Caswell # 641

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Wood Preservative Hearing Support -- Inhalation Absorption of Pentachlorophenol.
Caswell No. 641 & 614B

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On October 18, 1978, the Agency published in the Federal Register a notice of rebuttable presumption against the registration (PD-1) of wood preservative pesticides containing inorganic arsenicals, creosote and pentachlorophenol. Public comment was also requested. The comments on the PD 1 were evaluated and the Agency's response (PD-2/3) was published in January 1981. The final Agency position (PD-4) was published in July 1984. Chapman Chemicals Company, one of the registrants of wood preservatives, has asked for an administrative law judge hearing concerning the Agency's July 13, 1984 Notice of Intent to Cancel certain uses of these wood preservatives.

In preparation for the hearing, Michael Winer of OGC in an August 3, 1985 memorandum to John Melone, asked Hazard Evaluation Division to thoroughly examine the assumptions and supporting information which formed the bases for the exposure assessments leading to the July 13, 1984 Notice. This reviewer was asked to address the scientific basis for the Agency's assumption for using 100% absorption rates for estimating inhalation exposures to pentachlorophenol (PCP).

This request was precipitated by industry comments that challenged the 100% absorption rate. However, no evidence was presented by the opposition to justify a lower rate.

The following general discussion presents information to support the continued use of the 100% absorption rate assumption.

Pentachlorophenol Exposures

The major commercial forms of pentachlorphenol are the unmodified phenol (PCP) and the sodium salt, sodium pentachlorophenolate (NaPCP). Both of these materials are solid, and they are usually applied to wood as 5% solutions, either in organic solvents or water. Granular (prilled) or flaked formulations of the technical grade material are used by commercial applicators to make up end-use dilutions. The end-use dilutions are applied in pressure treatment systems, dip treatments, surface spray or brush treatments.

The vapor pressure of PCP at room temperature (25°C) is relatively low, 1.6×10^{-4} mm Hg and increases with temperature (1.2×10^{-1} at 100°C). Measureable levels of PCP vapor (in the microgram/cu. m. ranges) have been found at application sites and in unventilated areas where wood has been treated with PCP. NaPCP does not have an appreciable vapor pressure. Spray applications with either PCP or NaPCP can however result in exposures to aerosols. The exposures of concern are for the applicator/workers who apply the preservative to wood products or who handle treated wood products as well as to the general population who work or live in quarters that are made from wood products treated with PCP.

Absorption and Deposition of Inhaled Chemicals.

Two main physiological functions of the respiratory tract are to take up oxygen and excrete carbon dioxide. Environmental contaminants in the form of gases or aerosols can also be deposited in the respiratory tract and subsequently be absorbed into the body. The term, "absorption" refers to the process whereby a chemical is taken into the tissues of the lung and/or taken up by the blood stream. Absorption needs to be differentiated from "deposition", a term usually applied to particles. Deposition is the process whereby an inhaled particle impacts or settles on the surface of the pulmonary system and may or may not be absorbed into the body from the lung. This would be the case for insoluble particles which are carried out of the lung by the action of cilia.

The respiratory tract (Figure 1) includes the nasal and pharyngeal cavities, the trachea, bronchi, bronchioles and alveoli. Figure 1 depicts the pulmonary system as three functional subdivisions: the nasal pharyngeal region (NP), the tracheobronchial region (TB) and the parenchymal or "pulmonary" region (P). These different areas have been identified because they represent different areas of deposition of aerosols and gases and help explain different pathological effects localized to these areas.

Absorption of Inhaled Gases. Gases and vapors are generally carried into the deep lung (alveoli) where they are absorbed by the process of diffusion. There are several physical and chemical factors which can augment or retard rate of diffusion of a gas into pulmonary tissues and through to the blood:

1) Solubility. Gases which are absorbed into the body need to first be dissolved in tissue fluids and then in the blood. Chemicals such as acetone or ether which are readily soluble diffuse through the lung tissues. Chemicals of low solubility will not readily penetrate pulmonary tissue and will not readily be absorbed into the body. Both PCP and NaPCP are sufficiently soluble to be taken up by the blood and tissues.

