Appendix F: Estimating Human Equivalent Concentrations Using the U.S. EPA Default Approach

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F.1 Estimating Human Equivalent Concentrations Using the U.S. EPA Default Approach

The United States Environmental Protection Agency (U.S. EPA) Human Equivalent Concentration (HEC) approach (U.S.EPA, 1994a) is designed to adjust the dose in an animal inhalation experiment to the dose that a human would receive at the same air concentration. The adjustment is based on some of the physiological differences between humans and animals. The Office of Environmental Health Hazard Assessment has recommended the necessary physiological parameters for children from the literature needed to adjust the dose in an animal inhalation experiment to the dose that children would receive at the same air concentration.

The U.S. EPA HEC approach was initially adopted by OEHHA for derivation of chronic inhalation Reference Exposure Levels (RELs). The U.S. EPA has proposed a number of different HEC schemes depending on the physicochemical characteristics of the substance (reactive gases, water soluble gases, water-insoluble gases, and particles) and on the site of toxic action (respiratory effects and systemic effects). For both the U.S. EPA Reference Exposure Concentrations (RfCs) and earlier OEHHA chronic RELs, the U.S. EPA default HEC approach was used when more data-intensive methods and specific parameters were unavailable.

The U.S. EPA HEC methods are presented in detail in U.S. EPA (1994a) and will be briefly reviewed here (Section F.1). Modifications to the U.S. EPA method developed by OEHHA to incorporate child-specific parameters are also described (Section F.2).

The U.S. EPA HEC method assumed that interspecies toxicokinetic differences were adequately accounted for by the method and thus the value of the interspecies uncertainty factor (UF_A) was reduced from 10 to $\sqrt{10}$. However, the U.S. EPA HEC procedure deals only with deposition of the original material. It does not consider interspecies differences in distribution of the parent compound after absorption into the respiratory system, in metabolism, or in the distribution of metabolites. The present guidance therefore regards this procedure as providing only a partial estimate of toxicokinetic differences, and an additional uncertainty factor of at least 2 is recommended (*i.e.* the full value of UF_A would be 6 if, as is most often the case, there is no reduction of the toxicodynamic component of interspecies uncertainty). A larger uncertainty factor to account for remaining toxicokinetic differences may be warranted in special cases where evidence indicates a larger interspecies toxickinetic difference (with humans being the more sensitive species).

F.1.1 Gases with Respiratory Effects

The regional gas dose ratio (RGDR) is calculated as the relative minute volume (MV) to relative surface area (SA) for the lung region of concern:

$$RGDR = (MV_a/MV_h) / (SA_a/SA_h)$$

Default lung surface area estimates presented by U.S. EPA (1994a) are used (Table F.1.1).

TABLE F.1.1. DEFAULT LUNG SURFACE AREA ESTIMATES

Species	Extrathoracic Surface Area (cm^2)	Tracheobronchial Surface Area (cm^2)	Pulmonary Surface Area (cm^2)
Guinea pig	30	200	9,000
Hamster	14	20	3,000
Human	200	3,200	540,000
Mouse	3	3.5	500
Rabbit	30	300	59,000
Rat	15	22.5	3,400

U.S. EPA, 1994a

Minute volume (volume inhaled per minute) is the product of inhaled volume and respiratory rate. Minute volumes (MV) in L/min for five animal species were estimated from body weights (BW) in kg with allometric relationships presented by U.S. EPA (1994):

$$\log_e(MV) = b_0 + b_1 \log_e(BW)$$

where b_0 and b_1 are empirically derived factors from a database of MV and BW values for various species and strains.

Body weights were estimated from the published experimental study under review or, when necessary, from strain and gender specific default values presented by U.S. EPA (1994a). Intercept (b_0) and slope (b_1) values are presented in Table F.1.2.

