Risk and Exposure Assessment to Support the Review of the Carbon Monoxide Primary National Ambient Air Quality Standards:

Second External Review Draft

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U.S. Environmental Protection Agency
Office of Air Quality Planning and Standards
Health and Environmental Impacts Division
Research Triangle Park, North Carolina

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Table of Contents

List of Figures

List of Tables

1 INTRODUCTION

This draft 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). This draft report, *Risk and Exposure Assessment to Support the Review of the Carbon Monoxide Primary National Ambient Air Quality Standards: Second External Review Draft*, is being provided to the Clean Air Scientific Advisory Committee (CASAC) CO Panel and the public for review in advance of a public meeting of the CASAC CO panel planned for March 22-23, 2010. Following that meeting, we will take CASAC and public comments into account in preparing the final document. We plan to complete the final Risk and Exposure Assessment report in May 2010. Given the significant time constraints of this review,[1] results of the assessment are provided in this document without substantial interpretation. Rather, interpretative discussion of these results is provided in the draft Policy Assessment.

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 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

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

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) 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, 2010a), 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 second draft Risk and Exposure Assessment (REA) describing the quantitative assessment conducted by

[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 is not intending to do a quantitative risk assessment for the secondary standard review.

the Agency to support the review of the primary CO standards. This second draft document is a concise presentation of the methods, key results, observations, and related uncertainties associated with the quantitative analyses performed. This REA builds upon the health effects evidence presented in the final ISA, as well as CASAC advice (Brain and Samet, 2009; Brain and Samet, 2010) 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 draft REA (US EPA, 2009b). The final REA will reflect consideration of CASAC and public comments on this second draft REA. The final REA will be completed by May 28, 2010, consistent with the court order governing the schedule for completion of this review. The court order also specifies 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 final ISA and final REA will inform the policy assessment and rulemaking steps that will lead to final decisions on the CO NAAQS. The policy assessment will be described in a Policy Assessment (hereafter, "PA") document, which will include staff analysis of the scientific basis for alternative policy options for consideration by the Administrator prior to rulemaking. The PA will integrate and interpret information from the ISA and the REA to frame policy options for consideration by the Administrator. The PA is intended to help "bridge the gap" between the Agency's scientific and technical assessments, presented in the ISA and REA and the judgments required of the Administrator in determining whether it is appropriate to retain or revise the standards. The PA is also intended to facilitate 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. A draft PA is being prepared (USEPA, 2010b) for release for review by CASAC, as well as for public comment, in conjunction with CASAC review and public comment of this document.

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 exercise-induced aggravation of angina 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).

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 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%. 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). While these indoor sources were shown to contribute to total CO exposure, it was determined to be of limited utility in the risk assessment because these 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 on a draft exposure analysis methodology document, Estimation of Carbon Monoxide Exposures and Associated Carboxyhemoglobin Levels in Denver Residents using pNEM/CO (Version 2.0) (Mauderly, 1999; Johnson, 1999). 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 the Total Risk Integrated Methodology (TRIM) system. A subsequent draft technical report (Johnson et al., 2000) was produced documenting the application of the CO

[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).

[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 (USEPA, 1992).

exposure and dose modeling methodology for two study areas (Denver and Los Angeles). The exposure and dose estimates were obtained by applying pNEM/CO version 2.1, a predecessor to APEX, to adults with IHD residing within each urban area.[5] 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.[6] 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) concentrations, 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% upon just meeting the current 8-hour standard.[7] 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 an important contributor to COHb though these impacted 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 much greater percentage than that estimated in the absence of indoor sources (i.e., <1%).

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[5] This is consistent with the demographic group modeled in the 1992 assessment described above (Johnson et al., 1992; USEPA, 1994), and drew from updated information with regard to prevalence demographics (Johnson et al., 2000, p. section 2.5.2).

[6] 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.

[7] 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).

1.3 CURRENT REVIEW, CASAC ADVICE AND PUBLIC COMMENT

In preparing the Scope and Methods Plan for the REA, we considered the scientific evidence presented in the first draft ISA (US EPA, 2009c) and the key science policy issues raised in the IRP (US EPA, 2008b). EPA held a consultation with CASAC to solicit comments on the Scope and Methods Plan during a May 2009 CASAC meeting at which CASAC also provided comments on the first draft ISA (Brain, 2009). Public comments were also requested (74 FR 15265). Those CASAC and public comments were considered in advance of the conduct of the analyses and results presented in the first draft REA (US EPA, 2009b).

As a result of the notable limitations in available ambient monitoring and microenvironmental concentration data, staff implemented a much-simplified, screening-level approach to assess population exposure and dose for the first draft APEX/CO REA (US EPA, 2009b). Two urban study areas, Denver and Los Angeles, were defined as all census tracts within 20 km of a single fixed-site monitor, using the design value monitor (i.e., the monitor recording the highest concentration in each area) for the specified year of the assessment. Therefore, ambient monitoring data associated with the site measuring the highest CO concentrations were applied to all people within the surrounding study area. This was the case for scenarios that included *as is* air quality (year 2006 for either location) and air quality adjusted to just meeting the current standard (adjusted from 1995 for Denver and from 1997 for Los Angeles). In the first draft REA, no adjustment was made for spatial variability in ambient concentrations across each area and at most two microenvironments were included in the exposure model simulations (in-vehicle and all others). The in-vehicle microenvironmental factor was constrained to a point estimate of 2.0, that is, these microenvironmental concentrations would always be twice that observed at the single ambient monitor. In the design of the assessment, it was noted that this focus on high concentration CO monitors and other model simplifications would have a tendency to produce higher CO exposures in most simulated persons than results generated from the 2000 pNEM/CO assessment. The results were consistent with this statement. The estimated percent of the population at any COHb level was greater in the first draft REA than that estimated by Johnson et al. (2000).

On November 16-17, 2009, the CASAC CO panel met to discuss the first draft REA. The final written comments and recommendations were provided to EPA in February 2010 (Brain and Samet, 2010). The design of the current second draft REA builds upon these recommendations from CASAC, information presented in the final ISA (US EPA, 2010a), as well as comments made by the public.[8] Specifically in this assessment, EPA has:

[8] Public Comments on the first draft REA were submitted to the docket for this review and also presented in November, 2009 at the CASAC meeting.

- Expanded each of the modeling domains to include a greater number of ambient monitors used as input to APEX;
- Increased the number of microenvironments modeled from two to eight;
- Improved the representation of variability in estimated microenvironmental concentrations, including in-vehicles;
- Included an algorithm that adjusts for spatial heterogeneity in estimated outdoor concentrations across each model domain;
- Implemented the mass-balance model for estimating concentrations in all indoor microenvironments;
- Implemented the algorithm that allows commuters to experience home-tract and work-tract ambient concentrations; and
- Expanded the at-risk population to address the undiagnosed persons with CHD.

The purpose of this second draft REA is to seek CASAC review and public comment regarding our characterization of the results presented considering the improvements made to the assessment design and inputs used, and CASAC's advice on the role of this assessment in informing the current review of the CO NAAQS.

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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 relevant microenvironments (section 2.2), identification of at-risk populations (section 2.3), the dose metric (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.

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). However, the focus of this REA, which is 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).

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

The exposure modeling in this assessment does not quantitatively estimate the contribution of indoor sources to an individual's total exposure and dose. This assessment does however qualitatively draw upon available information regarding potential indoor source contributions to estimated population exposure and dose (described in section 2.2 below).

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 in Baltimore, MD (ISA, section 3.6.5.2; Chang et al., 2000). On average, the indoor-to-ambient and outdoor-to-ambient concentration ratios were about one, though most of the 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 were generally above one, few ratios were 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/microenvironmental-to-ambient and outdoor-to-ambient concentration ratios is the result of spatial and temporal variability in outdoor concentrations with respect to simultaneously measured ambient concentrations at fixed-site monitors, and also reflects the impact of lag time associated with attaining steady state relationships, as well as potential presence of non-ambient sources.

Typically the highest CO exposure concentrations are experienced while inside vehicles. Because motor vehicles 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).[2] Given this relationship, it should not be surprising that while about 8% of a person's time per day is spent in transit, 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).

A similar influence of mobile source-influenced microenvironments 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).[3] 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 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.

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

[3] 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).

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, indicates 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).[4] Under these stated conditions, the I/O ratio would ultimately converge to unity.

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

[4] See section 3.6.2 of the ISA.

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 likely 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 value 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 define this relationship.

Although not the focus of this review, indoor sources such as gas stoves and environmental tobacco smoke can, where present, also be important contributors to total CO exposure and may be of concern for such at-risk populations as individuals with cardiovascular disease, among others (see section 2.3 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, as summarized in section 1.2 above.[5]

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) ambient and nonambient[6] CO exposures (ISA, section 4.5).[7] Levels of endogenous COHb 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. 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 accumulation of COHb in some circumstances. 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

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[5] 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.

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

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

disorders that can make an individual more susceptible to the potential adverse effects of low levels of CO, especially during exercise.

As described in section 4.4.7 below, 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 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)[8] 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

[8] 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).

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[9] 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).

Other populations considered to be potentially at increased risk relative to the general population due to gender differences, aging, or preexisting disease or because of the use of medications or alterations in their environment, include fetuses and young infants; the elderly, especially those with compromised cardiovascular function; individuals with hematologic diseases (e.g., anemia) that affect oxygen-carrying capacity or transport in the blood; those with chronic obstructive pulmonary disease; people using medicinal or recreational drugs with central nervous system depressant properties; individuals exposed to other chemical substances that increase endogenous formation of CO; individuals who have not adapted to high altitude and are exposed to a combination of high altitude and CO; and people that spend a substantial amount of time on or near heavily traveled which may contribute to higher CO exposures (ISA, section 5.7). 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). Additionally, although there are no controlled human exposure or epidemiological studies examining potential CO-induced effects in people suffering with anemia, it is reasonable to assume that the potential combination of hypoxic effects of CO together with reduced oxygen availability and/or elevated

[9] 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., coronary heart disease [CHD], CAD, myocardial infarction, and angina), congestive heart failure, and disturbances of cardiac rhythm (dysrhythmias and arryhthmias) (2000 AQCD, p. 7-7).

baseline COHb levels in people suffering with anemia[10] may make this population susceptible to CO-induced effects (ISA, section 5.7.1.4). Asthma and COPD are other oxygen-limiting diseases which may be exacerbated by CO-related oxygen limitation. Other individuals that may be potentially susceptible to CO are those 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).

Based on the current evidence, most particularly with regard to quantitative information of COHb levels and association with specific health effects, the primary target population for purposes of the quantitative assessment described in this document is adults with CHD (also known as ischemic heart disease IHD or CAD), both diagnosed and undiagnosed.[11] Little empirical evidence is available by which to specify health effects associated with 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 limited and does not include COHb levels related to health effects in these groups. 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 population simulated in this assessment is individuals with CAD (diagnosed and undiagnosed and inclusive of individuals with angina pectoris and heart attacks). We note, however, that the larger cardiovascular disease population and the potential susceptibility of other populations is further considered with regard to the review of the CO NAAQS in the draft Policy Assessment document (US EPA, 2010b).

2.5 HEALTH ENDPOINTS

Carbon monoxide elicits various health effects by binding to reduced iron in heme proteins and altering the functioning of a number of heme proteins (ISA, sections 4.6 and 5.1). 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.

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

[11] 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).

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[12] and effects on exercise duration and maximal aerobic capacity observed in controlled exposure studies of healthy adults.[13] As noted in the ISA, the decreases in exercise duration

[12] 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. 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.

[13] 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).

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[14] 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[15] (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-min 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) and 253 ppm (range 143-357 ppm). After the 50- to 70-min 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%[16] 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).

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

[15] 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).

[16] 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).

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., 1991; Allred et al., 1989b). 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., 1991; Allred et al., 1989b). 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; Allred et al., 1989a,1989b, 1991).

Other controlled human exposure studies (Adams et al. 1988, Anderson et al. 1973, Kleinman et al. 1989, Kleinman et al., 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., 1990; Sheps et al., 1987). 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 in study protocols and analytical methods do not allow for an informative pooled or quantitative metaanalysis 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).

2.5.2 Other Effects

Other health effects for which the evidence is suggestive of causal relationships with short-term 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 a relationship close to ambient levels is less clear (ISA, pp. 5-49). Further, the evidence indicates that healthy adults may be protected against such effects at ambient levels through compensatory responses such as increased cardiac output and cerebral blood flow, although these compensatory mechanisms may be impaired among susceptible groups, including those with reduced cardiovascular function (ISA, section 5.3.3). Limited evidence indicates an association of CO exposure during early pregnancy with pre-term births and birth defects (ISA, p. 2-8). New epidemiologic studies report positive associations for CO-induced lung-related 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).

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; Brain and Samet, 2010). As summarized in section 1.2 above, 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 (USEPA, 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 exercise-induced aggravation of angina in controlled human exposure studies involving short-term (shorter than 8 hours) exposures of patients with diagnosed CAD[17] 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 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 (USEPA, 1991, 2000, 2010). The strength of the evidence more broadly continues to support the use of

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

COHb level as the internal dose metric for assessing exposure to ambient levels of CO and characterizing associated potential for 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 population expected to experience maximum end-of-hour COHb levels of interest based on findings of those studies.

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).[18] These studies have observed associations between ambient monitor CO concentrations and increases in emergency department visits and hospital admissions for cardiovascular effects (ISA, sections 5.2.1.9). While these studies are coherent with the controlled human exposure studies (ISA, section 5.2.6), we recognize a number of uncertainties that complicate their use for our purposes in a quantitative risk assessment (ISA, pp. 2-14 to 2-17, section 5.2.3).

- "This [epidemiological] evidence for ischemia-related outcomes is coherent with effects observed in controlled human exposure studies, although uncertainty regarding the extent of reduced O_2 delivery to tissues following exposure to ambient CO concentrations contributes to the uncertainty in quantitative interpretation of effect estimates." [ISA, p. 2-14]
- The correlation between concentrations of CO and other combustion-related pollutants "complicates the quantitative interpretation of effect estimates in these studies to apportion the relative extent to which CO at ambient concentrations is independently associated with cardiovascular or other effects, and the extent to which CO acts as a marker for the effects of another combustion-related pollutant or mix of pollutants." [ISA, p. 2-16]
- Although the epidemiological evidence indicates that CO associations generally remain robust in copollutant models, uncertainty associated with the use of these models "complicates quantitative interpretation of the effect estimates reported in epidemiologic studies" [ISA, p. 2-16]
- "Some of these uncertainties [identified in 2000 AQCD] remain and complicate the quantitative interpretation of the epidemiologic findings, particularly regarding the biological plausibility of health effects occurring at COHb levels resulting from exposures to ambient CO concentrations measured at AQS monitors." [ISA, p. 2-17]

Given these uncertainties in the quantitative interpretation of epidemiological studies for CO, and the longstanding body of evidence that links exposures to effects through an internal dose metric, we have characterized health risk of ambient CO exposures in this assessment using

[18] One additional controlled exposure study in CHD patients is available since the last review. It involved higher COHb levels than the study by Allred et al (1989a, 1989b, 1991) and is not a focus here (2000 AQCD, section 6.2.2).

estimates of associated COHb levels and a benchmark level approach, with benchmarks identified in consideration of the controlled human exposure literature.[19] This is supported by the fact that COHb levels reported in controlled human exposure studies are a better indicator of personal exposure and dose than concentrations measured at fixed site ambient monitors. In addition, controlled human exposure studies can examine the health effects of short-term exposure to CO in the absence of co-pollutants that can confound results in epidemiologic analyses; thus, health effects observed in controlled human exposure studies can confidently be attributed to a defined COHb dose level resulting from short-term CO exposures.

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,b, 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 3.9%[20] 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 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).

[19] 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.

[20] 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,b, 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 COHb estimates developed in this assessment with attention to both COHb in absolute terms and also based on consideration of the contribution to COHb associated with ambient CO exposures. With regard to COHb in absolute terms, 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 (USEPA, 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 draft 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 draft Policy Assessment document. We additionally consider, however, the observations of the multi-laboratory clinical study with regard to response per 1% increase in COHb concentration 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).[21]

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 for cardiovascular effects in individuals with CHD when exposed to CO. That is, 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 draft Policy Assessment.

2.7 KEY OBSERVATIONS

Presented below are key observations regarding the current evidence for health effects associated with exposures to ambient CO.

- 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.
- 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 CO health effects of concern.
- 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 to contribute susceptibility to CO effects. Other populations potentially at risk include individuals with diseases such as chronic

[21] 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).

obstructive pulmonary disease (COPD), anemia, or diabetes, and individuals in prenatal or elderly life stages.

- Cardiovascular effects are the health endpoint for which the evidence is strongest and indicative of a likely causal relationship with CO exposures. Other endpoints for which the evidence is suggestive of such a relationship include effects on the central nervous system, reproduction and prenatal development, and the respiratory system.
- Risk is characterized in this REA through evaluation of COHb estimated to result from ambient CO exposure in individuals with CHD (including undiagnosed persons) considering potential health effect benchmarks for daily maximum COHb levels. Results are reported in terms of percent of population expected to experience daily maximum COHb levels at or above a series of levels that range as low as 1%. These results are considered in the Policy Assessment document in light of potential health effects benchmarks ranging 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 associated with adverse effects in those studies.

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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 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 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 pollutants (CO, SO_2, NO_2, and Pb) where measured levels were well below the applicable NAAQS and air quality problems were not expected. CO monitoring activities have been maintained at some SLAMS and these measurements of CO are required to continue until discontinuation is approved by the EPA Regional Administrator.

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

- **Microscale:** Data represent concentrations within a 100 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, 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 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, 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 FEMs.[4] Specifications for CO monitoring are designed to help states utilize equipment that has

[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).

[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

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 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 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, 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 are a growing body of ambient data from high sensitivity CO instruments is becoming available. Among newer GFC high sensitivity instruments, manufacturer-declared LDLs range from 0.02 – 0.04 ppm, with 24-hour zero drift varying between 0.5% 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

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(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).

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. The majority 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 well-operating legacy CO monitors as well as the possibility that monitoring requirements for CO might either encourage or require such technological improvements.

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), 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 contribute about 98% of total CO emissions. 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 U.S. 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 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 (i.e., 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).

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

[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 monitoring scale for 16 (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.

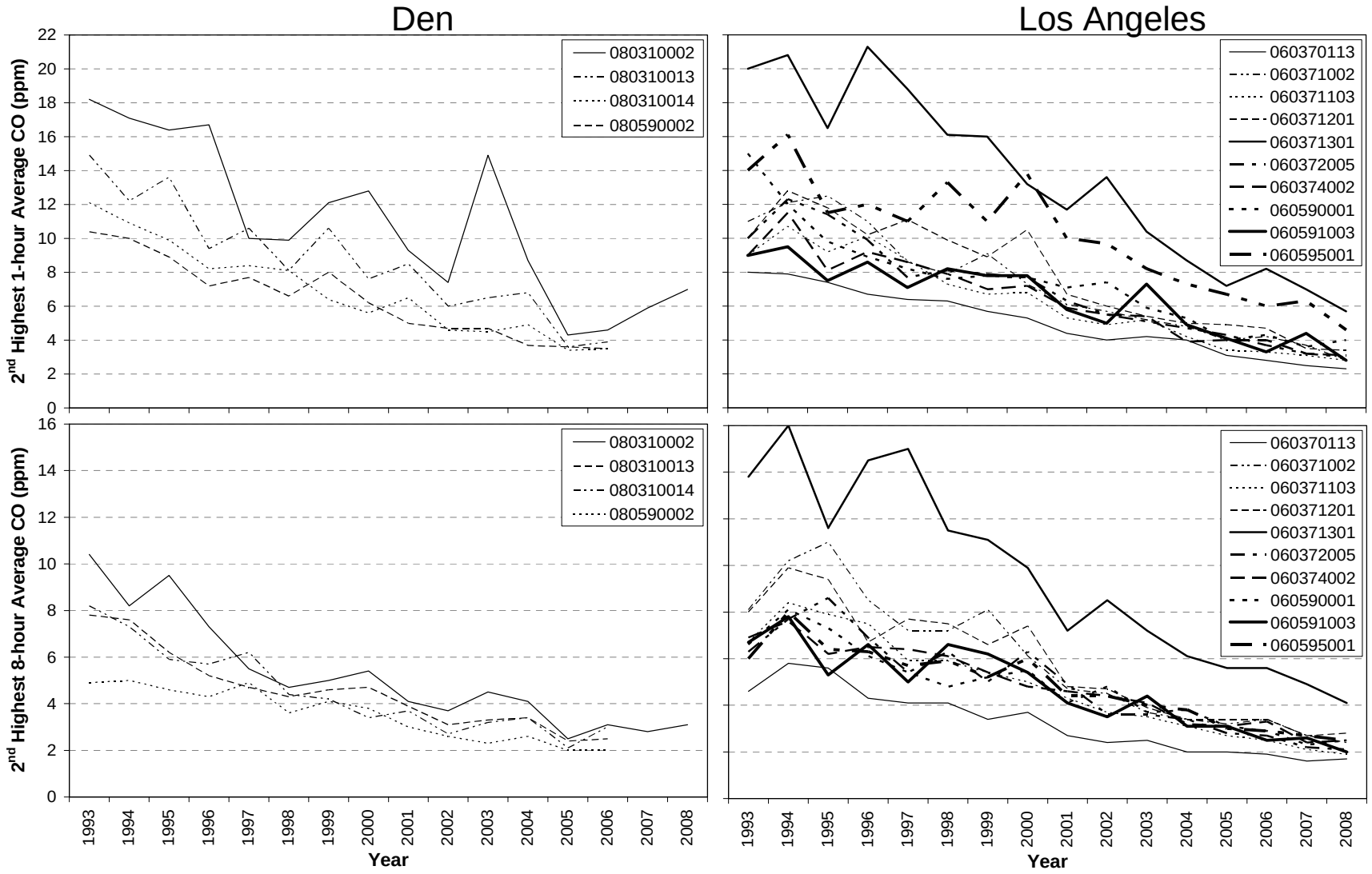

Figure 3-1. Spatial and Temporal Trends in the 2nd Highest 1-hour (top) and 8-hour Average (bottom) CO Ambient Monitoring Concentrations in Denver, Colorado (left) and Los Angeles, California (right), Years 1993 – 2008.

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, beyond consideration of AQS attributes such as monitoring scale and traffic count, local meteorology, would likely need to be performed (e.g., using GIS to determine monitor distance from roads, 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 90^{th} and 95^{th} 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

[10] Staff also recognizes some uncertainty in how well the AQS AADT estimates reflect current conditions at this monitor site.

selected percentiles, though a few locations (e.g., Phoenix, Los Angeles, Seattle) did have a more pronounced late afternoon peak (ISA, Figure 3-37).

Staff 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 currently (year 2006) most commuting times are associated with concentrations ranging from between 1 and 5 ppm. The weekend profile exhibits some variation when considering either year, with maximum concentration levels and variability exhibited during the overnight hours.

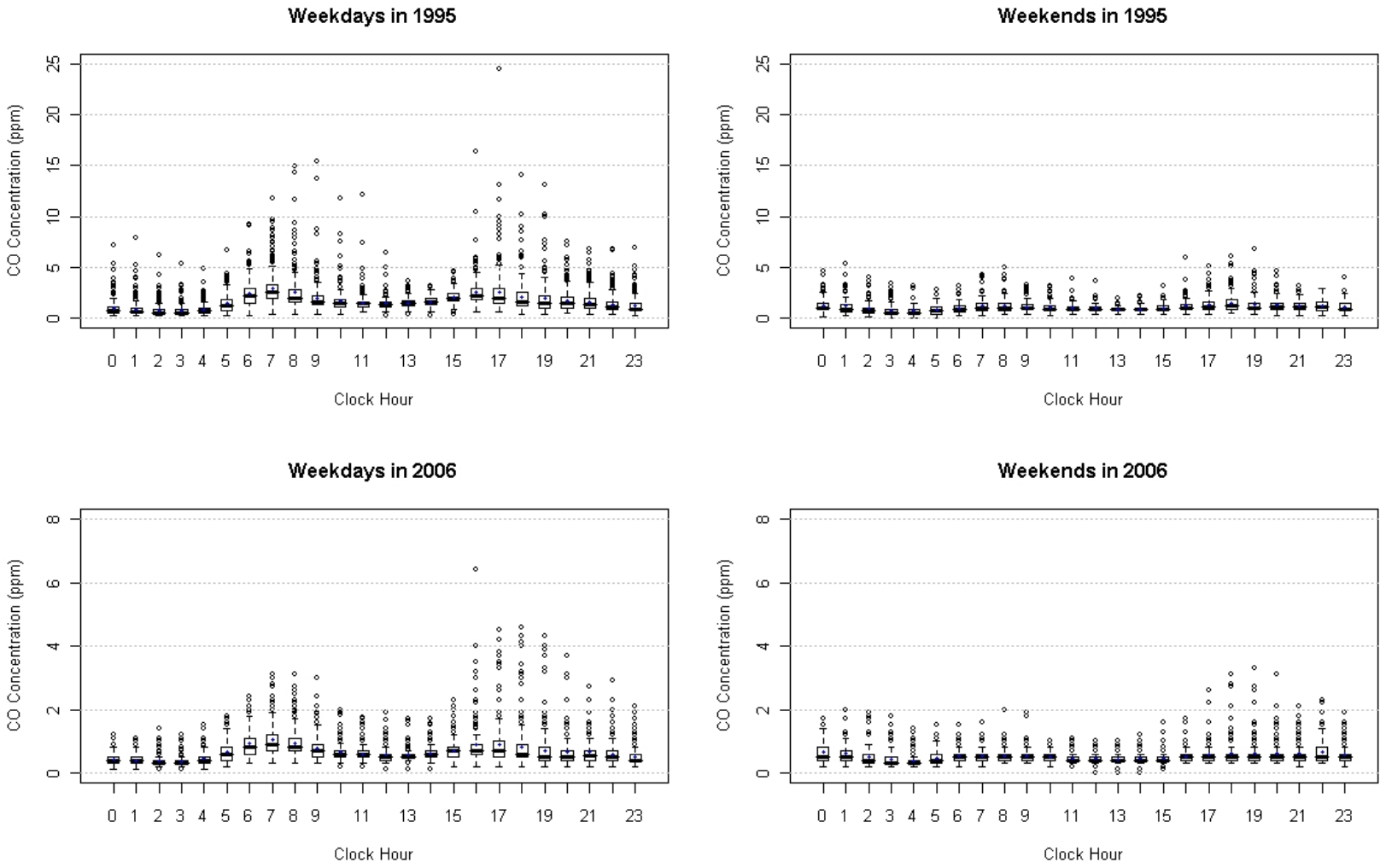

Figure 3-2. **Diurnal Distribution of 1-hour CO Concentrations in Denver (Monitor 080310002) by Day-type (weekdays-left; weekends-right), Years 1995 (top) and 2006 (bottom).** The box encompasses concentrations from the 25th to 75th percentiles or Interquartile range (IQR), the line bisecting the box 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 time periods.