2) Metabolism and Excretion. Gaseous agents which are not metabolized or excreted to an appreciable extent tend to accumulate in the blood stream and retard the rate of diffusion of the agent across the alveolar membranes thereby decreasing the rate of absorption. In such cases (which is common with many of the anesthetic gases) there is established an equilibrium in which the amount of the agent absorbed into the body is equal to that which is excreted from the blood back out into the alveoli.

3) Airborne Concentration. Figure 2 shows a decrease in the rates of absorption of 1,1-dichloro-ethylene with increases in the concentration of the vapor administered to rats. At high airborne concentrations, the diffusion of gases into the body may be limited by the solubility and the rates of metabolism and/or excretion. Therefore the relative absorption rates (that is the percent of the inhaled gases which is retained) may be reduced. At low airborne concentrations of the same chemical, solubility, metabolism and excretion may not be limiting absorption and therefore higher relative rates of absorption (approaching 100% of the inspired air) can be expected.

4) Ventilation Rate. The ventilation rate is dependent on the depth of the breath and the number of breaths with time. In normal individuals, the ventilation rate is dependent on the rate of work being performed. This

is least at rest and increases considerably with increase in the amount of work. Deposition and absorption usually increase with an increase in the ventilation rate.

Absorption of Aerosols. Aerosols are suspensions of liquid particles (sprays) or solid particles (dusts). Many pesticides are applied by sprays and dusts which are made of particles which are not readily inhaled through the nose. These are generally in the range of 200 um or more. However, smaller particles, especially those that remain in the air over time, are usually readily inhaled through the nose and can reach into different levels of the pulmonary tract as indicated in Figure 1. The extent to which such particles may be deposited in various parts of the respiratory tract will vary as depicted in Figure 3. The deposition of the larger particles (between 1 and 100 um) occurs primarily in the nasal-pharyngeal portion of the respiratory system and the smaller particles (0.01 to 8 um) in the deeper alveolar portions of the lung (referred to as "pulmonary") in the figure. Total deposition of the larger particles is shown at or near 100% and at the lowest particles sizes (0.01 um) the total deposition is shown as exceeding 90%.

Deposited particles which are soluble may be absorbed into the pulmonary tissues and taken up by the blood. Insoluble particles may be taken into the lymphatic system or may be carried up the the respiratory tract by the action of cilia where they can be swallowed. Particles which are very insoluble may be carried through the intestinal tract and not be absorbed into the body at all. Particulate PCP is soluble enough to be absorbed directly from the lung and from the intestinal tract.

Absorption of Inhaled of Pentachlorophenol.

Hoben et al. (1975) published a series of papers which studied the deposition of inhaled PCP in rats. The rats were exposed to aerosols of NaPCP in nose-only chambers. Different groups of rats were exposed for 20 minutes a day, for one to 5 days. The investigators measured the amounts of PCP in the plasma, lung, liver and urine with time after the different exposures. From calculated crude estimates of the amount of NaPCP that the animals may have breathed during their exposures, they presented figures (such as Figure 4) on the percent of the "dose" administered to the rats that was found in the different tissues. This ranged from 75% to 121% depending on the experiment, based only on the percent of the calculated doses found in the plasma, lung, liver and urine. These calculations do not take into account the amounts of the PCP which might be retained by the rest of the animals tissues.

Several aspects of these experiments should be noted. The concentrations to which the animals were exposed were quite high, in the range of approximately 77 mg/L (77,000 ug/cu.m.). Worker ~~and~~ exposure concentrations are in the range of microgram/cu. m. (1 to 10 ug/cu.m.). The particle sizes of the aerosols to which the rats were exposed were not determined. Thus, it was not determined how much of the airborne PCP was respirable for the animal. The assumed ventilation rates of the animals were obtained from other studies and may not be applicable to the animals used in these studies. Results from Hoben's studies were from exposures to NaPCP aerosols rather than to PCP vapors.

Defense of the 100% Absorption Factor.

Based on the general discussion of absorption from the lung, inhalation conditions can be obtained in which the 100% absorption rate of gases and aerosols is not unreasonable. The Hoben et al. studies in rats also indicated that 100% absorption of NaPCP aerosols can be expected. We do not, however, have specific data on absorption of PCP vapors in humans under conditions which simulate expected exposures in humans. The data which is available supports the assumption that the 100% absorption rate is reasonable.