TABLE F.1.2. INTERCEPT AND SLOPE PARAMETERS FOR ESTIMATING MINUTE VOLUME FROM BODY WEIGHT

Species	b_0	b_1
Guinea pig	-1.191	0.516
Hamster	-1.054	0.902
Mouse	0.326	1.05
Rabbit	-0.783	0.831
Rat	-0.578	0.821

F.1.2 Gases with Systemic Effects

Gases leading to systemic health effects were calculated using the default assumptions used by the U.S. EPA for all systemic RfCs developed to date. The default methodology adjusts the average exposure concentration by the regional gas dose ratio (RGDR), which for systemically-acting gases is assumed to be the ratio of the animal blood:air partition coefficient $(H_{b/g})_A$ to the human blood:air partition coefficient $(H_{b/g})_H$. The following formulae describe the calculation of the RGDR and HEC:

$$RGDR = (H_{b/g})_A / (H_{b/g})_H$$

$$HEC = \text{Average exposure concentration} \times (H_{b/g})_A / (H_{b/g})_H$$

Where the relevant blood:air coefficients are unknown, U.S. EPA recommends assuming that $(H_{b/g})_A$ is equal to $(H_{b/g})_H$ and thus the RGDR for systemic effects is assumed to equal one. This assumption was used for all RfCs that have been developed for systemically-acting gases. Chemical-specific data, where available, were used to estimate the HEC for additional REL values determined by OEHHA. Where species-specific, but not chemical-specific, data were available, the default assumption of RGDR = 1 was used. Where both species-specific and chemical-specific data were lacking, no HEC calculation was used, and a 10-fold interspecies UF was applied.

F.1.3 Particulates with Respiratory Effects

The U.S. EPA HEC method for particulates (U.S.EPA, 1994a) estimates fractional deposition in different lung regions for both animal species and humans, and calculates the regional deposited dose ratio (RDDR) as the ratio of animal fractional deposition to human fractional deposition. Fractional deposition is assumed to be dependent on minute volume, mass median aerodynamic diameter (MMAD), geometric standard deviation (σ_g), and prior deposition in regions through which the particles have already passed. Deposition efficiency (DE), which is unaffected by prior deposition, is calculated from minute volume, MMAD, and σ_g using a fitted logistic function. The function uses impaction diameter (x) estimated from MMAD and minute volume and is fitted for a given species with two parameters (α and β, Table F.1.3):

$$\text{Flow rate } (Q) \approx MV / 30$$

$$x = MMAD^2 \times Q$$

$$DE = 1 / (1 + e^{\alpha + \beta \log_{10} x})$$

Then, fractional deposition is determined by sequentially determining deposition in extrathoracic (ET), tracheobronchial (TB), and pulmonary (PU) regions.

U.S. EPA RDDR software (U.S. EPA, 1994a) has been used to calculate RDDR and HEC for OEHHA RELs for particulates with respiratory effects. Parameters used include experimentally-determined values for the particle distribution, characterized by the mass median aerodynamic diameter (MMAD) and σ_g, the experimental species, and experimentally-determined or estimated

body weights. Minute volumes are estimated from body weights and default estimates of lung surface areas were used. Deposition and RDDRs are estimated for different lung regions.

TABLE F.1.3. PARAMETERS FOR DEPOSITION EFFICIENCY EQUATION

Species	α (ET)	β (ET)	α (TB)	β (TB)	α (PU)	β (PU)
Human	7.13	-1.96	3.30	-4.59	0.52	-1.39
Rat	6.60	-5.52	1.87	-2.09	2.24	-9.46
Mouse	0.66	-2.17	1.63	-2.93	1.12	-3.20
Hamster	1.97	-3.50	1.87	-2.86	1.15	-7.22
Guinea pig	2.25	-1.28	2.52	-0.87	0.75	-0.56
Rabbit	4.31	-1.63	2.82	-2.28	2.58	-1.99

F.2 Human Equivalent Concentration Calculation for Children

OEHHA examined differences related to postnatal development of the lung, including such factors as differences in respiratory frequency, minute volume, lung surface area, lung deposition, and lung compliance. We also noted other factors such as mouth vs. nasal breathing habits and differences in physical activity. Different scenarios can lead to somewhat different results, but, in general, most differences between children and adults are no greater than several-fold in magnitude. The patterns of postnatal development indicate that susceptibility may change throughout childhood, and exposure during the first year of life may be of special concern.

OEHHA compares the human adult physiological and anatomical parameters used by U.S. EPA with the same parameters for children. We then examine the difference that the use of these child specific parameters would make in the HEC calculations. We thus determine if the HEC adjustment to a NOAEL derived from an animal study is protective of children.

