plained of light nausea, lightheadedness, and headache at COHb levels of 4.1-12.8% (Atkins and Baker 1985). These effects are below the lethality threshold. At slightly higher COHb levels (5-6%), there may be an increase in cardiac activity in subjects with coronary artery disease (WHO 1999a). Therefore, a total uncertainty factor of 3 for intraspecies variability was considered adequate based on the following supporting evidence in susceptible subpopulations:

1. Exposure to the derived AEGL-3 concentrations will result in COHb values of about 14-17% in adults (see Table B-4 in Appendix B). In the reported cases of myocardial infarction, the measured COHb was normally above 20%, except in one case in which the measured COHb was about 15%. In this case (Grace and Platt 1981), the man was exposed during several weeks to (presumably) the same high CO concentration in his home and presented two times to the emergency room with signs of CO intoxication (which were misdiagnosed) until the infarction occurred. Therefore, the derived AEGL-3 values are considered to protect heart patients against CO-induced myocardial infarction. It should be noted, however, that a clear threshold for this end point cannot be defined because myocardial infarction might be triggered at lower COHb in hypersusceptible individuals, and myocardial infarction can also occur spontaneously or by trigger effects (e.g., psychological stress and physical exertion), which have no relevant effects on the health of normal subjects.

2. With regard to stillbirths, a COHb of 14-17% was considered protective of lethal effects on the unborn because, in the case studies available, stillbirths were found only after measured maternal COHb of about 22-25% or higher (Caravati et al. 1988; Koren et al. 1991). In the clinic, a measured COHb of about 15-20% in pregnant women (implicating a higher end-of-exposure level) is considered a severe CO intoxication that could require hyperbaric oxygen treatment (Ellenhorn 1997; Tomaszewski 1998). Available animal studies reported increased rates of stillbirths after a 2-3-day exposure at a maternal COHb above 23% (Dominick and Carson 1983), after continuous exposure at a maternal COHb of 16-18% (Astrup et al. 1972), and after repeated short-term exposures at a maternal COHb of 16% (Rosenkrantz et al. 1986). Taken together, the animal data support the conclusion that pregnant women should not be exposed to COHb levels higher than about 14-17% to prevent lethal effects on the unborn.

3. In smokers with a background COHb of 3-8% from smoking, exposure to the AEGL-3 concentration–time combinations will result in COHb levels between 16.1 and 23.0% (see Table B-4 in Appendix B). Smokers may show an adaptive response to their chronically elevated COHb levels, as evidenced by increased red-blood-cell volumes or reduced plasma volumes (EPA 2000). This adaptive response is likely to reduce the effect level in smokers compared with nonsmokers exposed to the same total COHb level. The estimated COHb exposure level in smokers is considered protective of lethal effects if they are healthy adults. Also, from the discussion above, it is considered unlikely that smoking pregnant women will have an increase risk of stillbirths at the AEGL-3 exposure