appropriately reproducing the frequency and duration of pollutant exposures in human exposure models. In EPA's exposure models, longitudinal activity diaries for simulated persons are constructed from the 1-day cross sectional activity diaries in the Consolidated Human Activity Database (CHAD). Recently, new algorithms have been developed to construct longitudinal diaries from CHAD diaries based on realistic variance and autocorrelation properties of diary characteristics relevant to pollutant exposure. Characteristics of particular interest include time spent in particular microenvironments and time spent in activities that produce high ventilation rates. However, few multi-day data are currently available for estimating accurate statistical properties for these quantities. Results from a recent time-activity study of 10 adults and one newborn child are presented here. The participants recorded their personal location and activity for two-week periods in each of four seasons in 2006 and 2007. The data were recorded 24 hours a day, in increments as small as one minute. Additional recording periods for these same individuals are expected in the future. The diaries for all subjects were assessed to calculate the between-person variance, the within-person variance, and the autocorrelation for various lags in the time spent in outdoor, residence, indoor (non-residence), and vehicle microenvironments, as well as for time spent performing high-METS activities. The effectiveness of various day-type definitions (for example, weekend versus weekday, or workday versus non-workday) for grouping similar diary days is examined. Seasonal variation in activity patterns is analyzed. These data have the potential to aid in the development of improved input variance and autocorrelation statistics for longitudinal diary assembly algorithms in EPA's human exposure models.

INTRODUCTION

Recently, new methods of assembling multi-day diaries in human exposure models from cross-sectional single-day diaries have been proposed that are based on the variance and autocorrelation statistics of the simulated population (Glen et al. 2008). Appropriately modeling intra- and interindividual variability using such algorithms may be essential in producing appropriate estimates of exposure. In addition, reproducing realistic autocorrelations in key diary properties may be required for the modeling of episodic exposure patterns.

Previously, longitudinal time activity-location data collected in children in the Southern California Chronic Ozone Exposure Study (Geyh et al. 2000) have been analyzed to obtain estimates of appropriate measures of variance and autocorrelation for use in the longitudinal algorithm. Data from a new study in adults are now presented.

BACKGROUND

Exposure models require construction of human activity diaries that cover the entire simulation period of a model run. This period is often several months, a year, or even longer. In EPA's models, human activity diaries are usually drawn from EPA's CHAD (Consolidated Human Activity Database; McCurdy et al., 2000; http://www.epa.gov/chadnet1), which typically includes just one day (24 hours) of activities from each person. A "longitudinal" diary is one that covers the same person over a long period of time. While the SHEDS modeling period may be of user-specified duration, it is assumed in this section to be one year, to provide a concrete example.

Recently, a new longitudinal diary assembly algorithm has been developed (Glen et al. 2007) based on the variance and autocorrelation properties of the modeled simulation. The new method requires the user to:

1) Select the diary property most relevant to exposure for the current application (such as outdoor time or time spent in vehicles)

2) Specify the D statistic, which relates the within-person and between-person variances for this diary property; and

3) Specify the 1-day lag autocorrelation in this diary property.

The new method is currently implemented in EPA's APEX and SHEDS-Air Toxics models. The new method allows the modeler to apportion the total variance in the key diary property into the within- and between-person variances $\sigma_w 2$ and $\sigma_b 2$ by specifying the D statistic, defined to be:

$$D = \frac{\sigma_b^2}{\sigma^2} = \frac{\sigma_b^2}{\sigma_b^2 + \sigma_w^2}$$

D pertains to the population as a whole and is bounded by zero and one. A value of zero implies all persons have the same average behavior, whereas a value of one implies the greatest possible difference in mean behavior that is consistent with the total variance.

In addition to targeting the within-person and between-person variances through setting the D statistic, the new diary assembly method optionally allows targeting of the day-to-day autocorrelation. This is a measure of the tendency for similar diaries to occur on consecutive days. The lag-one autocorrelation in a variable y is for a person defined as:

$$A = \sum_{j=1}^{N-1} (y_j - \bar{y})(y_{j+1} - \bar{y}) / \sum_{j=1}^{N} (y_j - \bar{y})^2$$

The population autocorrelation A is the mean of the A values for all individuals. Autocorrelation could be of interest to the exposure modeler if the concentration time series were strongly episodic, for example. In the diary assembly, a positive autocorrelation indicates a tendency for diaries with x-scores near each other to be used on consecutive days, while a negative autocorrelation indicates a tendency for dissimilar x-scores to be used on consecutive days. Some preliminary values of A have been derived from the same data that were used to estimate D (Glen et al., 2008).

METHODS

Activity Diary Study

Activity-location data were collected from 10 adults. Nine of the adults were working professionals; one was a stay-at-home parent. Nine of the adults recorded their personal location and activity for two-week periods in each of four seasons in 2006 and 2007. Additional data were collected in one of the male subjects in 1999, another male (the 10th adult) in 2002, and in one of the females in 2008 (collected during maternity leave). The data were recorded 24 hours a day, in increments as small as one minute. In this preliminary analysis, the time spent outdoors, indoors, in travel, and performing hard work each day were calculated from the diaries. "Hard work" was self-reported by each individual, as defined as activities requiring heavy breathing and/or sweating. Daily high temperatures and precipitation amounts were acquired for each day of the study.

Variance and Autocorrelation Statistics

Variance and lag-one autocorrelation statistics were calculated for the studied individuals. Variance statistics were estimated for both the raw measured variables (i.e. time in minutes) and the scaled ranks of the variable for each person on a given day. The ratio of the between-person variance to the total variance (the sum of the between- and within-person variance) was calculated for the population. This ratio, calculated using the raw variables, is the intraclass correlation coefficient (ICC), while the same ratio, calculated using the ranks, is D, the diversity statistic. The autocorrelation A was also calculated using both the raw variables and the scaled ranks of the variables on each day for each person in the study.

Analysis of Time Spent in Locations/Activities

The longitudinal data were assessed to support decisions on optimal diary pools for exposure modeling. Time spent in each of the examined locations/activities were assessed as a function of day of the week (weekday versus weekend), day type (workday versus non-workday), season, temperature, precipitation, and gender. These analyses were undertaken to assess the utility of different diary pool definitions. Optimal definitions of diary pools can adequately capture temporal patterns in activities while maximizing the number of activity diaries available for sampling on a given day for a simulated individual. Differences between groups were assessed with the Wilcoxon signed rank test (for 2 groups) or the Kruskal-Wallis test (for more than 2 groups). The Wilcoxon rank sum (two-sample) test was used to test differences between genders.

RESULTS AND DISCUSSION

Individual Variability

Figure 1 shows an example of the individual variability in time spent in different locations/activities for a single male subject; a 367-day period from this subject is depicted. Distributions of time for this subject are also shown. These figures demonstrate the large amount of intra-individual variability that can be seen in longitudinal activity studies. Distributions of time spent in locations/activities for the population is shown in **Figure 4[*sic 2*]**.

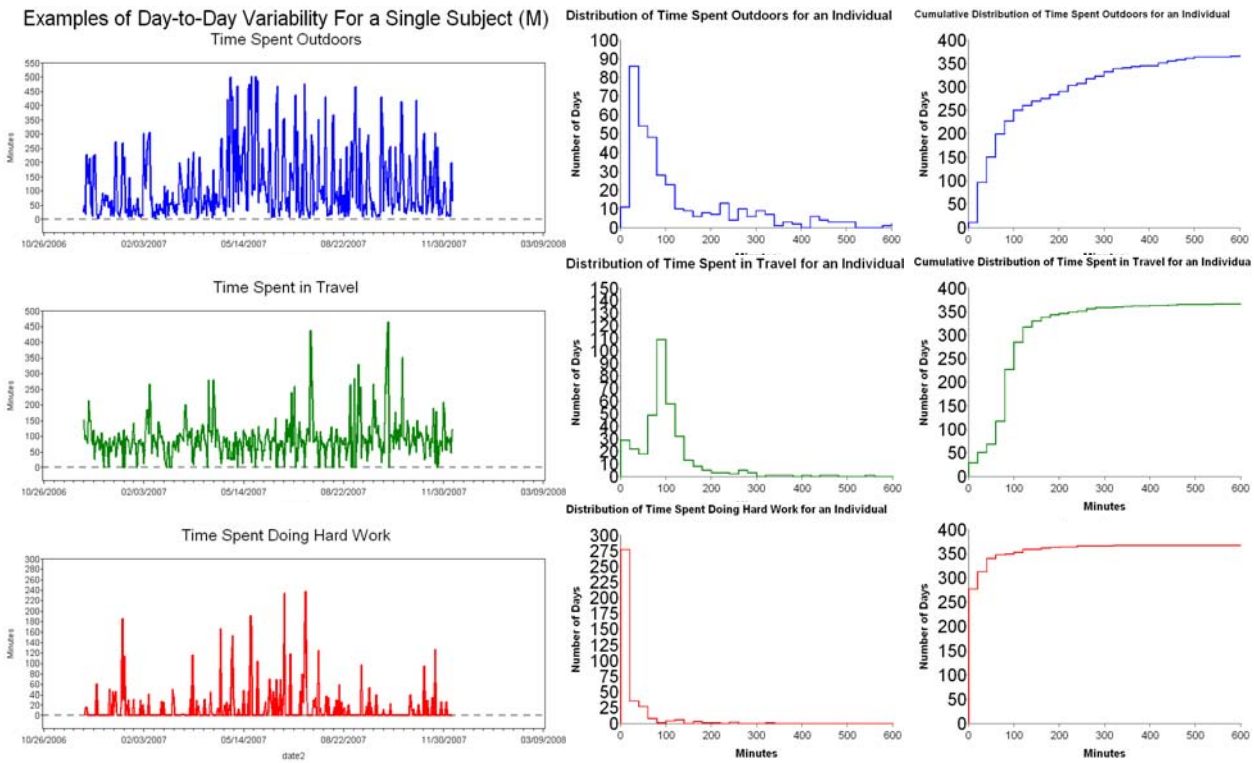

Figure 1. Time series and distributions of time spent in locations/activities for 367 days of data from a single male subject. Note high degree of interpersonal variability in behavior.

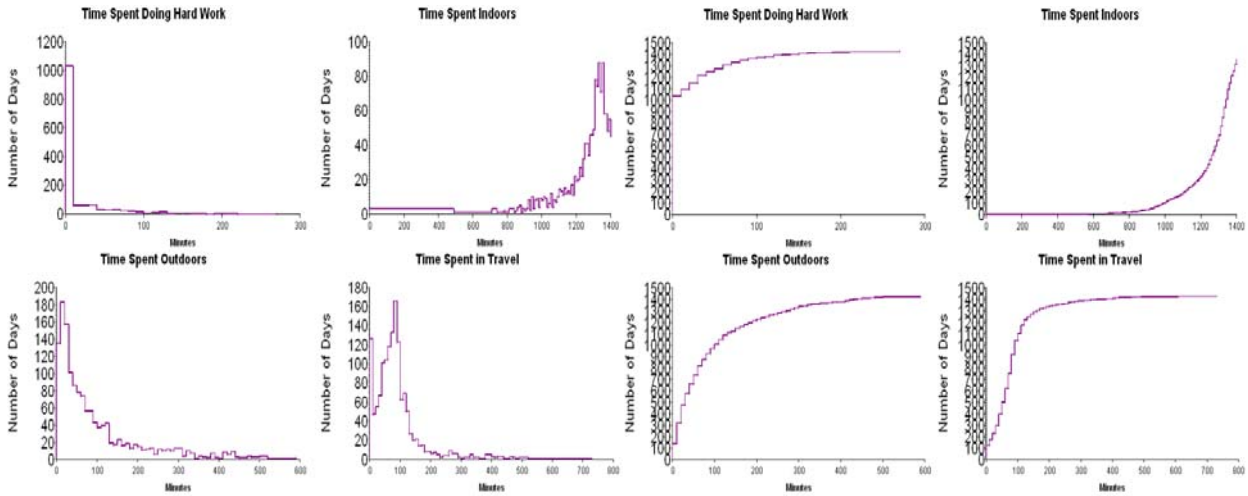

Figure 2. Distributions of time spent in different activities for all days for all subjects.

