SILICONES ENVIRONMENTAL, HEALTH AND SAFETY COUNCIL NORTH AMERICA

Phone: 703.904.4322
Fax: 703.925.5955
www.sehsc.com
11921 Freedom Drive
Suite 550
Reston, VA 20190

Guidance for Aerosol Applications of Silicone-Based Materials

This document provides information for formulating an aerosol product containing silicone-based materials. It addresses aerosol particle size considerations in aerosol product applications of silicone polymers and emulsions. Silicone-based materials may be safely used in industrial applications where exposure to aerosols can be minimized through appropriate industrial hygiene practices. The considerations and guidance set forth in this document should be followed for aerosol applications, such as consumer spray applications, in which industrial hygiene practices are not available.

What Are Aerosols?

Aerosols are liquid or solid particles that remain suspended in air for an extended period of time. The particles remain suspended because they are small and, therefore, do not fall (or sediment) rapidly under the force (or pull) of gravity. Many chemicals can be inhaled as aerosols. Just as liquid and solid aerosol particles can sediment in air, so can they sediment in the lung, if inhaled. The rate at which a particle sediments in the lung is a function of the particle diameter. (For the interested reader, the relationship between sedimentation rate and particle diameter is presented in the Appendix in Table 1.)

As liquid or aerosol particles sediment in the lung following inhalation, they deposit at various regions in the lung. The degree of deposition in the lung and of regional deposition is controlled by a number of factors. What is important when considering regional deposition are: (1) particles in the range of 5-30 μm are largely deposited in the nasopharyngeal region (i.e., the nose and throat region), (2) the majority of the particles in the range of 1-5 μm pass through the nasopharyngeal region and are deposited in the tracheobronchial regions (i.e., the trachea and upper part or large airways of the lungs), and (3) particles < 0.5 μm penetrate the alveoli (i.e., the small air sacs of the lungs) by diffusion.

Potential Effects

A number of potentially serious health effects can result from aerosol inhalation. Chemical pneumonitis, lipoid pneumonia, and petroleum distillate pneumonitis are all terms that describe pulmonary (deep lung) tissue damage, edema, fibrosis, or other inflammatory changes in the lungs. Aspiration or inhalation of an aerosol of oily or fatty-type materials into the alveolar region of the lung can cause these changes. Regional release of endogenous lipoid (fatty) or oily material within the lung in certain disease states also can result in a pneumonitis reaction. Ostensibly, this damage is not due to a specific mechanism of chemical toxicity but rather is driven by a physical disturbance of the alveolar lining and subsequent attempts by inflammatory cells within the lung to resolve the lesion.

Considerations

Silicone polymers and emulsions have a wide variety of uses including applications for consumer use. It is known that some silicone polymers and emulsions demonstrate acute toxicity in experimental animals when inhaled as an aerosol. The acute inhalation effects of these materials have been confined primarily to the lungs. The Silicones Environmental, Health and Safety Council (SEHSC), the Centre Européen des Silicones (CES), and the Silicone Industry Association of Japan (SIAJ) have evaluated the data from a variety of the polymers and emulsions assessed in acute aerosol inhalation studies.

The industry assessment revealed that no one parameter was predictive of the acute aerosol inhalation toxicity of the silicone polymers or emulsions. Therefore, it is recommended that if a silicone polymer or emulsion is being developed for an aerosol application, the developer should pay particular attention to the particle size Mass Median Aerodynamic Diameter (MMAD) that will be generated. An acute aerosol inhalation study should be performed if an analysis of the MMAD indicates a potential for lung penetration to an extent where a toxic response may occur. (See the Appendix for further discussion of particle size and potential toxicity.)

Guidance

When considering a consumer aerosol application for any silicone-based material, regardless of the method of aerosol generation, the particle size MMAD should be at least 30 μm with no more than 1% of the particles having an aerodynamic diameter of 10 μm or less. Following this guidance ensures that virtually all aerosol particles will be trapped in the nasopharyngeal region and very few if any particles will be deposited in the tracheobronchial region. The following references can be consulted for information on methods for determining the particle size distribution for an aerosol:

- Vincent, James, H. 1995. *Aerosol Science for Industrial Hygienists.* New York: Elsevier Science.
- Hinds, William C. 1982. *Aerosol Technology*. New York: John Wiley and Sons.

Appendix

Aerosol Inhalation

Many chemicals can be inhaled as aerosols and many toxic substances enter the body in this way. Aerosols are liquid or solid particles that remain suspended in air for some period of time because they are small and do not sediment rapidly under the force of gravity. Table 1 provides sedimentation rate as a function of particle diameter computed from Stoke's law for the viscous drag on a moving sphere.