F.2.1 Respiratory Differences between Children and Adults

Various factors can affect particle deposition. The respiratory tract is often considered to consist of three anatomically and functionally distinct units: (a) the extra-thoracic (ET - from the mouth and nose to the larynx); (b) the tracheo-bronchial (TB – from the larynx through the conducting airways; and (c) the alveolar (AL – the gas exchange zone). In general, more serious pollution-related health outcomes are related to effects in the TB and AL regions. The patterns of particle deposition in the respiratory tract do not, however, correspond well to the categories used to classify particles (PM10, fine (PM2.5) and coarse (PM10 – PM2.5) fractions). Generally, larger particles demonstrate a greater fractional deposition in the ET and upper TB areas, while smaller particles show greater deposition in the deep lung (lower TB and AL). These regional patterns reflect principally the mechanisms of deposition that differentially influence particles by size.

Mechanisms of nonfibrous particle deposition include: (i) gravitational settling, for particles more dense than air; (ii) impaction on the wall of a bronchus or bronchiole, due to inertia maintained when the airstream changes direction at an anatomical bend or bifurcation; (iii) diffusion related to Brownian motion; and (iv) electrostatic attraction, which is generally considered of lesser importance than the other three. Settling and diffusion are more important for particles less than about 3 μm, while inertial impaction generally affects larger particles, particularly in the ET and upper TB area (Foster, 1999). For ultrafine particles (with diameters <0.1 μm in diameter), diffusion represents the dominant mode of deposition.

The ET region and especially the nose effectively filter out a large fraction of inhaled particles, mainly those above 1 μm in diameter, and also ultrafine particles. In general, inertial impaction predominates in the ET region, so increasing particle size and increasing flow rates will tend to increase particle deposition. However, fractional deposition of ultrafine particles (inhaled at flow rates between 5.9 and 22 liters/min) in the nose has also been reported to be very high (in excess of 93%) (Swift and Strong, 1996).

In the TB and AL areas, increased depth of breathing tends to enhance the deposition of fine particles, while an increased respiratory rate has the opposite effect (Foster, 1999). Exercise and increased respiratory rates also tend to result in greater deposition in larger, central airways, and less in the AL region (Foster, 1999). Using inert particles 1, 3, and 5 μm in diameter, Kim et al. (1996) showed that, even in healthy adults, there is striking heterogeneity of deposition patterns, with airway surface doses 2 to 16.6 times greater in large airways and up to 4.5 times greater in small airways than in the alveolar region for larger (3 and 5 μm) particles. A similar, but less pronounced, pattern was also observed for particles of 1 μm diameter.

Among healthy adults, airway caliber (measured by specific airway resistance) appears to be an important determinant of particle deposition, with a generally inverse relationship between airway diameter and deposition efficiency (Bennett et al., 1996). This may result from the decreased cross-sectional distance that particles have to traverse (by inertial velocity, gravitational settling, or diffusion) before depositing. Women tended to display a greater deposition fraction than men of 3-5 μm particles (perhaps because of a smaller respiratory tract anatomy overall), particularly in the ET and TB regions (Kim and Hu, 1998).

Individuals with asthma and chronic obstructive lung disease experience greater fractional deposition of fine particles (1 μm in diameter) than individuals with healthy, normal lungs, with the degree of particle retention roughly proportionate to the severity of airway obstruction (Kim and Kang, 1997). Anderson et al. (1990) showed a similar increase in deposition efficiency of fine and ultrafine particles, defined here as those with 0.02 – 0.24 μm in diameter, in several individuals with asthma and COPD relative to healthy subjects.

In such individuals, one can observe focal hyperdeposition of particles, often in sites of airflow limitation in central airways, even when nominal ambient particle concentrations are relatively low (Foster, 1999). Airway hyperresponsiveness, which is one of the hallmarks of asthma, is likewise associated with enhanced regionalization of deposition to the central airways (Foster, 1999). The work of Kim and Kang (1997) indicates that such dose amplification can occur because individuals with obstructive lung disease: (1) ventilate only a portion of their lungs, (2) experience increased deposition compared with healthy individuals, and (3) if symptomatic, tend

to have increased minute ventilation. Assessing these factors together, Kim and Kang (1997) estimate that such individuals may have more than three-fold greater total lung deposition than healthy subjects, with this enhanced deposition concentrated in small areas of the lung.

One group of investigators modeled short-term particle deposition in various regions of the respiratory tract using a dosimetry model developed by the International Committee on Radiological Protection (Snipes et al., 1997). They identified large differences in deposition between the ET, TB and AL regions. Daily deposition of all particle sizes was estimated to be greater (by one to three orders of magnitude) in the TB compared with the AL region.