Variance and Autocorrelation Statistics

D, ICC, and A values for the population for time spent in different locations/activities are given in **Table 1**. Values of the ICC are lower than D; while A for the raw variables were higher than A for the scaled ranks. These trends were also consistent with observed tends in the Southern California data. Values were also calculated by gender (**Table 2**), temperature categories (**Table 3**), and day types (**Table 4**) where possible.

The D and ranked A values were compared to those calculated for children from the Southern California Chronic Ozone Exposure Study (SCCOES). The diversity (D) for this group of adults for outdoor time were higher than those calculated for the children (0.38 versus 0.19). The D values for travel time in the current study were also higher (0.18 in children versus 0.36 in this study). These differences reflect the increased heterogeneity in these variables in the studied adults versus the (relatively homogenous) studied children. The A values calculated for outdoor time in this study were virtually identical to those estimated using data from SCCOES.
In general, differences between D by temperature and day types were notable, even considering the small number subjects in this study. There were gender differences observed in D; the mechanism of these differences is unclear, but is likely influenced by the activity patterns of the female who was not a worker.

There were observed differences in A by temperature, but especially by day type. This is not unexpected, as it is reasonable that the behavior of working adults is more consistent day-to-day on workdays. These trends should be confirmed by analysis of other longitudinal data. Note however, that such differences in are only important when strongly episodic behavior or exposure is of interest. In general, the values of D are much more relevant to exposure.

Table 1. Variance and Autocorrelation Statistics: All Days/Subjects

Location/Activity	ICC	D	A (Raw)	A (Ranks)
Indoors	0.26	0.33	0.23	0.34
Outdoors	0.16	0.38	0.22	0.31
Travel	0.14	0.31	0.12	0.19
Hard Work	0.18	0.22	0.17	0.19

Table 2. Variance and Autocorrelation Statistics: By Gender

Location/Activity	ICC	D	A (Raw)	A (Ranks)
Males				
Indoors	0.36	0.54	0.25	0.16
Outdoors	0.14	0.22	0.24	0.22
Travel	0.36	0.46	0.17	0.08
Hard Work	-0.01	0.15	0.22	0.20
Females				
Indoors	0.08	0.09	0.37	0.25
Outdoors	0.07	0.27	0.35	0.18
Travel	0.05	0.16	0.15	0.11
Hard Work	0.15	0.24	0.16	0.21

Table 3. Variance and Autocorrelation Statistics: By Temperature

Location/Activity	ICC	D	A (Raw)	A (Ranks)
Days with max temp less than 50 degrees				
Indoors	0.37	0.37	0.23	0.19
Outdoors	0.20	0.27	0.33	0.18
Travel	0.23	0.37	0.20	0.09
Hard Work	0.21	0.31	0.14	0.14
Days with max temp greater or equal to 50 degrees				
Indoors	0.12	0.26	0.45	0.23
Outdoors	0.09	0.24	0.39	0.20
Travel	0.10	0.24	0.34	0.09
Hard Work	0.01	0.20	0.35	0.14

Table 4. Variance and Autocorrelation Statistics: By Daytype

Location/Activity	ICC	D	A (Raw)	A (Ranks)
Workday				
Indoors	0.37	0.47	0.56	0.05
Outdoors	0.19	0.31	0.78	0.07
Travel	0.45	0.47	0.30	0.01
Hard Work	0.20	0.25	0.53	-0.12
NonWorkday				
Indoors	0.12	0.21	0.59	0.24
Outdoors	0.11	0.14	0.60	0.19
Travel	0.09	0.24	0.38	0.08
Hard Work	0.06	0.07	0.43	0.18

Time Spent in Different Locations/Activities

The time spent in different locations/activities for different day types, seasons, temperature categories are presented in **Figures 3-6**. The effects of gender and precipitation were also studied. There were no significant differences for these categories, and thus plots are not shown. The plotted data represent all days for all subjects. The medians are represented by the midline of the boxes, the first and third quartiles by the ends of the boxes, and the means by the stars. The whiskers extend to cover data that lies beyond the boxed but within the quartiles plus 1.5 times the interquartile range. Points outside this range are plotted.

Results by day of the week and day type are presented in **Figure 3**. Day type (workday versus non-workday) was at least as good as day of the week in categorizing time/activities. This trend is similar to that seen in a recent analysis of the larger, cross-sectional database of diaries from The National Human Activity Pattern Survey (NHAPS, data not shown). That analysis indicated that a workday/non-workday was a better discriminator of time spent outside than a weekday/weekend split. As such, further comparisons are also presented for both workdays and non-workdays.

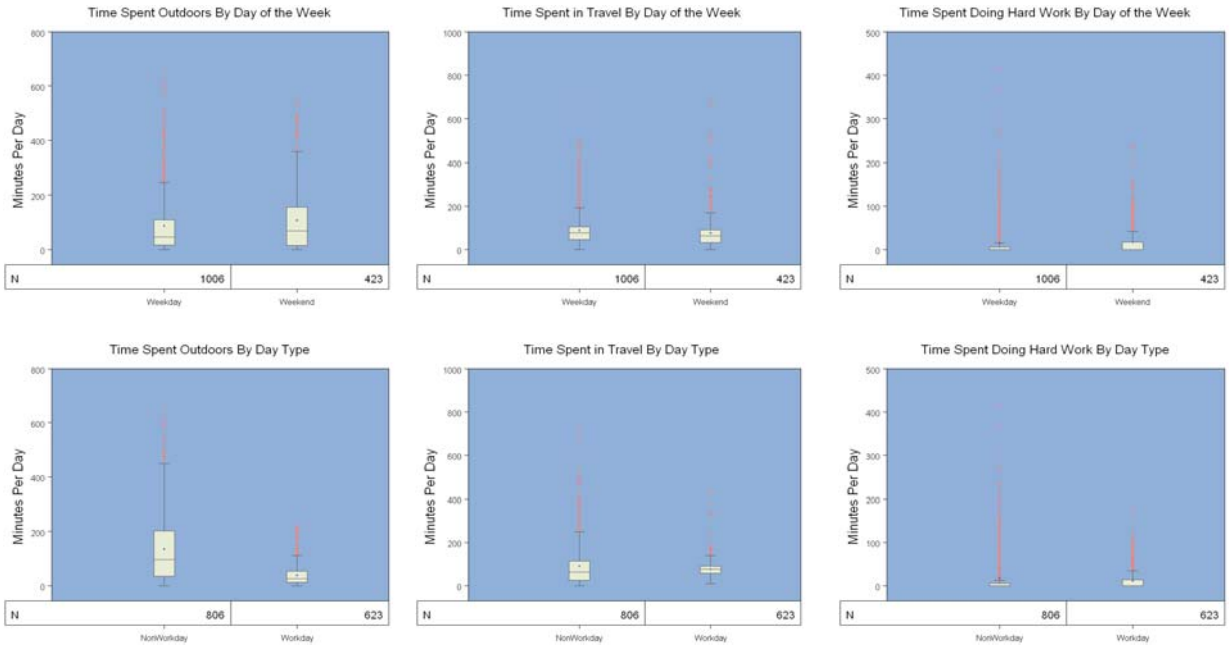

Figure 3. Time spent in different locations/activities as a function of day of the week, and daytype (workday versus non-workdays).

The effect of season on time spent in locations/activities is shown in **Figure 4**. Seasonal effects were apparent for time spent outdoors on non-workdays, and for time spent doing hard work. Travel was also affected by season, likely due to the large number of work-related travel days in the fall for this particular group of workers.

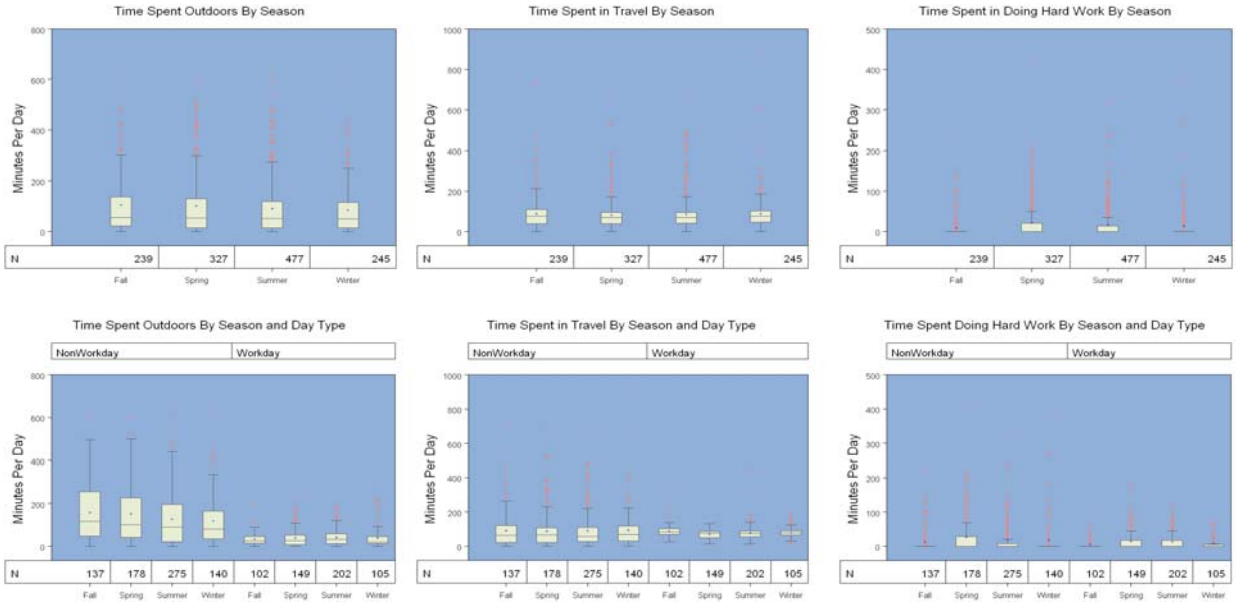

Figure 4. Time spent in different locations/activities as a function of season and daytype.

The effect of temperature category is shown in **Figure 5**. The temperature category was defined as warmer = maximum temperature greater than or equal to 75 degrees, colder= maximum temperature less than 75 degrees. Temperature category was better than or as good as season in discriminating behavior in time spent outdoors, even when day type was considered.