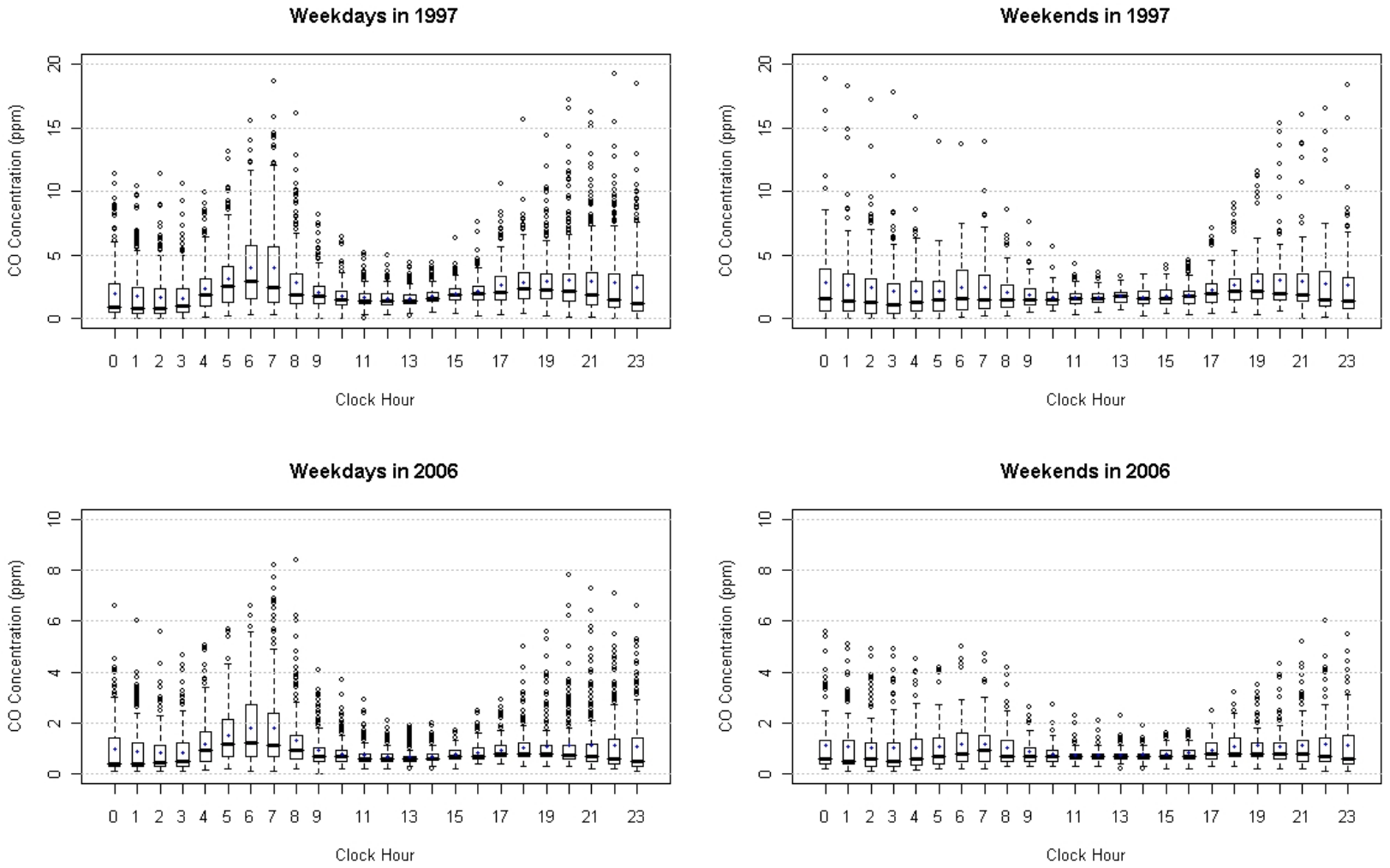

Figure 3-3. Diurnal distribution of 1-hour CO concentrations in Los Angeles (Monitor 060371301) by day-type (weekdays-left; weekends-right), years 1997 (top) and 2006 (bottom). The box encompasses concentrations from the 25th to 75th percentiles or IQR, the line bisecting the box is the median, the solid 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 time periods.

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 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 within 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 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. Staff 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 draft REA. Ambient CO concentration data were obtained for several monitors in Los Angeles for two years: 1997 – representing a high concentration year and 2006 – representing a low

concentration year. First, all reported hourly CO concentrations were used to calculate the full percentiles of the distribution (0-100 by 1 pct increments) for each year. Then the percentiles for the high concentration year were plotted against that of the low concentration year for each individual monitor (Figure 3-4). A simple linear regression was also plotted, along with the regression slope, intercept, and fit statistic (R^2). As shown by the relationships, there is a very strong linear relationship when comparing each year of data within each monitor, and the regression intercepts for most of the monitors are small, indicating there is adequate support for adjusting air quality by a proportional method.

Staff was 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 concentration in a year. The next two air quality metrics compared by staff were the 99th percentile 1-hour and 8-hour daily maximum CO concentrations.

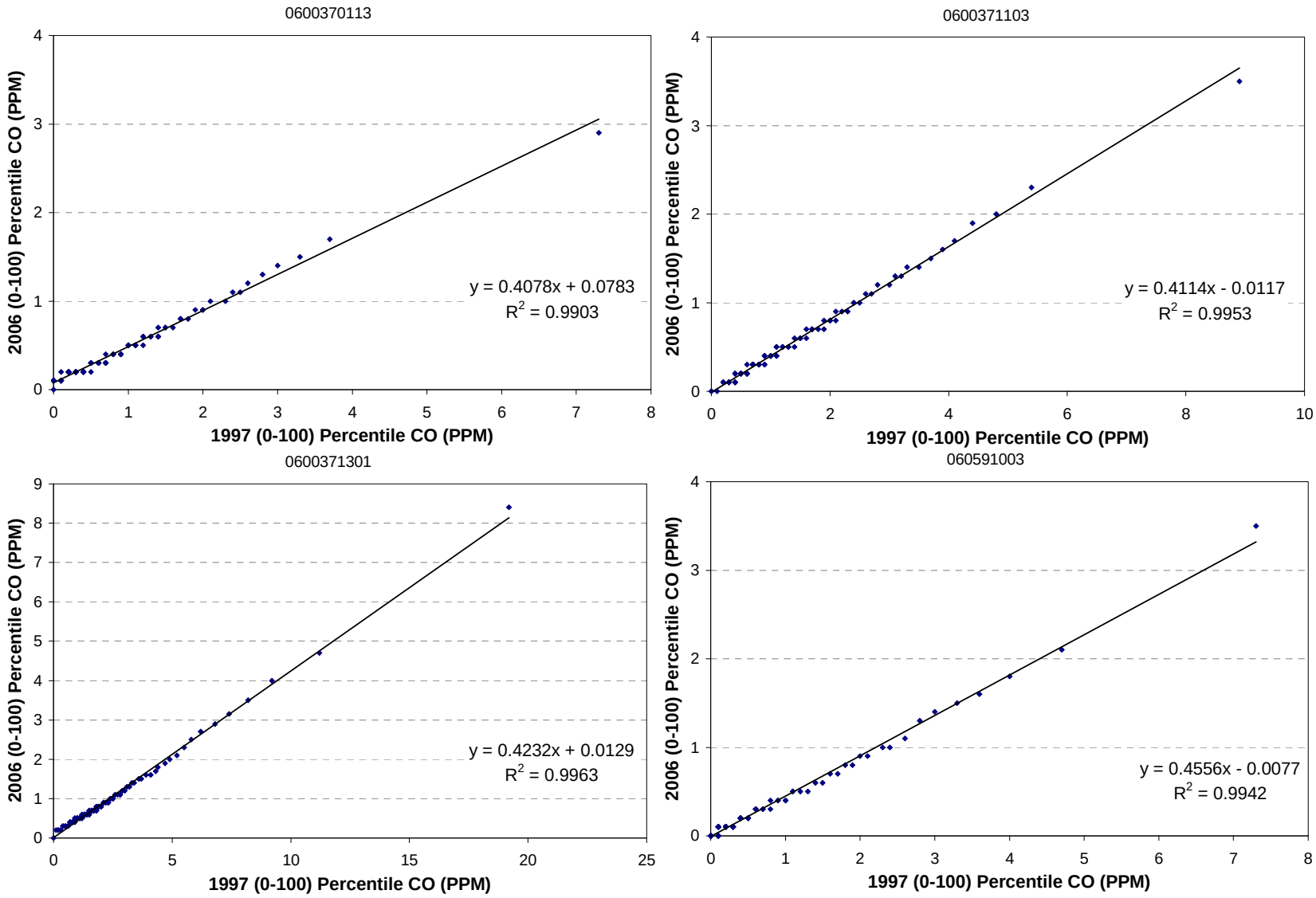

Figure 3-4. Comparison of a high concentration year (1997) with a low concentration year (2006) in Los Angeles. The 0 through 100th percentiles of the hourly air quality distribution are plotted for each monitor-year.

Staff 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 by staff to represent historical and recent air quality, respectively. Staff 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 first air quality metric 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),[11] is generally 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). 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 and 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 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 year-to-year spatial variability for this metric is consistent with that stated above. In Denver, the COV on average was less for the recent air quality when compared with 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).

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

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	1995	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	1995	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	1995	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

Staff 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 from exposure to CO. In addition, of 10 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 limited to roads where traffic density described for them is moderate (<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 peaks 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 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 is relatively small across a three year monitoring period, particularly when considering recent air quality.

3.4 REFERENCES

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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 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

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 (U.S. EPA 2008a, 2008b), and other supporting documentation, can be found at http://www.epa.gov/ttn/fera.

both home and work locations for individuals who work away from home.

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 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 rely 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 PC instead of a mainframe. The next version, APEX2, was substantially different, particularly in the use of a personal profile approach rather than a 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 parameters. Johnson and Capel (2003) describe a case study in which 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 ozone (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 coronary heart disease (CHD);
- 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 this population. APEX4.3 then generates a personal profile for each simulated person that specifies various parameter values required by the model. 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, 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 weather 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, b). 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.

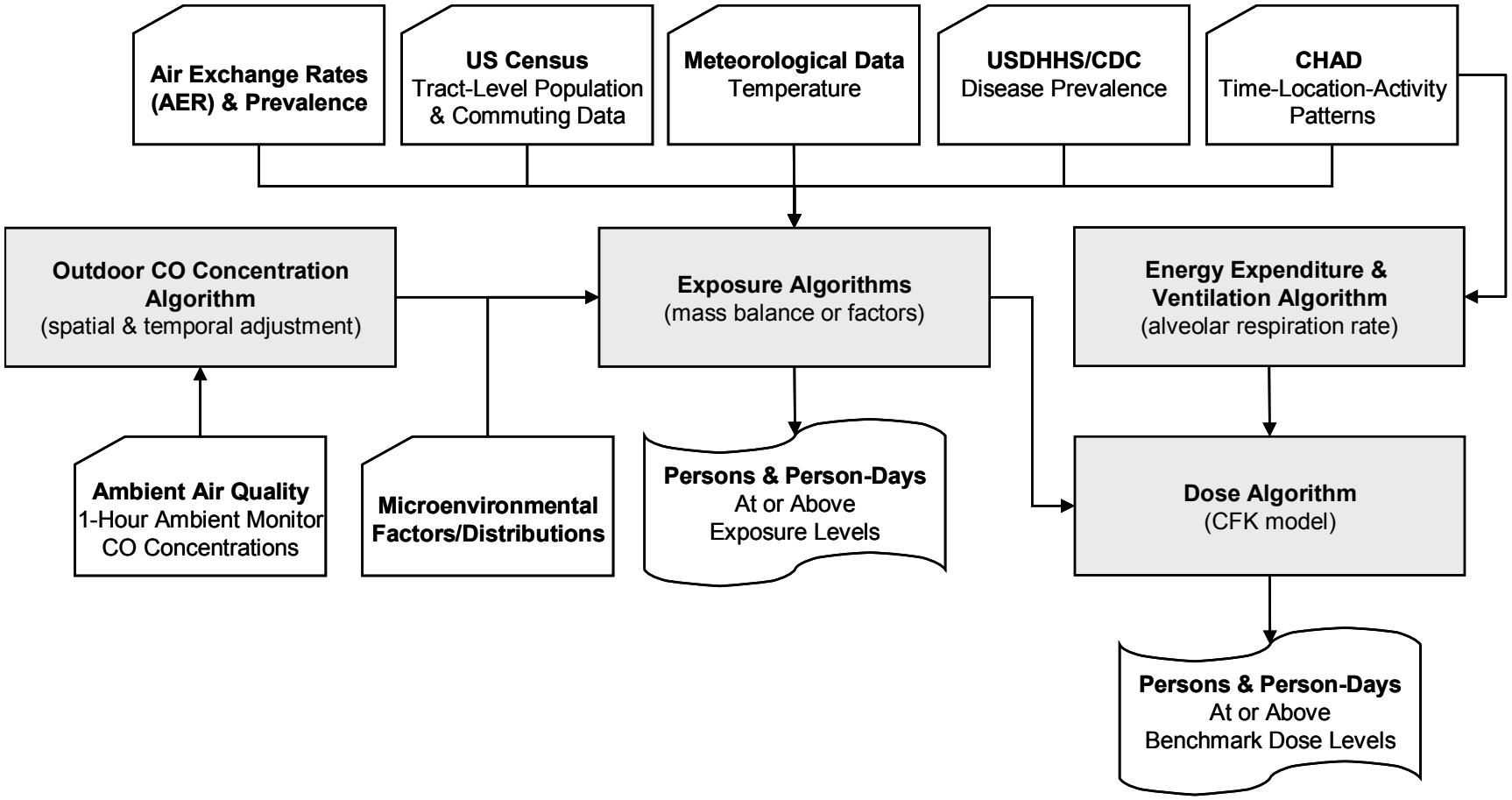

Figure 4-1. Conceptual model and simplified data flow for estimating population exposure and dose using APEX4.3.

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 and then APEX4.3 calculates the distances to the center of the study area of all the sectors included in the sector location database, and finally 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. 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 to be not employed.

4.4.2.2 Commuting Database

In addition to using estimates of employment by 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 draft CO REA and associated appendices can be found in US EPA (2008a, b).

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 containing daily diaries of human activities performed, locations visited, and personal attributes (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., specific microenvironments modeled in this CO assessment). 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,b)
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)
- 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. A study individuals' diary can vary in length from one to 15 days (i.e., referring to the number of person-days). 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, sleep), while others, such as athletic endeavors or manual labor, are represented by normal, lognormal, or similar 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.
- 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 (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 it is best to estimate the outdoor (ambient) CO concentration in the immediate vicinity of each microenvironment. This is 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 accomplish this. 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 grids). 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 algorithm (either the mass balance model or factors method) employed to estimate CO microenvironmental concentrations.

Staff selected a statistically-based approach to adjust 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.

The microenvironmental algorithm and data used by pNEM/CO to estimate variable parameters 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 is described in section 4.4.4.4. The details regarding selection of 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:

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

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

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

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

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

The solution to this differential equation is

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

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:

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

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

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

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 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 without 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:

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

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 Model

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

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

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 multiplier (> 0) specific to cohort c, microenvironment m, and district d (held constant for all hours),
$T(c,m,d,h)$ = time-of-day multiplier (> 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 zero 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 zero 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, there is no change in CO concentration as ambient (outdoor) air moves into a microenvironment, though the CO concentration within the microenvironment will be affected by air exchange rate and the presence of 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 Model Parameters

During a residential monitoring study described by Wilson, Colome, and Tian (1995), researchers measured 10-minute CO concentrations outside 293 residences throughout California in 1992. These residences were 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 (not part of the Los Angeles study area) and homes for which valid CO data were not available, analysts used the 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] The 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). The valid 10-minute values were then averaged by clock hour to permit comparison with hourly-average CO concentrations reported by nearby fixed-site monitors.

Analysts determined that the negative values in the 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 (which could not be used in fitting equation 4-11), analysts added a constant offset of 0.5 ppm to each hourly-average value measured outside a residence. In addition, seventeen (0.2%) of the original hourly averages less than or equal to -0.5 ppm were discarded. Each of the resulting one-hour outdoor 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)]. This approach yielded a final database containing 6,330 pairs of hourly average concentrations, in which each pair was indexed by date, time, residence identifier, fixed-site monitor identifier, and fixed-site monitor scale (e.g., neighborhood).

The *M(m)* values of equation 4-11 were based on data provided by 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

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

microenvironment assigned to each PEM reading was determined from entries made in a real-time diary carried by the subject.

Researchers created a data base in which each PEM value was matched to the corresponding hourly-average CO concentration reported by the nearest fixed-site monitor. The data were first processed by excluding cases with missing measurements, cases in which measurements failed a quality control check, and cases in which applicable diary data indicated the potential 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 Wilson, Colome, and Tian (1995) database, all cases with a zero measurement from the personal exposure monitor 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 Model Equation

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 models could have been developed. In specifying the model that was ultimately used (i.e., equation 4-11), 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. Most of the model development was based on a comparison of hourly averages of 10-minute CO concentrations measured outside residences in southern California (Wilson, Colome, and Tian, 1995) with hourly average CO concentrations measured at the nearest fixed-site monitor. For this case, *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 impossible negative outdoor concentrations, 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:

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

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 model:

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

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

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

where

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

[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.

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

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

Several alternative statistical models were considered by analysts during the development of the selected model 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 models similar to equation 4-11 in which the exponent *A* varied with microenvironment. These models were rejected due to the need for parsimony and 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 31-0002). 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 model, 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 model 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 California study conducted by Wilson, Colome, and Tian (1995), whereas the specific *M(m)* values were based on data provided by the Denver Personal Monitoring Study (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, σ_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 outdoor personal exposure measurement (PEM) values reported by the Denver study 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 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

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[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.

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

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 Model 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

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

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:

$$\text{Ambient} = [CO_{mon}(d,h)]^A \quad (4\text{-}18)$$
$$\text{Proximity} = M(m) \times L(c, m, d) \quad (4\text{-}19)$$
$$\text{Penetration} = T(c,m,d,h). \quad (4\text{-}20)$$

which gives

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

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

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

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 each of 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 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	Minimum (5^{th} pct)	Maximum (95^{th} 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.

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

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

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 i^{th} activity on day j for person k. Equation 4-23 can now be expressed as

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

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

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

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).[6] However, CO and oxygen can compete for binding with the available hemoglobin and, therefore,

[6] US EPA (2009b).

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 4^{th}-order Taylor's series with subintervals. This method, first incorporated in APEX3 (Glen, 2002), is summarized in Appendix B. The selected method (4^{th}-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 available (e.g., Bruce and Bruce (2003) multi-compartment model), 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)

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

tabulations of hourly exposure, ventilation, and energy expenditure. Detailed event-level information can also be output. 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, staff have 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.

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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.

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 exposure to carbon monoxide (CO) 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 second draft 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 to include the major comments and recommendations made by the CASAC and public regarding the geographically constricted and simplified exposure modeling approach used in the first draft CO REA (US EPA, 2009a).

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).

5.3 STUDY AREAS

As discussed in section 3.2, staff selected areas within Denver, Colorado, and Los Angeles, California, 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 these 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.

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 31-0014 (Denver - Julian) for the city center and set the "CityRadius" equal to 20 km (Figure 5-1). Staff used the location of monitor ID 37-1103 (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 monitoring 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.

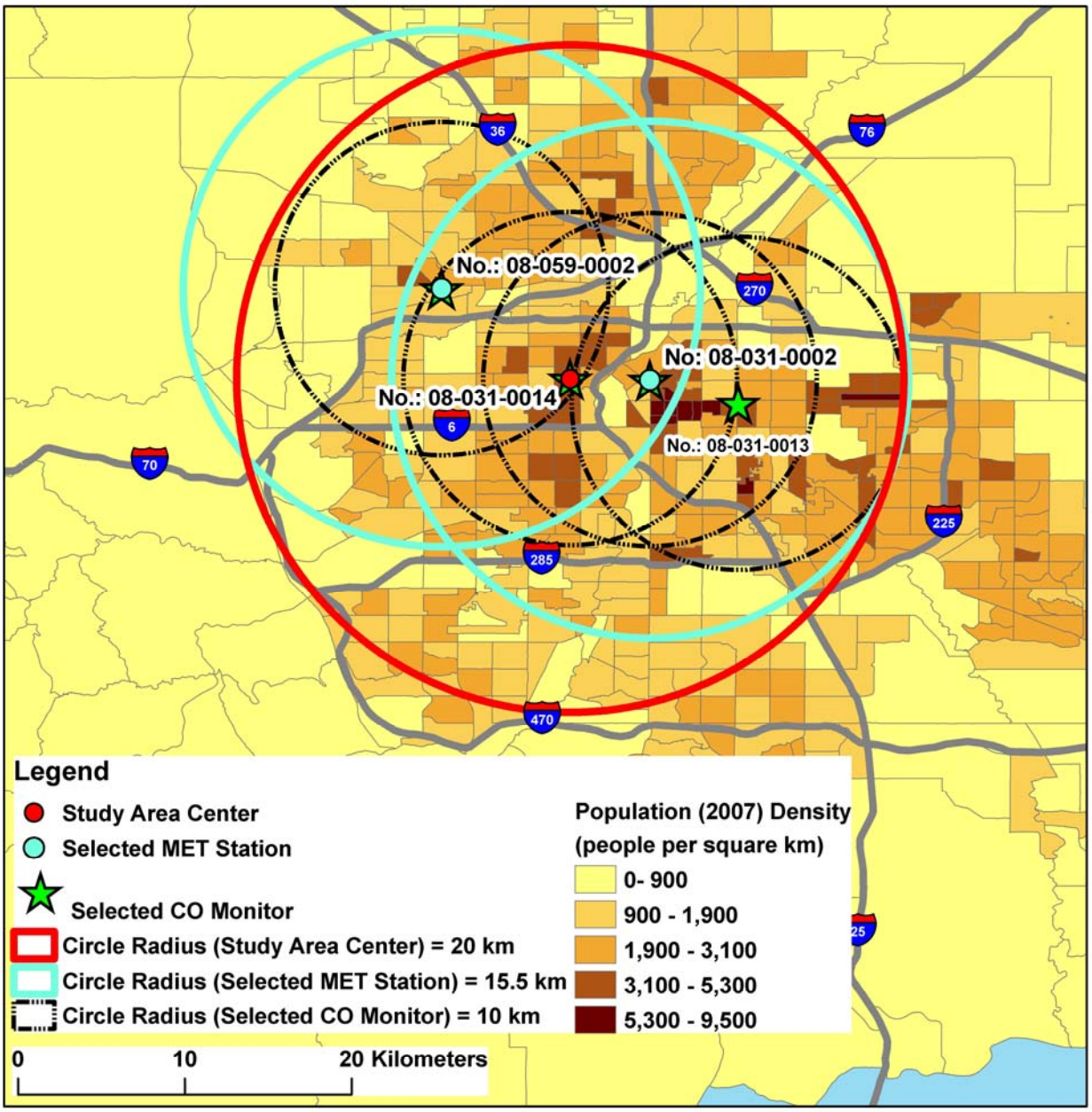

Figure 5-1. Ambient monitor locations, air districts (black circles), meteorological zones (blue circles), and study area (red circle) for the Denver exposure modeling domain.

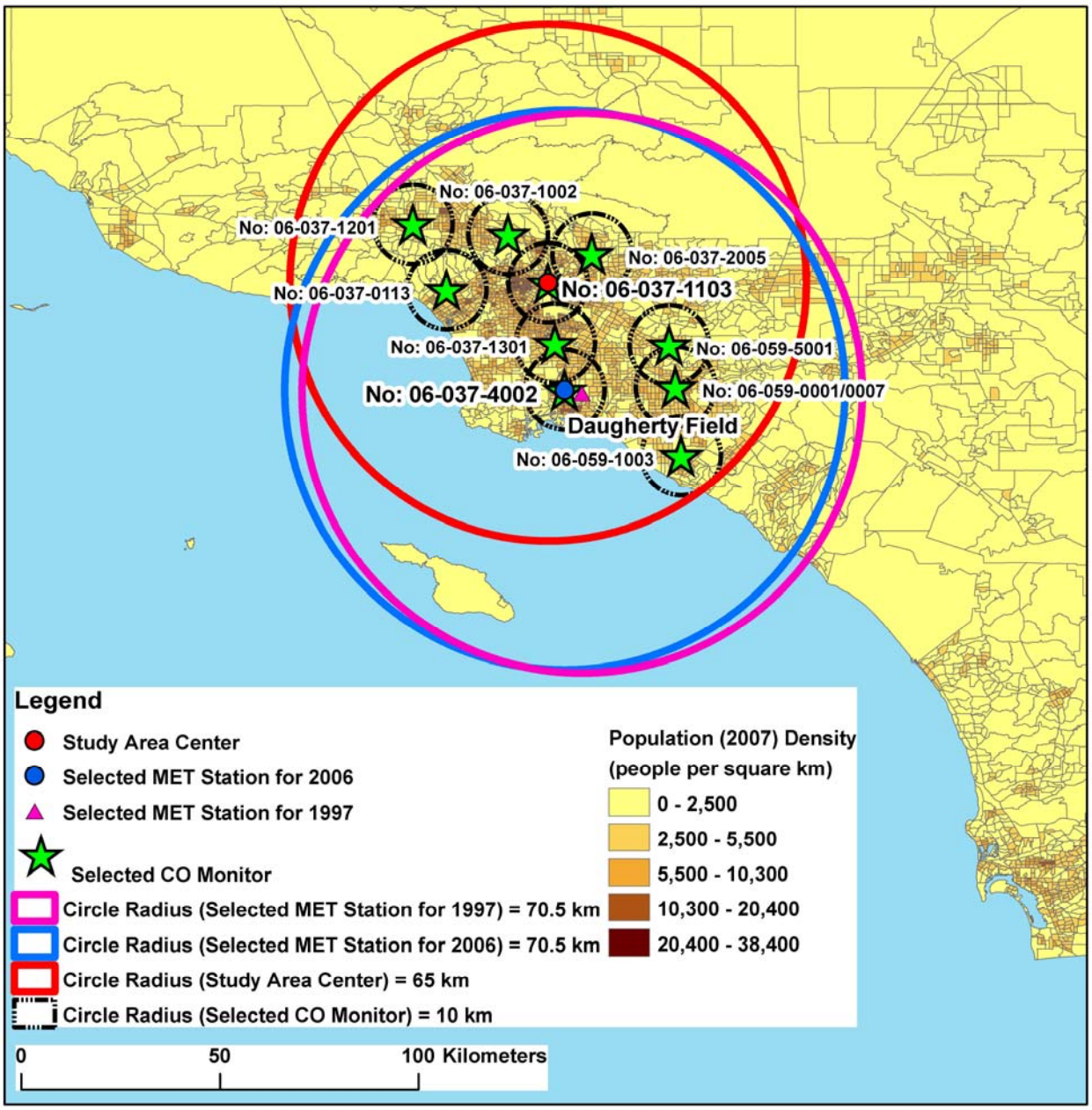

Figure 5-2. Ambient monitor locations, air districts (black circles), meteorological zones (blue and pink circles), and study area (red circle) for the Los Angeles exposure modeling domain.