Results of the deposition modeling forming the basis for the report by Snipes et al. (1997) are presented in slightly different form in the 1996 U.S. EPA Criteria Document for particulate matter (U.S. EPA, 1996; vol II, chapter 10). For normal adult males in the general population exposed to a Phoenix-like aerosol (tending to coarse mode), the model predicted daily deposition of 2 and 6 μg/day of fine and coarse mode particles, respectively, in the bronchi, 3 (fine) and 4 (coarse) μg/day in the bronchioles, and 17 (fine) and 12 (coarse) in the alveolar region. Particle doses were estimated to increase substantially in all zones of the lower respiratory tract among "mouth breathers (U.S. EPA, 1996). Higher doses were also predicted to occur as a result of light or heavy work (involving increased breathing rates). Somewhat lower doses were estimated to result from exposure to a Philadelphia-like aerosol, which is characterized by a particle distribution favoring smaller particles. The model employed in these deposition exercises is based on average doses and does not take into account the potential impacts of age, gender, disease states or inter-individual variations in anatomy, ventilation patterns, short-term peak exposures, and so forth.

The human respiratory system undergoes developmental changes throughout childhood. Full lung maturity may not occur until the age of 20 or 25 (Yu and Xu, 1987).

The structural development of the respiratory system varies markedly among species (Mauderly, 2000). Humans as well as rabbits and dogs have developed alveoli at birth, but these structures have not yet developed their mature form, and undergo septal wall thinning and capillary fusion postnatally. Humans form 80% of alveoli postnatally (Plopper and Fanucchi, 2004). Human alveolar multiplication can continue until about 8 years of age (Boyden, 1971). Development of intra-acinar vessels also occurs postnatally (Boyden, 1971). Guinea pigs and sheep have morphologically mature alveoli at birth that only increase in number and size after birth. At birth rats, mice, and hamsters have immature lungs that lack developed alveoli. Thus different species are at markedly different stages of development and may differ in susceptibility to toxicants during the early postnatal period.

There are significant anatomic and physiological differences between the developing lungs of children and those of mature adults (Snodgrass, 1992). These include differences in the size and shape of the conducting airways, the number and orientation of physiologically active gas exchange regions, and ventilation rates. Though the basic structure of the airways is established *in utero*, most of the alveoli (≈ 85%) develop in infancy and early childhood. Alveolar multiplication coincides with incorporation of elastin and collagen in the lung, which are responsible for the mature lung's mechanical properties (Lipsett, 1995). With growth and development other patterns of anatomical differences emerge. For instance, TB airways increase

in diameter and length until adulthood. Lung volume expands disproportionately in relation to the increasing number of alveoli during somatic growth, indicating enlargement of individual alveoli (Murray, 1986).

Because of differences in anatomy, activity, and ventilation patterns, children are likely to inhale and retain larger quantities of pollutants per unit body surface area than adults (Adams, 1993). Phalen et al. (1985) developed a model incorporating airway dimensions measured in lung casts of people (aged 11 days to 21 years) and predicted that particle deposition efficiency would be inversely related to body size, which would tend to accentuate differences in exposure related to activity and ventilation patterns. Phalen et al. (1985) estimated that 5 micron diameter particles will deposit in a 6-fold higher dose per kilogram body weight in the tracheobronchial region in a resting newborn compared to a resting adult. Corroborative evidence for this was provided by Oldham et al. (1997), who found that in models of the proximal TB airways (i.e., the trachea and the first two bronchial bifurcations) of 4- and 7-year-old children and an adult, deposition efficiencies for radiolabelled particles 1.2, 4.5, 9.7 and 15.4 μm in median aerodynamic diameter were greater in the child models in almost all cases. As expected, particle deposition efficiency increased markedly with increasing particle size in this model system. For instance, in the model of the four-year-old child, the deposition efficiency increased from 0.3% to 10.7% when the smallest and largest particle sizes were used, respectively.

