level. As discussed above, a threshold for the induction of myocardial infarction by CO exposure cannot be defined. Therefore, heavy smokers with coronary artery disease, which have a higher risk for myocardial infarction already from smoking (American Heart Association 2002), may be at somewhat higher risk compared with nonsmoking patients.

The values are listed in Table 2-16.

8. SUMMARY OF AEGLs

8.1. AEGL Values and Toxicity End Points

The AEGL values for various levels of effects and various time periods are summarized in Table 2-17. They were derived using the following key studies and methods.

AEGL-1 values are not recommended because susceptible persons may experience more serious effects (equivalent to AEGL-2) at concentrations that do not yet cause AEGL-1 effects in the general population.

The AEGL-2 was based on cardiovascular effects in patients with coronary artery disease, who constitute the most susceptible subpopulation. For the derivation of AEGL-2 values, a level of 4% COHb was chosen. At this exposure level, patients with coronary artery disease may experience a reduced time until onset of angina (chest pain) during physical exertion. The changes in the electrocardiogram (ST-segment depression of 1 mm or greater) associated with angina symptoms were fully reversible. An exposure level of 4% COHb is unlikely to cause a significant increase in the frequency of exercise-induced arrhythmias. A mathematical model (Coburn et al. 1965; Peterson and Stewart 1975) was used to calculate exposure concentrations resulting in a COHb of 4% at the end of exposure periods of 10 and 30 min and 1, 4, and 8 h. An intraspecies uncertainty factor of 1 was used. A total uncertainty factor of 1 was used. An intraspecies uncertainty factor of 1 was considered adequate because the values are based on observations in the most susceptible human subpopulation (patients with coronary artery disease).

The AEGL-3 values were based on COHb levels of 40% in human blood derived from a weight-of-evidence analysis of lethal and nonlethal poisoning cases (Nelson 2006a). A threshold for lethality of

40% is also supported by experimental studies by Chiodi et al. (1941), Henderson et al. (1921), and Haldane (1895), in which exposures resulting in COHb of 34-56% did not cause lethal effects in healthy individuals. Further support comes from the studies of Kizakevich et al. (2000), Stewart et al. (1970), and Nielsen (1971) that reported headache as the only symptom when health adults were exposed to 20-33% COHb. A level of 40% COHb was used as the basis for AEGL-3 derivation. A mathematical model (Coburn et al. 1965; Peterson and Stewart 1975) was used to calculate exposure concentrations resulting in a COHb of 40% at the end of exposure periods of 10 and 30 min and