5.5 STUDY POPULATION

5.5.1 Total and Simulated Population

The population estimates obtained from the 2000 US Census were used "as is" for each study area and scenario modeled; there were no adjustments made for modeling the most recent air quality data (2006) or for each of the alternative exposure scenarios modeled (a hypothetical year). The total population in this study was restricted to those aged 18 years or older. Based on the census tracts included and removal of residents commuting outside of the study area, the total modeled population was 617,020 persons (or 81.1% of the total population). The corresponding figure for Los Angeles was 5,017,551 persons (or 88.5% of the total population within the modeled census tracts). 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.

5.5.2 Selected at-Risk Subpopulation

The at-risk population simulated within each study area is comprised of adults ages 18 and older with CHD (diagnosed and undiagnosed). This focus on adults is 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 CHD in younger individuals is extremely small (CDC, 2009). In this assessment, the term CHD is used consistent with its use in the National Health Interview Survey (NHIS) where it is inclusive of coronary heart disease, angina pectoris and heart attack (CDC, 2009).

For estimates of adults with diagnosed CHD, staff obtained CHD prevalence data from the NHIS for 2007 (CDC, 2009). The estimated CHD prevalence for the population above 18 years of age is about 6% (ISA, section 5.7.2.1).[1] Staff 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. Staff desired the prevalence rates to be stratified by age *and* gender, though 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.

[1] 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 5-3. National prevalence rates for coronary heart disease by age range.

Age range	Prevalence rate (fraction) for coronary heart disease[a]
18 to 44	0.009
45 to 64	0.067
65 to 74	0.187
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.

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

Age range	Prevalence rate (fraction) for 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. National prevalence rates for coronary heart disease, stratified by age and gender.

Age range	Prevalence rate (fraction) for coronary heart disease[a]	
	Males	Females
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 for males and 0.74 for females using data from Table 5-4.

Staff has expanded the selected at-risk population 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[2] were stratified by age and sex (Adams and Marano,

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

1995) and constituted approximately 8.0 million individuals in the civilian, non-institutionalized population.[3] In addition, as many as three to four million persons were estimated to have silent ischemia or undiagnosed IHD (American Heart Association, 1990). Staff used this information to provide estimates of the undiagnosed IHD population for use in the pNEM/CO model. Staff 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 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 1990. The total prevalence listed for each gender (diagnosed and undiagnosed combined) was used by APEX in estimating the selected at-risk population.

When using these 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 same selected at-risk population.

Table 5-6. 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	0.039	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	0.136	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. Staff assumed CHD and IHD are identical with respect to the ratio of undiagnosed cases (3.5 million) to diagnosed cases (8.0 million) and that this ratio has not changed since 1990 (see Appendix F of Johnson et al. (2000)).

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

5.5.3 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.

5.5.4 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 ($< 55.0\ ^{\circ}F$, between 55.0 and 83.9 $^{\circ}F$, and $\geq 84.0\ ^{\circ}F$) and two day-types (i.e., weekend and weekday); thus, there were 3 x 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 second draft 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 adjusted high concentration year ambient data in each location (i.e., the 1995 monitoring data in Denver and the 1997 monitoring data in Los Angeles). 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 adjusted air quality exposure scenarios considered ambient concentrations adjusted to just meeting the 8-hour average CO NAAQS of 9 ppm. This particular form was selected when considering the two current standard forms (8-hour average and 1-hour) because it is the controlling standard.[4] The second of these exposure scenarios using the historical monitoring data also considered the current 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 the 99th percentile daily maximum 8-hour average CO concentrations, while the second considered the same form though with a 1-hour averaging time. Details regarding the concentration adjustments associated with each of the current and potential alternative standards are provided in section 5.7.3.

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 location and monitoring year (Tables 5-7 to 5-10). As expected, CO concentrations are about a factor of two or greater when comparing the high concentration year (1995 or 1997) to the more recent year (2006) of ambient monitoring data in either location. In general, there is similarity in the concentration distribution for both locations within a given year, with the following exceptions. There is one monitor in Los Angeles (ID 37-1301) reporting exceptionally high concentrations at each of the percentiles of the distribution in this location when compared with the other Los Angeles monitors for either year. In addition,

[4] 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).

there is a sharper rate of increase in the upper percentile concentrations (i.e., ≥95th percentiles) in Denver when compared with the Los Angeles ambient concentration distribution, for either year.

5.7.2 Method for Estimating of 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 a time-of-day and at each 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 5-7 to 5-10 provide the descriptive statistics for 1-hour CO concentrations in each data set, before and after estimating missing values. The agreement between these statistics indicates that the addition of the estimated missing-value concentrations did not significantly affect the overall distribution of the hourly CO concentrations in either year or location.

Table 5-7. 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 5-8. 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 5-9. 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 5-10. 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 the potential alternative standards. 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:

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

$CO(m,h)$ 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. [5]

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.

[5] 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.[6] 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.[7] The final potential alternative standard that staff evaluated was a 99th percentile daily maximum 1-hour CO concentration of 8.0 ppm. Table 5-11 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 5-11. 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	0.380
	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.

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

[7] It was assumed that there are an infinite number of zeros, that is, the level is exactly 5.0 ppm. This rounding convention applies to the other potential alternative standard selected, the level is exactly 8.0.

Table 5-12 and 5-13 provides 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 5-12. 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 5-13. 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 5-14 and 5-15 list the meteorological stations staff selected for use 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 have 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) will be 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, staff set this at 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 5-14. 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 5-15. 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 of 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 5-14 and 5-15). To generate the full year of temperature data set, we estimated the missing values for the selected meteorological (MET) stations in Denver and Los Angeles as follows.

For the Denver study area, staff 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 this gap. In these instances, staff applied an alternative approach whereas 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 was missing from 1AM to 11pm on 2/8/1995, staff averaged the hourly temperature of 2/7/1995 and 2/9/1995 for 1AM, 2AM …, 11PM to fill the missing hours (all eleven hours have an individual value).[8]

For Los Angeles, staff evaluated the two sites noted 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), staff 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

[8] 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 by staff 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.[9]

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 the previous assessment (Johnson et al., 2000).

5.9.1 The Micronenvironmental 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

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

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 mean (GM_T) equal to 1.0 and geometric standard deviation (GSD_T) equal to 1.6289.

[9] This was done in SAS using a procedure "PROC EXPAND" with "JOIN" option.

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 REA Table 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 produces 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, Colome, and Tian (1995) which have compared outdoor concentrations with simultaneously measured fixed-site concentrations.

Table 5-16. Parameters of Bounded Lognormal Distributions Defined for Proximity Factors to be Used in the Proposed 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 (5^{th} pct)	Maximum (95^{th} 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 persons 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. See Appendix D Figure D-1 that 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 Appendix D Figure D-1) 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 methods available in APEX for calculating pollutant levels within microenvironments are mass balance or a factors approach. Table 5-17 lists the microenvironments used in this study and the calculation method used.

Table 5-17. 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	Outdoor	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[10] 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 5-18 and 5-19

[10] 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, classified by A/C prevalence and temperature categories. For all other indoor microenvironments, the AER distributions used here (Tables 5-18 and 5-19) were based 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 (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 is dependent on temperature.

Table 5-18. 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.

Table 5-19. 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	0.9185	1.8589	0.1	10.0
		50 – 68	0.5636	1.9396	0.1	10.0
		68 – 77	0.4676	2.2011	0.1	10.0
		77 – 86	0.4235	2.0373	0.1	10.0
		86+	0.5667	1.9447	0.1	10.0
	No	≤ 50	0.9258	2.0836	0.1	10.0
		50 – 68	0.7333	2.3299	0.1	10.0
		68+	1.3782	2.2757	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.

5.10 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.
- The selected at-risk population was simulated by combining the tract-specific age and gender population distribution and the CHD prevalence, also stratified by age and gender. In using this approach, staff can represent the variability that exists in the CHD population that resides in each census tract and within each study area.
- Staff expanded the selected at-risk population to include an estimate of persons with undiagnosed CHD.
- Compared with the single-monitor approach used for the first draft CO REA, staff expanded the number of ambient monitors used in this second draft CO REA to better capture the spatial variability in ambient concentrations. In Denver, a total of four monitors were used, in Los Angeles, the total number of monitors was ten.
- Compared with the two microenvironments modeled in the first draft CO REA, staff has expanded the number modeled in each location to eight. This approach is designed to better represent the expected variability in microenvironmental CO concentrations.

- Compared with the approach used to estimate microenvironmental concentrations in the first draft CO REA (factors approach only), all indoor microenvironments were modeled using a mass balance model in this second draft assessment. Use of the mass balance model will better represent temporal variability in indoor CO concentrations with respect to the outdoor CO concentration variability. In addition, distributions of microenvironmental factors were used in this second draft CO REA for all microenvironments rather than using point estimates (as was done for the first draft CO REA). Using distributions of microenvironmental factors will better represent both spatial and temporal variability in estimated microenvironmental CO concentrations.

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6 SIMULATED EXPOSURE AND COHB DOSE 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) *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 5.4 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.

The chapter is divided into five main sections. The first section (6.1) summarizes the estimated exposures associated with each of the five air quality scenarios. The simulated at-risk population 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 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 dose levels for persons in the simulated at-risk population residing in each study area. The 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 recorded. In section 6.3, staff compares the dose estimates in this second draft CO REA with those estimated in the 2000 exposure assessment (Johnson et al., 2000). The fourth section (6.4) presents an evaluation of endogenous CO production for the APEX simulated individuals. This includes analysis of the COHb ambient contribution attributed to ambient CO in a select group of simulated persons. Finally, key observations are presented in the final section (6.5). As mentioned in Chapter 1, exposure and risk results are provided here without substantial interpretation. Rather, interpretative discussion of these results is provided in the CO Policy Assessment.

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[1] As described in section 5.5 above, 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) provided by the National Health Interview Survey (which includes CHD, angina pectoris and heart attack) and corresponding 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*.

6.1 ESTIMATED EXPOSURES

The section summarizes the estimated exposures for the simulated individuals in a series of tables, separated by the five air quality scenarios and study areas considered.

6.1.1 Air Quality "As Is"

As described in section 5.6, ambient monitoring data from each location for 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 population in the Denver Study area. About 80% of the simulated CHD population did not experience a 1-hour daily maximum exposure above 9 ppm; 99.9% did not experience a 1-hour daily maximum exposure concentration above 20 ppm. Of the nearly 20 million 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 above 8 ppm (0.4% of the CHD population). Approximately 99% of simulated person-days were associated with 8-hour daily maximum exposure concentrations of less than 3 ppm. These results are consistent with the ambient concentration distribution used to represent this scenario, where upper percentile concentrations range from about 2 to 6.4 ppm (see Table 5-8). Note also that the highest estimated 1-hour daily maximum exposures are likely a function of microenvironmental concentrations (e.g., in-vehicles or near-roads) that, in general, may be a factor of two to five times higher than ambient CO concentrations.

In Los Angeles, there were a greater number of individuals experiencing exposures at each of the selected exposure levels (Table 6-2) when compared with Denver (Table 6-1), given that the overall exposure modeling domain extended over a larger area with a higher total 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 population was estimated to experience a 1-hour daily maximum exposure of at least 9 ppm in Los Angeles (Table 6-2) 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 (section 5.7.1).

In addition, the maximum 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 the population (<0.1%). The corresponding maximum 1-hour daily maximum exposure in the Denver study area was at or above 20 ppm but less than 25 ppm, and was experienced by approximately 0.1% of the CHD 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 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 (0.8%) experienced 8-hour daily maximum exposures above 8 ppm. These exposure results are also consistent with the distribution of ambient air quality used to represent this scenario, where upper percentile concentrations extend from about 2 to 8.4 ppm (Table 5-10).

Table 6-1. Estimated Number (and Percentage) of Persons and Person-Days with a Daily Maximum 1-Hour or 8-hour Exposure At or Above the Specified Level – Adults With Coronary Heart Disease (CHD) in the Denver Study Area –"As Is" Air Quality.

Daily Maximum Exposure (ppm)	1-Hour				8-Hour			
	Persons		Person-days		Persons		Person-days	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
0	53,656	100	19,580,000	100	53,656	100	19,580,000	100
3	53,397	100	2,188,000	11.2	31,036	58	189,500	1.0
6	32,517	60.6	170,400	0.9	1,715	3.2	2,851	<0.1
9	10,662	19.9	24,560	0.1	62	0.1	86	<0.1
12	3,048	5.7	4,677	<0.1	12	<0.1	12	<0.1
15	876	1.6	1,061	<0.1	0	0	0	0
20	62	0.1	62	<0.1	0	0	0	0
25	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
Unadjusted ambient concentrations from four monitors in 2006 were used to represent the *As Is* air quality scenario.								

Table 6-2. Estimated Number (and Percentage) of Persons and Person-Days with a Daily Maximum 1-Hour or 8-hour Exposure At or Above the Specified Level – Adults With Coronary Heart Disease (CHD) in the Los Angeles Study Area – Air Quality As Is.

Daily Maximum Exposure (ppm)	1-Hour				8-Hour			
	Persons		Person-days		Persons		Person-days	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
0	383,040	100	139,800,000	100	383,040	100	139,800,000	100
3	382,739	100	23,620,000	16.9	294,430	77	3,793,000	2.7
6	287,606	75.1	2,423,000	1.7	36,528	9.5	72,150	0.1
9	122,428	32.0	408,300	0.3	3,011	0.8	3,412	<0.1
12	42,850	11.2	83,990	0.1	301	0.1	301	<0.1
15	13,949	3.6	20,170	<0.1	0	0	0	0
20	2,208	0.6	2,509	<0.1	0	0	0	0
25	401	0.1	502	<0.1	0	0	0	0
30	100	<0.1	100	<0.1	0	0	0	0
40	0	0	0	0	0	0	0	0
Unadjusted ambient concentrations from four monitors in 2006 were used to represent the *As Is* air quality scenario.								

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 needed to be adjusted downwards to meet a 2nd highest 8-hour average concentration of 9.4 ppm. Note that even with a downward proportional adjustment, these ambient concentrations remain higher than *as is* ambient air quality. Table 6-3 summarizes the CHD population exposure results generated for 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 CHD 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 maximum 1-hour daily maximum exposure was estimated to be at or above 40 ppm when considering air quality adjusted to just meet the current standard, though only experienced by 0.2% of the CHD population. Thus, there is a wider range in the exposure levels experienced by the CHD population. 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 CHD population was estimated to experience an 8-hour daily maximum exposure at or above 9 ppm (Table 6-3) when considering air quality just meeting the current 8-hour standard. Most of the CHD population

(99.6%) would not experience an 8-hour daily maximum concentration at that same level when considering the *as is* air quality scenario (Table 6-1).

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 6-4), 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 40 ppm, but less than 60 ppm for this scenario. This estimate of an upper level is consistent with the maximum in-vehicle concentration of 46 ppm measured by Shikiya (1989) during 112 southern California commutes in wintertime. However, Rodes et al. (1998) reported maximum in-vehicle and on road CO concentrations of only 7.6 and 9.0 ppm during Los Angeles commutes in 1997. Note though the scripted commutes in this study were time-averaged for two hours, the sample size was limited (about 30 total samples), and conducted over a nine days in the fall.

When comparing the overall population distribution for Los Angeles to Denver for this exposure scenario, there are a greater percentage of persons and person-days estimated for the Denver CHD population at the same 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 6-4), while in Denver, the estimated percent of the CHD population exposed at this level was over a factor of three greater (9.4%) (Table 6-3). 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.

Table 6-3. Estimated Number (and Percentage) of Persons and Person-Days with a Daily Maximum 1-Hour or 8-hour Exposure At or Above the Specified Level – Adults With Coronary Heart Disease (CHD) in the Denver Study Area – Air Quality Just Meeting the Current 8-Hour Standard.

Daily Maximum Exposure (ppm)	1-Hour				8-Hour			
	Persons		Person-days		Persons		Person-days	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
0	53,656	100	19,580,000	100	53,656	100	19,580,000	100
3	53,656	100	8,638,000	44.1	52,706	98	2,690,000	13.7
6	53,039	98.9	1,625,000	8.3	23,879	44.5	97,760	0.5
9	44,598	83.1	404,800	2.1	5,060	9.4	9,724	<0.1
12	28,469	53.1	127,300	0.7	1,037	1.9	1,382	<0.1
15	16,610	31.0	46,710	0.2	309	0.6	346	<0.1
20	6,022	11.2	10,290	0.1	37	0.1	37	<0.1
30	691	1.3	802	<0.1	0	0	0	0
40	86	0.2	86	<0.1	0	0	0	0
60	0	0	0	0	0	0	0	0
Ambient concentrations from 1995 were adjusted to just meet a 2nd highest 8-hour average concentration of 9.4 ppm.								

Table 6-4. Estimated Number (and Percentage) of Persons and Person-Days with a Daily Maximum 1-Hour or 8-hour Exposure At or Above the Specified Level – Adults With Coronary Heart Disease (CHD) in the Los Angeles Study Area – Air Quality Just Meeting the Current 8-Hour Standard.

Daily Maximum Exposure (ppm)	1-Hour				8-Hour			
	Persons		Person-days		Persons		Person-days	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
0	383,040	100	139,800,000	100	383,040	100	139,800,000	100
3	383,040	100	36,430,000	26.1	342,598	89	8,655,000	6.2
6	335,975	87.7	4,826,000	3.5	75,966	19.8	262,600	0.2
9	189,563	49.5	982,300	0.7	10,336	2.7	18,670	<0.1
12	83,693	21.8	257,200	0.2	1,505	0.4	2,308	<0.1
15	36,126	9.4	80,180	0.1	301	0.1	401	<0.1
20	8,731	2.3	14,450	<0.1	100	<0.1	100	<0.1
30	803	0.2	803	<0.1	0	0	0	0
40	0	0	0	0	0	0	0	0
60	0	0	0	0	0	0	0	0
Ambient concentrations from 1997 were adjusted to just meet a 2nd highest 8-hour average concentration of 9.4 ppm.								

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 selected averaging times, forms and target levels would affect the estimated exposure

concentrations (section 5.7.3). The data for the 1-hour and 8-hour daily maximum exposure concentrations are presented here, only with a focus on the number and percent of persons exposed at selected concentrations. Table 6-5 summarizes the 1-hour exposure results for each of the three alternative standards scenarios in the Denver study area, while the following table presents the same information for the Los Angeles study area (Table 6-6). Tables 6-7 and 6-8 contain the corresponding 8-hour exposure distribution for the potential alternative standard scenarios in each respective location.

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 CHD population 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 CHD population in Denver (Table 6-5) when compared with that of Los Angeles (Table 6-6) when considering the same potential alternative standard. This is also consistent patterns in the estimated distribution of 8-hour daily maximum exposures experienced by the CHD population, 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 (Tables 6-7 and 6-8). 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 5.4 ppm best 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 6-7). 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 and below 30 ppm.

Table 6-5. Estimated Number (and Percentage) of Persons with a Daily Maximum 1-Hour Exposure At or Above the Specified Level – Adults With Coronary Heart Disease (CHD) in the Denver Study Area – Air Quality Just Meeting Potential Alternative Standards.

Daily Maximum 1-hour Exposure (ppm)	2nd highest 8-hour average of 5.4 ppm		99th pct 8-hour Daily Max of 5.0 ppm		99th pct 1-hour Daily Max of 8.0 ppm	
	Persons		Persons		Persons	
	Number	Percent	Number	Percent	Number	Percent
0	53,656	100	53,656	100	53,656	100
3	53,656	100	53,656	100	53,656	100
6	47,264	88.1	50,534	94.2	48,239	89.9
9	25,174	46.9	32,147	59.9	26,877	50.1
12	11,082	20.7	16,326	30.4	12,192	22.7
15	4,850	9.0	7,676	14.3	5,282	9.8
20	975	1.8	1,888	3.5	1,222	2.3
30	62	0.1	136	0.3	74	0.1
40	0	0	0	0	0	0
60	0	0	0	0	0	0
Ambient concentrations from 1995 were adjusted to just meet the level of the potential alternative standard indicated.						

Table 6-6. Estimated Number (and Percentage) of Persons with a Daily Maximum 1-Hour Exposure At or Above the Specified Level – Adults With Coronary Heart Disease (CHD) in the Los Angeles Area – Air Quality Just Meeting Potential Alternative Standards.

Daily Maximum 1-hour Exposure (ppm)	2nd highest 8-hour average of 5.4 ppm		99th pct Daily 8-hour Max of 5.0 ppm		99th pct Daily 1-hour Max of 8.0 ppm	
	Persons		Persons		Persons	
	Number	Percent	Number	Percent	Number	Percent
0	383,040	100	383,040	100	383,040	100
3	378,624	99.0	379,728	99.0	381,535	99.6
6	215,454	56.2	229,302	59.9	260,913	68.1
9	68,540	17.9	77,571	20.3	98,244	25.6
12	19,769	5.2	24,285	6.3	34,721	9.1
15	6,322	1.7	7,827	2.0	10,738	2.8
20	903	0.2	1,305	0.3	2,709	0.7
30	0	0	0	0	0	0
40	0	0	0	0	0	0
60	0	0	0	0	0	0
Ambient concentrations from 1997 were adjusted to just meet the level of the potential alternative standard indicated.						

Table 6-7. Estimated Number (and Percentage) of Persons with a Daily Maximum 8-Hour Exposure At or Above the Specified Level – Adults With Coronary Heart Disease (CHD) in the Denver Study Area – Air Quality Just Meeting Potential Alternative Standards.

Daily Maximum 8-hour Exposure (ppm)	2nd highest 8-hour average of 5.4 ppm		99th pct 8-hour Daily Max of 5.0 ppm		99th pct 1-hour Daily Max of 8.0 ppm	
	Persons		Persons		Persons	
	Number	Percent	Number	Percent	Number	Percent
0	53,656	100	53,656	100	53,656	100
3	44,574	83.1	48,819	91.0	45,808	85.4
6	6,590	12.3	10,650	19.8	7,380	13.8
9	839	1.6	1,555	2.9	926	1.7
12	111	0.2	296	0.6	123	0.2
15	25	<0.1	49	<0.1	25	<0.1
20	0	0	0	0	0	0
30	0	0	0	0	0	0
40	0	0	0	0	0	0
60	0	0	0	0	0	0
Ambient concentrations from 1995 were adjusted to just meet the level of the potential alternative standard indicated.						

Table 6-8. Estimated Number (and Percentage) of Persons with a Daily Maximum 8-Hour Exposure At or Above the Specified Level – Adults With Coronary Heart Disease (CHD) in the Los Angeles Area – Air Quality Just Meeting Potential Alternative Standards

Daily Maximum 8-hour Exposure (ppm)	2nd highest 8-hour average of 5.4 ppm		99th pct Daily 8-hour Max of 5.0 ppm		99th pct Daily 1-hour Max of 8.0 ppm	
	Persons		Persons		Persons	
	Number	Percent	Number	Percent	Number	Percent
0	383,040	100	383,040	100	383,040	100
3	214,149	55.9	230,807	60.3	264,425	69.0
6	17,060	4.4	20,672	5.4	28,801	7.5
9	903	0.2	1,204	0.3	2,007	0.5
12	301	<0.1	301	<0.1	301	<0.1
15	0	0	100	<0.1	100	<0.1
20	0	0		0		0
30	0	0		0		0
40	0	0		0		0
60	0	0		0		0
Ambient concentrations from 1997 were adjusted to just meet the level of the potential alternative standard indicated.						

6.2 ESTIMATED COHB DOSE LEVELS

Consistent with section 6.2, this section summarizes the estimated COHb levels for the simulated CHD population in a series of tables, separated by the air quality scenarios and study areas considered. In addition to reporting the number and percentage of persons and person-days associated with the dose metric of interest (daily maximum end-of-hour COHb level), staff provides the person-days *per person* at or above the selected COHb levels. This dose metric can be calculated in two manners. The first, termed *on average*, is the number of person-days at a given level divided by the total number of CHD persons in each model simulation. Therefore, this metric gives an estimate of, on average, the number of days an individual in the entire CHD population might experience a daily maximum end-of-hour COHb concentration at or above the selected COHb level. The second, termed *at level*, is calculated by dividing number of person-days estimated for a given level by the number of persons estimated for the same COHb level. Therefore, this 2nd metric will provide an estimate of, for persons that experience a selected COHb level, the average number of days in the year they may experience that selected level. This second metric (at level) will always be larger than the first (on average) because it only includes the persons experiencing a selected COHb dose level.[3]

6.2.1 Air Quality "As Is"

Table 6-9 provides the COHb levels (%) for the simulated COHb population in Denver, when considering the *as is* air quality. No persons were estimated to have a daily maximum end-of-hour COHb level at or above 2.0%, while only a few (<0.1%) were estimated to have a COHb dose level ≥1.8%. Over 99% of the CHD population had a daily maximum end-of-hour COHb level below 1.5%. Most of the person-days were associated with daily maximum end-of-hour COHb levels below 1.0%. It follows that the majority of the person-days per person *on average* were also limited to COHb levels at or below 1.0%. When individuals did have an estimated daily maximum end-of-hour COHb level at or above 1.5%, it occurred on multiple days (i.e., between 8 and 14 (Table 6-9), depending on the level).

Similarly in Los Angeles, very few persons (98.5%) had an estimated daily maximum end-of-hour COHb level at or above 1.5% when considering the *as is* air quality (Table 6-10). There were, however, a few persons (0.1%) estimated to have daily maximum end-of-hour COHb levels at or above 2.0% in this study area. Of these 301 simulated individuals, all were estimated to have only one person-day per person at that level. The majority of the person-days and person-days per person *on average* were limited to COHb levels at or below 1.0%.

[3] This averaging of person-days would underestimate the number of person-days any one simulated individual might experience above a given benchmark in a year. For example, 10 exceedances occurring in one individual would give the same average as 1 exceedance occurring in 10 individuals.

Table 6-9. Estimated Number (and Percentage) of Persons and Person-Days with a Daily Maximum End-of-hour COHb Level At or Above the Specified Level – Adults With Coronary Heart Disease (CHD) in the Denver Study Area – Air Quality As Is.

COHb Level (%)	Persons		Person-days		Person-days/person	
	Number	Percent	Number	Percent	On Average	At Level
0.0	53,656	100	19,580,000	100	365	365
1.0	7,873	14.7	293,000	1.5	5.5	37.2
1.5	333	0.6	4,652	<0.1	<0.1	14.0
1.8	12	<0.1	99	<0.1	<0.1	8.2
2.0	0	0	0	0	0	0
2.5	0	0	0	0	0	0
3.0	0	0	0	0	0	0
4.0	0	0	0	0	0	0
Unadjusted ambient concentrations from four monitors in 2006 were used to represent the *As Is* air quality scenario.						

Table 6-10. Estimated Number (and Percentage) of Persons and Person-Days with a Daily Maximum End-of-hour COHb Level At or Above the Specified Level – Adults With Coronary Heart Disease (CHD) in the Los Angeles Study Area – Air Quality As Is.