Inhalation experiments comparing particle deposition patterns in children and adults have produced somewhat inconsistent results. Schiller-Scotland et al. (1994) reported greater fractional deposition in healthy children, aged 3 – 14 years, compared with adults, when breathing 1, 2 or 3 μm particles spontaneously through a mouthpiece. The differences were greater with the larger particles. However, as noted by the authors, these children were breathing more deeply than expected, which is a common tendency when breathing through a mouthpiece. This propensity may result in greater time-dependent deposition of fine particles (by sedimentation and diffusion). Schiller-Scotland et al. (1994) also noted that, among the older children (mean age = 10.9 years) who were capable of controlled breathing in time with a metronome, particle deposition was inversely related to body height, so that the shorter children demonstrated greater fractional deposition (for 1 and 2 μm particles, the only categories analyzed in this manner). In contrast, Bennett and Zeman (1998) found no significant differences between children (7 – 14 yr), adolescents (14 to 18 yr), and young adults (19 – 35 yr) in deposition (measured as deposition fraction or rate) of 2 μm particles during spontaneous breathing at rest. Unlike the study by Schiller-Scotland et al. (1994), this investigation tailored the participants' mouthpiece breathing patterns to those measured during unencumbered breathing, in order to control for the tendency to breathe more deeply through a mouthpiece. Another difference between the study by Bennett and Zeman (1998) and that by Schiller-Scotland et al. (1994) is that the former did not include very young children, who would have had difficulty in mimicking their normal breathing patterns while using a mouthpiece. However, Schiller Scotland et al. (1994) found that older children (mean age = 10.9 years) as well as the younger ones (mean age = 5.3 years) also showed increased fractional particle deposition relative to adults.

Children demonstrate lower absolute minute ventilation at rest than adults, despite having higher breathing rates. Relative to lung volume, however, children demonstrate a higher minute ventilation than adults. Thus, Bennett and Zeman (1998) noted that children tended to have a somewhat greater normalized deposition rate (by about 35%) than the combined group of

adolescents and adults, suggesting that children at rest would receive higher doses of particles per unit of lung surface area than adults. This tendency might be additionally enhanced by activity patterns, as children spend more time than adults in activities requiring elevated ventilation rates. However, it is unknown whether flow-dependent deposition mechanisms operative at higher ventilation rates in children would offset the decreases that would occur in time-dependent mechanisms (sedimentation and diffusion). If this offset does occur, then particle deposition would likely be shifted more towards the larger, more central airways, which would tend to increase the dose per surface area in children versus adults (Bennett and Zeman, 1998).

Investigators using models from the ICRP reported that the dosimetry of particles for the 3 month old is different than the adults by region of the respiratory tract (Ginsberg et al., 2005b). The model showed two to fourfold greater deposition of particles in the pulmonary region especially in the submicron size range. In the bronchiolar region, adults had higher deposition rates than the 3 month old lung. Particle deposition was similar for adults and 3 month old children in the extrathoracic and tracheobronchiolar region.

The above studies suggest that children may experience proportionately greater particle deposition than adults. It is also possible that, especially in very young children, immature respiratory defenses may result in lower clearance rates in relation to those observed in adults. For instance, Sherman et al. (1977) reported that alveolar macrophages of neonatal rabbits (1 day old) ingested significantly fewer bacteria than older animals (7 days). To the extent that this phenomenon may also apply across species and to nonbiological particles, the immaturity of the neonatal human lung may result in slower and less complete particle clearance.

In summary, there is substantial evidence to conclude that childhood exposures may differ significantly from those experienced by adults. In some cases doses received by children may be substantially greater than those received by adults. However, the differences may be complex and change somewhat over the period of lung development.

F.2.2 Calculation of Adult and Child HECs

The regional gas dose ratio (RGDR) for gases with respiratory effects is calculated as the relative minute volume (MV) to relative surface area (SA) for the lung region of concern.

Minute volume (volume inhaled per minute) is calculated as the product of tidal volume and respiratory frequency. Using empirical formulas for humans,

$$\text{Tidal volume } (\text{cm}^3) = 21.7 + 35.15t - 0.64\,t^2$$

and

$$\text{Respiratory frequency (per minute)} = 15.17 / (0.25t + 0.5) + 11.75,$$

where t is age in years (Hofmann, 1982). Minute volumes (MV) in L/min for five animal species were estimated from body weights (see Section 1.1 and Table 2).

F.2.2.1 Gases with Extrathoracic Effects

Many pollutants fall into the category of gases with extrathoracic effects. These include ammonia, chlorine, formaldehyde, hydrogen chloride, and hydrogen sulfide. Data to estimate child nasopharyngeal surface area are very limited. A simple assumption is that growth of the extrathoracic surface area is proportional to body weight, body surface area, or overall lung surface area.

