

In patients with coronary artery disease, which constitute the most susceptible subpopulation, the time to onset of angina and the time to 1-mm ST-segment change in the electrocardiogram during physical exercise were significantly reduced at a COHb of 2.0% or 4.0% (Allred et al. 1989a,b; 1991).

### 5.2. Animal Data Relevant to AEGL-1

No studies in experimental animals were located that were considered relevant for the derivation of AEGL-1 values. The studies describing effects of CO on cardiac function, such as Sekiya et al. (1983), DeBias et al. (1976), and Aronow et al. (1979), normally use models in which the heart was damaged additionally by an electric stimulus or by coronary artery ligation. Effects of CO exposure found in these systems can hardly be extrapolated quantitatively to humans.

### 5.3. Derivation of AEGL-1

CO is an imperceptible toxic gas. Until very severe symptoms occur (inability to walk) none or only nonspecific symptoms were noted in healthy humans and monkeys (Haldane 1895; Purser and Berrill 1983).

In patients with coronary artery disease, which constitute the most susceptible subpopulation, effects, such as significant electrocardiogram changes, reduced time to the onset of angina, and increased cardiac arrhythmia, start occurring at exposure concentrations little higher than current ambient air quality guidelines (e.g., the U.S. national air quality guideline of 9 ppm for 8 h) (National Air Pollution Control Administration 1970; 65 Fed. Regist.50201[2000]; EPA 2000; Raub 2000), the WHO air quality guideline of 10 mg/m<sup>3</sup> (9 ppm) for 8 h (based on 2.5% COHb) (WHO 1999a), and the designated European Union limit value of 10 mg/m<sup>3</sup> (9 ppm) for 8 h (EC 1999). These cardiac effects were considered above the AEGL-1 and thus would not constitute a suitable basis for the derivation of AEGL-1 values.

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.

In addition, CO exposure concentrations encountered frequently in everyday life are at or above the concentration range in which an AEGL-1 would have to be set: smokers have COHb concentrations in the range of 3-8% (Radford and Drizd 1982), and CO concentrations between about 10 and 50 ppm, which can be found on heavily traveled roads; inside motor vehicles; and in homes with gas-, coal-, wood- or kerosene-fired heaters, and stoves, correspond to an equilibrium COHb range of 1.8-7.5% (see Figure 2-2 and Table 2-14).