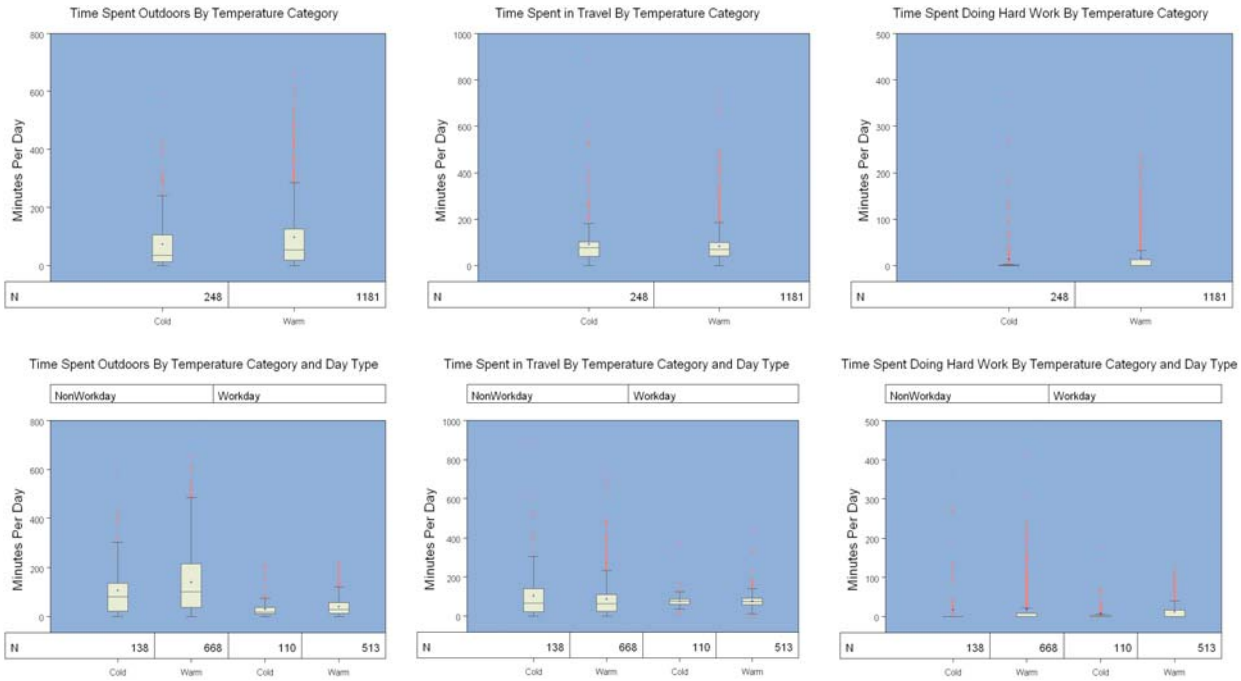

Figure 5. Time spent in different locations/activities as a function of temperature category (colder: max temp< 75 degrees, warmer: max temp≥ 75 degrees) and day type.

CONCLUSIONS

- The diversity (D) and autocorrelation (A) for this group of adults for outdoor time were higher than those calculated for children in a previous study. Thus these data provide some justification for considering age when considering D and A input values for EPA's exposure models.
- While the current data suggest possible effects of temperature, day type and gender on diversity (D) and autocorrelation (A), more data from this and other studies are needed to confirm these findings. Such results could aid in the fine-tuning of the longitudinal diary algorithm.
- The analysis of the time spent in locations was consistent with recent findings from cross-sectional diary studies indicating that workdays/non-workdays may be a better grouping for diary pools than weekdays/weekends.
- Temperature category was at least as good as season in discriminating behavior for this population for time spent outdoors, especially when day type was considered. Such breakdowns by temperature and day type may eliminate the need for diary pools for different seasons, providing larger pools for diary sampling on a given day. Further analysis with other time-activity data can confirm this trend.

FUTURE WORK

We plan to repeat this type of study periodically. Data will be compared to/combined with analyses of other available longitudinal time/location/activity studies.

DISCLAIMER

The information in this document has been funded wholly (or in part) by the U. S. Environmental Protection Agency (EPA contract 68-D-00-206). It has been subjected to review by the EPA and approved for publication. Approval does not signify that the contents necessarily reflect the views of the Agency, nor does mention of trade names or commercial products constitute endorsement or recommendation for use.

REFERENCES

Geyh AS, Xue J, Ozkaynak H, Spengler JD. (2000). The Harvard Southern California Chronic Ozone Exposure study: assessing ozone exposure of grade school-age children in two southern California communities. *Environ Health Perspect*. 108:265–270.

Glen G, Smith L, Isaacs K, McCurdy T, Langstaff J. (2008). A new method of longitudinal diary assembly for human exposure modeling. *J Expo Sci Environ Epidemiol*. 18(3):299-311.

McCurdy T, Glen G, Smith L, Lakkadi L. (2000). The National Exposure Research Laboratory's Consolidated Human Activity Database. *J Expo Anal Environ Epidemiol*. 10:566-78.

Isaacs et al. (2009) in original poster format:

Statistical Properties of Longitudinal Time-Activity Data for Use in EPA Exposure Models

Kristin Isaacs[1], Thomas McCurdy[2], April Errickson[3], Susan Forbes[3], Graham Glen[1], Stephen Graham[4], Lisa McCurdy[5], Melissa Nysewander[1], Luther Smith[1], Nicolle Tulve[2], and Daniel Vallero[2]

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ABSTRACT

Realistic simulation of longitudinal activity patterns is necessary for appropriately reproducing the frequency and duration of pollutant exposures in human exposure models. In EPA's exposure models, longitudinal activity diaries for simulated persons are constructed from the 1-day cross sectional activity diaries in the Consolidated Human Activity Database (CHAD). Recently, new algorithms have been developed to construct longitudinal diaries from CHAD diaries based on realistic variance and autocorrelation properties of diary characteristics relevant to pollutant exposure. Characteristics of particular interest include time spent in particular microenvironments and time spent in activities that produce high ventilation rates. However, few multi-day data are currently available for estimating accurate statistical properties for these quantities. Results from a recent time-activity study of 10 adults and one newborn child are presented here. The participants recorded their personal location and activity for two-week periods in each of four seasons in 2006 and 2007. The data were recorded 24 hours a day, in increments as small as one minute. Additional recording periods for these same individuals are expected in the future. The diaries for all subjects were assessed to calculate the between-person variance, the within-person variance, and the autocorrelation for various lags in the time spent in outdoor, residence, indoor (non-residence), and vehicle microenvironments, as well as for time spent performing high-METS activities. The effectiveness of various day-type definitions (for example, weekend versus weekday, or workday versus non-workday) for grouping similar diary days is examined. Seasonal variation in activity patterns is analyzed. These data have the potential to aid in the development of improved input variance and autocorrelation statistics for longitudinal diary assembly algorithms in EPA's human exposure models.

INTRODUCTION

Recently, new methods of assembling multi-day diaries in human exposure models from cross-sectional single-day diaries have been proposed that are based on the variance and autocorrelation statistics of the simulated population (Glen et al. 2007). Appropriately modeling intra- and interindividual variability using such algorithms may be essential in producing appropriate estimates of exposure. In addition, reproducing realistic autocorrelations in key diary properties may be required for the modeling of episodic exposure patterns.

Previously, longitudinal time activity-location data collected in children in the Southern California Chronic Ozone Exposure Study (Geyh et al. 1999) have been analyzed to obtain estimates of appropriate measures of variance and autocorrelation for use in the longitudinal algorithm. Data from a new study in adults are now presented.

BACKGROUND

Exposure models require construction of human activity diaries that cover the entire simulation period of a model run. This period is often several months, a year, or even longer. In EPA's models, human activity diaries are usually drawn from EPA's CHAD (Consolidated Human Activity Database; McCurdy et al., 2000; http://www.epa.gov/chadnet1), which typically includes just one day (24 hours) of activities from each person. A "longitudinal" diary is one that covers the same person over a long period of time. While the SHEDS modeling period may be of user-specified duration, it is assumed in this section to be one year, to provide a concrete example.

Recently, a new longitudinal diary assembly algorithm has been developed (Glen et al. 2007) based on the variance and autocorrelation properties of the modeled simulation. The new method requires the user to:

1) select the diary property most relevant to exposure for the current application (such as outdoor time or time spent in vehicles)

2) specify the D statistic, which relates the within-person and between-person variances for this diary property; and

3) specify the 1-day lag autocorrelation in this diary property.

The new method is currently implemented in EPA's APEX and SHEDS-Air Toxics models.

The new method allows the modeler to apportion the total variance in the key diary property into the within- and between-person variances $\sigma_w 2$ and $\sigma_b 2$ by specifying the D statistic, defined to be

$$D = \frac{\sigma_b^2}{\sigma^2} = \frac{\sigma_b^2}{\sigma_b^2 + \sigma_w^2}$$

D pertains to the population as a whole and is bounded by zero and one. A value of zero implies all persons have the same average behavior, whereas a value of one implies the greatest possible difference in mean behavior that is consistent with the total variance.

In addition to targeting the within-person and between-person variances through setting the D statistic, the new diary assembly method optionally allows targeting of the day-to-day autocorrelation. This is a measure of the tendency for similar diaries to occur on consecutive days. The lag-one autocorrelation in a variable y is for a person defined as

$$A = \sum_{j=1}^{N-1}(y_j - \bar{y})(y_{j+1} - \bar{y}) / \sum_{j=1}^{N}(y_j - \bar{y})^2$$

The population autocorrelation A is the mean of the A values for all individuals. Autocorrelation could be of interest to the exposure modeler if the concentration time series were strongly episodic, for example. In the diary assembly, a positive autocorrelation indicates a tendency for diaries with x-scores near each other to be used on consecutive days, while a negative autocorrelation indicates a tendency for dissimilar x-scores to be used on consecutive days. Some preliminary values of A have been derived from the same data that were used to estimate D (Glen et al., 2007).

METHODS

Activity Diary Study

Activity-location data were collected from 10 adults. Nine of the adults were working professionals; one was a stay-at-home parent. Nine of the adults recorded their personal location and activity for two-week periods in each of four seasons in 2006 and 2007. Additional data were collected in one of the male subjects in 1999, another male (the 10th adult) in 2002, and in one of the females in 2008 (collected during maternity leave). The data were recorded 24 hours a day, in increments as small as one minute. In this preliminary analysis, the time spent outdoors, indoors, in travel, and performing hard work each day were calculated from the diaries. "Hard work" was self-reported by each individual, as defined as activities requiring heavy breathing and/or sweating. Daily high temperatures and precipitation amounts were acquired for each day of the study.

Variance and Autocorrelation Statistics

Variance and lag-one autocorrelation statistics were calculated for the studied individuals. Variance statistics were estimated for both the raw measured variables (ie. time in minutes) and the scaled ranks of the variable for each person on a given day. The ratio of the between-person variance to the total variance (the sum of the between- and within-person variance) was calculated for the population. This ratio, calculated using the raw variables, is the intraclass correlation coefficient (ICC), while the same ratio, calculated using the ranks, is D, the diversity statistic. The autocorrelation A was also calculated using both the raw variables and the scaled ranks of the variables on each day for each person in the study.

Analysis of Time Spent in Locations/Activities

The longitudinal data were assessed to support decisions on optimal diary pools for exposure modeling. Time spent in each of the examined locations/activities were assessed as a function of day of the week (weekday versus weekend), day type (workday versus nonworkday), season, temperature, precipitation, and gender. These analyses were undertaken to assess the utility of different diary pool definitions. Optimal definitions of diary pools can adequately capture temporal patterns in activities while maximizing the number of activity diaries available for sampling on a given day for a simulated individual.

Differences between groups were assessed with the Wilcoxon signed rank test (for 2 groups) or the Kruskal-Wallis test (for more than 2 groups). The Wilcoxon rank sum (two-sample) test was used to test differences between genders.

Figure 1. Time series and distributions of time spent in locations/activities for 367 days of data from a single male subject. Note high degree of interpersonal variability in behavior.

Figure 2. Distributions of time spent in different activities for all days for all subjects.