The approach applied here uses estimates of head volume derived from head growth charts to estimate relative extrathoracic surface area. It assumes that overall extrathoracic surface area is proportional to the surface area of a horizontal plane through the nasopharyngeal region. Based on these assumptions, children are predicted to have lower extrathoracic exposures than adults (Table F.2.1).

TABLE F.2.1. RELATIVE MINUTE VOLUME (MV) TO SURFACE AREA (SA) RATIOS FOR PULMONARY, TRACHEOBRONCHIAL, AND EXTRATHORACIC SPACES IN CHILDREN

A. Chronic Exposure

Age Range (years)	Pulmonary Relative MV/SA	Tracheobronchial Relative MV/SA	Extrathoracic Relative MV/SA
0 to 1	3.0	0.5	0.5
1 to 2	2.0	0.5	0.5
2 to 4	1.5	0.6	0.6
4 to 8	1.5	0.8	0.7
8 to 15	1.3	0.9	0.9
15-25	1.1	1.0	1.0

B. Acute Exposure

Age (years)	Pulmonary Relative MV/SA[1]	Tracheobronchial Relative MV/SA[2]	Extrathoracic Relative MV/SA[3]
0	3.8	0.5	0.5
1	2.2	0.5	0.5
2	1.8	0.5	0.5
4	1.6	0.7	0.6
8	1.4	0.8	0.8
15	1.2	1.0	0.9

[1]Pulmonary calculations based on the lung growth model of Yu and Xu (1987).

[2]Tracheobronchial calculations based on the data of Phalen *et al*. (1985). Calculations are based on flux per surface area in accordance with the U.S. EPA HEC methodology, and do not take into account increased absorption and greater particle deposition due to much greater relative tracheobronchial surface area in children. For example, Phalen *et al*. (1985) predicted a 6-fold increased tracheobronchial deposition of 5-micron particles in newborns compared with adults.

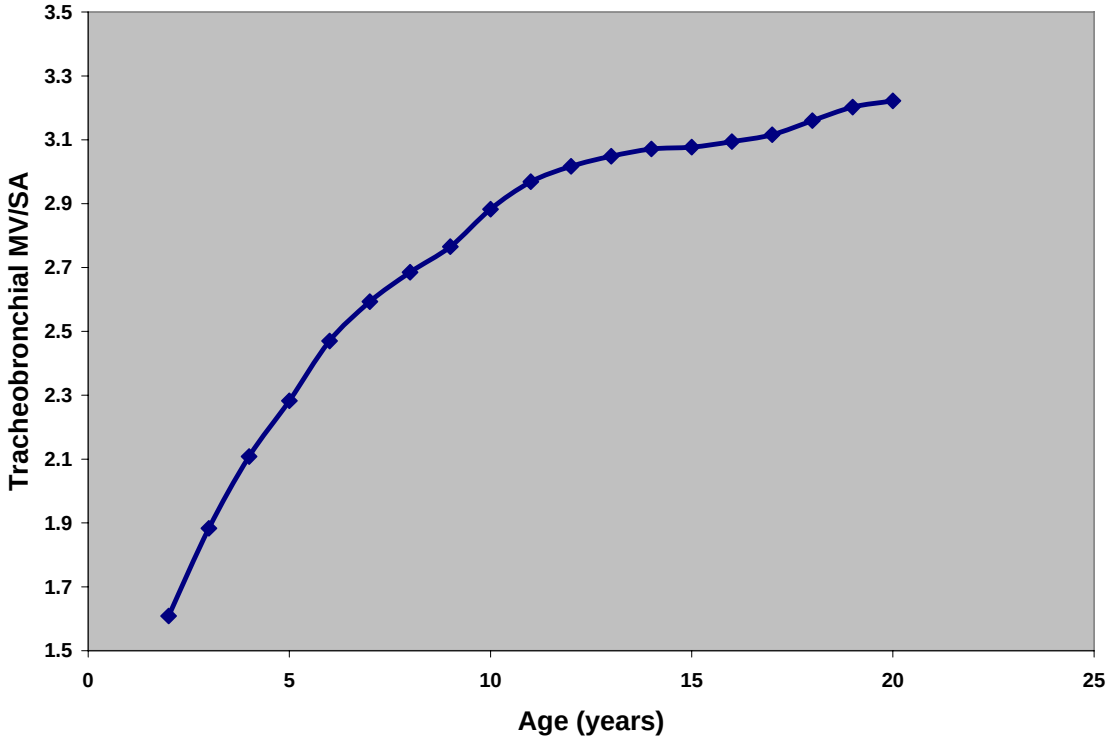
[3]Extrathoracic calculations based on head growth data of Tanner in Dattani and Preece (1978). The increase in extrathoracic surface area is presumed to be proportional to the increase in head volume.