References.

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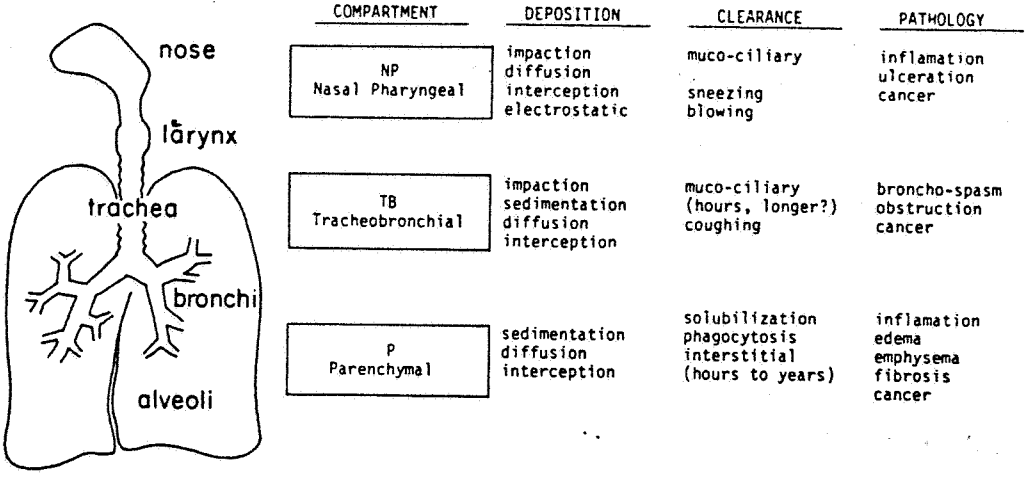
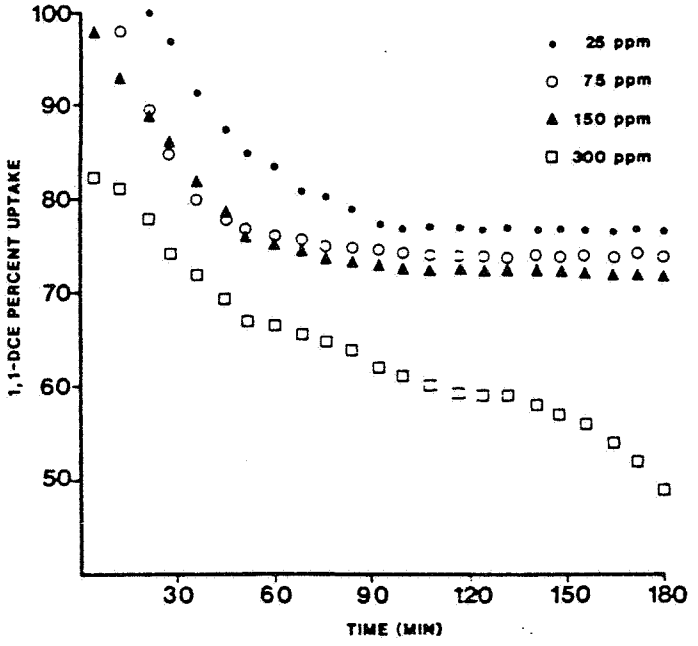


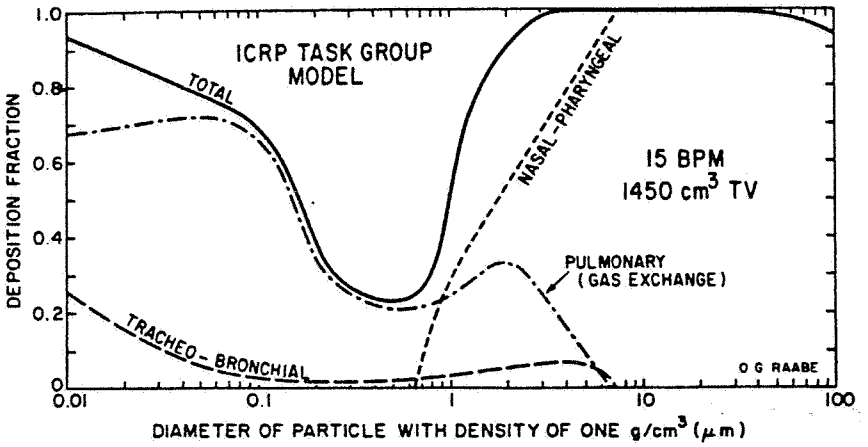
~~FIGURE 1~~. Compartmental model of the respiratory tract of the Task Group on Lung Dynamics of the ICRP.