Impaction is a term used to describe the deposition of aerosol particles in the respiratory tract. The degree of impaction is determined by the rates of sedimentation, diffusion, and inertial precipitation. In considering the rate of movement of substances within the respiratory tract, diffusion may be ignored except for very small particles. Inertial precipitation arises from the tendency of a particle moving in a stream of air to continue in its original direction when the air stream changes direction, and thus, to impact upon some tissue. This occurs, for example, at bronchial branch points.

The extent of impaction in different parts of the human respiratory tract may be computed for particles of varying sizes and, in such computations, have been confirmed by some experimental data. Figures 1 and 2 show the various regions of the respiratory tract for reference. In the nasal passages large particles (>10 μm) are almost completely removed. Particles 5 μm in diameter are removed to an extent of about one-half and particles 2 μm in diameter are removed to an extent of about one-fifth. Below 1μm nasal impaction is negligible. Table 2 provides theoretical results for particle sizes ranging from 0.2 to 20 μm at two values of tidal air.

The following conclusions can be drawn: (1) The larger the particle the greater its tendency to impact and be retained in the upper respiratory tract; (2) At high tidal volume and the same respiratory rate, the airstream velocity is greater, thus particles of all sizes tend to be driven deeper into the lung; (3) As particles become smaller, their retention is primarily limited to the most peripheral parts of the pulmonary tree beyond the terminal bronchioles, but the total retention is less than for larger particles; and (4) When particles become extremely small the total retention begins to increase because diffusion becomes a significant factor.

As far as regional deposition is concerned, the following conclusions can be drawn: (1) Particles in the range of 5-30 μm are largely deposited in the nasopharyngeal region; (2) The majority of the particles in the range of 1-5 μm pass through the nasopharyngeal region and are deposited in the tracheobronchial regions; and (3) Particles <0.5 μm penetrate the alveoli by diffusion.

Aerosol Inhalation Toxicity and Pulmonary Toxicity from Oils and Lipid Materials

The aim of this section is to provide an overview of pulmonary toxicity arising from mist inhalation or liquid aspiration into the lung, of organic oils of various origins in order to provide perspective to the current (and future) aerosol inhalation toxicity data being obtained for silicone compounds. After a detailed literature review, two excellent papers emerged as providing the best review and experimental background to this overview (Skyberg, et al., 1990, Spickard and Hirschmann, 1994).

Much of the content of these papers together with current knowledge of the pulmonary toxicity of oil mists is summarized here, along with their significance for the aerosol (mist) toxicology of silicones. Chemical pneumonitis, lipoid pneumonia, petroleum distillate pneumonitis are all terms which describe pulmonary (deep lung) tissue damage, oedema, fibrosis, and other inflammatory changes which are caused by the aspiration or mist inhalation of oily and lipoid materials into the alveolar region of the lung.

These effects have been shown to be produced by synthetic oils of mineral, animal, or vegetable origin that have been aspirated after ingestion or inhaled as a mist during industrial exposure, medicinal use and abuse, aspiration of foodstuffs, use of oral and nasal lubricants, and so forth.

Some variation in the lung damage caused by exogenous oils is known to be due to their origin, i.e., whether animal, vegetable, or mineral. It has even been noted that endogenous lipids (i.e., those occurring naturally in the body) are capable of causing lipoid pneumonia; this is known to occur in certain disease states where damage to alveoli or other lung tissue allows release of lipids (usually cholesterol and its esters) to escape into the alveolar space. Endogenous and exogenous lipoid pneumonia are distinguishable by histopathological examination of the affected lung tissue.

In summary, a pneumonitis reaction in the deep lung can be elicited by the aspiration, mist inhalation or even *in situ* release of any lipoid or oily material from a wide range of sources; indeed this should be expected to occur if such exposure situations arise, not primarily due to a specific mechanism of chemical toxicity but rather driven by a physical disturbance of the alveolar lining and subsequent attempts by inflammatory cells to resolve the lesion.

Existing data on aerosol inhalation toxicity of silicones and future such test data should be assessed with this perspective in mind.

References

Skyberg, k., Skaug, V., Gylseth, B., Pedersen, J. R. and Iversen, O.H. 1990. Subacute Inhalation Toxicity of Mineral Oils, C_{15}-C_{20} Alkylbenzenes, and Polybutene in Male Rats. *Environmental Research*, 53(1), 48-61.

Spickard, A. and Hirshmann, J.V. 1994. Exogenous Lipoid Pneumonia. *Arch. Intern. Med*., 154(6), 686-692.