Using the HEC model, the observed concentration divided by the appropriate relative MV/SA factor may be used as an estimate of equivalent childhood exposure. Thus in terms of relative MV/SA, pulmonary effects are predicted to be greater in children, whereas tracheobronchial and extrathoracic effects are predicted to be less in children. The approach does not take into account other differences between adults and children, such as differences in deposition, mouth breathing, and susceptibility.

F.2.2.2 Gases with Tracheobronchial Effects

Other pollutant gases, such as chlorine dioxide and toluene diisocyanate, have primarily tracheobronchial effects. Good data are available to estimate child tracheobronchial surface areas. Figure F.2-1 below depicts changes in the relative ratio of minute volume to tracheobronchial surface area as children age. This approach results in lower tracheobronchial regional gas doses for children than adults (Table F.2.1).

FIGURE F.2-1. CHANGES IN MINUTE VOLUME/TRACHEOBRONCHIAL SURFACE AREA WITH AGE.



F.2.2.3 Gases with Pulmonary Effects

For gases with pulmonary effects, an opposite result is obtained. There are good data to estimate child pulmonary surface areas. As shown in Figure F.2-2, the number of alveoli increases dramatically from birth to age 8. Figure F.2-3 depicts changes in the relative ratio of minute volume to tracheobronchial surface area as children age. This approach results in higher regional gas doses for children than adults (Table F.2.1). This is most pronounced in newborns and infants.

FIGURE F.2-2. INCREASE IN NUMBER OF ALVEOLI FROM BIRTH TO AGE 8.

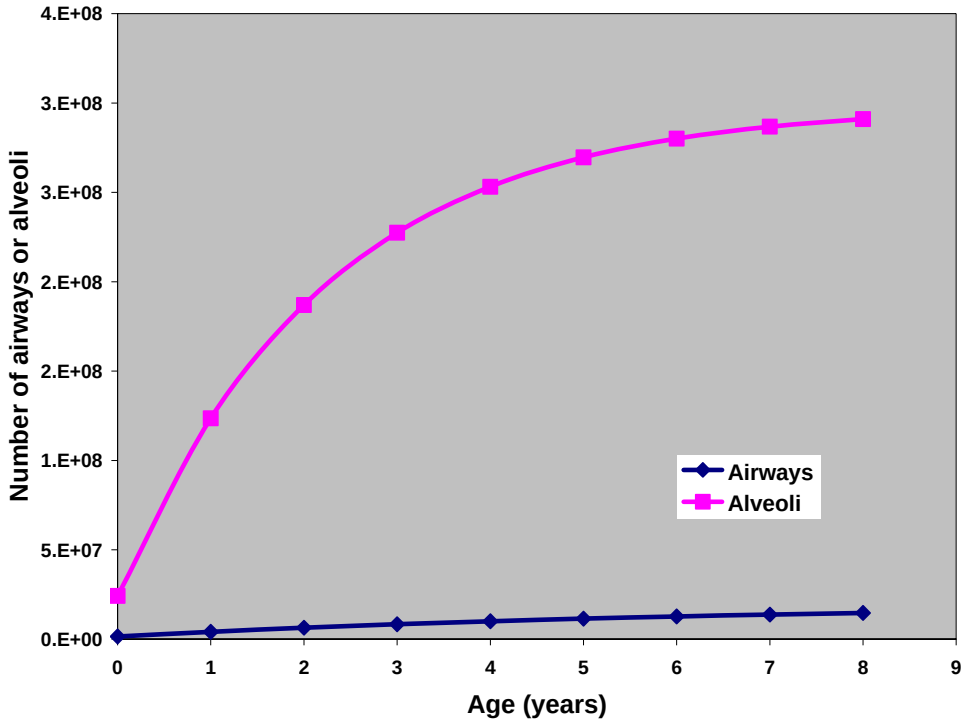
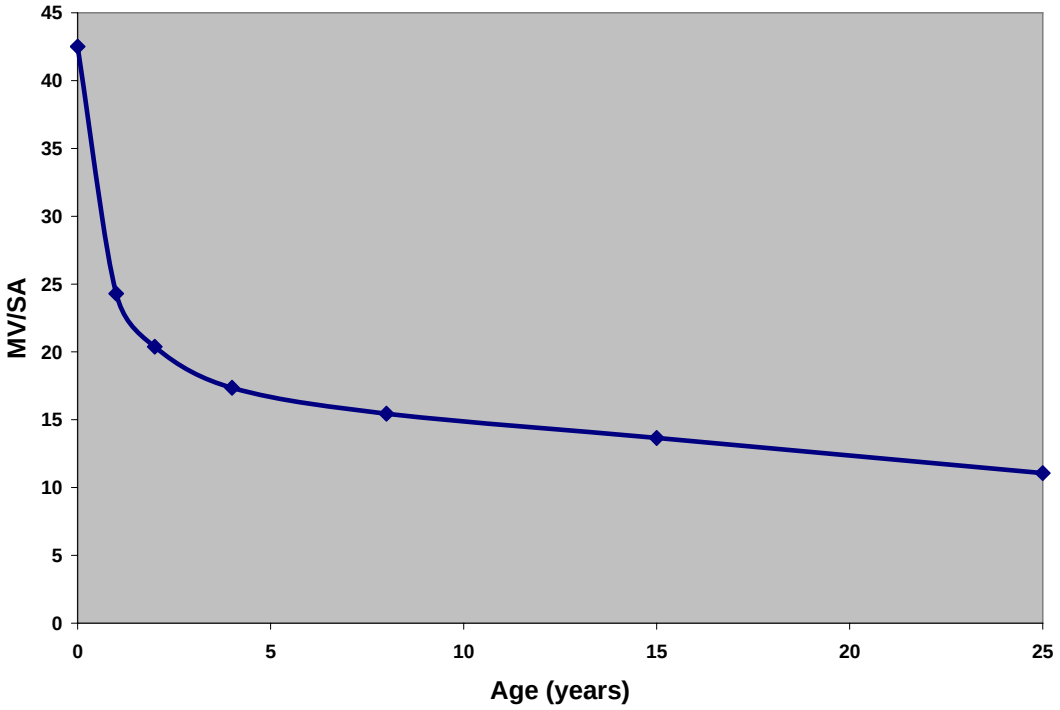