COHb Level (%)	Persons		Person-days		Person-days/person	
	Number	Percent	Number	Percent	On Average	At Level
0.0	383,040	100	139,800,000	100	365	365
1.0	98,043	25.6	1,645,000	1.2	4.3	16.8
1.5	5,820	1.5	86,800	0.1	0.2	14.9
1.8	1,505	0.4	8,630	<0.1	<0.1	5.7
2.0	301	0.1	301	<0.1	<0.1	1.0
2.5	0	0	0	0	0	0
3.0	0	0	0	0	0	0
4.0	0	0	0	0	0	0
Unadjusted ambient concentrations from ten monitors in 2006 were used to represent the *As Is* air quality scenario.						

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

Consistent with the estimated exposure concentrations, dose levels experienced by the CHD population in each study area were greater when considering simulated 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 3% of the CHD population was estimated to have a daily maximum end-of-hour COHb level at or above 2.0% (Table 6-11). There were no persons in Denver estimated above this COHb level based on estimated ambient exposures associated with *as is* air quality. A similar pattern is observed for the CHD population in Los Angeles

(Table 6-12), though a lower percentage of persons (0.5%) was estimated to have daily maximum end-of-hour COHb levels at or above 2.0% when compared results for Denver. In both study areas, a few persons had daily maximum end-of-hour COHb levels extending upwards to 3.0%. Most of the persons that did experience these higher COHb levels (≥2.0%) however, experienced them for fewer than 2 days in a year (Table 6-12).

Table 6-11. Estimated Number (and Percentage) of Persons and Person-Days with a Daily Maximum End-of-hour COHb Level At or Above the Specified Level – Adults With Coronary Heart Disease (CHD) in the Denver Study Area – Air Quality Just Meeting the Current 8-hour Standard.

COHb Level (%)	Persons		Person-days		Person-days/person	
	Number	Percent	Number	Percent	On Average	At Level
0.0	53,656	100	19,580,000	100	365	365
1.0	40,921	76.3	829,300	4.2	15.5	20.3
1.5	10,267	19.1	35,520	0.2	0.7	3.5
2.0	1,814	3.4	2,480	<0.1	<0.1	1.4
2.5	346	0.6	370	<0.1	<0.1	1.1
3.0	86	0.2	86	<0.1	<0.1	1.0
4.0	0	0	0	0	0	0
Ambient concentrations from 1995 were adjusted to just meet a 2nd highest 8-hour average concentration of 9.4 ppm.						

Table 6-12. Estimated Number (and Percentage) of Persons and Person-Days with a Daily Maximum End-of-hour COHb Level At or Above the Specified Level – Adults With Coronary Heart Disease (CHD) in the Los Angeles Study Area – Air Quality Just Meeting the Current 8-hour Standard.

COHb Level (%)	Persons		Person-days		Person-days/person	
	Number	Percent	Number	Percent	On Average	At Level
0.0	383,040	100	139,800,000	100	365	365
1.0	155,243	40.5	2,472,000	1.8	6.4	15.9
1.5	17,561	4.6	120,100	0.1	0.3	6.8
2.0	2,007	0.5	3,111	<0.1	<0.1	1.6
2.5	301	0.1	401	<0.1	<0.1	1.3
3.0	100	<0.1	100	<0.1	<0.1	1.0
4.0	0	0	0	0	0	0
Ambient concentrations from 1997 were adjusted to just meet a 2nd highest 8-hour average concentration of 9.4 ppm.						

6.2.3 Air Quality Adjusted to Just Meet Alternative Air Quality Scenarios

Consistent with results described for the exposure, the percentage of persons estimated to experience maximum end-of-hour COHb at selected levels are general similar across the three potential alternative standard scenarios. For example, in Denver most of the population (>99%) were estimated to not experience a daily maximum end-of-hour COHb level above 2.0% (Table 6-13). There are a few study area differences worthy of note. As expected, the corresponding estimated percent of the CHD population in Denver is greater than that estimated for Los Angeles, even when considering the same potential alternative standard form and air quality level (Table 6-14). For example, when considering a 99th percentile daily maximum 8-hour average CO concentration of 5.0 ppm, 0.8% of the CHD population had an estimated daily maximum end-of-hour COHb level at or above 2.0%; in Los Angeles this dose level was estimated for only 0.1% of the CHD population.

Table 6-13. Estimated Number (and Percentage) of Persons with a Daily Maximum End-of-hour COHb Level At or Above the Specified Level – Adults With Coronary Heart Disease (CHD) in the Denver Study Area – Air Quality Just Meeting Potential Alternative Standards.

COHb Level (%)	2nd highest 8-hour average of 5.4 ppm		99th pct Daily Max 8-hour of 5.0 ppm		99th pct Daily Max 1-hour of 8.0 ppm	
	Persons		Persons		Persons	
	Number	Percent	Number	Percent	Number	Percent
0.0	53,656	100	53,656	100	53,656	100
1.0	19,560	36.5	26,692	49.7	21,040	39.2
1.5	2,061	3.8	3,826	7.1	2,271	4.2
1.8	444	0.8	1,012	1.9	568	1.1
2.0	197	0.4	407	0.8	234	0.4
2.5	62	0.1	86	0.2	62	0.1
3.0	0	0	12	<0.1	0	0
4.0	0	0	0	0	0	0
Ambient concentrations from 1995 were adjusted to just meet the level of the potential alternative standard indicated.						

Table 6-14. Estimated Number (and Percentage) of Persons with a Daily Maximum End-of-hour COHb Level At or Above the Specified Level – Adults With Coronary Heart Disease (CHD) in the Los Angeles Study Area – Air Quality Just Meeting Potential Alternative Standards.

COHb Level (%)	2nd highest 8-hour average of 5.4 ppm		99th pct Daily Max 8-hour of 5.0 ppm		99th pct Daily Max 1-hour of 8.0 ppm	
	Persons		Persons		Persons	
	Number	Percent	Number	Percent	Number	Percent
0.0	383,040	100	383,040	100	383,040	100.0
1.0	53,086	13.9	60,913	15.9	77,772	20.3
1.5	2,408	0.6	3,312	0.9	5,319	1.4
1.8	602	0.2	803	0.2	1,204	0.3
2.0	301	0.1	301	0.1	401	0.1
2.5	0	0	0	0	0	0
3.0	0	0	0	0	0	0
4.0	0	0	0	0	0	0
Ambient concentrations from 1997 were adjusted to just meet the level of the potential alternative standard indicated.						

6.3 COMPARISON OF COHB ESTIMATES OBTAINED FROM THE 2000 PNEM/CO AND DRAFT 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 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 called CHD and with regard to characterizing the population of interest with regard to demographics (age and sex), 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) second draft 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,[4] and defined at-risk population. There are some differences that exist when comparing the specific methodologies:

- number of ambient monitors used (e.g., previously 6 in Denver versus 4 used here),
- location of ambient monitors used (e.g., only 7 of the same monitors used previously were used here for Los Angeles),
- number of microenvironments modeled (previously 15 versus the 8 modeled here)

[4] When considering the exposure scenario that uses air quality just meeting the current standard.

- use of mass balance modeling (previously all 12 enclosed MEs used mass balance, here only indoor MEs use mass balance)
- cohort approach (pNEM) versus individual approach (APEX) , and
- two indoor sources of CO included in the 2000 pNEM/CO assessment for residential microenvironments: gas stoves and passive smoking.

Despite these differences and others not listed, staff still did not expect to see greatly different results when comparing the two assessments given the similarities in the likely influential variables (i.e., ambient concentrations, microenvironmental approach, CFK module used, etc.). Table 6-15 presents estimates for the percentage of Denver adults with CHD estimated to experience a daily maximum end-of-hour COHb level at or above the specified level under the specified air quality conditions for 1995. Table 6-16 presents similar estimates for Los Angeles using the adjusted 1997 ambient air quality to just meet the current 8-hour standard. Each table provides two sets of estimates for the 2000 pNEM/CO assessment (indoor sources "on" and "off") and one set generated for the current (2010) second draft APEX/CO REA.

As expected, the COHb levels estimated by the 2000 pNEM/CO assessment are higher when internal sources are turned on, though in the absence of indoor sources, the range of dose estimates are generally similar in both study areas. 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 3.4% 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.

Table 6-15. Percentage of Denver Adults with Coronary Heart Disease (CHD) Estimated to Experience a Daily Maximum End-of-hour COHb Level At or Above the Specified Percentage – Air Quality Just Meeting the Current Standard.

COHb Level (%)	Percentage of CHD Adults at or Above COHb Level		
	Johnson et al. (2000) pNEM/CO[a]		2010 2nd draft REA APEX/CO[b]
	Internal sources on	Internal sources off	Internal sources off
6.0	0.2	0	0
5.0	0.6	0	0
4.0	1.6	0	0
3.0	5.5	< 0.1	0.2
2.5	10.4	0.2	0.6
2.0	19.9	0.5	3.4
1.5	37.6	6.7	19.1
1.0	83.2	65.0	76.3
0	100	100	100

[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).

Table 6-16. Percentage of Los Angeles Adults with Coronary Heart Disease (CHD) Estimated to Experience a Daily Maximum End-of-hour COHb Level At or Above the Specified Percentage – Air Quality Just Meeting the Current Standard.

COHb Level (%)	Percentage of CHD Adults at or Above COHb Level		
	Johnson et al. (2000) pNEM/CO[a]		2010 2nd draft REA APEX/CO[b]
	Internal sources on	Internal sources off	Internal sources off
6.0	0.2	0	0
5.0	0.8	0	0
4.0	2.2	0	0
3.0	5.1	<0.1	<0.1
2.5	9.0	<0.1	0.1
2.0	16.8	0.5	0.5
1.5	32.3	5.2	4.6
1.0	79.0	58.1	40.5
0	100	100	100

[a] Los Angeles 1997 ambient CO concentrations adjusted to just meet the current 8-hour standard (9.4 ppm).

6.4 EVALUATION OF ENDOGENOUS CO CONTRIBUTION TO COHB LEVELS IN APEX SIMULATED INDIVIDUALS

As summarized in section 4.4.7 and described fully in Appendix B, staff 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. Staff has performed such a simulation using APEX for both study locations. The results of these simulations, conducted in a similar manner as the above exposure scenarios (i.e., a 50,000 person simulation and the random assignment of the CHD population from this simulation) only in the absence of environmental CO concentrations, are provided in section 6.3.1. A second set of simulations was performed to better characterize the endogenous CO production rate and its impact on estimated COHb levels. This second set of simulations considered both the estimated COHb levels associated with and without ambient exposures for an identical, yet smaller, set of individuals. The purpose of this focused analysis was to determine the contribution of the endogenous CO and ambient exposure to total COHb levels. Because the generation of these data required hourly concentration output and multiple model runs, the sample size was restricted to less than 100 simulated persons to maintain a manageable data file. In addition, this subpopulation was a random sample from the entire adult population residing within the Denver study area. Details of this second set of simulations are provided in section 6.4.2.

6.4.1 Estimation of Endogenous CO Contribution to Population COHb Levels

As mentioned above, these two additional simulations were conducted in each the Denver and Los Angeles study areas. Fifty thousand persons were simulated, as was done when considering the five exposure scenarios. The only difference between these APEX simulations and those for the five air quality scenarios was the ambient concentration input files used. In these two model runs, all ambient CO concentrations equaled zero. The same output described above for the five air quality scenarios were generated, only in this instance, the distribution of population exposures effectively equals zero. We evaluated smaller bins of the maximum end-of-hour COHb level below 1.0% in these simulations (i.e., 0.25%) given that even when using *as is* air quality, most persons had COHb levels at or below 1.0%. We report the daily maximum end-of-hour COHb levels for the simulated CHD population and, given this, the results can be considered as a single view of population-level endogenous CO production.[5] We caution against assuming that there is a direct correlation between the endogenous CO production estimated here and the total COHb levels estimated for each study area in the prior sections. That is, the daily maximum end-of hour COHb level estimated to result from endogenous CO production

[5] Theoretically the APEX model can estimate all hourly values as was done in section 6.4.2.

exclusively may not necessarily be correlated with the daily maximum end-of hour COHb level for the sum of endogenous CO production and ambient CO exposures. Nevertheless, it still provides some information regarding the potential effect of the endogenous CO production on estimated COHb levels in the simulated population.

Table 6-17 summarizes the daily maximum end-of-hour COHb levels estimated for the CHD population in Denver and Los Angeles, with no ambient CO exposure contribution. In general, the population distributions for the two areas are very similar, with the majority of the population (about 99%) having a daily maximum end-of-hour COHb level of less than 1.0%. The mean and median COHb level would approximately fall between 0.25 and 0.50% in both populations, with the percent population estimated to experience maximum end-of-hour COHb levels at or above 1.0% greater in the Denver study area (1.5%) than in the LA area (0.8%). These estimated distributions do not appear outside of what might be expected given some of the available data reported in the extant literature. However, as a reminder, these output data are for the maximum value that occurred in an entire year simulation. The distribution for the average end-of-hour COHb level associated with endogenous CO production would surely be less than that indicated here and likely more comparable to any available measurement data. Staff notes that these distributions represent a population sample and is unique in its own right; even if a mean estimate could be constructed it may not be comparable to measurements performed on a smaller (and possibly not random) population of limited study subjects.

Table 6-17. Estimated Number (and Percentage) of Persons with a Daily Maximum End-of-hour COHb Level At or Above the Specified Level – Adults With Coronary Heart Disease (CHD) in the Denver and Los Angeles Study Areas – Zero Ambient Exposures.

COHb Level (%)	Denver		Los Angeles	
	Persons	Percent	Persons	Percent
0.00	53,656	100	383,040	100
0.25	47,362	88.3	327,546	85.5
0.50	13,537	25.2	85,098	22.2
0.75	3,209	6.0	17,260	4.5
1.00	790	1.5	3,211	0.8
1.25	140	0.3	803	0.2
1.50	12	<0.1	301	<0.1
1.80	0	0	100	<0.1
2.00	0	0	0	0

6.4.2 Contribution of Endogenous CO Production and Ambient Exposures to COHb Level in Limited Simulations

Two APEX model simulations were performed for this second evaluation: one using 1995 Denver ambient concentrations adjusted to just meet the current standard (9.4. ppm) and the second using ambient concentrations equal to zero. Each of the new runs simulated 8,760 hours of exposure for each of 92 persons (n = 92 people x 8,760 hrs/person = 805,920 person-hours per run). 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 across the two runs hour by hour. We first calculated all 805,920 hour-by-hour ambient contributions (*COHb ambient contribution*) in 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. Table 6-18 provides the descriptive statistics for the COHb ambient contribution experienced by the selected population. Below are listed selected statistics for COHb ambient contribution based on the entire hourly data set (N = 805,920). Figure 6-1 provides the same information only in graphical form; note that most of the ambient contribution to COHb levels values fall between 0.1 and 0.4% COHb and can be well represented by a lognormal distribution {GM 0.205, GSD 1.57}. The complete distribution of the endogenous contribution to COHb levels is also provided in Table 6-18. Most of the simulated hours for the population had an endogenous end-of-hour COHb level contribution of less than 0.5%, though for a limited number of hours, the endogenous contribution could be over 1.0% COHb. On average, this limited population was estimated to have just over half of their hourly total COHb level attributed to endogenous COHb production.[6]

Table 6-18. Descriptive statistics for the % COHb ambient contribution estimated using Denver 1995 ambient concentrations adjusted to just meet the current standard.

Statistic (N = 805,920)	COHb Ambient Contribution (% COHb)	COHb Endogenous (% COHb)	COHb Total (% COHb)
Arithmetic Mean	0.2264	0.255	0.4814
Arithmetic SD	0.109	0.1476	0.1757
Geometric Mean	0.2046	0.2206	0.4529
Geometric SD*	1.5682	1.7085	1.4151
Minimum	0.003	0.0329	0.0988
10^{th} percentile	0.1155	0.1106	0.2912
20^{th} percentile	0.1416	0.1373	0.3378

[6] One should not go beyond comparing the means or 50^{th} percentiles of the ambient and endogenous contribution as the other percentiles of the distribution are likely not correlated.

Statistic (N = 805,920)	COHb Ambient Contribution (% COHb)	COHb Endogenous (% COHb)	COHb Total (% COHb)
30th percentile	0.1628	0.1631	0.3766
40th percentile	0.1833	0.1882	0.413
50th percentile	0.2046	0.2177	0.4504
60th percentile	0.2284	0.2544	0.4915
70th percentile	0.2573	0.299	0.5407
80th percentile	0.2965	0.3526	0.6063
90th percentile	0.3615	0.4404	0.7098
95th percentile	0.4268	0.5343	0.8034
98th percentile	0.5192	0.6405	0.9332
99th percentile	0.5949	0.778	1.062
99.5th percentile	0.6759	0.9006	1.188
99.8th percentile	0.8006	1.07	1.319
99.9th percentile	0.9086	1.2	1.394
Maximum	1.9158	1.541	2.323
Notes: * dimensionless			

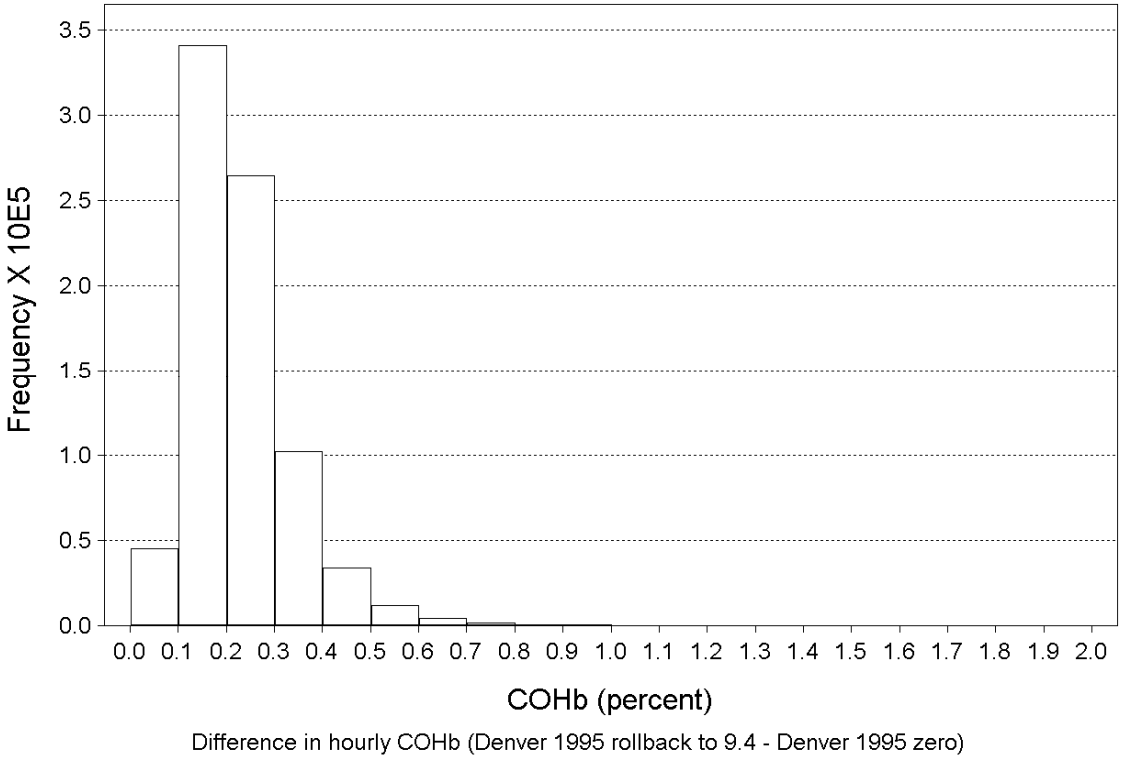

Figure 6-1. Histogram of the % COHb ambient contribution estimated using Denver 1995 ambient CO concentrations adjusted to just meet the current standard.

Two other metrics were calculated for each individual using the same hourly output for the limited simulation run. First, staff calculated the 1-hour COHb ambient contribution

associated with the maximum total 1-hour COHb (i.e., endogenous and ambient contribution) and second, the 1-hour total COHb associated with the maximum COHb ambient contribution. The purpose of these metrics was to determine the relative contribution the endogenous CO production and ambient exposure have on the maximum hourly COHb level.

Figure 6-2 illustrates the contribution of endogenous CO production relative to that of each person's maximum end-of-hour COHb level. As can be seen in the figure, there is not a strong relationship between the two variables, that is, the endogenous CO production does little to influence a persons maximum end-of-hour COHb level, given this air quality scenario (i.e., just meeting the current standard in Denver). Consistent with the population distribution described above (section 6.4.1), there are very few individuals that were estimated to have maximum end-of-hour COHb levels at or above 1.0% in the absence of ambient CO exposure. As described earlier, it was expected that there would not be a relationship between the contribution of endogenous CO production to COHb level and the ambient exposure contribution to COHb. This expectation is confirmed by the results presented in Figure 6-3.

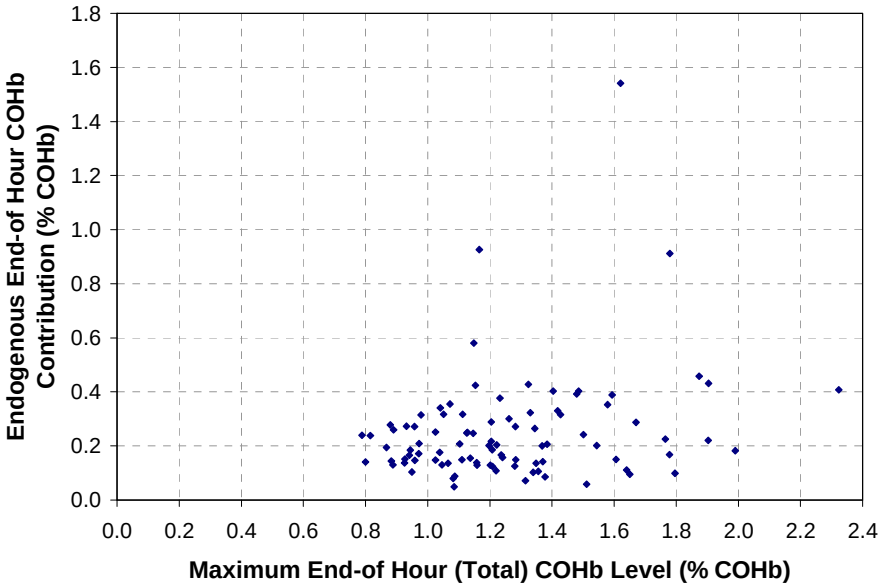

Figure 6-2. The contribution of endogenous CO production relative to an individual's maximum end-of-hour COHb level using 1995 Denver ambient concentrations adjusted to just meet the current standard.

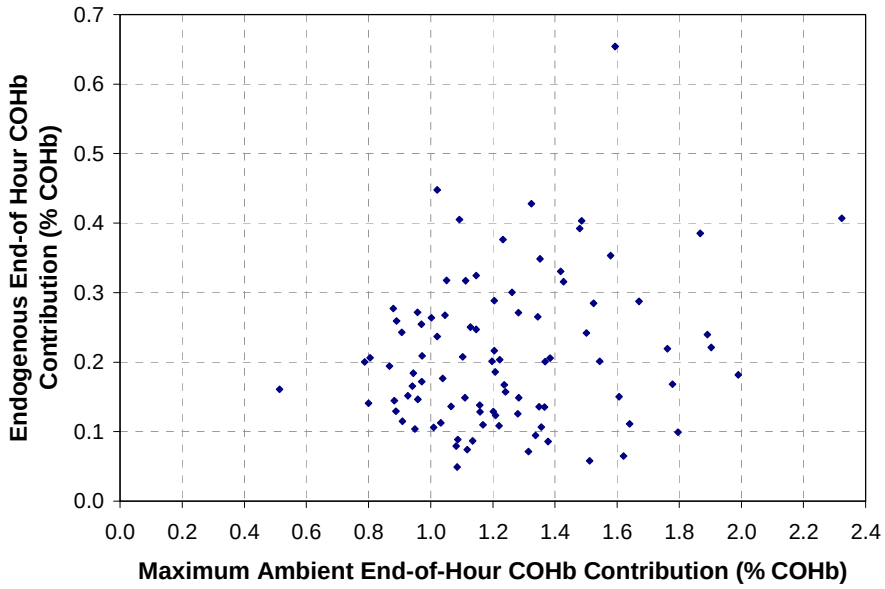

Figure 6-3. Comparison of endogenous CO production relative to an individual's maximum COHb ambient contribution using 1995 Denver ambient concentrations adjusted to just meet the current standard.

Alternatively, one can see the strong relationship between the maximum end-of-hour COHb level and the contribution from ambient exposure (Figure 6-4). For the majority of the 92 simulated persons, the maximum end-of-hour total COHb level (i.e., the combined contribution from both endogenous CO production and ambient CO exposure) is largely driven by the contribution from ambient CO exposure.

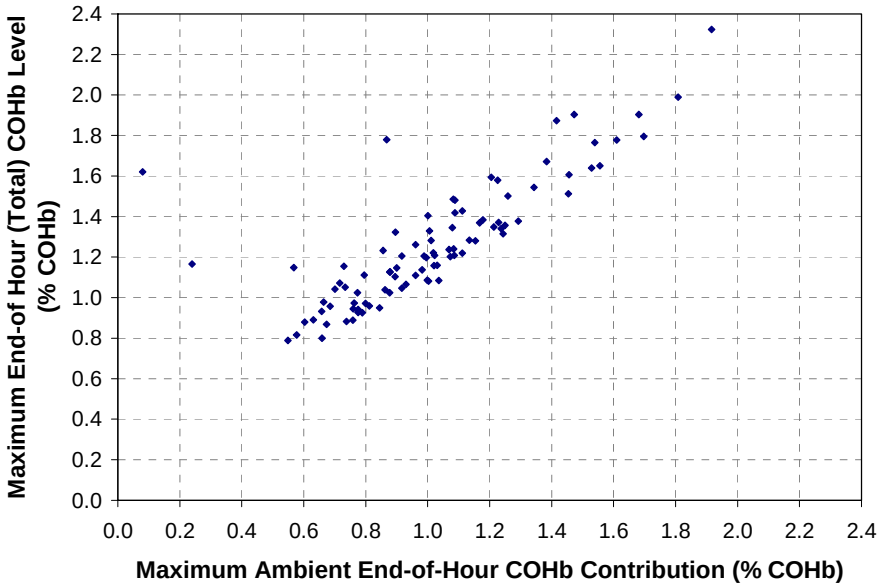

Figure 6-4. Comparison of endogenous CO production relative to an individual's maximum COHb ambient contribution using 1995 Denver ambient concentrations adjusted to just meet the current standard.

6.5 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 exposed individuals were estimated for populations in two study areas in the Los Angeles and Denver areas under 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.
- More than 98% of the simulated at-risk population in each study area was estimated to experience a daily maximum end-of-hour COHb level below 1.5% over the course of a year considering *as is* air quality in either study area, with more than 99.9% of the selected at-risk population in both areas having daily maximums COHb levels below 2%.
- The distribution of maximum end-of-hour COHb levels extended slightly higher for the Los Angeles population when using *as is* air quality, while the Denver population was

estimated to experience higher levels under conditions of air quality adjusted to just meet the current standard.