Figure 1 - taken from Phalen (1984a) p. 36.



~~FIG. 3~~. Percentage systemic uptake of 1,1-DCE during inhalation exposures. Rats were exposed to 25, 75, 150, or 300 ppm 1,1-DCE for 3 hr. Percentage uptake was determined at 8-min intervals. Each point represents the mean percentage uptake in four animals per group. Standard deviation brackets are omitted for sake of clarity.

Figure 2 - taken from page 145 of Dallas et al 1983.



~~Figure 4.B-1.~~ — Total and regional deposition fractions for various sizes of inhaled airborne spherical particles with physical density of 1.0 g/cm^3 in the human respiratory tract as calculated by the International Commission on Radiological Protection (ICRP) Task Group on Lung Dynamics[6] for nasal breathing at a rate of 15 breaths per minute (BPM) and tidal volume (TV) of 1450 cm^3.[2]

Figure 3. Taken from Phalen (1984b)

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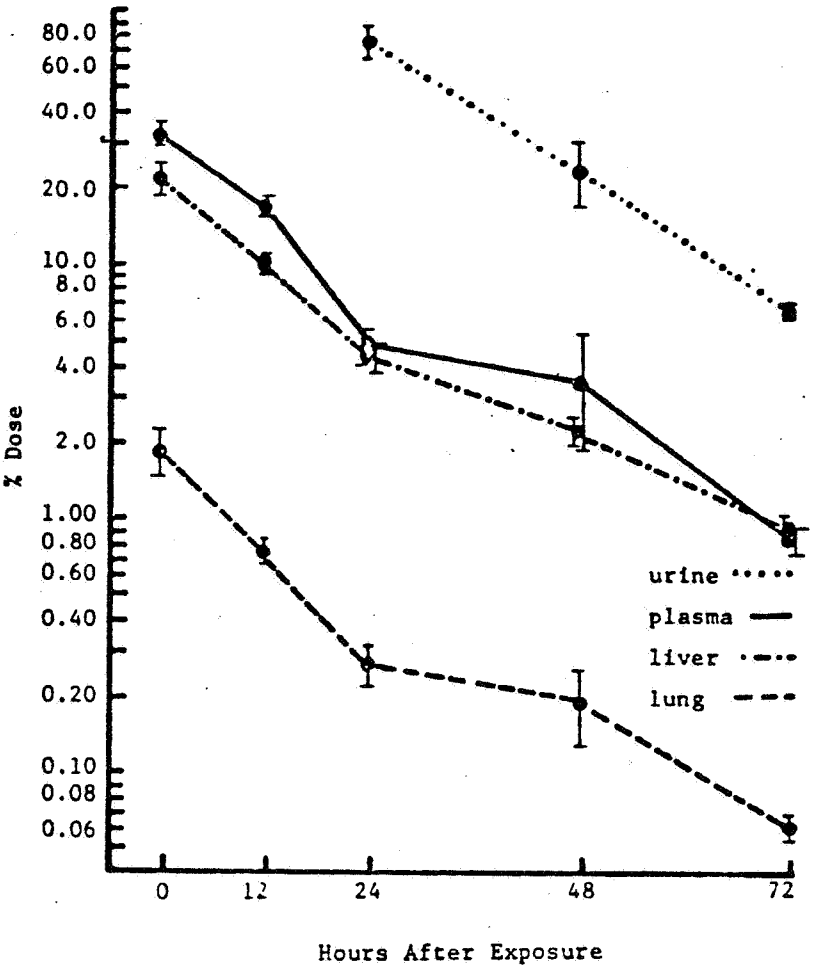

~~Fig. V.~~ Distribution and elimination of inhaled PCP after 5 daily exposures.

Figure 4. Taken from Hoben et al (1976).