Table 1. Variance and Autocorrelation Statistics: All Days/Subjects

Location/Activity	ICC	D	A (Raw)	A (Ranks)
Indoors	0.29	0.33	0.23	0.24
Outdoors	0.16	0.38	0.22	0.31
Travel	0.14	0.31	0.12	0.19
Hard Work	0.18	0.33	0.17	0.19

Table 2. Variance and Autocorrelation Statistics: By Gender

Location/Activity	ICC	D	A (Raw)	A (Ranks)
Males				
Indoors	0.36	0.54	0.25	0.16
Outdoors	0.14	0.22	0.24	0.22
Travel	0.36	0.46	0.17	0.08
Hard Work	-0.01	0.15	0.22	0.20
Females				
Indoors	0.08	0.09	0.37	0.25
Outdoors	0.07	0.27	0.35	0.18
Travel	0.05	0.16	0.15	0.11
Hard Work	0.15	0.24	0.16	0.21

Table 3. Variance and Autocorrelation Statistics: By Temperature

Location/Activity	ICC	D	A (Raw)	A (Ranks)
Days with max temp less than 50 degrees				
Indoors	0.37	0.37	0.23	0.19
Outdoors	0.20	0.27	0.33	0.16
Travel	0.23	0.37	0.20	0.09
Hard Work	0.21	0.31	0.14	0.14
Days with max temp greater or equal to 50 degrees				
Indoors	0.12	0.26	0.16	0.23
Outdoors	0.09	0.24	0.30	0.20
Travel	0.10	0.24	0.31	0.09
Hard Work	0.01	0.20	0.36	0.14

Table 4. Variance and Autocorrelation Statistics: By Daytype

Location/Activity	ICC	D	A (Raw)	A (Ranks)
Weekend	0.17	0.43	0.24	0.21
Outdoors	0.13	0.14	0.09	0.18
Travel	0.08	0.09	0.08	0.08
Hard Work	0.08	0.07	0.13	0.18
Weekday				
Indoors	0.31	0.37	0.24	0.21
Outdoors	0.16	0.38	0.22	0.31
Travel	0.14	0.31	0.12	0.19
Hard Work	0.18	0.33	0.17	0.19

Figure 3. Time spent in different locations/activities as a function of day of the week, and daytype (workday versus nonworkdays).

Figure 4. Time spent in different locations/activities as a function of season and daytype.

Figure 5. Time spent in different locations/activities as a function of temperature category (colder: max temp< 75 degrees, warmer: max temp≥ 75 degrees) and daytype.

RESULTS AND DISCUSSION

Individual Variability

Figure 1 shows an example of the individual variability in time spent in different locations/activities for a single male subject; a 367-day period from this subject is depicted. Distributions of time for this subject are also shown. These figures demonstrate the large amount of intra-individual variability that can be seen in longitudinal activity studies. Distributions of time spent in locations/activities for the population is shown in **Figure 4**.

Variance and Autocorrelation Statistics

D, ICC, and A values for the population for time spent in different locations/activities are given in **Table 1**. Values of the ICC are lower than D; while A for the raw variables were higher than A for the scaled ranks. These trends were also consistent with observed tends in the Southern California data. Values were also calculated by gender (**Table 2**), temperature categories (**Table 3**), and daytypes (**Table 4**) where possible.

The D and ranked A values were compared to those calculated for children from the Southern California Chronic Ozone Exposure Study (SCCOES). The diversity (D) for this group of adults for outdoor time were higher than those calculated for the children (0.38 versus 0.19). The D values for travel time in the current study were also higher (0.18 in children versus 0.36 in this study). These differences reflect the increased heterogeneity in these variable in the studied adults versus the (relatively homogenous) studied children. The A values calculated for outdoor time in this study were virtually identical to those estimated using data from SCCOES.

In general, differences between D by temperature and daytypes were notable, even considering the small number subjects in this study. There were gender differences observed in D; the mechanism of these differences is unclear, but are likely influenced by the activity patterns of the female who was not a worker.

There were observed differences in A by temperature, but especially by daytype. This is not unexpected, as it is reasonable that the behavior of working adults is more consistent day-to-day on workdays. These trends should be confirmed by analysis of other longitudinal data. Note however, that such differences in are only important when strongly episodic behavior or exposure is of interest. In general, the values of D are much more relevant to exposure.

Time Spent in Different Locations/Activities

The time spent in different locations/activities for different day types, seasons, temperature categories are presented in **Figures 3-6**. The effects of gender and precipitation were also studied. There were no significant differences for these categories, and thus plots are not shown.

The plotted data represent all days for all subjects. The medians are represented by the midline of the boxes, the first and third quartiles by the ends of the boxes, and the means by the stars. The whiskers extend to cover data that lies beyond the boxedbut within the quartiles plus 1.5 times the interquartile range. Points outside this range are plotted.

Results by day of the week and day type are presented in **Figure 3**. Day type (workday versus nonworkday) was at least as good as day of the week in categorizing time/activities. This trend is similar to that seen in a recent analysis of the larger, cross-sectional database of diaries from The National Human Activity Pattern Survey (NHAPS, data not shown). That analysis indicated that a workday/nonworkday was a better discriminator of time spent outside than a weekday/weekend split. As such, further comparisons are also presented for both workdays and nonworkdays.

The effect of season on time spent in locations/activities is shown in **Figure 4**. Seasonal effects were apparent for time spent outdoors on nonworkdays, and for time spent doing hard work. Travel was also affected by season, likely due to the large number of work-related travel days in the fall for this particular group of workers.

The effect of temperature category is shown in **Figure 5**. The temperature category was defined as warmer = maximum temperature greater than or equal to 75 degrees, colder= maximum temperature less than 75 degrees. Temperature category was better than or as good as season in discriminating behavior in time spent outdoors, even when daytype was considered.

CONCLUSIONS

- The diversity (D) and autocorrelation (A) for this group of adults for outdoor time were higher than those calculated for children in a previous study. Thus these data provide some justification for considering age when considering D and A input values for EPA's exposure models.
- While the current data suggest possible effects of temperature, daytype and gender on diversity (D) and autocorrelation (A), more data from this and other studies are needed to confirm these findings. Such results could aid in the fine-tuning of the longitudinal diary algorithm.
- The analysis of the time spent in locations was consistent with recent findings from from cross-sectional diary studies indicating that workdays/nonworkdays may be a better grouping for diary pools than weekdays/weekends.
- Temperature category was at least as good as season in discriminating behavior for this population for time spent outdoors, especially when daytype was considered. Such breakdowns by temperature and daytype may eliminate the need for diary pools different seasons, providing larger pools for diary sampling on a given day. Further analysis with other time-activity data can confirm this trend.

FUTURE WORK

- We plan to repeat this type of study periodically. Data will be compared to/combined with analyses of other available longitudinal time/location/activity studies.

DISCLAIMER

The information in this document has been funded wholly (or in part) by the U. S. Environmental Protection Agency (EPA contract 68-D-00-206). It has been subjected to review by the EPA and approved for publication. Approval does not signify that the contents necessarily reflect the views of the Agency, nor does mention of trade names or commercial products constitute endorsement or recommendation for use.

REFERENCES

Geyh A.S., Xue J., Ozkaynak H., and Spengler J.D. The Harvard Southern California Chronic Ozone Exposure study: assessing ozone exposure of gradeschool- age children in two southern California communities. Environ Health Perspect 2000: 108: 265–270.

Glen G., Smith L., Isaacs, K., and Langstaff, J. 2007. A new method of longitudinal diary assembly for human exposure modeling. *J Exposure Sci and Environmental Epi.*

Xue J., McCurdy T., Spengler J., and Ozkaynak, H. 2004. Understanding variability in time spent in selected locations for 7-12-year old children. *J Exposure Sci and Environmental Epi.* 14:222-233.

McCurdy, T., G. Glen, L. Smith, and Y. Lakdadi, 2000, The National Exposure Research Laboratory's Consolidated Human Activity Database. *J Expo Anal Environ Epidemiol* 10:566-78.

Appendix D

Microenvironmental Mapping

Figure D-1 presents how CHAD codes are mapped to the eight microenvironments used to model exposure in the CO REA. Table D-1 provides the CHAD activity codes used to identify when a simulated individual was in a work air district.

Figure D-1. Microenvironmental Mapping Input File Showing Mapping of CHAD Location Codes to the Eight Microenvironments for Application of APEX4.3 to Carbon Monoxide.

```
! Mapping of CHAD location codes to nine APEX microenvironments defined
! by Option 4 of Memorandum dated 12/8/2009.
CHAD Loc.  Description                              APEX
---------  ---------------------------------------------
U          Uncertain of correct code            =  -1  U
X          No data                              =  -1  U
30000      Residence, general                   =   1  H
30010      Your residence                       =   1  H
30020      Other residence                      =   1  H
30100      Residence, indoor                    =   1  H
30120      Your residence, indoor               =   1  H
30121      ..., kitchen                         =   1  H
30122      ..., living room or family room      =   1  H
30123      ..., dining room                     =   1  H
30124      ..., bathroom                        =   1  H
30125      ..., bedroom                         =   1  H
30126      ..., study or office                 =   1  H
30127      ..., basement                        =   1  H
30128      ..., utility or laundry room         =   1  H
30129      ..., other indoor                    =   1  H
30130      Other residence, indoor              =   1  H
30131      ..., kitchen                         =   1  H
30132      ..., living room or family room      =   1  H
30133      ..., dining room                     =   1  H
30134      ..., bathroom                        =   1  H
30135      ..., bedroom                         =   1  H
30136      ..., study or office                 =   1  H
30137      ..., basement                        =   1  H
30138      ..., utility or laundry room         =   1  H
30139      ..., other indoor                    =   1  H
30200      Residence, outdoor                   =   7  H
30210      Your residence, outdoor              =   7  H
30211      ..., pool or spa                     =   7  H
30219      ..., other outdoor                   =   7  H
30220      Other residence, outdoor             =   7  H
30221      ..., pool or spa                     =   7  H
30229      ..., other outdoor                   =   7  H
```

30300	Residential garage or carport	=	1	H
30310	..., indoor	=	1	H
30320	..., outdoor	=	7	H
30330	Your garage or carport	=	1	H
30331	..., indoor	=	1	H
30332	..., outdoor	=	7	H
30340	Other residential garage or carport	=	1	H
30341	..., indoor	=	1	H
30342	..., outdoor	=	7	H
30400	Residence, none of the above	=	1	H
31000	Travel, general	=	8	O
31100	Motorized travel	=	8	O
31110	Car	=	8	O
31120	Truck	=	8	O
31121	Truck (pickup or van)	=	8	O
31122	Truck (not pickup or van)	=	8	O
31130	Motorcycle or moped	=	5	O
31140	Bus	=	8	O
31150	Train or subway	=	8	O
31160	Airplane	=	0	O
31170	Boat	=	7	O
31171	Boat, motorized	=	7	O
31172	Boat, other	=	7	O
31200	Non-motorized travel	=	7	O
31210	Walk	=	7	O
31220	Bicycle or inline skates/skateboard	=	7	O
31230	In stroller or carried by adult	=	7	O
31300	Waiting for travel	=	7	O
31310	..., bus or train stop	=	5	O
31320	..., indoors	=	4	O
31900	Travel, other	=	8	O
31910	..., other vehicle	=	8	O
32000	Non-residence indoor, general	=	3	O
32100	Office building/ bank/ post office	=	3	O
32200	Industrial/ factory/ warehouse	=	4	O
32300	Grocery store/ convenience store	=	3	H
32400	Shopping mall/ non-grocery store	=	3	O
32500	Bar/ night club/ bowling alley	=	3	O
32510	Bar or night club	=	3	O
32520	Bowling alley	=	3	O
32600	Repair shop	=	3	O
32610	Auto repair shop/ gas station	=	2	O
32620	Other repair shop	=	3	O
32700	Indoor gym /health club	=	3	O
32800	Childcare facility	=	4	O
32810	..., house	=	1	O
32820	..., commercial	=	4	O
32900	Large public building	=	3	O
32910	Auditorium/ arena/ concert hall	=	3	O
32920	Library/ courtroom/ museum/ theater	=	3	O
33100	Laundromat	=	3	H