- More than 95% of the simulated at-risk population in the Los Angeles study area was estimated to experience an annual daily maximum end-of-hour COHB level below 1.5%, and 99.5% with maximum COHb less than 2%, with air quality adjusted to just meet the current standard. In contrast, 80.1% of the simulated at-risk population in the Denver study area was estimated to experience a daily maximum end-of-hour COHB level below 1.5%, and greater than 95% with maximum COHb less than 2%, in air quality conditions adjusted to just meet the current standard.

- Alternative standards that we considered in this document included two potential alternative forms for the 8-hour standard and one potential alternative form for the1-hour standard. Beyond the results for alternative forms presented in this document, results for alternative standard levels for any given combination of averaging time and form are presented and discussed in the draft Policy Assessment.

- The three potential alternative standards considered in this document resulted in generally similar percentages of individuals exposed at selected concentrations and maximum end-of hour COHb levels. Each of these potential alternative standards generated fewer persons and a lower percent of the CHD population at or above selected COHb levels (e.g., <1% at a 2.0% COHb level in Denver) when compared with corresponding COHb levels associated with air quality adjusted to just meet the current 8-hour standard (e.g., 3.4% at a 2.0% COHb level in Denver). When considering the potential alternative standards in Los Angeles, only 0.1% of the CHD population was 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.

- A few simulations with a small number of individuals in which no external CO sources were included provided limited information regarding the contribution of endogenous COHb to the total COHb estimates produced. This quite limited information indicates that most simulated individuals have endogenous COHb levels below 1% and that the upper end of total COHb (reflecting ambient plus endogenous contributions) may arise as a result of an individual receiving high external CO exposures rather than having higher endogenous levels.

- 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). While the two assessments employed similar approaches and similar, although not identical, air quality data for this scenario, they used different versions of the exposure model (APEX vs. pNEM). Results were quite similar for the 1.5% and 2% COHb level in Los Angeles study area and somewhat different in the Denver study area.

6.6 REFERENCES

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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 and associated CO exposure and health risk across the study locations and population. In this second draft 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 CO population exposure and dose (e.g., time spent inside vehicles, moderate or greater exertion 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 and estimated parameters within the exposure and dose assessment performed rather than employing standard default assumptions and/or using point estimates to describe model inputs. The details regarding any 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 dose levels. As a result, APEX addresses much of the variability in factors that affect human exposure and dose. The variability accounted for in this analysis is summarized in Table 7-1.

Table 7-1. Summary of How Variability Was Incorporated Into the Second Draft CO REA.

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 persons visit and activities performed, 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.
	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	Three age-group (18-29, 30-59, and 60+) by gender specific regression equations 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 distribution with geometric mean (GM) and geometric standard deviation (GSD) distribution specific to age and gender 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 from analyses (Johnson, 1998) of height and weight data (Brainard and Burmaster, 1992) (see Appendix B for details).
	Blood volume	Values determined according to gender using equations based on work by 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 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.

Staff has used such an iterative process in characterizing the uncertainty associated with the approach and data used in the 1st draft REA. Following a review of that 1st draft REA by CASAC, a few sources of uncertainty were identified as most important in improving the

approach used to estimate exposure and dose for the second draft CO REA. This included 1) expanding the number of monitors used to better address spatial variability in ambient CO concentrations, 2) increasing the number of microenvironments modeled from two to eight, 3) using distributions of proximity factors to estimate all microenvironmental concentrations rather than simple point estimates, and 4) additional analysis of historical trends in ambient CO concentrations at individual monitors. These additional analyses and approaches used are not without their own uncertainties, and following this iterative process, also need to be characterized.

The 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 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 second draft 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 evaluate 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,

[1] This is synonymous with the "level of uncertainty" discussed in WHO (2008), section 5.1.2.2.

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 of particular model forms), though 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 provide 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 severity of the uncertainty as implied by the relationship between the source of the uncertainty and the exposure concentrations and COHb dose 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 5-7 through 5-10). There is still uncertainty in the approach used, since there are a variety of methods available to use. 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 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 high as *medium*. A characterization of *high* implies that a small change in the

source would have a large effect on results. This rating would be used where model was extremely sensitive to the identified source 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. There are several sources of uncertainty associated with this simplified approach for modeling CO population exposure/dose and associated potential health risk, each summarized and discussed in Table 7-2.

As mentioned in section 1 above, given the significant time constraints of this review, results of the assessment 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 draft Policy Assessment.

Table 7-2. Characterization of Key Uncertainties in the Second Draft CO REA for Denver and Los Angeles Areas.

Sources of Uncertainty		Influence of Uncertainty on Exposure/Dose Estimates		Knowledge-Base Uncertainty	Comments[a]
Category	**Element**	**Direction**	**Magnitude**		
Ambient CO Monitor Concentrations	Database Quality	Over	Low	Low	INF: There may be a limited number of poor quality high concentration data within the analytical data sets, potentially influencing the number of benchmark dose level exceedances. Note also that the uncertainty regarding low concentration data near the monitor detection limit is unlikely to influence the number of benchmark exceedances. KB: EPA's Air Quality System data used in the analyses are of high quality. There is no other source of monitoring data as comprehensive. Data are being used in a manner consistent with one of the defined objectives of ambient monitoring.
	Spatial and Temporal Representation	Both	Low - Medium	Medium	INF: Use of several ambient monitors better represents spatial-temporal variability in ambient CO levels throughout each study area when compared with the simplified approach used in the 1st draft CO REA. Analysis of the monitoring concentrations indicates there is spatial variability in monitoring concentrations across each area, but that it is relatively limited, particularly for more recent ambient concentrations (low magnitude). In comparing results generated using the simplified approach used in the 1st draft CO REA however, selection of the particular monitor(s) used may have a medium magnitude of influence on estimated exposures. KB: Each ambient monitor has specific objectives and monitoring scale that may not appropriately capture the true spatial and temporal variability in CO concentrations. In the absence of 1) a monitoring network designed to 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.
	Missing Data Substitution	Under	Low	Low	INF: Assuming there is an equal probability of missing low and high concentration hourly values, and that substituted data are limited by the bounds of the algorithm (i.e., as defined by limits in the measurement data), there may be a few missing high concentration data that could lead to underestimation in exposure concentrations and doses. This assumes that the substitution of low-level concentration data with potentially higher concentrations (within the bounds of the algorithm) does not affect exposure results. KB: All available measurement data are quality assured. Very few data values were substituted with respect to the number of measured values available in each location.
Adjustment of Air Quality to Simulate Just Meeting the Current and Potential Alternative Standards	Historical Data Used	Unknown	Low - Medium	Medium	INF & KB: Even though the historical data represent a real air quality condition that may be similar to concentrations levels expected to just meet the 8-hour current and potential alternative standards, the condition simulated is hypothetical. Based on observed trends in air quality over time and the results generated using adjusted ambient concentrations, staff judges that, at most, the magnitude of influence would be a medium level. However, there is uncertainty in how influential factors such as emission levels per vehicle, vehicular traffic, and meteorology compare between an earlier period of time and the hypothetical scenario of just meeting the current standard some time in the future. 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 knowledge base uncertainty as medium.

Sources of Uncertainty		Influence of Uncertainty on Exposure/Dose Estimates		Knowledge-Base Uncertainty	Comments[a]
Category	Element	Direction	Magnitude		
	Proportional Approach Used	Both	Low	Low	INF: The magnitude of the adjustment applied to historical ambient concentration data was wide ranging. For example, in Denver, to just meet the current standard 0.99 was the adjustment applied. In comparison, to just meet a 2nd highest 8-hour average CO concentration in Los Angeles, a greater adjustment was needed (0.36). However, in comparing recent and historical ambient CO concentrations for several ambient monitors in Los Angles (Figure 3-4), a strong proportional relationship is present when comparing the recent and historic CO concentrations. KB: A similar proportional 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). In addition, little difference was observed here when comparing exposure results using the1997 LA data adjusted downwards to level similar to that observed with the *as is* air quality with exposure results using the 2006 air quality.
APEX Inputs and Algorithms	Population Database	Both	Low	Low	INF & KB: Population data 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 dose results.
	Activity Pattern Database	Unknown	Low – Medium	Medium	INF: Data are actual records of the time spent in specific locations while performing specific activities in particular locations. While not specific to a particular area, the activity patterns of a population are generally well represented by the mainly population-based and nationally-representative survey data (e.g., see Table E-1 in Appendix E regarding the patterns of typical commuting in CHAD versus the urban locations modeled in this assessment). CHAD is comprised of data from individuals that may or may not have had an identified health condition and are assumed to represent the activities of persons with normal health status as well as those with certain health conditions that may not affect general activity patterns. 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). Activity patterns for persons with angina were compared to those individuals not having angina using various exertion level metrics and time spent outdoors or inside-vehicles. The percentages of time spent outdoors or in a vehicle were generally not statistically significant different between angina and non-angina subjects. While there were statistically significant differences in the exertion rate between angina and non-angina subjects, it was likely a function of the large sample size for the non-angina subjects since actual differences were generally numerically small compared to the mean values. The differences in activity and exertion 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. KB: Data are from a reliable and quality assured source (CHAD) and are from surveys of real persons. 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. However, there are several assumptions made that contribute to uncertainty in its use. For example, activity patterns of persons surveyed over 30 years ago are assumed to represent a current persons activity patterns.

Sources of Uncertainty		Influence of Uncertainty on Exposure/Dose Estimates		Knowledge-Base Uncertainty	Comments[a]
Category	Element	Direction	Magnitude		
	Longitudinal Profile Algorithm	Both	Low – Medium	Medium	INF: This assessment focused on persons having at least one exposure or dose above a selected level (low magnitude), however when considering multi-day exposures, the magnitude of potential influence is judged as medium. KB: In developing the longitudinal method, the evaluation indicated that both the *D* and *A* statistics are reasonably reproduced for the population. In addition, the approach was compared to two other independent methods used for constructing longitudinal activity patterns (see Appendix B, Attachment 5 of US EPA, 2009). Note however, long-term diary profiles (i.e., monthly, annual) do not exist for a population.
	Meteorological Data	Both	Low	Low	INF & KB: Data are from the National Weather Service, a well-known and quality-assured source. Daily maximum temperatures are used when selecting appropriate diaries to simulate individuals. The bin ranges used are wide such that erroneous temperature data would likely have limited impact to exposure results. Daily mean temperatures are used when selecting air exchange rates. Given the overlap of the AER distributions and the wide temperature ranges used to categorize them, there is likely limited impact by erroneous temperature data.
	Microenvironmental Algorithm and Input Data	Unknown	Medium	Medium	INF & KB: In this second draft CO 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 reasonable. However, how these data derived from a Denver study reflect similar relationships in Los Angeles 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, for most of the distributions, in particular those used to estimate high exposure microenvironments, there are other comparable measurement data and relationships available (albeit limited in number) to generally support the distributions applied in this assessment.
	Commuting Algorithm	Both	Low	Low	INF & KB: In this second draft 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.
	CHD Prevalence	Both	Low	Medium	INF & KB: 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.

Sources of Uncertainty		Influence of Uncertainty on Exposure/Dose Estimates		Knowledge-Base Uncertainty	Comments[a]
Category	Element	Direction	Magnitude		
	Physiological Factors	Unknown	Low – Medium	Medium	INF & KB: Many of the parameters used to estimate the physiological attributes of the CHD 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 conditions may not necessarily be associated with the simulated at-risk population, i.e., CHD individuals. In addition, some of the parameters used to estimate COHb levels are based on older publications (some dating back to the mid 20th century). It is possible that most of the 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.
Potential Health Effect Benchmark Levels	Simulated At-Risk Population	Unknown	Low	Medium	INF & KB: 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% 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 about the lowest benchmark level identified (i.e., 1.5%) and 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.

Notes:

[a]INF refers to comments associated with the influence rating; KB refers to comments associated with the knowledge-base rating.

[b]This entry focuses on the uncertainty associated with the benchmark levels in their application to estimated COHb levels for the simulated at-risk population (i.e., individuals with diagnosed/undiagnosed CHD, inclusive of angina pectoris and heart attacks). 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.

7.3 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 reasonable for the simulated population the assessment is intended to represent (i.e., the CHD population residing within the urban core of each study area). This is because:

- Only two sources of uncertainty were associated with a potential directional influence: data base quality (overestimation) and missing data substitution (underestimation), and both were judged to have a low magnitude of influence on estimated exposures and doses.
- Twelve of the identified sources of uncertainty were judged by staff to have either bidirectional influence (eight sources) or unknown (four sources) direction:
  - 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 eleven sources (i.e., spatial and temporal 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.
  - Six of the sources were judged to have a low magnitude of influence on estimated exposures and doses (i.e., proportional approach used, population database, meteorological data, commuting data, CHD prevalence, 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:

- Eight 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, CHD prevalence, 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, population database, meteorological data, commuting data.
- The knowledge-base uncertainty was also judged as low for the two sources identified above as being associated with either under- or overestimating exposures.

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 six sources (i.e., the spatial and temporal representation, 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.

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8 SUMMARY OF KEY OBSERVATIONS

Presented together below are the key observations made in each of the chapters.

Introduction

- This draft 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). The previous review of the CO NAAQS was concluded in 1994 with confirmation of the current standards. An assessment of ambient CO exposure/dose was developed in an earlier phase of this review in the late 1990s. The design of this 2nd draft REA builds upon recommendations from CASAC, information presented in the final ISA, as well as comments made by the public.

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.
- 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 CO health effects of concern.
- 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 to contribute susceptibility to CO effects. Other populations potentially at risk include individuals with diseases such as chronic obstructive pulmonary disease (COPD), anemia, or diabetes, and individuals in prenatal or elderly life stages.
- Cardiovascular effects are the health endpoint for which the evidence is strongest and indicative of a likely causal relationship with CO exposures. Other endpoints for which the evidence is suggestive of such a relationship include effects on the central nervous system, reproduction and prenatal development, and the respiratory system.
- Risk is characterized in this REA through evaluation of COHb estimated to result from ambient CO exposure in individuals with CHD (including undiagnosed persons) considering potential health effect benchmarks for daily maximum COHb levels. Results are reported in terms of percent of population expected to experience daily maximum COHb levels at or above a series of levels that range as low as 1%. These results are considered in the Policy Assessment document in light of potential health

effects benchmarks ranging 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 associated with adverse effects in those studies.

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 limited to roads where traffic density described for them is moderate (<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 peaks 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 standard and those reflecting current (*as is*) conditions.
- The temporal variability in selected upper percentile ambient concentrations (e.g., 99^{th} percentile 1-hour daily maximum) at individual monitors is relatively small across a three year monitoring period, particularly when considering recent air quality.

Overview Of Approach Used for Estimating Co Exposure and COHb Dose Levels

- 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, staff have 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.

Application of APEX4.3 in this Assessment

- 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.
- The selected at-risk population was simulated by combining the tract-specific age and gender population distribution and the CHD prevalence, also stratified by age and gender. In using this approach, staff can represent the variability that exists in the CHD population that resides in each census tract and within each study area.
- Staff expanded the selected at-risk population to include an estimate of persons with undiagnosed CHD.
- Compared with the single-monitor approach used for the first draft CO REA, staff expanded the number of ambient monitors used in this second draft CO REA to better capture the spatial variability in ambient concentrations. In Denver, a total of four monitors were used, in Los Angeles, the total number of monitors was ten.
- Compared with the two microenvironments modeled in the first draft CO REA, staff has expanded the number modeled in each location to eight. This approach is designed to better represent the expected variability in microenvironmental CO concentrations.
- Compared with the approach used to estimate microenvironmental concentrations in the first draft CO REA (factors approach only), all indoor microenvironments were modeled using a mass balance model in this second draft assessment. Use of the mass balance model will better represent temporal variability in indoor CO concentrations with respect to the outdoor CO concentration variability. In addition, distributions of microenvironmental factors were used in this second draft CO REA for all microenvironments rather than using point estimates (as was done for the first draft CO REA). Using distributions of microenvironmental factors will better represent both spatial and temporal variability in estimated microenvironmental CO concentrations

Simulated Exposure and COHb Dose Results

- Ambient CO exposures and resulting COHb levels in the blood of exposed individuals were estimated for populations in two study areas in the Los Angeles and Denver areas under 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.
- More than 98% of the simulated at-risk population in each study area was estimated to experience a daily maximum end-of-hour COHb level below 1.5% over the course of a year considering *as is* air quality in either study area, with more than 99.9% of the selected at-risk population in both areas having daily maximums COHb levels below 2%.
- The distribution of maximum end-of-hour COHb levels extended slightly higher for the Los Angeles population when using *as is* air quality, while the Denver population was

estimated to experience higher levels under conditions of air quality adjusted to just meet the current standard.

- More than 95% of the simulated at-risk population in the Los Angeles study area was estimated to experience an annual daily maximum end-of-hour COHB level below 1.5%, and 99.5% with maximum COHb less than 2%, with air quality adjusted to just meet the current standard. In contrast, 80.1% of the simulated at-risk population in the Denver study area was estimated to experience a daily maximum end-of-hour COHB level below 1.5%, and greater than 95% with maximum COHb less than 2%, in air quality conditions adjusted to just meet the current standard.

- Alternative standards that we considered in this document included two potential alternatives for the 8-hour standard and one potential alternative 1-hour standard. The results looking at alternative levels for any given combination of averaging time and form are presented and discussed in the draft Policy Assessment.

- For the three potential alternative standard scenarios for which results are presented in this document provided generally similar percent of individuals exposed at selected concentration levels and maximum end-of hour COHb levels. Each of these potential alternative standards generated fewer persons and a lower percent of the CHD population at or above selected COHb levels (e.g., <1% at a 2.0% COHb level in Denver) when compared with corresponding COHb levels and using air quality adjusted to just meeting the current standard (e.g., 3.4% at a 2.0% COHb level in Denver). When considering the potential alternative standard scenarios in Los Angeles, only 0.1% of the CHD population was estimated to experience a maximum end-of-hour COHb level of 2.0 % COHb compared to 0.5% at that same COHb level and using air quality adjusted to just meet the current standard.

- A few simulations with a small number of individuals in which no external CO sources were included provided limited information regarding the contribution of endogenous COHb to the total COHb estimates produced. This quite limited information indicates that most simulated individuals have endogenous COHb levels below 1% and that the upper end of total COHb (reflecting ambient plus endogenous contributions) may arise as a result of an individual receiving high external CO exposures rather than having higher endogenous levels.

- 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). While the two assessments employed similar approaches and similar, although not identical, air quality data for this scenario, they used different versions of the exposure model (APEX vs. pNEM). Results were quite similar for the 1.5% and 2% COHb level in Los Angeles study area and somewhat different in the Denver study area.

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 reasonable for the simulated population the assessment is intended to represent (i.e., the CHD population residing within the urban core of each study area). This is because:
    - Only two sources of uncertainty were associated with a potential directional influence: data base quality (overestimation) and missing data substitution (underestimation), and both were judged to have a low magnitude of influence on estimated exposures and doses.
    - Twelve of the identified sources of uncertainty were judged by staff to have either bidirectional influence (eight sources) or unknown (four sources) direction:
        - 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 eleven sources (i.e., spatial and temporal 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.
        - Six of the sources were judged to have a low magnitude of influence on estimated exposures and doses (i.e., proportional approach used, population database, meteorological data, commuting data, CHD prevalence, 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:
    - Eight 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, CHD prevalence, 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, population database, meteorological data, commuting data.
    - The knowledge-base uncertainty was also judged as low for the two sources identified above as being associated with either under- or overestimating exposures.

- 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 six sources (i.e., the spatial and temporal representation, 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.

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 draft 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.

Table of Contents

LIST OF FIGURES

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 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:

$$w_{combined} = \frac{1}{3} w_{2003-2004} \quad (1)$$

$$w_{combined} = \frac{2}{3} w_{1999-2002} \quad (2)$$

where $w_{combined}$ is the sampling weight for the combined dataset, $w_{2003-2004}$ is the weight for the subjects in the most recent study, and $w_{1999-2002}$ 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.

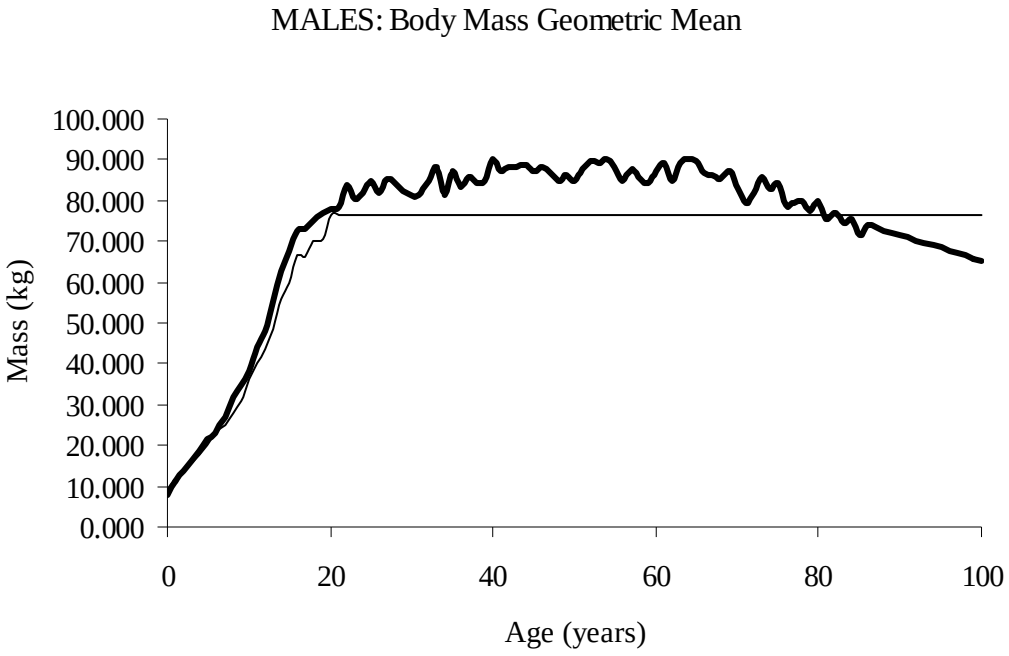
3.4 Body Mass Results.

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.



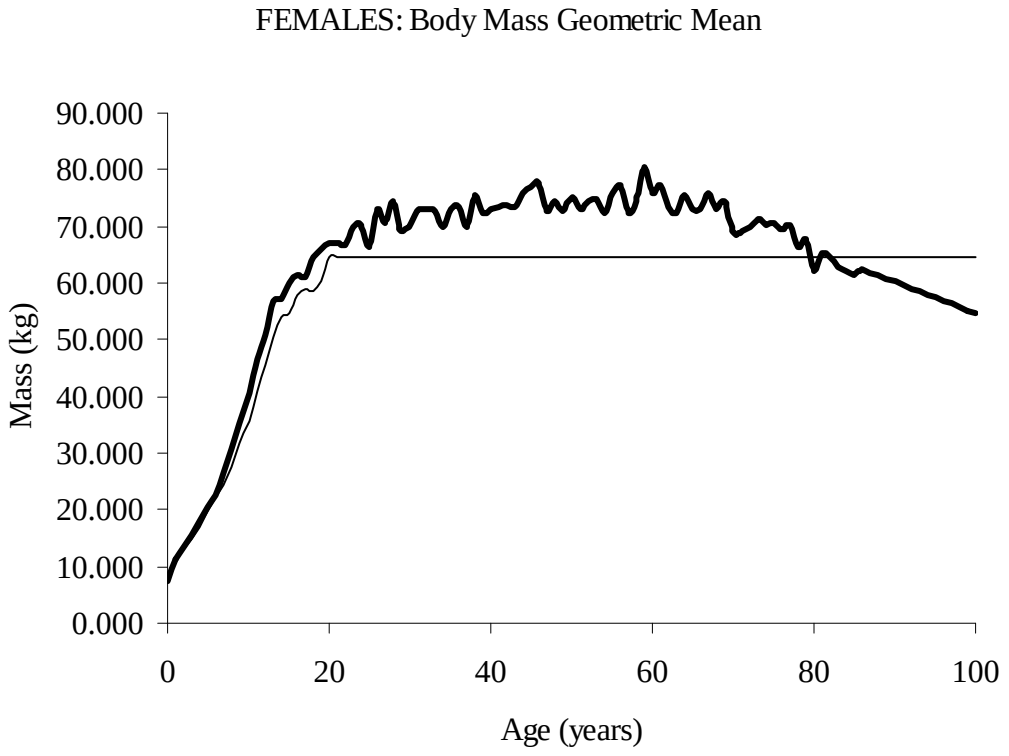
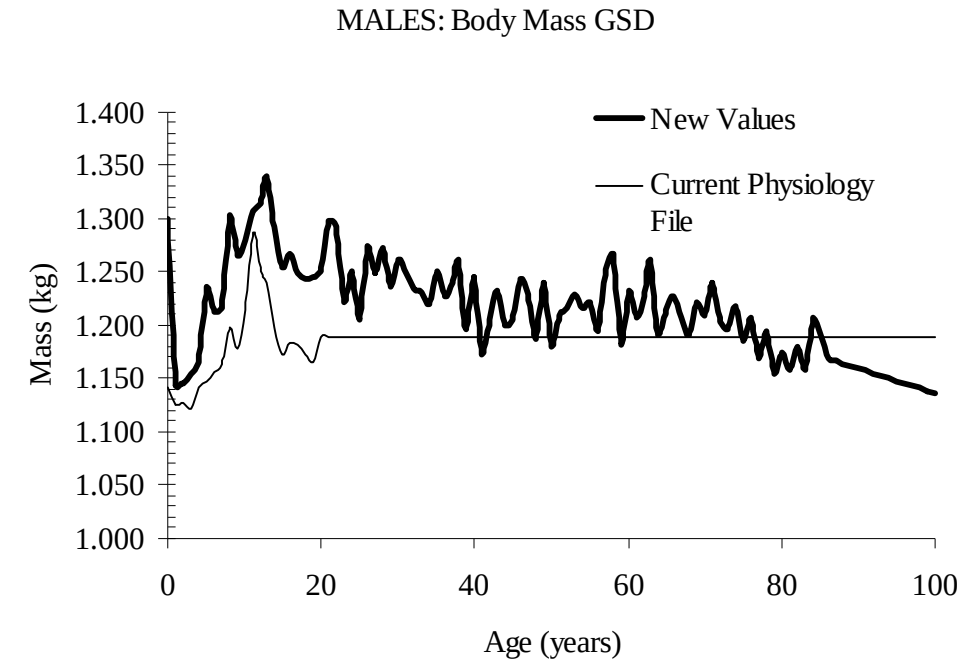


Figure 1. Geometric Means for the Best-fit Lognormal Distributions for Body Mass as a Function of Age, Derived from NHANES 1999-2004 Study Data.