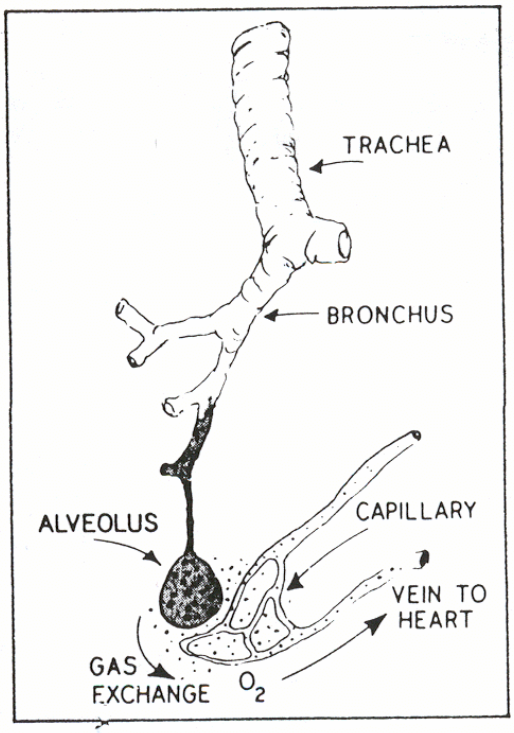

FIGURE 1 —The branching characteristic of the trachea into smaller airways, ending in an alveolus, is shown here.

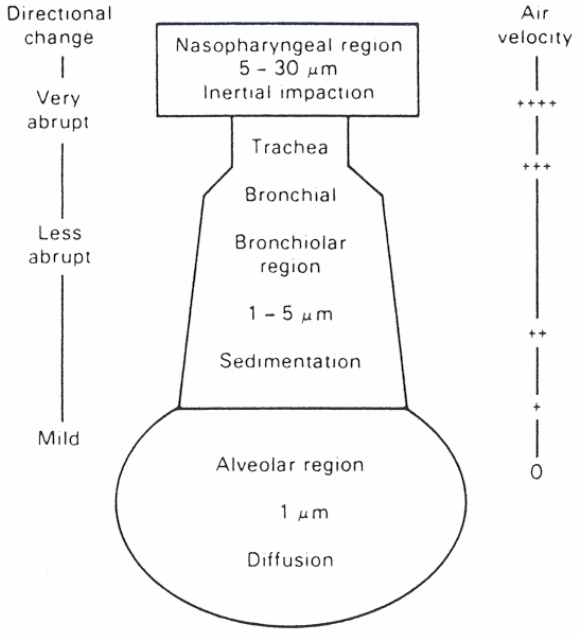

Figure 2 Parameters influencing particle deposition. [From Casarett, L. J.: The vital sacs: Alveolar clearance mechanisms in inhalation toxicology. In Blood, F. R. (ed.): *Essays in Toxicology*, Vol. 3. Academic Press, New York, 1972.]

TABLE 1. Rate of gravitational sedimentation in quiet air as a function of particle size. Sedimentation rates are computed from Stokes' law as described in the text.

Particle diameter, μm	Sedimentation rate, cm sec^{-1}
100	28.7
50	7.17
25	1.79
10	0.287
5	0.072
1	0.0029

TABLE 2. Percent retention of inhaled aerosol particles in various regions of the respiratory tract.
The figures in the columns are percent retention; the column headings are particle sizes in μm. A 4 sec respiratory cycle is assumed. (From Hatch and Gross.[11] Table 3-4.)

	Percent retention									
	450 cm^3 Tidal air					1500 cm^3 Tidal air				
	20	6	2	0.6	0.2	20	6	2	0.6	0.2
Mouth	15	0	0	0	0	18	1	0	0	0
Pharynx	8	0	0	0	0	10	1	0	0	0
Trachea	10	1	0	0	0	19	3	0	0	0
Pulmonary bronchi	12	2	0	0	0	20	5	1	0	0
Secondary bronchi	19	4	1	0	0	21	12	2	0	0
Tertiary bronchi	17	9	2	0	0	9	20	5	0	0
Quarternary bronchi	6	7	2	1	1	1	10	3	1	1
Terminal bronchioles	6	19	6	4	6	1	9	3	2	4
Respiratory bronchioles	0	11	5	3	4	0	3	2	2	4
Alveolar ducts	0	25	25	8	11	0	13	26	10	13
Alveolar sacs	0	5	0	0	0	0	18	17	6	7
Totals	93	83	41	16	22	99	95	59	21	29