33200	Hospital/ medical care facility	=	4	O
33300	Barber/ hair dresser/ beauty parlor	=	3	H
33400	Indoors, moving among locations	=	3	O
33500	School	=	4	O
33600	Restaurant	=	3	O
33700	Church	=	4	H
33800	Hotel/ motel	=	3	O
33900	Dry cleaners	=	3	H
34100	Indoor parking garage	=	6	O
34200	Laboratory	=	3	O
34300	Indoor, none of the above	=	3	O
35000	Non-residence outdoor, general	=	7	O
35100	Sidewalk, street	=	5	O
35110	Within 10 yards of street	=	5	O
35200	Outdoor public parking lot /garage	=	6	O
35210	..., public garage	=	6	O
35220	..., parking lot	=	6	O
35300	Service station/ gas station	=	2	O
35400	Construction site	=	7	O
35500	Amusement park	=	7	O
35600	Playground	=	7	H
35610	..., school grounds	=	7	O
35620	..., public or park	=	7	H
35700	Stadium or amphitheater	=	7	O
35800	Park/ golf course	=	7	O
35810	Park	=	7	O
35820	Golf course	=	7	O
35900	Pool/ river/ lake	=	7	O
36100	Outdoor restaurant/ picnic	=	7	O
36200	Farm	=	7	O
36300	Outdoor, none of the above	=	7	O

Table D-1. CHAD Work Related Activity Codes Used To identify Work Air Districts.

<10> Work and Other Income Producing Activities
10000: work and other income producing activities, general
10100: work, general
- 10110: work, general, for organizational activities
  - 10111: work for professional/union organizations
  - 10112: work for special interest identity organizations
  - 10113: work for political party and civic participation
  - 10114: work for volunteer/ helping organizations
  - 10115: work of/ for religious groups
  - 10116: work for fraternal organizations
  - 10117: work for child/ youth/ family organizations
  - 10118: work for other organizations
- 10120: work, income-related only
- 10130: work, secondary (income-related)

10200: unemployment
10300: breaks

Appendix E

Analysis of CHAD Diaries for Time Spent in Vehicles.

The US Census Bureau (2009) provides an on-line facility for accessing the detailed census data included in their Summary File 3 (SF3). We obtained information on travel time to work for workers ages 16 years and over specific to Denver County, Colorado and Los Angeles, CA (US Census Bureau, 2009, Table P31). Staff converted the counts listed in Table P31 for trips to work places other than home into the percentages listed in Columns 2 and 3 of Table E-1. Although the P31 statistics apply to people 16 years or older, staff assumed that the statistics were generally applicable to people 18 years or older.

We next determined the number of 24-hour diaries in EPA's Consolidated Human Activity Database (CHAD) (US EPA, 2002) that met the following criteria: the subject was ≥18 years of age and the diary reported at least one minute in a motor vehicle between 6 am and 9 am. The number of these diaries that had in-vehicle times corresponding to the bins listed in Table E-1 are given in Column 4 and were converted to the percentages listed in Column 5.

Table E-1. Comparison of Denver and LA commuting characteristics (US Census, 2009) to time spent in motor vehicles using CHAD Diaries (US EPA, 2002).

Travel time (minutes) (1)	Percent of commuters according to SF3 census data for Denver County (2)	Percent of commuters according to SF3 census data for Los Angeles County (3)	24-hour diaries meeting inclusion criteria[a]	
			Number in CHAD (4)	Percent in CHAD (5)
1 to 9	10.3	7.8	563	9.79
10 to 19	32.0	25.9	1,676	29.16
20 to 29	24.2	21.0	1,068	18.58
30 to 39	18.6	21.4	1,111	19.33
40 to 59	9.3	13.6	665	11.57
60 to 89	3.8	7.0	407	7.08
90+	1.7	3.4	258	4.49
Total	100	100	5,748	100

Notes:
[a] Subjects are 18+ years of age. Diaries are those having ≥one minute in motor vehicle time spent between 6 AM and 9 AM.

References

US Census Bureau. (2009). American Fact Finder. Census Summary File 3 (SF3) – custom tables. Available at: www.factfinder.census.gov.

US EPA. (2002). EPA's Consolidated Human Activities Database. Available at: http://www.epa.gov/chad/.

Appendix F

Differences in Human Activity Patterns Between Individuals With and Without Cardiovascular Disease

The following presents a memorandum by Cohen et al. (1999) that was included in the Johnson et al. (2000) CO exposure assessment (see Appendix J of that report). It is in its original form, with some minor editing performed by staff for inclusion into the CO REA.

M E M O R A N D U M

TO: Harvey Richmond

FROM: Jonathan Cohen, Sergey Nikiforov, and Arlene Rosenbaum

DATE: January 15, 1999

SUBJECT: EPA 68-DO-0062 Work Assignment 2-24: Task 2: Evaluation of Differences in Human Activity Patterns Between Individuals With or Without Cardiovascular Disease

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EVALUATION OF DIFFERENCES IN HUMAN ACTIVITY PATTERNS BETWEEN INDIVIDUALS WITH OR WITHOUT CARDIOVASCULAR DISEASE

SUMMARY

Activity pattern data from the National Human Activity Pattern Survey were used to compare activity patterns and exertion distributions between subjects with or without angina. The diary survey provided a 24-hour diary of activities. Exertion rates for each person in the survey were simulated 100 times. For each person, the body weight was simulated from a log-normal distribution specific to the age and gender. The resting metabolic rate was simulated using a regression against body weight, with coefficients depending on age and gender. Finally, the exertion rate was simulated for each activity and person by multiplying the simulated resting metabolic rate by a MET exertion ratio with a distribution specific to each type of activity. The current version of the probabilistic NAAQS Exposure Model for Carbon Monoxide (pNEM/CO), described in Johnson (1998), begins with the same set of physiological equations and statistical distributions for probabilistic simulation of exposure. The pNEM/CO model uses the much broader Consolidated Human Activity Data Base (CHAD) and simulates additional physiological variables, such as the ventilation rate. The description of the relevant probabilistic and physiological equations in this memorandum is largely based on Johnson (1998); see that memorandum for more detailed information.

Differences between angina and non-angina subjects were evaluated for several summary statistics: average and 95th percentile of the maximum daily 8-hour exertion, percentage of time spent outdoors or in a vehicle, average percentage of time at light, moderate or heavy exertion

levels. Age and gender have very significant effects on these summary statistics of activity and exertion. Since angina patients tend to be much older and tend to include more females than the general population, it is very important to adjust for age and gender effects when comparing angina and non-angina groups. Otherwise, one cannot distinguish between the angina effect and the effects of age and gender. Statistical analyses comparing angina to non-angina subjects were performed, adjusting for age and gender either by stratification (comparing subjects in a given age/gender subgroup), or by fitting a general linear model (with separate terms for age, gender, and angina effects and their interactions). These analyses showed that, overall, angina subjects tended to have less extreme exertion levels. More specifically, the maximum 8-hour exertion energies tended to be lower, as did the percentages of time above moderate or high exertion rate thresholds. The percentages of time spent outdoors or in a vehicle were generally not statistically significantly different between angina and non-angina subjects.

The large sample of NHAPS subjects produced, in many cases, statistically significant differences in the exertion rate summaries between angina and non-angina subjects. However, those differences were generally numerically small compared to the mean values. Therefore we conclude that the differences in activity and exertion between angina and non-angina subjects, although statistically significant, are not large enough to severely impact the validity of pNEM/CO modeling results that do not adjust for an angina/non-angina difference.

METHODOLOGY

For these analyses we used the National Human Activity Pattern Survey (NHAPS) database, a telephone survey of human activity patterns conducted for the USEPA between October 1992 and September 1994 by the Survey Research Center at the University of Maryland. See Klepeis et al. (1996, 1998) and Tsang and Klepeis (1996) for more details about the NHAPS study and various statistical analyses of those data. The NHAPS data (Triplett, 1996) are included in CHAD. (Other CHAD studies did not include questions about cardiovascular disease and so could not be used for these analyses comparing angina and non-angina respondents.) A nationally representative sample of 9,386 respondents completed a detailed diary listing all their activities and locations over a 24-hour period (either from the previous day or a previous weekend day). A few respondents did not state their age and/or gender and their data was not used in our analysis. Our analysis used 9,149 of the surveys. Respondents were also asked demographic questions, including age and gender, and health questions, including whether or not they have been told by a doctor that they have angina: 243 respondents (2.6 percent) had angina. Respondents were asked about employment status (e.g. full-time, part-time, or unemployed) but not about their occupation. Other follow-up questions (not used in our analyses) related to the respondent’s exposure to either water or air pollution on the diary day. For each household, the respondent was randomly selected to be either the adult or child (under 18) with the next birthday; an adult provided proxy responses for a child.

The EPA report (Klepeis, Tsang and Behar, 1996), Section 3, shows that the sample is reasonably representative of the national population with respect to gender and age distributions. The NHAPS population slightly underrepresented males (46 % NHAPS compared to 49 % from the 1990 Census). The fraction of weekend (Saturday or Sunday) respondents was 33 %, close to

the desired ratio of 2:7, but Thursdays, Fridays and Saturdays were underrepresented. The Fall season was significantly underrepresented. The database includes weights to adjust for varying selection probabilities, due to differences in the numbers of adults or children in a selected household, the numbers of non-business phones in a household, the numbers of non-business telephones in each census region, and to the survey stratification between weekend or weekdays and between children and adults. Based on discussions with the EPA WAM, it was decided that the weights would not be used in these analyses; the raw, unweighted data would be treated as an approximately simple random sample. Note that the statistical weights: 1) were not used in the pNEM/CO exposure modeling effort, 2) could not be used to accurately estimate standard errors of weighted means, and 3) were close to 1 for most respondents.

In pNEM/CO, each activity is assigned a probability distribution of the exertion rate (kilo-calories per minute). For this analysis, the 24-hour sequence of exertion rates was simulated 100 times for each person in the NHAPS sample; the sequence of activities is fixed but the simulated exertion rates vary. Following both CHAD and the exposure modeling methodology currently used in pNEM/CO, a constant simulated exertion rate is assumed throughout the time period of each listed activity in the 24-hour diary. If the individual repeats the same activity at a later time, with other activities intervening, the exertion rate is simulated again. SAS statistical software was used for the simulations and for the statistical analysis.

The assigned exertion rate distribution depends upon the type of activity, and the occupation, age, gender, and body weight of the respondent. The exertion rate (kilo-calories/minute = kcal/min), also referred to as average energy expenditure rate, EE, is defined as the product

$$EE = MET \times RMR.$$

MET is the metabolic equivalent of work, a dimensionless ratio (i.e., exertion compared to the resting metabolic rate) specific to each activity, and, in some cases, to an age group. RMR is the resting metabolic rate (kcal/min), approximately equal to the basal metabolic rate. We used the same set of MET statistical distributions supplied by Tom McCurdy that are currently used in pNEM/CO (and CHAD). For the work activity “at main job,” the MET distribution depends on the occupation. Since occupation was not recorded in NHAPS, we followed the pNEM methodology and randomly selected the occupation based on census fractions of persons in each activity. The same occupation is assumed throughout a simulated person-day (in case the person repeats the work activity), but is randomly selected again for the next simulated person-day. Note that this procedure may bias the comparison between angina and non-angina subjects, since the distribution of occupation is expected to differ between angina subjects and the general population.