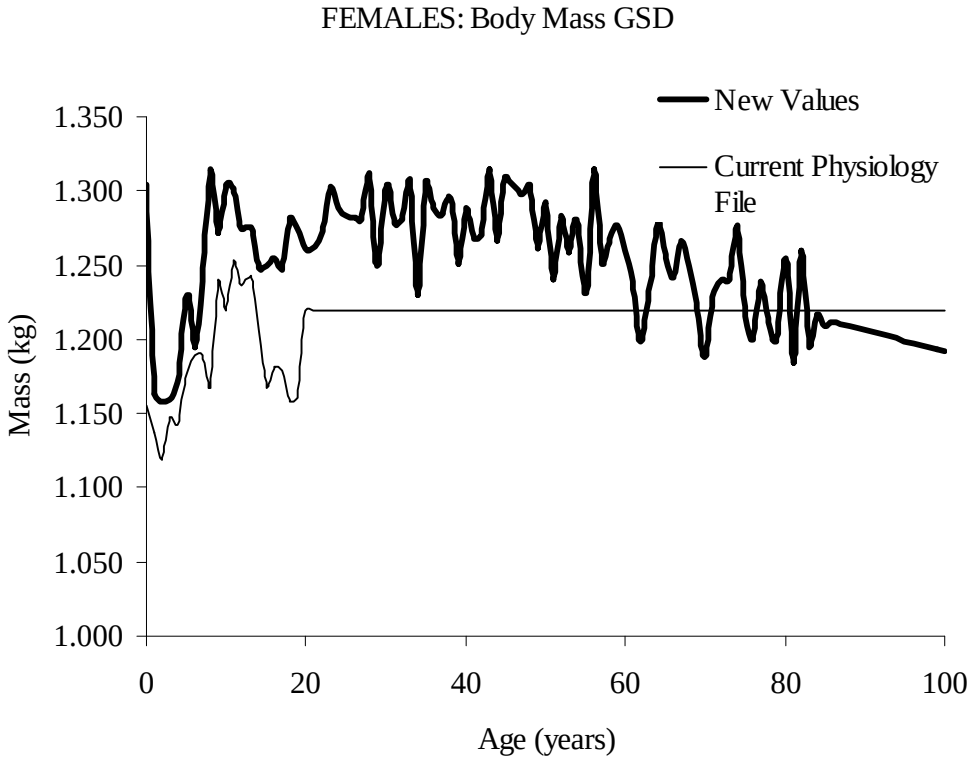
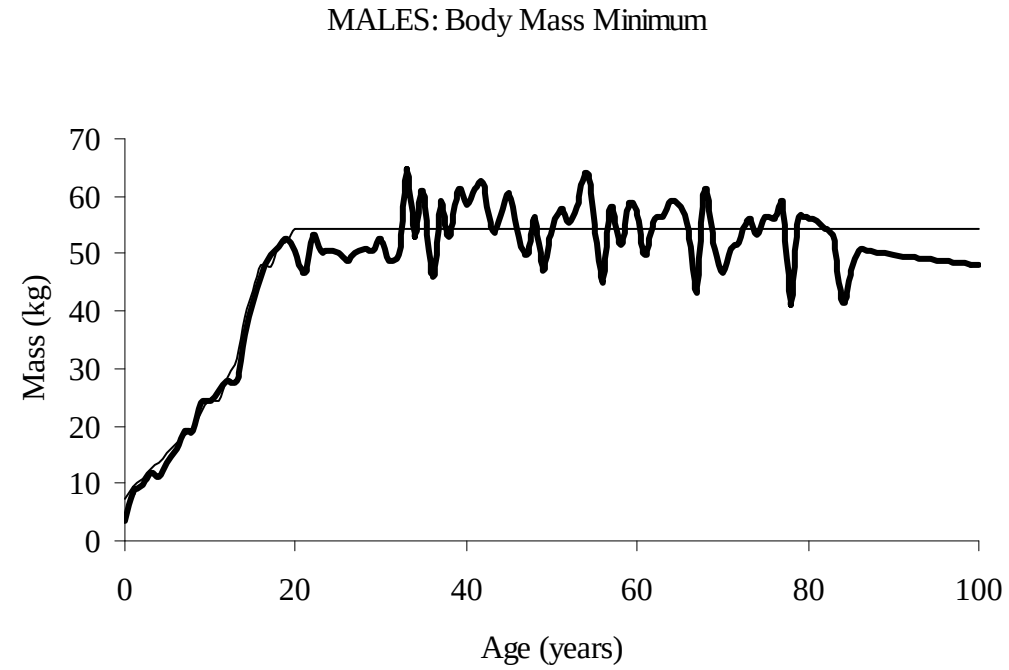


Figure 2. Geometric Standard Deviations for the Best-fit Lognormal Distributions for Body Mass as a Function of Age, Derived from NHANES 1999-2004 Study Data.



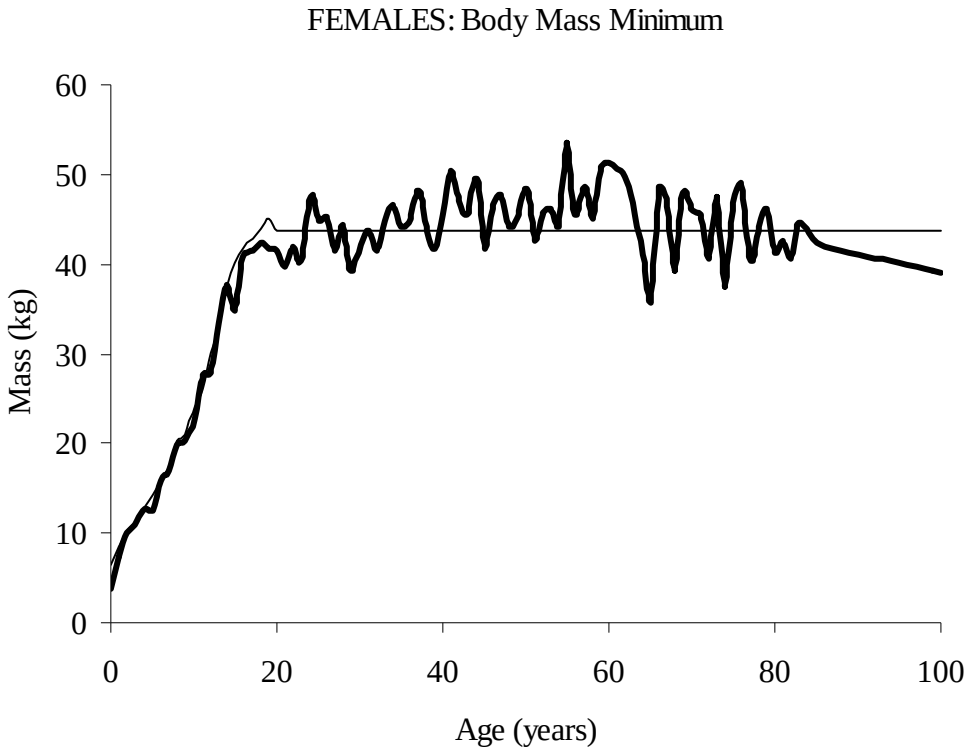
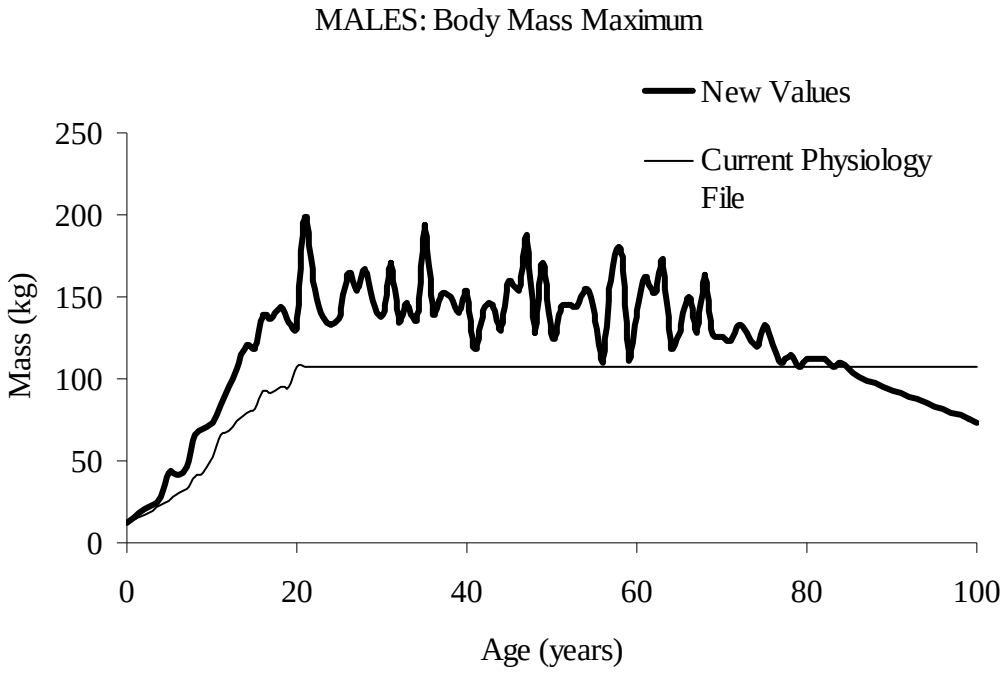


Figure 3. Minimums (1st Percentile) for Body Mass as a Function of Age, Derived from NHANES 1999-2004 Study Data.



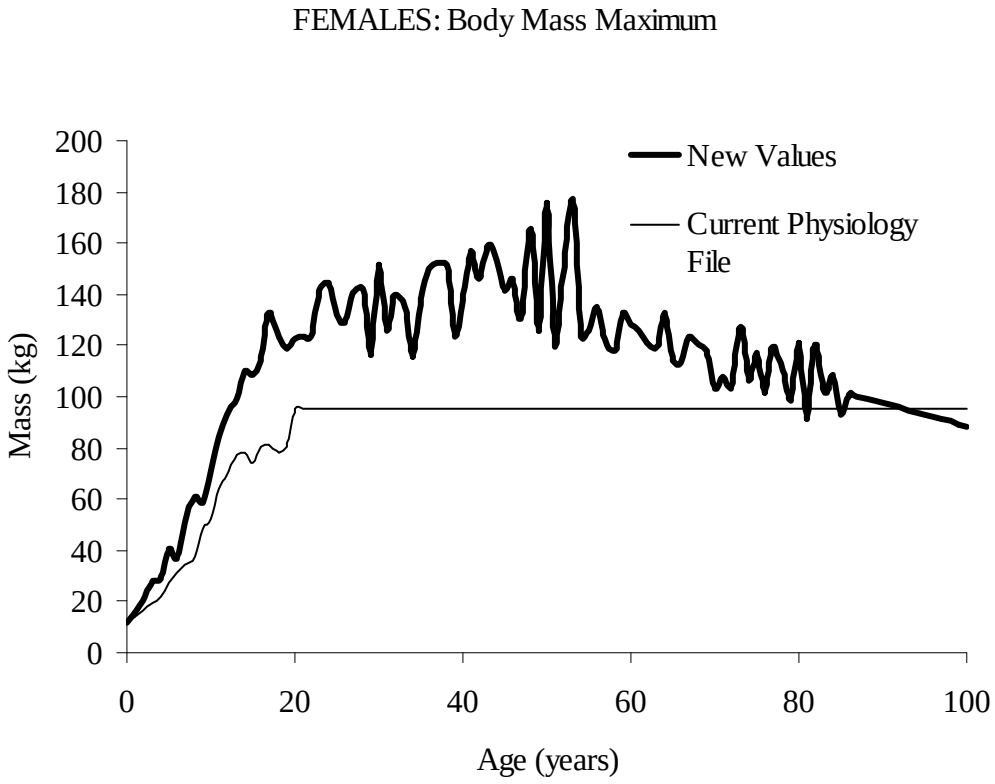


Figure 4. Maximums (99th Percentile) for Body Mass as a Function of Age, Derived from NHANES 1999-2004 Study Data.

4. DERIVATION OF NEW DISTRIBUTIONS FOR NORMALIZED VO2MAX

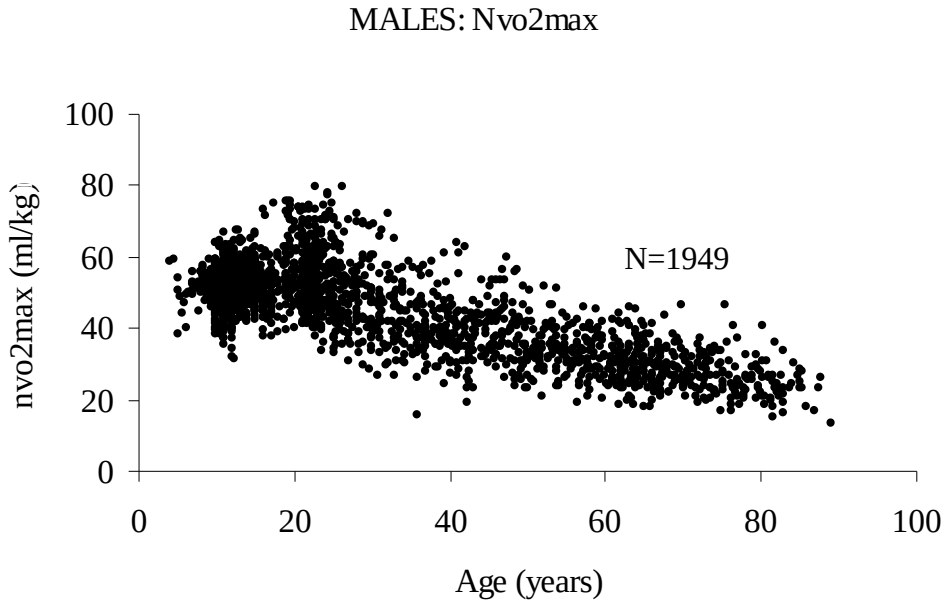
4.1 The Nvo2max Data

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.



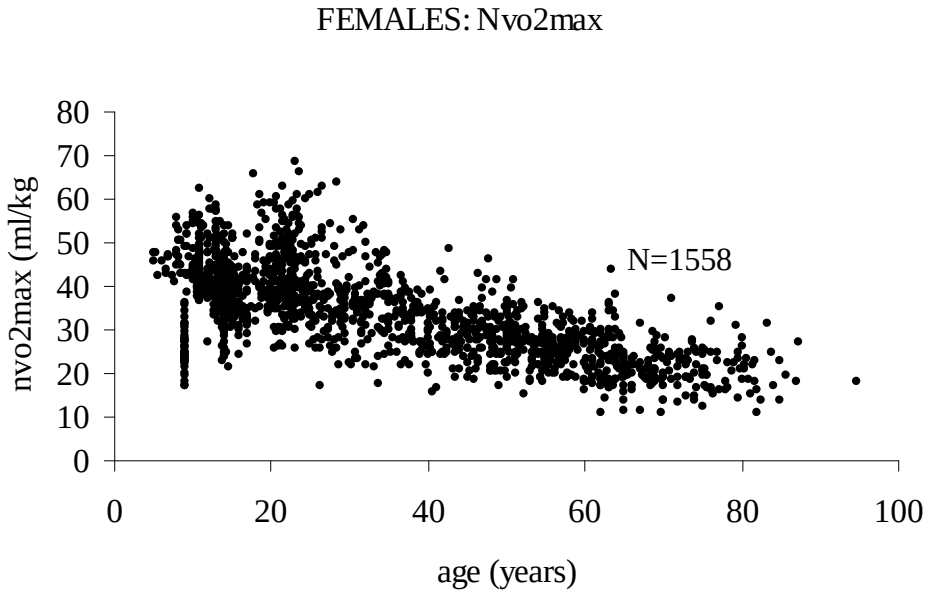


Figure 5. Individual Nvo2max Measurements for Males and Females, Derived from Literature Studies and Experimental Measurements.

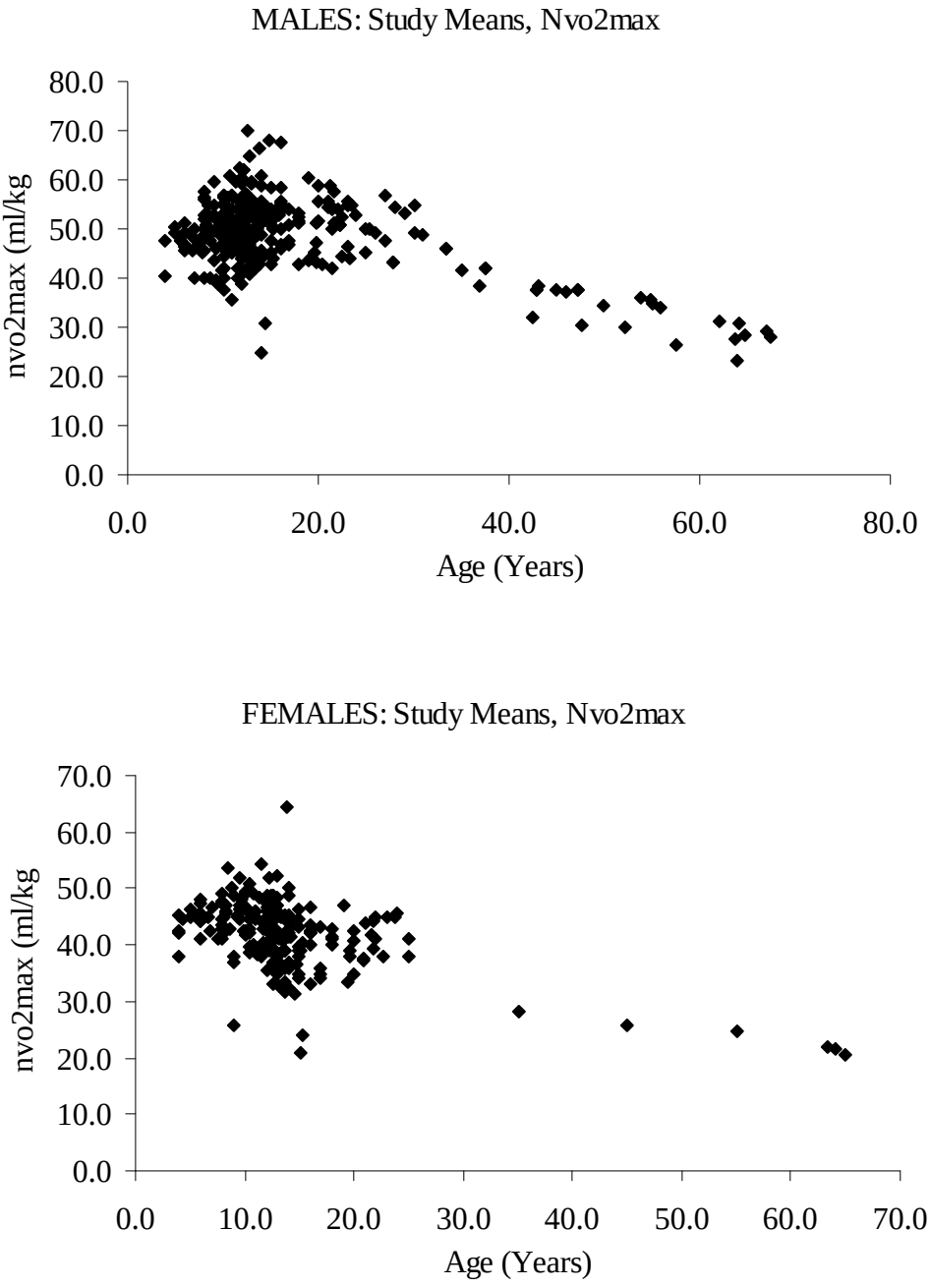


Figure 6. Grouped Mean Nvo2max Measurements for Males and Females, Derived from Literature Studies.

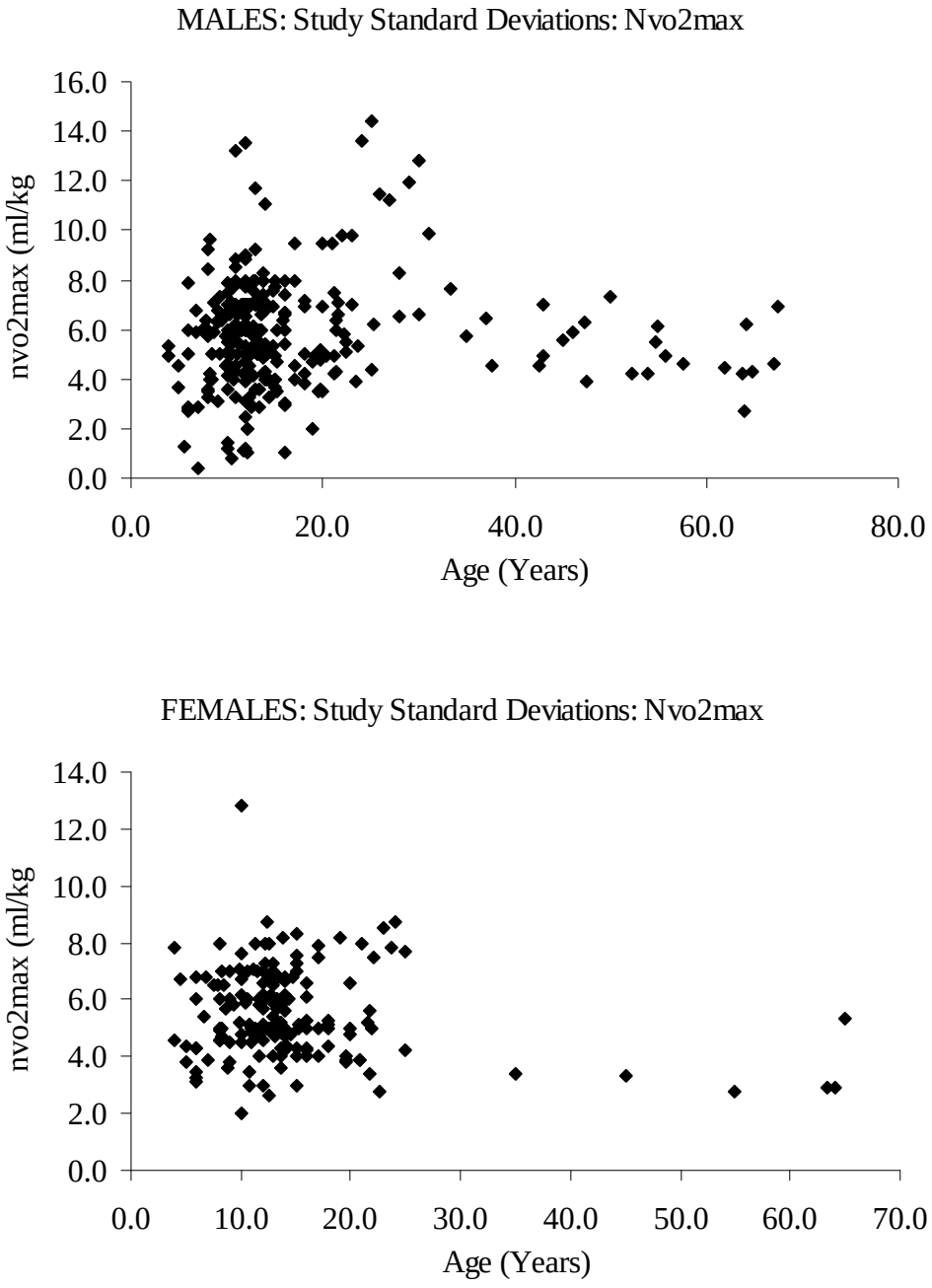


Figure 7. Nvo2max Standard Deviations for Males and Females, Derived from Literature Studies.

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.

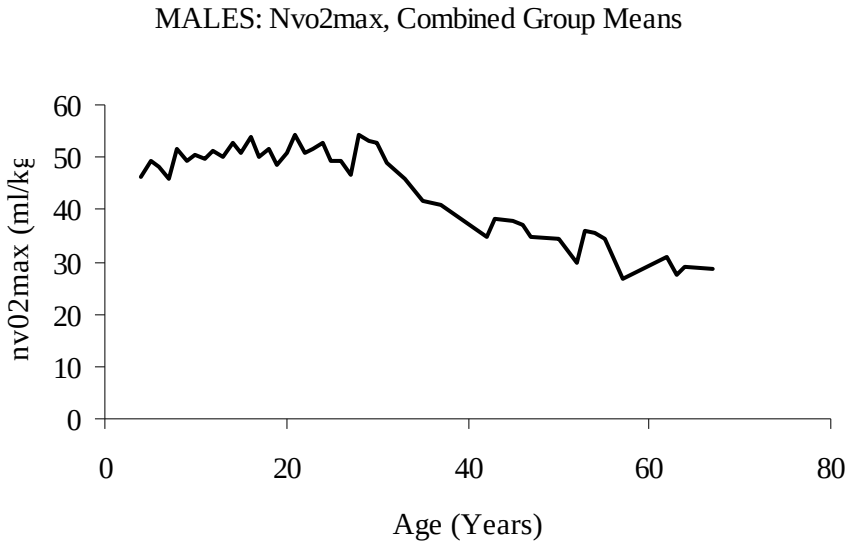
Both raw and smoothed nvo2max fits were calculated. Calculating 5-year running averages did not smooth the data considerably. Therefore, the smoothed fits were determined by choosing a best-fit functional form for the nv02max data. The data were fit to functions as follows:

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.



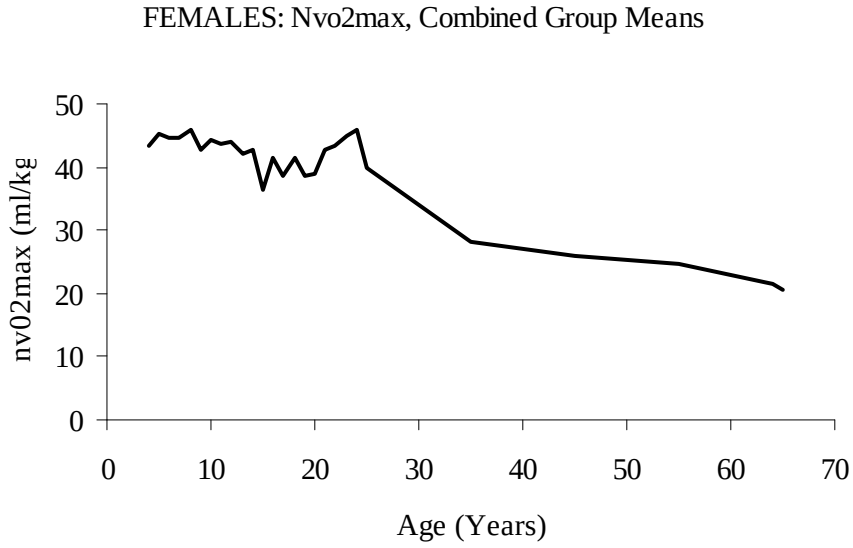
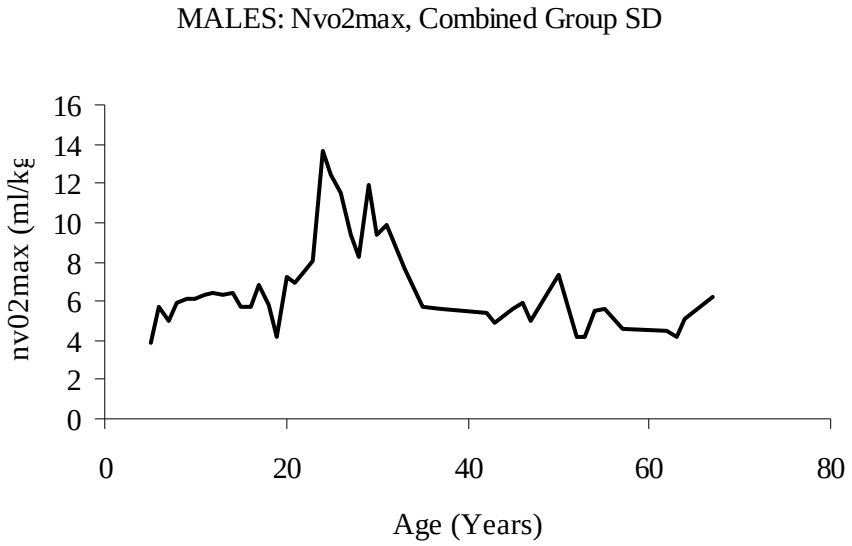


Figure 8. Combined Nvo2max Group Means for Males and Females



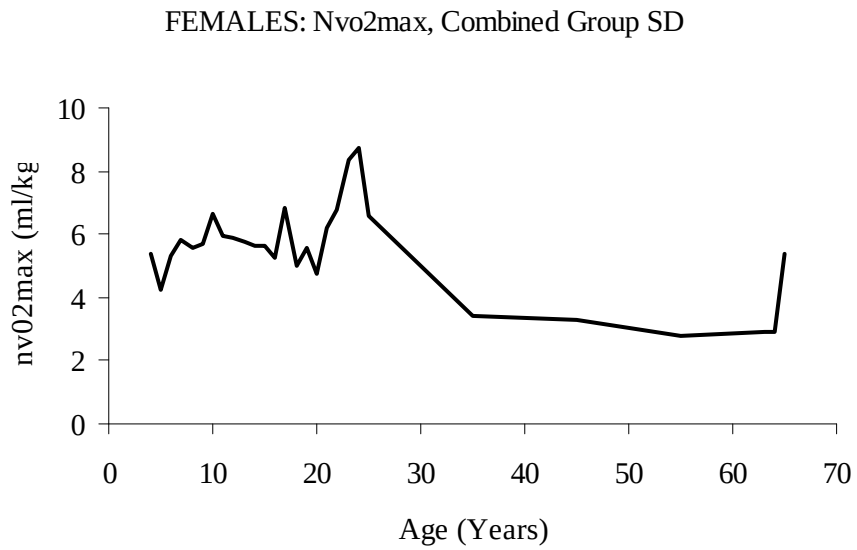


Figure 9. Combined Nvo2max Group Standard Deviations.