FIGURE F.2-3. DECLINE IN MINUTE VOLUME/TRACHEOBRONCHIAL SURFACE AREA WITH AGE.



F.2.2.4 Vapors with Systemic Effects

The RGDR calculation for systemic effects assumes:

$$RGDR = \lambda_{animal} / \lambda_{human}$$

where λ is the blood to air partition coefficient.

Experimental data for the blood to air partition coefficient were used. A default blood to air partition coefficient value of 1 was used where chemical-specific data were unavailable. Appropriate methods to account for differences between adults and children have not been developed.

F.2.2.5 Particulates/Aerosols/Mists

Deposition efficiency differs as a function of age, as do minute volume, surface area, and body weight. Total deposition fractions tend to be higher in children than adults (Oldham et al., 1997). Deposition fractions of 2 µm particles were 73% in a 7 month old and 38% in an adult (Musante and Martonen, 2000). Children under 8 years of age have the highest deposition fractions. Both tracheobronchial and pulmonary deposition fractions are higher in children. Children may receive a 3-fold higher deposited dose than adults.

Tracheobronchial deposition is inversely proportional to age. Alveolar deposition is maximal at age 4 to 6 as a result of later alveolar development. Aerosol deposition in the nose is also predicted to be greater in children than in adults (Phalen et al., 1989).

As noted earlier, the minute volume to respiratory surface area may be higher or lower for children relative to adults, depending on the region of interest. Thus the net relative RDDR may increase or offset the effect of increased deposition in children, depending on the region of interest.

F.3 Conclusions

Differences between children and adults for relative minute volume to surface area ratios are 4-fold or less. Such differences may be already accounted for in many cases by the 10-fold intraspecies uncertainty factor to protect sensitive subpopulations. There may be cases, however, where other factors lead to greater exposures or susceptibility among children. In these cases, children may be affected at concentrations more than 10-fold lower than concentrations affecting adults. Increased deposition among children can be addressed by child-specific deposition modeling. Known differences in susceptibility should be addressed separately.

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