A single RMR value was simulated to represent each person-day. Thus the same person would have 100 simulated RMRs, one for each of the 100 days simulated. This reflects the assumption that each person represents the activity pattern for a group of persons with the same age and gender. As in pNEM/CO, RMR was simulated from a normal distribution where the mean is of the form a + b (Body Mass), and the standard deviation is the constant _. The values of a, b, and _ are the values derived by Schofield (1985) for 12 age/gender combinations (this assumes basal

metabolic rate is equivalent to resting metabolic rate). In turn, the body mass was simulated using the log-normal distributions estimated by Brainard and Burmaster (1992) and Burmaster and Crouch (1994). The parameters of the log-normal distributions depend on age and gender.

The statistical analysis used the following summary statistics of the activity and simulated exertion patterns for each person in the NHAPS study. The selection of these summary statistics was based on recommendations from the EPA WAM:

- Average maximum 8-hour energy expenditure. For each 8-hour period in a simulated person-day, starting every 10 minutes, integrate the simulated EE to give the energy expenditure in Mcal (millions of calories), i.e. sum the products of activity time and energy expenditure rate. For each simulated day, compute the maximum 8-hour energy expenditure, treating the simulated day in circular fashion so that the respondent is assumed to repeat exactly the same activity and exertion rate patterns on the day after the diary day. For example, the simulated activities for the period starting at 10 pm are assumed to follow the reported sequence of activities for the diary day from 10 pm to midnight and then the reported sequence from the beginning of the diary day until 6 am. To represent a typical value for the selected person, compute the average maximum 8-hour energy expenditure across the 100 simulations.

- 95th percentile maximum 8-hour energy expenditure. As in the last bullet, compute the maximum 8-hour energy expenditure for each simulated day. To represent an extreme value for the selected person, compute the fifth highest maximum 8-hour energy expenditure among the 100 simulations.

- Percentage time spent outdoors. This number is the same for all simulations, since the activity patterns are held constant.

- Percentage time spent in a vehicle. This number is the same for all simulations, since the activity patterns are held constant.

- Percentage time spent outdoors or in a vehicle. This number is the same for all simulations, since the activity patterns are held constant.

- Average percentage time with exertion rate above 2.39 kcal/min. For each simulated person-day, the percentage of that day with an EE (rate) above the threshold level of 2.39 kcal/min was computed; then, this percentage was averaged over the 100 simulations for that person. The statistic estimates the percentage time spent at or above the threshold exertion rate level over a long period, assuming the daily activity pattern was the same every day. The threshold of 2.39 kcal/min, which equals 0.010 MJ/min, represents “light” exertion (see below).

- Average percentage time with exertion rate above 5.97 kcal/min. The threshold of 5.97 kcal/min, which equals 0.025 MJ/min, represents “moderate” exertion (see below).

- Average percentage time with exertion rate above 9.55 kcal/min. The threshold of 9.55 kcal/min, which equals 0.040 MJ/min, represents “heavy” exertion (see below).

The exertion rate thresholds used for these analysis were originally defined as 0.010, 0.025, and 0.040 mega-joules per minute, but were converted into the more commonly used calorie units (1 joule equals 0.2388 calories). For purposes of exposure assessment, exertion categories (i.e., light, moderate, or heavy exertion) are more usefully defined by the ventilation rate VE (liters air per minute) rather than the energy expenditure rate EE (kilo-calories per minute). For the EPA's Ozone Criteria Document, the Environmental Criteria and Assessment Office categorized VE into ranges of 0-23, 24-43, 44-63, and 64+ liters of air per minute to define light, moderate, heavy, and very heavy exertion, respectively (based on a reference male adult with body weight 70 kg). To convert from EE to VE, EE is first multiplied by an energy conversion factor, ECF, to give the oxygen uptake rate VO2 (liters of oxygen per minute). ECF varies across the population, but is approximately 0.2 liters oxygen per kcal (Esmail, Bhambhani, and Brintnell, 1995). The "ventilatory equivalent rate" (VER) is the dimensionless ratio of VE (liters per minute) divided by VO2 (liters per minute) and has typical values from about 24 for light exertion to about 32 for peak exertion. Thus the selected energy expenditure rates are approximately equivalent to the following ventilation rates:

EE = 0.010 MJ/min = 2.39 kcal/min:
VE = EE _ ECF _ VER = 2.39 _ 0.2 _ 24 = 11.5 liters/min = light exertion

EE = 0.025 MJ/min = 5.97 kcal/min:
VE = EE _ ECF _ VER = 5.97 _ 0.2 _ 28 = 33.4 liters/min = moderate exertion

EE = 0.040 MJ/min = 9.55 kcal/min:
VE = EE _ ECF _ VER = 9.55 _ 0.2 _ 32 = 61.1 liters/min = heavy exertion

The selected summary statistics were computed for each of the 243 angina subjects and 8,906 non-angina subjects in the NHAPS study. A statistical analysis compared the distributions of these summary statistics for persons with and without angina. For each summary statistic we compared the mean values between the angina and non-angina groups using standard t tests. The significance level (p-value) for the difference in means was computed using the Smith-Satterthwaite procedure, that tests for no difference in population means assuming that the two populations are normally distributed but may have different variances. P-values at or below 0.05 denote significant differences at the five percent level of significance. By the central limit theorem, the p-values for the t test comparisons should be reasonably accurate for the large samples used in the overall analyses, even if the normality assumption does not hold, but the p-values will be less accurate for the analyses of specific gender and age subgroups. We also compared variances using a standard F test, that assumes normality of the two populations.

Since the normality assumption may not be a sufficiently good approximation, we also applied two non-parametric tests that do not require specific parametric distributions. The non-parametric Wilcoxon test, also known as the Mann-Whitney-Wilcoxon test or the Rank Sum Test, was used to compare the central tendencies of the two distributions. This test assumes only that the populations have the same distributional shape, which may or may not be the normal distribution, but the distribution of values for angina population might be shifted by some

constant value, and thus might have a different median than the non-angina population. The Kolmogorov-Smirnov test was used to evaluate any possible differences between the two distributions, whether due to differences in means, medians, variances, or any other features of the distribution. This test uses the maximum absolute difference between the two cumulative distribution functions, assuming only that these distributions are continuous.

The mean, variance, median, and distribution function comparisons were made for all persons combined, separately for males and females, and then separately for four age groups within the male and female subgroups. Age groupings were chosen to include approximately 25 percent of angina subjects in each group. Separate comparisons for males and females are needed to distinguish whether any overall differences in exertion or activity are explained by the fact that angina subjects are more likely to be female than in the general population. Since activity patterns and exertion rates differ between males and females, any overall difference between the angina and non-angina groups might be explained by the greater propensity for females to get angina, rather than the direct effect of angina. Similarly, the subsetting by age group evaluates the effect of the different age distributions for angina subjects compared to the general population (angina subjects tend to be much older). This statistical analysis does not, and cannot, address questions as to whether the angina causes the change in exertion or activity patterns, or *vice versa*. We only examine whether or not the summary statistics of activity and exertion patterns are different for the two populations.

A general linear model approach was also used as an alternative method of adjusting for the effects of age and gender on the angina/non-angina comparison. We focused attention on a relatively simple statistical model with cubic terms in age (a simple linear function of age fitted poorly), gender, interactions between age and gender, and a single term for the effect of angina:

$$\begin{aligned}\text{Summary Statistic} = \; & I(\text{male})\{_ + _(\text{age}) + _(\text{age})^2 + _(\text{age})^3\} \\ & + I(\text{female})\{_ + _(\text{age}) + _(\text{age})^2 + _(\text{age})^3\} \\ & + _I(\text{angina}) + \text{error}\end{aligned}$$

where: I(male) = 1 for males, 0 for females; I(female) = 1 for females, 0 for males; I(angina) = 1 for persons having angina, 0 for persons not having angina. The errors are assumed to be normally distributed, statistically independent, and have mean zero and some constant variance.

This statistical model assumes that the expected value of the summary statistic is a cubic function of age, but is a different function for males and females. The selected model has the same coefficient for the cubic term for males and females, but different coefficients for the intercept, linear, and quadratic effects. The model also assumes that having angina changes the mean by a constant amount, which is the same factor for all age groups and both genders. A more sophisticated model might allow for interactions between angina and the age and gender variables, to allow for the possibility that the angina effect varies by gender and/or age. Note, however, that our statistical analysis clearly showed that age and gender were much more significant predictors of exertion patterns than the angina indicator, explaining most of the variability in the summary statistics.

Project resources were insufficient for a detailed exploration of alternative statistical models. We tried using logarithmic transformations to improve the model fit, but could not reasonably use such models in view of the large number of cases where the observed summary statistic was zero (the logarithm is then undefined). The model fit for the selected model (without taking logarithms) varied with the summary statistic. R squared goodness-of-fit statistics were extremely low, less than 0.05, for the percentages of time spent outdoors and/or in a vehicle. For the summary statistics based on the maximum 8-hour exertion and the percentages of time above exertion rate thresholds, the R squared statistics ranged from a poor fit, 0.25, to a fairly good fit, 0.48. The cases of poor fitting models may be because the selected statistical models poorly represent the relationship between age, gender, and angina and the activity/exertion summary statistic and/or because the activity/exertion pattern varies substantially between people of the same age, gender, and angina status.

RESULTS

Age, Gender, and Angina Disease Distributions

Table 1 shows the number of subjects with or without angina by gender and by age group. The four age groups were chosen to have approximately the same numbers of angina subjects. The strong association between angina and age is illustrated by the fact that 52/243 = 21 % of angina subjects are under 55 but 6877/8906 = 77 % of non-angina subjects are under 55. Angina subjects tend to be significantly older than the general population. The association between angina and gender is weaker. 103/243 = 42.3 % of angina subjects are male, but 4116/8906 = 46.2 % of non-angina subjects are male.

Overall Comparisons of Activity and Exertion Summary Statistics between Angina and Non-Angina Subjects

Table 2 compares the means between the angina and non-angina subjects, without stratification by age or gender. The average and 95th percentile of the maximum eight hour exertion has a statistically significantly lower mean for angina subjects. Furthermore, for each of the exertion levels 2.39, 5.97, and 9.55 kcal/min (0.010, 0.025, and 0.040 MJ/min), the mean percentage of time above each level was statistically significantly lower for the angina subjects. Non-angina subjects spend an average of 2.8 percent of their time doing activities requiring moderate or higher levels of exertion, defined by exertion rates above 5.97 kcal/min (0.025 MJ/min); angina subjects spend an average of 2.2 percent of their time doing such activities. All subjects spend over 75 percent of time in light or sedentary activities, with extertion rates below 2.39 kcal/min, including sleeping. All these exertion distribution comparisons show that angina subjects tend to do activities with less exertion than the general population. However, since the summary analyses in Table 2 do not take into account the marked differences between the age and gender distributions of angina and non-angina subjects, the lower exertion rates could be associated with the tendency for angina subjects to be older (and female) rather than the disease itself. The average percentages of time spent outdoors are nearly identical, and are not statistically significantly different between angina and non-angina subjects, but angina subjects spend statistically significantly less time in vehicles (4.5 % rather than 5.5 %, on average).