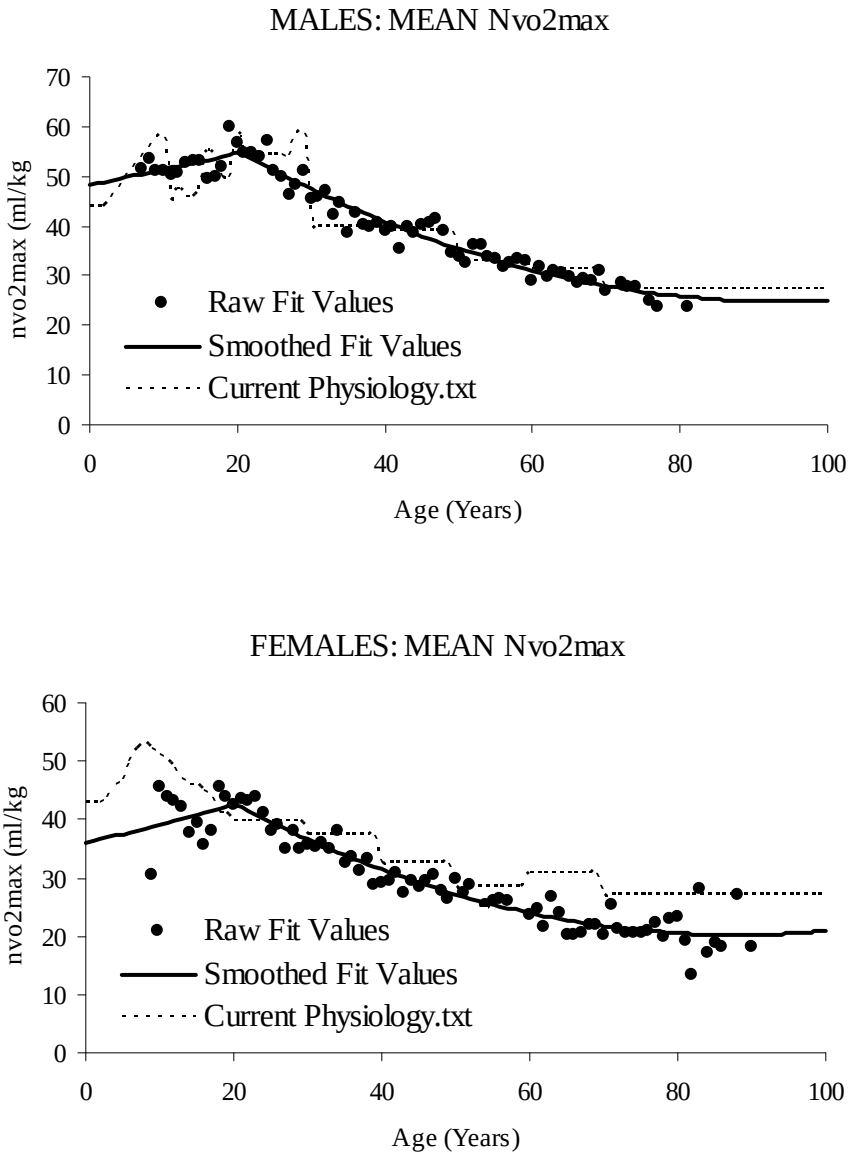
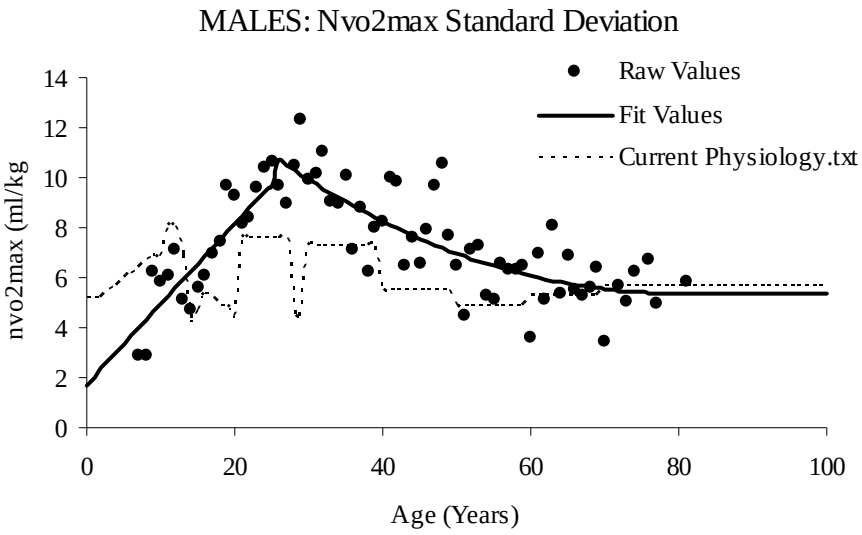


Figure 10. Nvo2max Normal Distribution Fits: Raw Fit Means and Smoothed Fits.



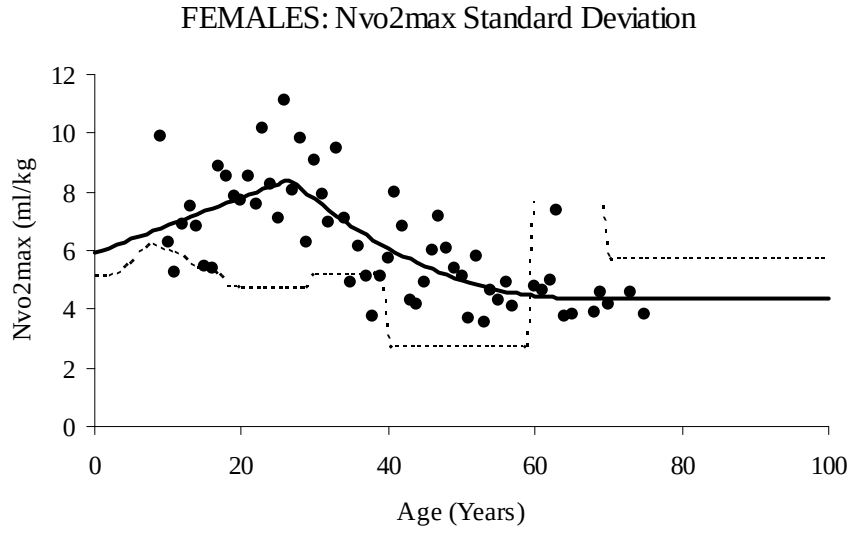
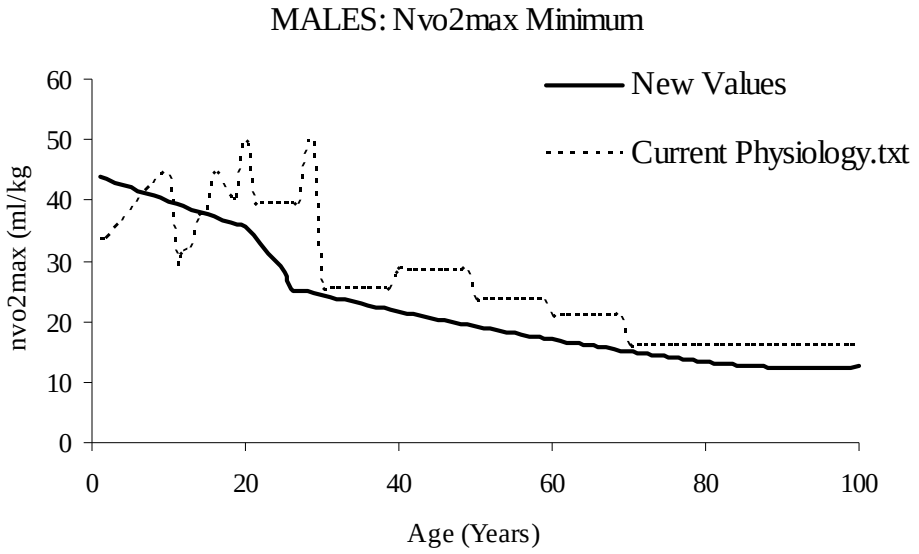


Figure 11. Nvo2max Normal Distribution Fits: Raw Fit Standard Deviations and Smoothed Fits.



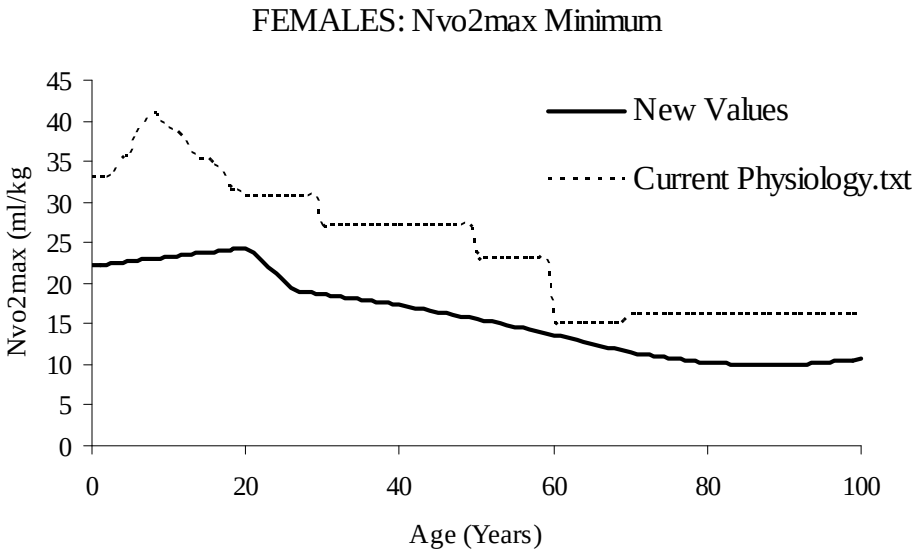


Figure 12. Nvo2max Minimums. 1st Percentile of the Best-fit Normal Distribution.

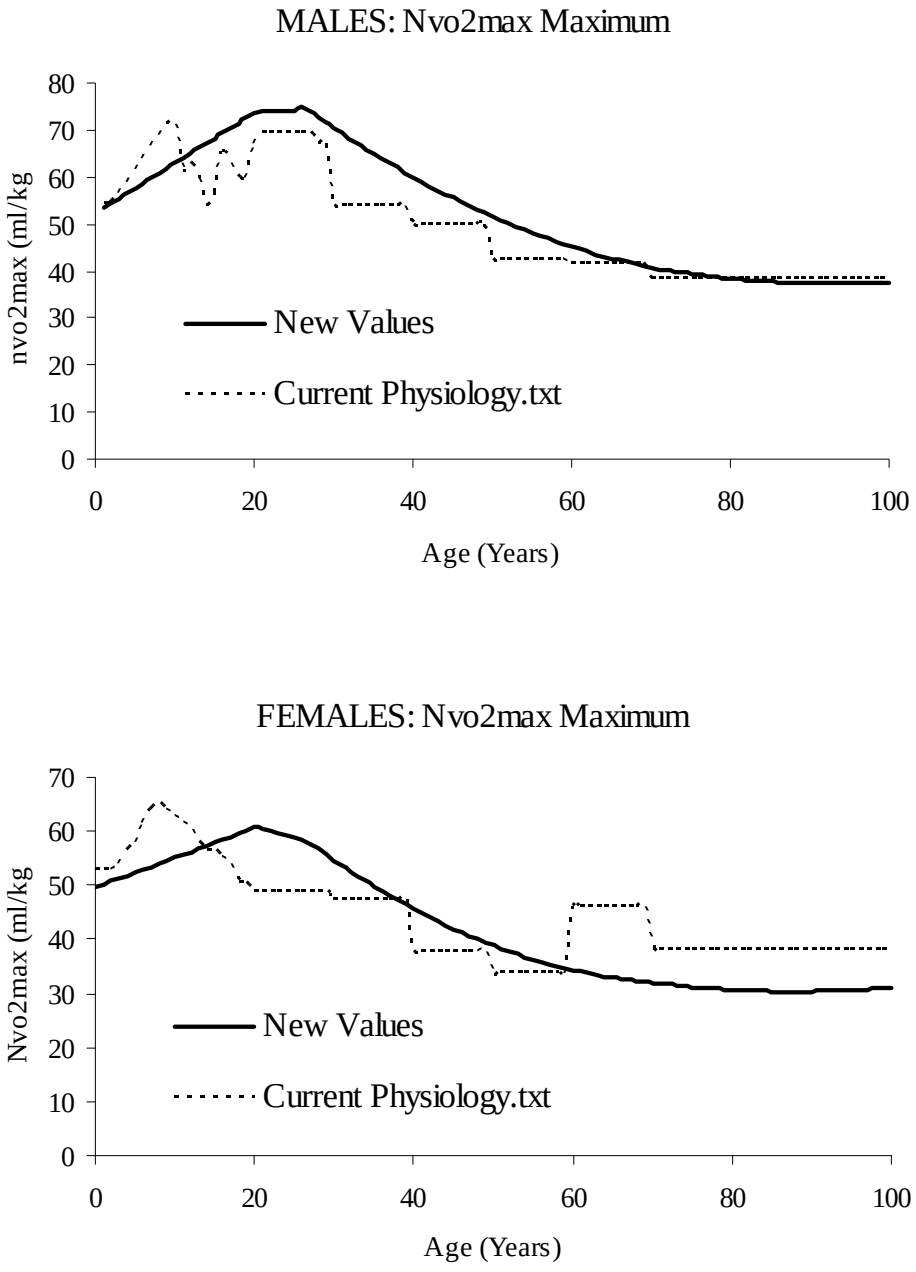


Figure 13. Nvo2max Maximums. 99th Percentile of the Best-fit Normal Distribution.

5. DERIVATION OF NEW DISTRIBUTIONS FOR HEMOGLOBIN CONTENT (HEMOGLOBIN DENSITY)

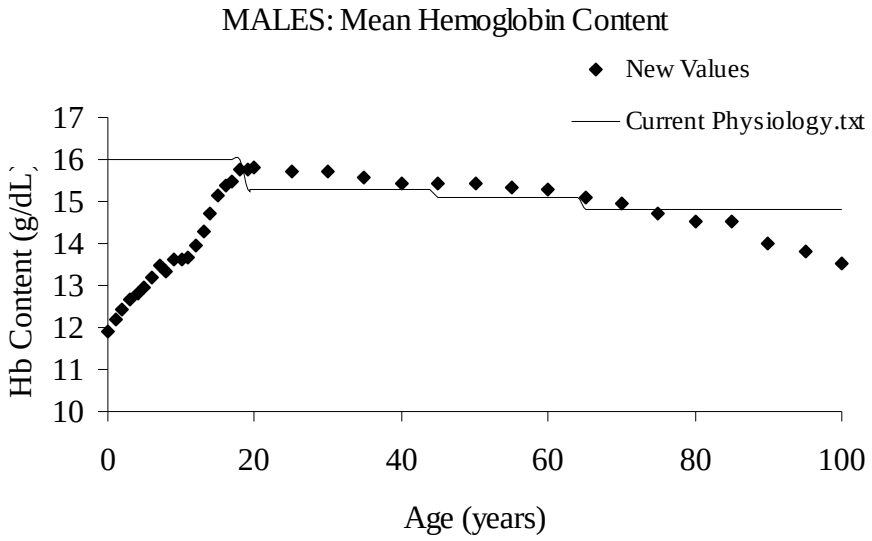
The new hemoglobin content values were derived from the combined NHANES 1999-2000 and 2001-2002 datasets. As of December 2005, hemoglobin data had not yet been released for the 2003-2004 study. The age data was provided in the Demographic datasets (Demo.xpt and Demo_b.xpt, previously downloaded for the 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.



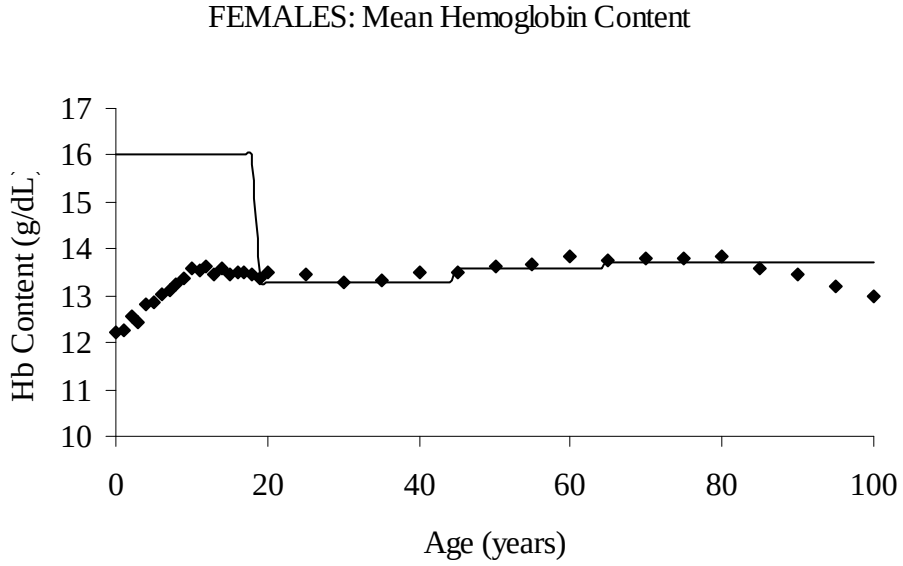
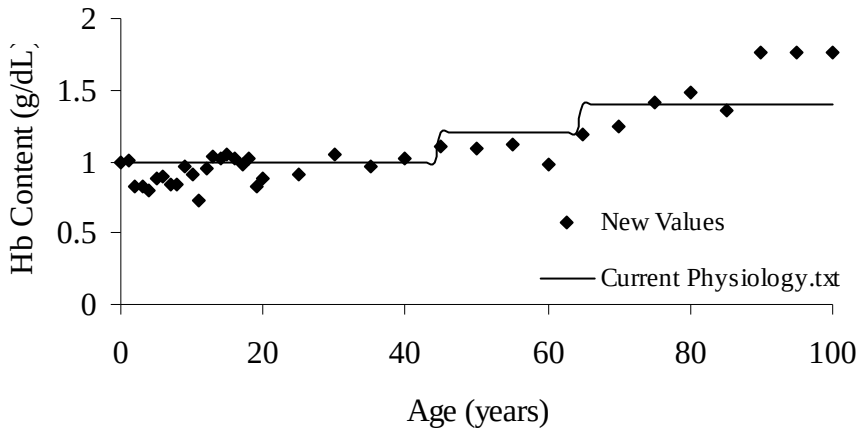


Figure 14. Mean Values of Hemoglobin Content as Derived from the 1999-2002 NHANES Dataset, with Comparison to Current Physiology.txt Values

MALES: Hemoglobin Content Standard Deviation



FEMALES: Hemoglobin Content Standard Deviation

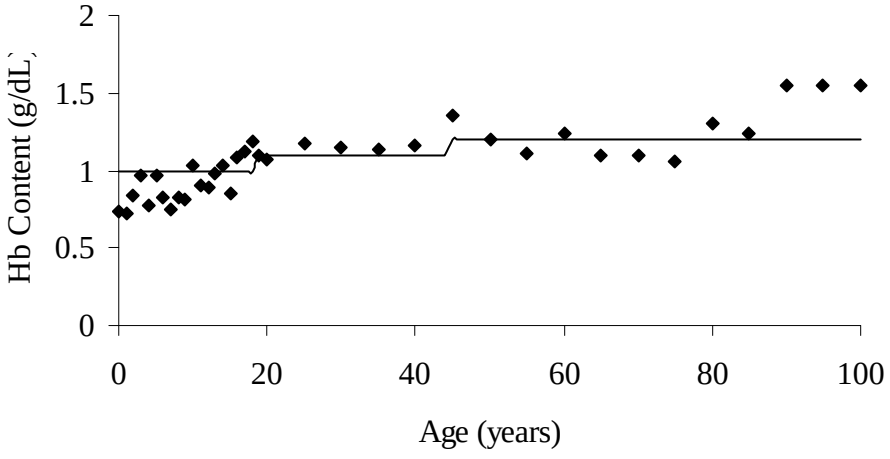


Figure 15. Values of Hemoglobin Content Standard Deviation as Derived from the 1999-2002 NHANES Dataset, with Comparison to Current Physiology.txt Values

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.

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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;

   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;


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;

   keep SEQN Hb gen ageyrs agemonths wt;
run;

proc sort data=Hb;
   by gen ageyrs;


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					
	MEAN	MEAN	SD	SD	MIN	MAX
Age	Raw Fit Values	Smoothed Fit Values	Raw Fit Values	Smoothed Fit Values	(1st Pctl)	(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

	MALES					
Age	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

	FEMALES					
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		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
20.00	42.52	42.50	7.69	7.80	24.35	60.65

	FEMALES					
Age	MEAN Raw Fit Values	MEAN Smoothed Fit Values	SD Raw Fit Values	SD Smoothed Fit Values	MIN (1st Pctl)	MAX (99th Pctl)
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
65.00	20.26	22.74	3.83	4.39	12.53	32.95

	FEMALES					
Age	MEAN Raw Fit Values	MEAN Smoothed Fit Values	SD Raw Fit Values	SD Smoothed Fit Values	MIN (1st Pctl)	MAX (99th Pctl)
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.

Age	MALES				FEMALES			
	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
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

Age	MALES Geometric Mean	GSD	Min	Max	FEMALES Geometric Mean	GSD	Min	Max
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
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

Age	MALES Geometric Mean	GSD	Min	Max	FEMALES Geometric Mean	GSD	Min	Max
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
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

Age	MALES Geometric Mean	GSD	Min	Max	FEMALES Geometric Mean	GSD	Min	Max
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
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

Age	MALES				FEMALES			
	Geometric Mean	GSD	Min	Max	Geometric Mean	GSD	Min	Max
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.

Age	MALES MEAN	MALES STD	FEMALES MEAN	FEMALES 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 in 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).

B.1 The 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 draft 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-Menton 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 C.2 of this appendix. A more detailed description can be found in the Programmer's Guide for the APEX3 model (Glen, 2002).

B.2 The CFK Model for Estimation of Carboxyhemoglobin

Table C-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 can vary 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:

$$CO + O_2Hb \leftrightarrow O_2 + COHb \qquad \text{(Eq. B-3)}$$

The following equation, 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-Menton kinetics model which can be integrated. The integration yields:

$$-(C_O + C_1)t + \%[COHb] - \%[COHb]_O - (100 - \%[COHb]_\infty)\ln\frac{(\%[COHb]_\infty - \%[COHb])}{\%[COHb]_\infty - \%[COHb]_O} = 0 \qquad \text{(Eq. B-15)}$$

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 (2008).

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 (C-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:

$$D_0 = 1 - N(0) / 100 \qquad \text{(Eq. B-18)}$$

$$A_0 = C_0 / (C_0 + C_1) \qquad \text{(Eq. B-19)}$$

$$A_1 = C_1 / (C_0 + C_1) \qquad \text{(Eq. B-20)}$$

$$D = D_0 - A_1 \qquad \text{(Eq. B-21)}$$

$$z = (C_0 + C_1)\, t / (100 * D_0 * D_0) \qquad \text{(Eq. B-22)}$$

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

$$N`(z) = D_0\ 2\ A_0 - D_0\ 2\ A_1\ N(z) / (\ 100 - N(z)\ ) \qquad \text{(Eq. B-23)}$$

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 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

Description of APEX4.3 for CO

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 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), which is described in Section 4.4.3 of the draft 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 which is a function of the average elevation of an 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.

C.4 Computation of Input Data for the COHb Module

As discussed in the previous section and in Sections 4.4.5 of the draft 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 (2008). 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 in minutes, 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. For each event it requires the following data.

Time duration of event, min
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

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 distribution with geometric mean (GM) and geometric standard deviation (GSD) distribution specific to age and gender 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). height = 34.43 inches + (6.67)[ln(weight)] + (2.38 inches)(z) Males: height = 48.07 inches + (3.07)[ln(weight)] + (2.48 inches)(z) Females: 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 which are based on work by Allen et al. (1956) which was 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 obtained from data from the National Health and Nutrition Examination Survey (NHANES), for the years 1999-2004 (see Isaacs and Smith, 2005 in 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: $D_{L_{CO}}(Adjusted) = D_{L_{CO}}(Base) + 0.000845\dot{V}_A - 5.7$

Parameter	Algorithm(s) Containing Parameter	Other Parameters Required for Calculating Parameter	Method Used to Estimate Parameter Value
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. 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).
Resting metabolic rate (RMR)	Ventilation rate	Gender Age Body Weight	See Section 4.4.5 of draft CO REA and Chapter 5 of US EPA (2008).
Energy conversion factor (ECF)	Ventilation rate	Gender	See Section 4.4.5 of draft CO REA and Chapter 5 of US EPA (2008).
NVO_{2max}	Ventilation rate	Gender Age	See Section 4.4.5 of draft CO REA and Chapter 5 of US EPA (2008).
VO_{2max}	Ventilation rate	NVO_{2max} Body Weight	See Section 4.4.5 of draft CO REA and Chapter 5 of US EPA (2008).

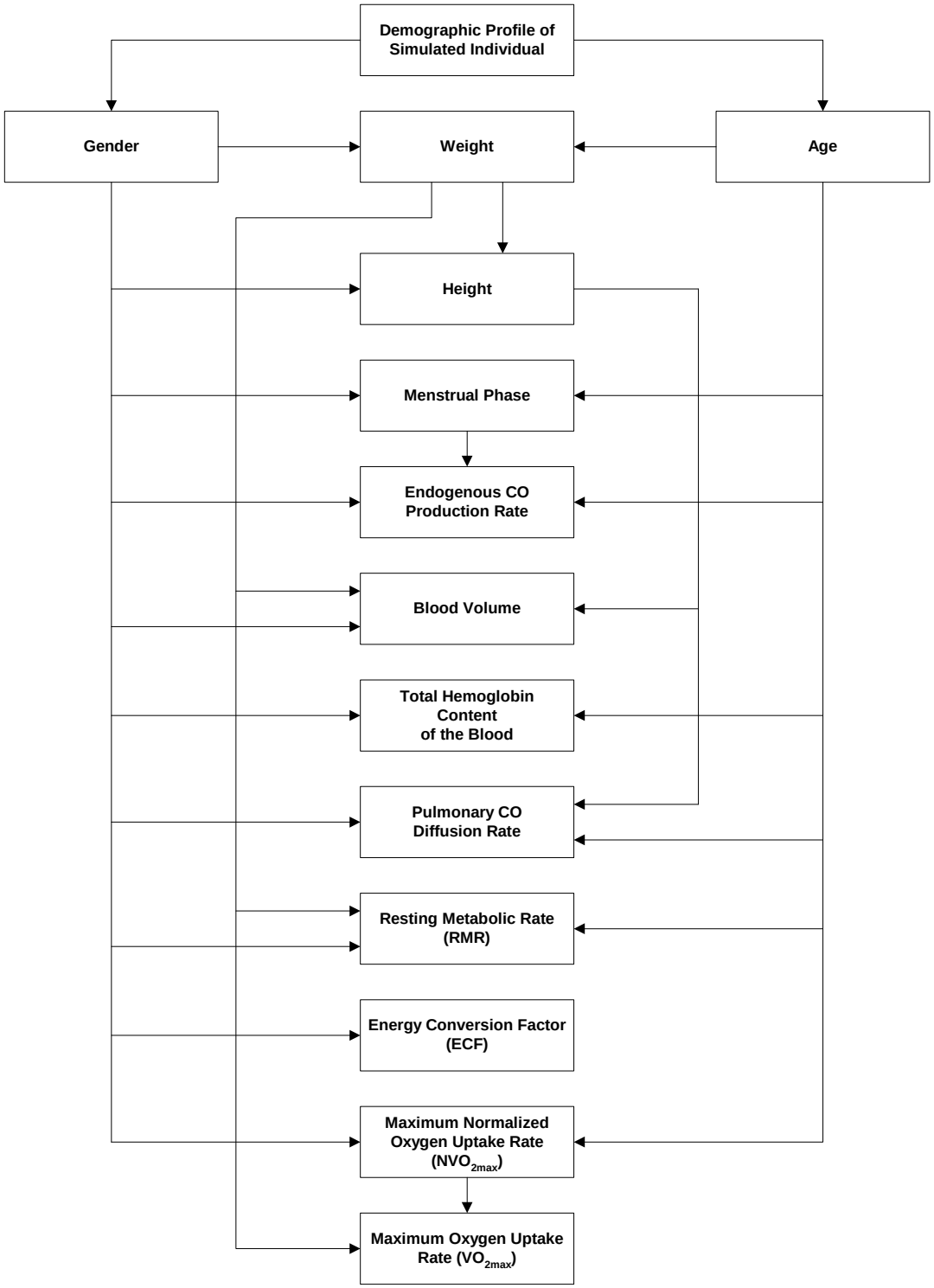

Figure B-1. Flow Diagram for Physiological Profile Generator. Input data is supplied at the start of the APEX4.3 computation.

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). Often times a value 100 torr is commonly used as 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 extent 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 (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, EPA analysts 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 C.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 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. study, it was determined that the Salorinne 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.

INPUT DATA SUPPLIED 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:

$$D_{L_{CO}}(Adjusted) = D_{L_{CO}}(Base) + 0.000845\dot{V}_A - 5.7 \qquad \text{(Eq. B-36)}$$

Table B-3. Literature Data Used to Derive Geometric Mean and Standard Deviation Lognormal Distribution of Endogenous CO Production Rate.

Study Author	Values for Endogenous CO Production Rate							
Brouillard et al. (1975)	0.81	0.57	0.33	0.7	0.58	0.38	0.51	0.55
	0.37	0.49	0.45	0.5	0.33	0.45	0.36	
Burke et al. (1974)	0.43	0.58	0.52	0.59	0.8	0.72	0.54	
Coburn et al. (1963)	0.35	0.4	0.39	0.43	0.35	0.51	0.42	0.57
	0.45							
Delivoria-Papadopoules et al. (1974)	0.45	0.26	0.6	0.45	0.39	0.4		
	0.57	0.54	0.72	0.99	0.48	0.53	0.43	
	0.23	0.51	0.34	0.41	0.26	0.16	0.3	
Luomanmaki and Coburn (1969)	0.38	0.42	0.41	0.54	0.38			
Lynch and Moede (1972)	0.4	0.81	0.26	0.65	0.51	0.62	0.44	
	0.72	0.37	0.23	0.33	0.42	0.44	0.29	0.48
	0.48	0.23	0.25	0.2	0.22	0.15	0.21	
Merke et al. (1975)	0.64	0.86	0.35	0.52	0.8	0.54	0.68	0.28
	0.4	0.47	0.23	0.24	0.55	0.32	0.43	0.35
Werner and Lindahl (1980)	0.54	0.76	0.48	0.31	0.7	0.36	0.65	

B.5 References

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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

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]

[1]Alion Science and Technology, Research Triangle Park, NC, [2]Human Exposure and Atmospheric Sciences Division, National Exposure Research Laboratory, US Environmental Protection Agency, Research Triangle Park, NC, [3]School of Information and Library Science, University of North Carolina at Chapel Hill, Chapel Hill, NC, [4]Office of Air Quality Planning and Standards, US Environmental Protection Agency, Research Triangle Park, NC, [5]Homemaker, Durham, NC.

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*]**.

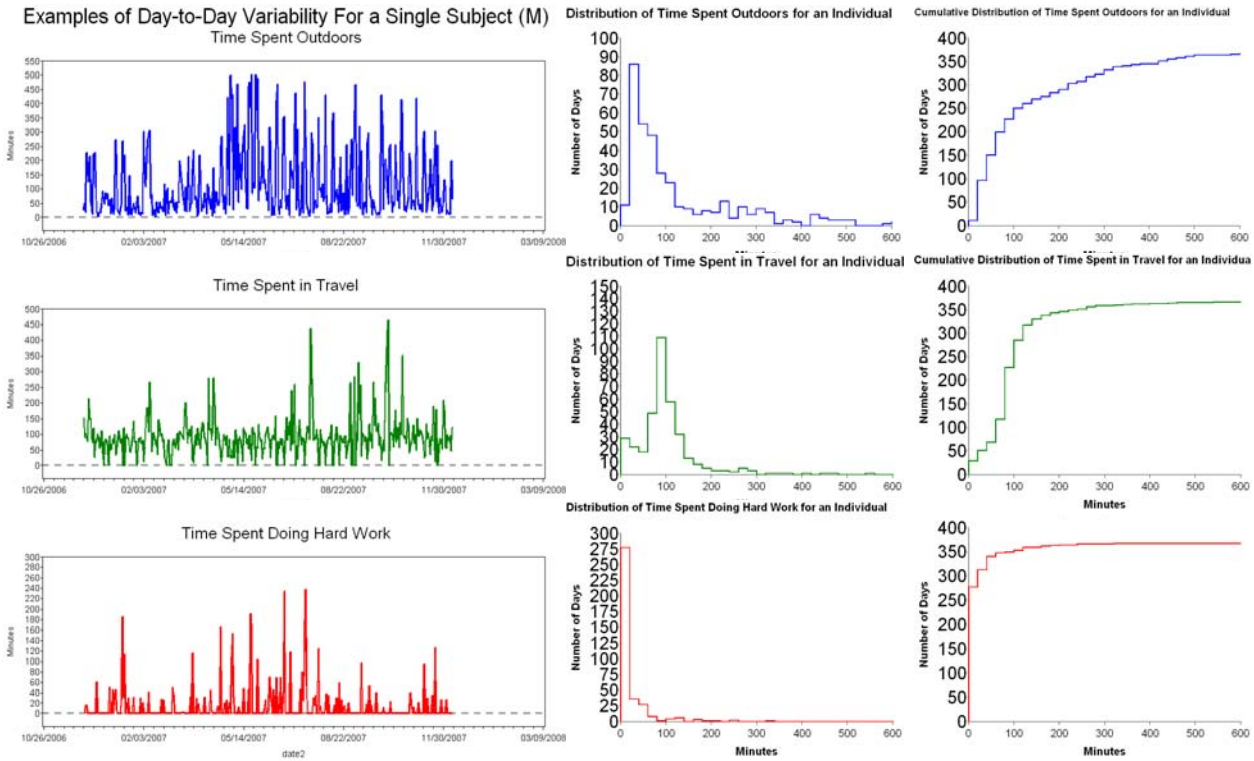

Figure 1. Time series and distributions of time spent in locations/activities for 367 days of data from a single male subject. Note high degree of interpersonal variability in behavior.

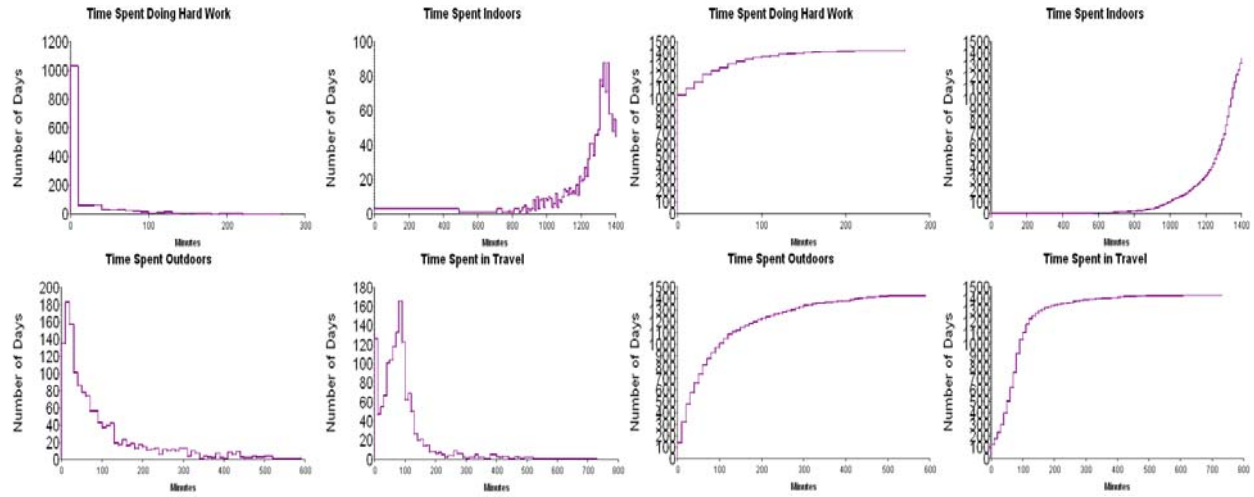

Figure 2. Distributions of time spent in different activities for all days for all subjects.

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.

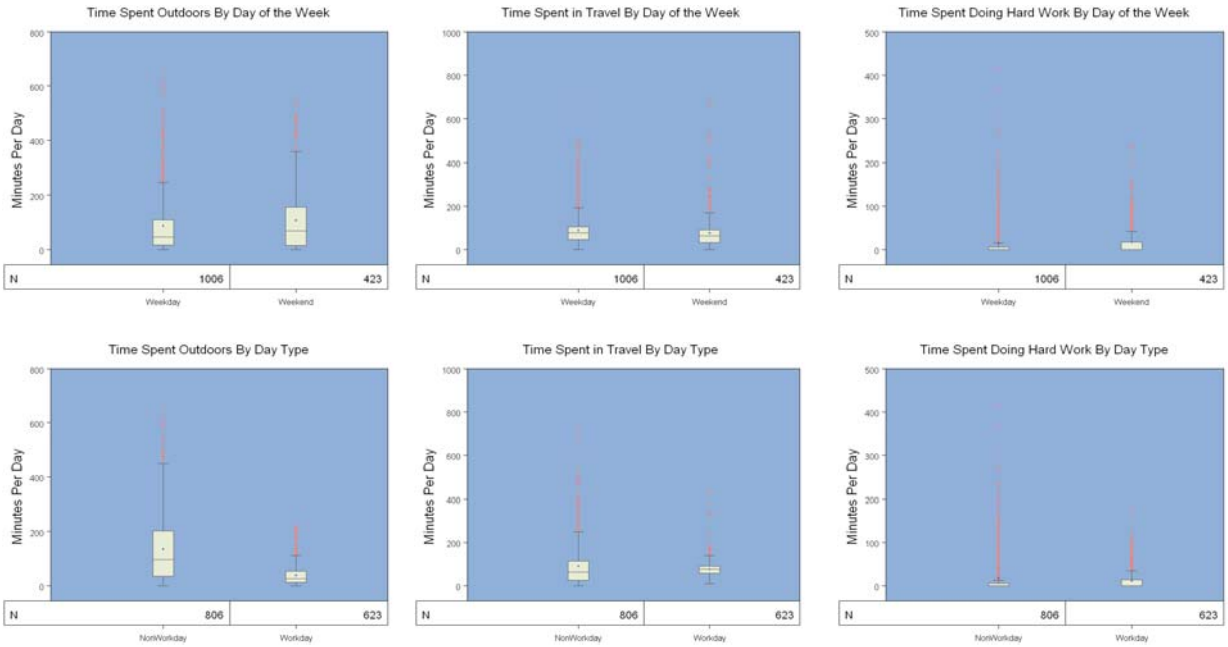

Figure 3. Time spent in different locations/activities as a function of day of the week, and daytype (workday versus non-workdays).

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.

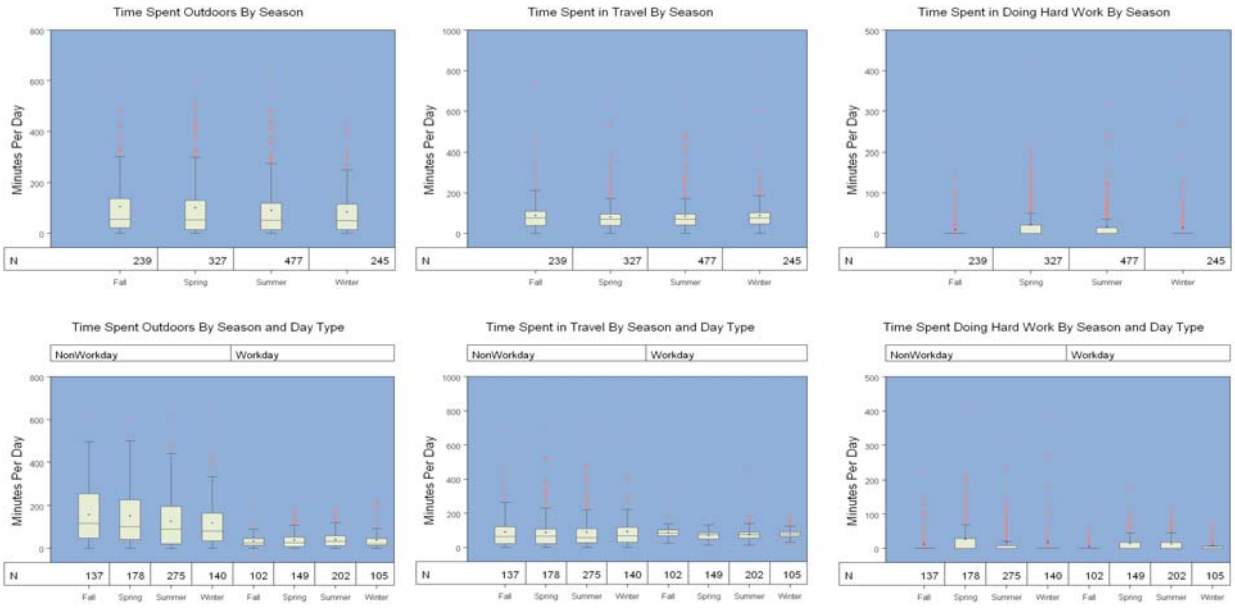

Figure 4. Time spent in different locations/activities as a function of season and daytype.

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.

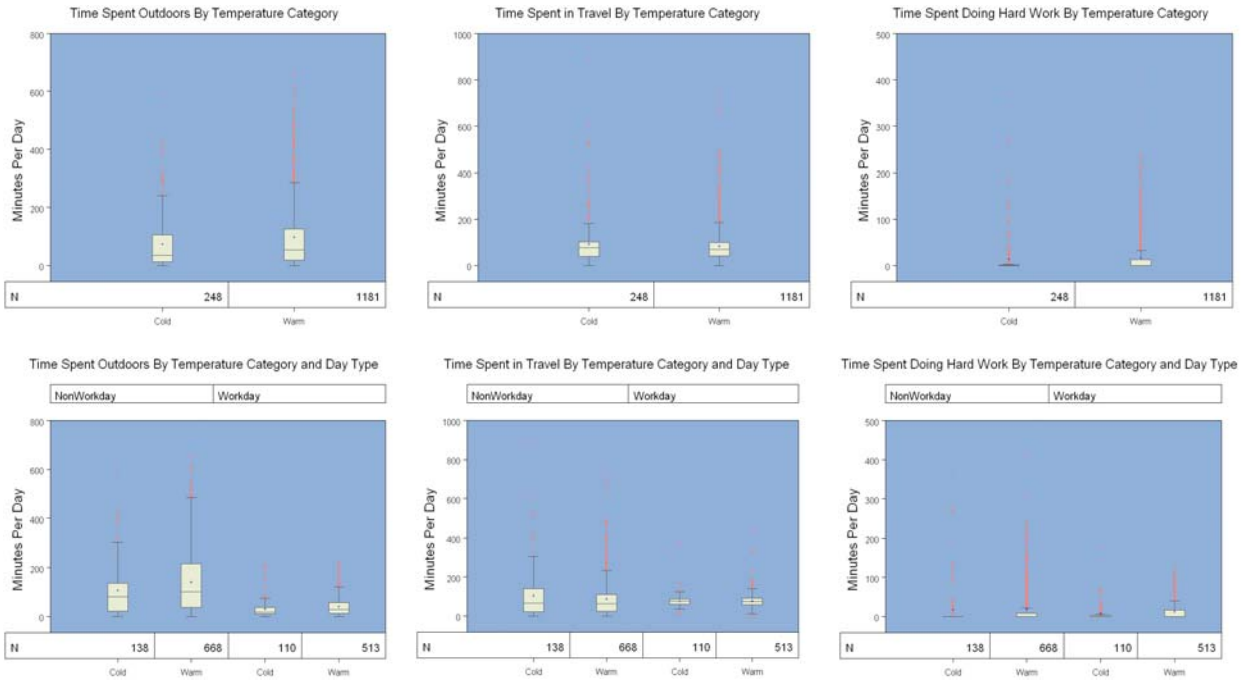

Figure 5. Time spent in different locations/activities as a function of temperature category (colder: max temp< 75 degrees, warmer: max temp≥ 75 degrees) and day type.

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

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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.

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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]

[1]Alion Science and Technology, Research Triangle Park, NC, [2]Human Exposure and Atmospheric Sciences Division, National Exposure Research Laboratory, US Environmental Protection Agency, Research Triangle Park, NC, [3]School of Information and Library Science, University of North Carolina at Chapel Hill, Chapel Hill, NC, [4]Office of Air Quality Planning and Standards, US Environmental Protection Agency, Research Triangle Park, NC, [5]Homemaker, Durham, NC.

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 σ_w^2 and σ_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, if 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. One 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	0.26	0.33	0.23	0.24
Outdoors	0.16	0.36	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	0.16
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	0.15	0.23
Outdoors	0.09	0.24	0.30	0.20
Travel	0.10	0.21	0.31	0.09
Hard Work	0.01	0.20	0.35	0.14

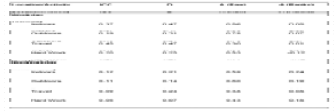

Figure 3. Time spent in different locations/activities as a function of day of the week, and daytype (workday versus nonworkdays).

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.

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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.*

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Appendix D

Microenvironmental Mapping

Figure D-1 presents how CHAD codes are mapped to the eight microenvironments used to model exposure in the draft 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 this second draft 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.

- 95^{th} 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 95^{th} 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 95^{th} 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 95^{th} 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.

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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.									

Age group	**Gender** **Males** **Angina(%)**	**Non-angina(%)**	**All**	**Females** **Angina(%)**	**Non-angina(%)**	**All**	**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		
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	0.00	0.00
Percentage of time spent in vehicle	4.55	5.55	0.01	6.19	7.13	0.00	0.22	0.23
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			
	55-64	0.00			0.34				
	65-74	1.48	1.77		0.48	0.48		0.02	0.02
	75+	0.00			0.86			0.01	0.02
		1.39	1.49		0.47	0.48		0.41	0.82
		0.36			0.96			0.51	0.95
		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			
	55-64	0.17			0.13				
	65-74	2.40	2.90		1.21	1.14		0.22	0.06
	75+	0.04			0.61			0.02	0.03
		1.91	2.17		0.78	0.94		0.26	0.63
		0.14			0.31			0.55	0.88
		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			
	55-64	0.02			0.00				
	65-74	9.28	10.02		14.26	13.86		0.01	0.01
								0.65	1.00
								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 value Angina	Mean Non-angina	St. Dev. Angina	St. Dev. Non-angina	P-value	P-value
	75+	0.79		0.78			
		6.43	10.40	11.38	14.34		
		0.13		0.20		0.58	0.66
		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		
	55-64	0.92		0.63			
	65-74	3.99	6.87	3.78	9.63	0.89	0.52
	75+	0.00		0.00		0.18	0.19
		7.20	5.88	9.04	7.80	0.82	0.93
		0.51		0.29		0.44	0.54
		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		
	55-64	0.02		0.05			
	65-74	13.27	16.89	15.30	16.18	0.02	0.02
	75+	0.24		0.76		0.17	0.22
		13.63	16.29	15.87	15.91	0.19	0.29
		0.45		1.00		0.69	0.41
		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 value Angina	Mean Non-angina	St. Dev. Angina	St. Dev. Non-angina	P-value	P-value
percentage of time	55-64	0.00		0.34			
with exertion	65-74	24.60	30.07	14.51	12.03		
above 2.39	75+	0.06		0.14		0.06	0.14
kcal/min		21.92	23.32	13.23	12.48	0.67	0.84
= 0.010MJ/min		0.63		0.64		0.39	0.74
(light)		18.24	15.87	11.13	10.37		
		0.41		0.63			
Average	0-54	6.63	4.46	6.37	4.31		
percentage of time	55-64	0.05		0.00			
with exertion	65-74	3.43	5.44	3.55	4.41	0.02	0.01
above 5.97	75+	0.01		0.17		0.01	0.01
kcal/min		2.27	3.27	2.47	3.46	0.20	0.40
= 0.025 MJ/ min		0.08		0.06		0.43	0.59
(moderate)		2.02	1.62	2.42	2.41		
		0.53		0.92			
Average	0-54	0.662	0.735	0.792	0.986		
percentage of time	55-64	0.59		0.11			
with exertion	65-74	0.565	0.846	1.068	1.222	0.55	0.15
above 9.55	75+	0.19		0.40		0.05	0.17
kcal/min		0.155	0.388	0.361	0.716	0.06	0.04
= 0.040 MJ/ min		0.01		0.00		0.55	0.96
(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	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	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		
	55-64	0.69		0.32	0.33	1.00		
	65-74	1.21	1.27	0.30	0.31	0.94	0.72	0.73
	75+	0.33		0.33	0.30	0.34	0.56	0.22
		1.05	1.10				0.31	0.44
		0.29					0.44	0.66
		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 value Angina	Mean Non-angina	P-value	St. Dev. Angina	St. Dev. Non-angina	P-value	P-value	P-value
percentile of	55-64	0.86			0.69				
maximum 8hr	65-74	1.79	1.92		0.80	0.77			
exertion (Mcal)	75+	0.41			0.68			0.33	0.28
		1.42	1.51		0.53	0.57		0.31	0.62
		0.26			0.57			0.43	0.47
		1.27	1.31		0.56	0.52			
		0.59			0.43				
Percentage of time	0-54	3.64	5.11		7.29	9.58			
spent outdoors	55-64	0.42			0.20				
	65-74	4.31	4.59		9.53	8.22		0.43	0.91
	75+	0.88			0.23			0.23	0.63
		2.84	4.14		5.51	7.34		0.49	0.53
		0.14			0.02			0.76	1.00
		3.79	2.27		12.04	4.60			
		0.40			0.00				
Percentage of time	0-54	4.54	5.35		5.48	5.98			
spent in vehicle	55-64	0.55			0.72				
	65-74	4.21	5.60		7.53	7.23		0.40	0.35
	75+	0.35			0.71			0.06	0.12
		5.26	4.15		5.94	6.18		0.15	0.19
		0.23			0.77			0.72	0.96
		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 value Angina	Mean Non-angina P-value	St. Dev. Angina	St. Dev. Non-angina P-value	P-value	P-value
spent outdoors or	55-64	0.36		0.57			
in vehicle	65-74	8.52	10.18	12.15	10.42		
	75+	0.48		0.22		0.04	0.05
		8.10	8.29	8.21	9.38	0.99	0.86
		0.88		0.26		0.77	0.97
		6.61	5.21	12.36	6.25		
		0.45		0.00			
Average	0-54	23.50	21.40	12.28	12.15		
percentage of time	55-64	0.49		0.86			
with exertion	65-74	19.04	21.04	10.34	10.47	0.41	0.69
above 2.39	75+	0.33		1.00		0.51	0.54
kcal/min		13.97	15.46	8.45	9.53	0.43	0.76
= 0.010MJ/min		0.26		0.31		0.51	0.89
(light)		11.31	11.84	9.75	8.61		
		0.73		0.24			
Average	0-54	1.44	1.59	1.66	1.97		
percentage of time	55-64	0.71		0.44			
with exertion	65-74	0.79	1.31	1.27	2.07	0.73	0.74
above 5.97	75+	0.05		0.00		0.04	0.06
kcal/min		0.65	0.68	1.35	1.56	0.51	0.88
= 0.025 MJ/ min		0.87		0.22		0.84	0.67
(moderate)		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 value 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				
with exertion	65-74	0.095	0.093		0.277	0.198			
above 9.55	75+	0.96			0.01			0.67	1.00
kcal/min		0.028	0.030		0.076	0.110		0.85	0.99
= 0.040 MJ/ min		0.89			0.00			0.28	0.83
(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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