Table 2 compares the standard deviations using a F-test based on the variance ratio for angina vs. non-angina subjects. In most cases the F tests show statistically significantly different variances (and, therefore, standard deviations).

Table 2 also uses the non-parametric Wilcoxon test to compare the central tendencies of the two distributions without the normality assumption required by the T test. Corresponding to the T test comparisons, the Wilcoxon test finds that the angina and non-angina distributions are significantly different in almost all cases; the angina subjects have a lower median value for each of the selected summary statistics. Exceptions are for the average maximum 8-hour exertion, just significant at the 7 % level, and the percentage of time spent outdoors, which has a non-significant p-value of 22 %.

Finally, Table 2 compares the distribution functions using the Kolmogorov-Smironov test. The distributions are statistically significantly different at the five and one percent levels in all cases except for the percentage of time spent outdoors, which shows no significant difference. For that variable, the T and Wilcoxon tests showed no statistically significant differences in central tendency although the F test showed a statistically significant difference in the population variances. If the population variances are different, so are the two distribution functions. The discrepancy between the F and Kolmogorov-Smirnov tests is partly explained by the fact that the F test is very sensitive to the assumption of normal distributions, whereas the Kolmogorov-Smirnov test only requires the distributions to be continuous. (Both tests assume that the mean and variances are constant for each population, which is inconsistent with the variation of the means and variances with age and gender shown in the stratified analyses in Tables 3 and 4.) The discrepancy is also partly explained by the fact that the Kolmogorov-Smirnov test is less powerful (less likely to detect a difference) than the other tests, because it makes the fewest assumptions and considers the widest class of alternative hypotheses.

Stratified Comparisons of Activity and Exertion Summary Statistics between Angina and Non-Angina Subjects

Tables 3 and 4 provide the same statistical comparisons as Table 2, stratified by gender and age group. The results show the mean values for the selected summary statistics are not consistently lower for each age and gender subgroup of angina subjects. For example, Table 2 showed that the angina subjects had a lower overall mean value of the average maximum 8-hour exertion than the non-angina subjects. Tables 3 and 4 show the mean is actually higher for angina subjects 0-54 of either gender and for males 75 or older. The mean average maximum 8-hour exertions are consistently higher for males of all age groups, with or without angina, compared to females. Similar patterns are found for the 95th percentile of the maximum 8-hour exertion.

The comparisons of the percentages of time spent outdoors or in a vehicle also vary across age and gender subgroups. The largest, and most surprising, angina vs. non-angina difference is for the mean percentage of time spent outdoors by 0-54 year old males: angina subjects have a mean of 17 % compared to the mean of 9 % for non-angina subjects. However the angina subjects in the 55-64 and 65-74 age groups of either gender spend less time outdoors, on average, than non-

angina subjects.

The Table 3 and 4 comparisons of the mean percentages of time above the light, moderate or high exertion levels show a variety of patterns for different age groups, genders, and exertion levels.

Comparisons of Activity and Exertion Summary Statistics between Angina and Non-Angina Subjects Adjusted for Age and Gender Differences

Table 5 gives the results of the fitted general linear model. As explained above, the fitted model assumes that for each gender, the average value of the summary statistic is a cubic function of age. Furthermore, having angina changes the expected value by a fixed amount, which is assumed to be the same value for every age and gender. This angina effect is the coefficient reported in the table, together with its standard error and p-value. P-values less than or equal to 0.05 indicate summary statistics where the angina effect was statistically significant at the 5 percent significance level. The angina coefficient can be thought of as the effect of angina after adjusting for age and gender. The effects of age and gender are not reported, but in all cases were extremely statistically significant compared to the angina effect.

Table 5 also reports the R squared goodness-of-fit statistic, which is the squared correlation between the observed and predicted values. R squared values vary from 0 (the worst possible fit) to 1 (a perfect fit), and are often interpreted as the fraction of the variability in the dependent variable (summary statistic) that is explained by the regression model.

The first two rows of Table 5 show that the angina effect on the average and 95th percentile maximum 8-hour exertion is a statistically significant reduction (at the 6 and 1 % levels, respectively) for angina subjects compared to non-angina subjects. However, these reductions of 0.04 Mcal and 0.16 Mcal are small when compared to the overall mean values of 1.4 and 2.3 Mcal (non-angina subjects) reported in Table 2. The next three rows show that angina subjects tend to spend a little more time (0.7 percentage points) outdoors and a little less time (0.5 percentage points) in a vehicle compared to non-angina subjects; those differences are not statistically significant. The last four rows show that angina subjects tend to spend less time at moderate or high levels of exertion, after adjusting for age and gender, although the differences are at most 1 percentage point and are not statistically significant. For example, the unadjusted average percentage time above 2.39 kcal/min (0.010 MJ/min) was 23.5 % for non-angina subjects (Table 2), and the effect of angina is to reduce the expected percentage of time by 0.7. As shown in Tables 3 and 4, this is due to average reductions of up to 5 percentage points for ages 55 and older but increases of 6 (males) and 2 (females) percentage points for the 0-54 age group.

R squared goodness-of-fit statistics were extremely low, 0.05 or less, for the percentages of time spent outdoors and/or in a vehicle. Thus the regression models for those percentages give very poor predictions. There are two possible reasons for this. First, the combination of age, gender, and angina status may be strongly associated with the percentages of time spent outdoors or in a vehicle but the assumed form of the regression model may poorly represent the functional

relationship. Second, the combination of age, gender, and angina status may be poorly associated with the percentages of time spent outdoors or in a vehicle so that those activity percentages vary mainly with the effects of factors other than age, gender, and angina status. In either case, those regression models are not recommended for use in predicting the activity percentages.

For the summary statistics based on the maximum 8-hour exertion and the percentages of time above exertion rate thresholds, the R squared statistics ranged from a poor fit, 0.25, to a reasonably good fit, 0.48. As above, the cases of poor fitting models may be because the selected statistical models poorly represent the relationship between age, gender, and angina and the activity/exertion summary statistic and/or because the activity/exertion pattern varies substantially between people of the same age, gender, and angina status. Alternative general linear models, or the more sophisticated generalized linear models, could be developed to improve the predictive ability of the statistical models.

REFERENCES

Brainard, J., and Burmaster, D. E. 1992. "Bivariate Distributions for Height and Weight of Men and Women in the United States." *Risk Analysis* 12:2, pp. 267-275.

Burmaster, D. E., and Crouch, E. A. C. 1994. "Lognormal Distributions of Body Weight as a Function of Age for Males and Females in the United States." *Risk Analysis* 17:4, pp. 499-508.

Esmail, Bhambhani, and Brintnell. 1995. "Gender Differences in Work Performance on the Baltimore Therapeutic Equipment Work Simulator." *Amer. J. Occup. Therapy* 49, pp. 405-411.

Johnson, T. R, 1998. *Proposed Probabilistic Algorithm for Estimating Ventilation Rate in the 1998 Version of pNEM/CO*. Memorandum submitted to EPA (September 25, 1998).

Klepeis, N. E., Tsang, A. E., and Behar, J. V. 1996. *Analysis of the National Human Activity Pattern Survey (NHAPS) Respondents from a Standpoint of Exposure Assessment*. EPA/600/R-96/074.

Klepeis, N. E., Nelson, W. C., Tsang, A. M., Robinson, J. P., Hern, S. C., Engelmann, W. H., and Behar, J. V. 1998. "The National Human Activity Pattern Survey (NHAPS): Data Collection Methodology and Selected Results." Submitted to *Journal of Exposure Analysis and Environmental Epidemiology*.

Schofield, W. N. 1985. "Predicting Basal Metabolic Rate, New Standards, and Review of Previous Work." *Hum Nutr Clin Nutr*. 39C (Supp 1), pp. 5-41.

Triplett, T. 1996. National Human Activity Pattern Survey, CD-ROM Version 2.0. University of Maryland Survey Research Center.

Tsang, A. M. and Klepeis, N. E. 1996. *Descriptive Statistics Tables from a Detailed Analysis of the National Human Activity Pattern Survey (NHAPS) Data*. EPA/600/R-96/148.

Table 1. Distribution of subjects according to their age, gender and disease status

	Males			Females			All		
Age Group	**Angina (%)**	**Non-angina (%)**	**All**	**Angina (%)**	**Non-angina (%)**	**All**	**Angina (%)**	**Non-angina (%)**	**All**
0-54	35 (1.0)	3307 (98.9)	3342	17 (0.5)	3570 (95.5)	3587	52 (0.8)	6877 (99.2)	6929
55-64	28 (6.5)	400 (93.5)	428	28 (5.4)	491 (94.6)	519	56 (5.9)	891 (94.1)	947
65-74	23 (7.9)	267 (92.1)	290	48 (9.6)	450 (91.4)	498	71 (9.0)	717 (91.0)	788
75+	17 (10.7)	142 (89.3)	159	47 (14.4)	279 (85.6)	326	64 (13.2)	421 (86.8)	485
Total	103 (2.4)	4116 (97.6)	4219	140 (2.8)	4790 (97.2)	4930	243 (2.6)	8906 (97.4)	9149
This table was modified by staff on 2-22-10 from the below original version due to issues related to the conversion from Word Perfect to Microsoft Word.									

Gender	**Males**			**Females**			**All**		
Age group	**Angina(%)**	**Non-angina(%)**	**All**	**Angina(%)**	**Non-angina(%)**	**All**	**Angina(%)**	**Non-angina(%)**	**All**
	35 (1.0)	3307 (98.9)	3342	17 (0.5)	3570 (95.5)	3587	52 (0.8)	6877 (99.2)	6929
	28 (6.5)	400 (93.5)	428	28 (5.4)	491 (94.6)	519	56 (5.9)	891 (94.1)	947
	23 (7.9)	267 (92.1)	290	48 (9.6)	450 (91.4)	498	71 (9.0)	717 (91.0)	788
	17 (10.7)	142 (89.3)	159	47 (14.4)	279 (85.6)	326	64 (13.2)	421 (86.8)	485
	103 (2.4)	4116 (97.6)	4219	140 (2.8)	4790 (97.2)	4930	243 (2.6)	8906 (97.4)	9149

Table 2. Statistical Tests for the Association between Angina and Various Variables Representing Physical Exertion. All

Variable	T Test Comparison of Means			F Test Comparison of Standard Deviations			Wilcoxon Test	Kolmogorov -Smirnov Test
	Mean Angina	Mean Non-angina	P-value	St. Dev. Angina	St. Dev. Non-angina	P-value	P-value	P-value
Average maximum 8hr exertion (Mcal)	1.28	1.40	0.00	0.48	0.49	0.68	0.00	0.00
Ninety fifth percentile of maximum 8hr exertion (Mcal)	1.87	2.25	0.00	0.97	1.13	0.00	0.00	0.00
Percentage of time spent outdoors	6.73	6.74	0.99	12.87	11.63	0.02	0.22	0.23
Percentage of time spent in vehicle	4.55	5.55	0.01	6.19	7.13	0.00	0.00	0.00
Percentage of time spent outdoors or in vehicle	11.27	12.29	0.27	14.33	13.45	0.15	0.00	0.00
Average percentage of time with exertion above 2.39 kcal/min = 0.010MJ/min (light)	19.98	23.53	0.00	13.56	13.78	0.75	0.00	0.00
Average percentage of time with exertion above 5.97 kcal/min = 0.025 MJ/ min (moderate)	2.17	2.78	0.01	3.68	3.56	0.46	0.00	0.00
Average percentage of time with exertion above 9.55 kcal/min	0.213	0.406	0.00	0.554	0.761	0.00	0.00	0.00

= 0.040 MJ/ min (heavy)

Table 3. Statistical Tests for the Association between Angina and Various Variables Representing Physical Exertion. Males

Variable	Age Group	T Test Comparison of Means			F Test Comparison of Standard Deviations			Wilcoxon Test	Kolmogorov-Smirnov Test
		Mean value Angina	Mean Non-angina	P-value	St. Dev. Angina	St. Dev. Non-angina	P-value	P-value	P-value
Average maximum 8hr exertion (Mcal)	0-54	1.85	1.59		0.49	0.55		0.02	0.02
	55-64	0.00			0.34			0.01	0.02
	65-74	1.48	1.77		0.48	0.48		0.41	0.82
	75+	0.00			0.86			0.51	0.95
		1.39	1.49		0.47	0.48			
		0.36			0.96				
		1.27	1.20		0.44	0.42			
		0.52			0.65				
Ninety fifth percentile of maximum 8hr exertion (Mcal)	0-54	2.94	2.68		1.06	1.30		0.22	0.06
	55-64	0.17			0.13			0.02	0.03
	65-74	2.40	2.90		1.21	1.14		0.26	0.63
	75+	0.04			0.61			0.55	0.88
		1.91	2.17		0.78	0.94			
		0.14			0.31				
		1.73	1.67		0.69	0.76			
		0.71			0.68				
Percentage of time spent outdoors	0-54	16.86	8.85		19.16	13.75		0.01	0.01
	55-64	0.02			0.00			0.65	1.00
	65-74	9.28	10.02		14.26	13.86		0.12	0.13

Table 3. Statistical Tests for the Association between Angina and Various Variables Representing Physical Exertion. Males

Variable	Age Group	T Test Comparison of Means			F Test Comparison of Standard Deviations			Wilcoxon Test	Kolmogorov-Smirnov Test
		Mean Angina	Mean Non-angina	P-value	St. Dev. Angina	St. Dev. Non-angina	P-value	P-value	P-value
	75+	0.79			0.78			0.58	0.66
		6.43	10.40		11.38	14.34			
		0.13			0.20				
		8.23	7.09		12.63	10.05			
		0.72			0.16				
Percentage of time spent in vehicle	0-54	5.96	6.09		7.55	8.10		0.89	0.52
	55-64	0.92			0.63			0.18	0.19
	65-74	3.99	6.87		3.78	9.63		0.82	0.93
	75+	0.00			0.00			0.44	0.54
		7.20	5.88		9.04	7.80			
		0.51			0.29				
		2.29	3.34		2.54	3.94			
		0.14			0.05				
Percentage of time spent outdoors or in vehicle	0-54	22.83	14.94		19.28	15.52		0.02	0.02
	55-64	0.02			0.05			0.17	0.22
	65-74	13.27	16.89		15.30	16.18		0.19	0.29
	75+	0.24			0.76			0.69	0.41
		13.63	16.29		15.87	15.91			
		0.45			1.00				
		10.51	10.43		12.86	10.39			
		0.98			0.19				
Average	0-54	34.76	27.78		13.33	15.18		0.02	0.05

Table 3. Statistical Tests for the Association between Angina and Various Variables Representing Physical Exertion. Males

Variable	Age Group	T Test Comparison of Means			F Test Comparison of Standard Deviations			Wilcoxon Test	Kolmogorov -Smirnov Test
		Mean Angina	Mean Non-angina	P-value	St. Dev. Angina	St. Dev. Non-angina	P-value	P-value	P-value
percentage of time	55-64	0.00			0.34			0.06	0.14
with exertion	65-74	24.60	30.07		14.51	12.03		0.67	0.84
above 2.39	75+	0.06			0.14			0.39	0.74
kcal/min		21.92	23.32		13.23	12.48			
= 0.010MJ/min		0.63			0.64				
(light)		18.24	15.87		11.13	10.37			
		0.41			0.63				
Average	0-54	6.63	4.46		6.37	4.31		0.02	0.01
percentage of time	55-64	0.05			0.00			0.01	0.01
with exertion	65-74	3.43	5.44		3.55	4.41		0.20	0.40
above 5.97	75+	0.01			0.17			0.43	0.59
kcal/min		2.27	3.27		2.47	3.46			
= 0.025 MJ/ min		0.08			0.06				
(moderate)		2.02	1.62		2.42	2.41			
		0.53			0.92				
Average	0-54	0.662	0.735		0.792	0.986		0.55	0.15
percentage of time	55-64	0.59			0.11			0.05	0.17
with exertion	65-74	0.565	0.846		1.068	1.222		0.06	0.04
above 9.55	75+	0.19			0.40			0.55	0.96
kcal/min		0.155	0.388		0.361	0.716			
= 0.040 MJ/ min		0.01			0.00				
(heavy)		0.132	0.157		0.331	0.512			

Table 3. Statistical Tests for the Association between Angina and Various Variables Representing Physical Exertion. Males

Variable	Age Group	T Test Comparison of Means			F Test Comparison of Standard Deviations			Wilcoxon Test	Kolmogorov -Smirnov Test
		Mean value Angina	Mean Non-angina	P-value	St. Dev. Angina	St. Dev. Non-angina	P-value	P-value	P-value
		0.79			0.05				

Table 4. Statistical Tests for the Association between Angina and Various Variables Representing Physical Exertion. Females

Variable	Age Group	T Test Comparison of Means			F Test Comparison of Standard Deviations			Wilcoxon Test	Kolmogorov -Smirnov Test
		Mean value Angina	Mean Non-angina	P-value	St. Dev. Angina	St. Dev. Non-angina	P-value	P-value	P-value
Average maximum 8hr exertion (Mcal)	0-54	1.30	1.27		0.31	0.38	0.34	0.72	0.73
	55-64	0.69			0.32	0.33	1.00	0.56	0.22
	65-74	1.21	1.27		0.30	0.31	0.94	0.31	0.44
	75+	0.33			0.33	0.30	0.34	0.44	0.66
		1.05	1.10						
		0.29							
		0.96	0.98						
		0.63							
Ninety fifth	0-54	1.98	2.01		0.82	0.91		0.99	0.86

Table 4. Statistical Tests for the Association between Angina and Various Variables Representing Physical Exertion. Females

Variable	Age Group	T Test Comparison of Means			F Test Comparison of Standard Deviations			Wilcoxon Test	Kolmogorov-Smirnov Test
		Mean Angina	Mean Non-angina	P-value	St. Dev. Angina	St. Dev. Non-angina	P-value	P-value	P-value
percentile of maximum 8hr exertion (Mcal)	55-64	0.86			0.69			0.33	0.28
	65-74	1.79	1.92		0.80	0.77		0.31	0.62
	75+	0.41			0.68			0.43	0.47
		1.42	1.51		0.53	0.57			
		0.26			0.57				
		1.27	1.31		0.56	0.52			
		0.59			0.43				
Percentage of time spent outdoors	0-54	3.64	5.11		7.29	9.58		0.43	0.91
	55-64	0.42			0.20			0.23	0.63
	65-74	4.31	4.59		9.53	8.22		0.49	0.53
	75+	0.88			0.23			0.76	1.00
		2.84	4.14		5.51	7.34			
		0.14			0.02				
		3.79	2.27		12.04	4.60			
		0.40			0.00				
Percentage of time spent in vehicle	0-54	4.54	5.35		5.48	5.98		0.40	0.35
	55-64	0.55			0.72			0.06	0.12
	65-74	4.21	5.60		7.53	7.23		0.15	0.19
	75+	0.35			0.71			0.72	0.96
		5.26	4.15		5.94	6.18			
		0.23			0.77				
		2.82	2.94		4.37	4.34			
		0.86			0.91				
Percentage of time	0-54	8.18	10.46		9.93	11.27		0.18	0.27

Table 4. Statistical Tests for the Association between Angina and Various Variables Representing Physical Exertion. Females

Variable	Age Group	T Test Comparison of Means			F Test Comparison of Standard Deviations			Wilcoxon Test	Kolmogorov -Smirnov Test
		Mean Angina	Mean Non-angina	P-value	St. Dev. Angina	St. Dev. Non-angina	P-value	P-value	P-value
spent outdoors or in vehicle	55-64	0.36			0.57			0.04	0.05
	65-74	8.52	10.18		12.15	10.42		0.99	0.86
	75+	0.48			0.22			0.77	0.97
		8.10	8.29		8.21	9.38			
		0.88			0.26				
		6.61	5.21		12.36	6.25			
		0.45			0.00				
Average percentage of time with exertion above 2.39 kcal/min = 0.010MJ/min (light)	0-54	23.50	21.40		12.28	12.15		0.41	0.69
	55-64	0.49			0.86			0.51	0.54
	65-74	19.04	21.04		10.34	10.47		0.43	0.76
	75+	0.33			1.00			0.51	0.89
		13.97	15.46		8.45	9.53			
		0.26			0.31				
		11.31	11.84		9.75	8.61			
		0.73			0.24				
Average percentage of time with exertion above 5.97 kcal/min = 0.025 MJ/ min (moderate)	0-54	1.44	1.59		1.66	1.97		0.73	0.74
	55-64	0.71			0.44			0.04	0.06
	65-74	0.79	1.31		1.27	2.07		0.51	0.88
	75+	0.05			0.00			0.84	0.67
		0.65	0.68		1.35	1.56			
		0.87			0.22				
		0.75	0.43		1.73	1.31			
		0.23			0.01				
Average	0-54	0.101	0.184		0.170	0.324		0.63	0.80

Table 4. Statistical Tests for the Association between Angina and Various Variables Representing Physical Exertion. Females

Variable	Age Group	T Test Comparison of Means			F Test Comparison of Standard Deviations			Wilcoxon Test	Kolmogorov -Smirnov Test
		Mean Angina	Mean Non-angina	P-value	St. Dev. Angina	St. Dev. Non-angina	P-value	P-value	P-value
percentage of time	55-64	0.06			0.00			0.67	1.00
with exertion	65-74	0.095	0.093		0.277	0.198		0.85	0.99
above 9.55	75+	0.96			0.01			0.28	0.83
kcal/min		0.028	0.030		0.076	0.110			
= 0.040 MJ/ min		0.89			0.00				
(heavy)		0.025	0.016		0.075	0.077			
		0.44			0.90				

Table 5. General Linear Models for the Association between Angina and Various Variables Representing Physical Exertion.

Variable	Angina Coefficient[1]	Standard Error	P-value	R squared
Average maximum 8hr exertion (Mcal)	-0.0445	0.0237	0.0608	0.4819
Ninety fifth percentile of maximum 8hr exertion (Mcal)	-0.1553	0.0581	0.0075	0.4114
Percentage of time spent outdoors	+0.6975	0.7648	0.3618	0.0388
Percentage of time spent in vehicle	-0.4805	0.4679	0.3045	0.0325
Percentage of time spent outdoors or in vehicle	+0.2170	0.8777	0.8047	0.0520
Average percentage of time with exertion above 2.39 kcal/min = 0.010 MJ/min (light)	-0.7359	0.6996	0.2929	0.4239
Average percentage of time with exertion above 5.97 kcal/min = 0.025 MJ/min (moderate)	-0.1730	0.1910	0.3650	0.3570
Average percentage of time with exertion above 9.55 kcal/min = 0.040 MJ/min (heavy)	-0.0933	0.0439	0.0334	0.2494

1. The angina coefficient is the expected difference (angina minus non-angina) between the summary statistic for angina and non-angina subjects of the same age and gender.

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