. . . it is much easier to generate dust clouds from amphiboles [than from chrysotile].

So, . . . people who were exposed to amphiboles in the past almost certainly were exposed to very high levels [compared to the levels of chrysotile to which people were exposed] (Tr. 7/9, p. 35).

Using a similar line of argument, Dr. Hans Weill of Tulane University suggested that epidemiologic studies show a fiber-specific risk differential because "it is likely . . . that a cloud of asbestos dust contains a higher proportion of respirable 'carcinogenic' fibers if crocidolite is present . . Crocidolite might therefore be more likely to be deposited in the deep portion of the lung and migrate more easily to the pleural surfaces" (Ex. 99, pp. 17–18).

Although the higher levels of amphiboles to which workers were exposed in the past may partly explain the different findings between epidemiologic and animal studies, physical differences between chrysotile and the amphiboles that affect the ability of the lung to clear fiber particles may also have led to these different findings. A number of studies have shown that chrysotile is more rapidly cleared from the lung than are the amphiboles (Exs. 84–171, 84–175, 84–178, 84–202, 312). For example, Glyseth et al. (Ex. 312) examined the asbestos content of lung tissue samples taken from asbestos cement workers who had died of pleural mesothelioma or lung cancer. Although more than 90 percent of the fibers used by the workers were chrysotile, 86 to 99 percent of the fibers found in the lung tissues were amosite, crocidolite, and anthophyllite. The *differential lung retention of various* fiber types has also been demonstrated in animals. Castleman (Ex. 121) discussed a study by Wagner (1982) that found that animals exposed to chrysotile fibers developed lung cancer even though a smaller amount of chrysotile was retained in the lung compared to similar tests with amphiboles. He suggested that "chrysotile fibers engaged in a process that led to cancer before removal and decomposition of . . . [the fibers] occurred" (Ex. 121, p. 2). Dr. Weill believed that "these differences in tissue persistence may wholly or partially explain the observations [that exposure to amphiboles are associated with a higher prevalence of mesothelioma] in human . . . populations . . . Non-confirmation of fiber type differences in animal experiments may be related to the much shorter life span . . . [of experimental animals, which would not allow] the effects of varying tissue persistence to be expressed" (Ex. 99, p. 18).

Dr. Davis also testified that the differential lung retention of chrysotile and the amphiboles may account for the conflicting results of human and animal studies, albeit by a different mechanism. He explained this view as follows:

[I suggest] that chrysotile or sufficient chrysotile is able to remain in the lung tissue for two or three years. Enough of it [to induce cancer] will stay for the [entire] life span of the rat. That means it can exert its maximum effect in the rat, and it means that the rat results showing chrysotile as being [more] hazardous are genuine.

I believe that chrysotile is largely removed from human lung tissue during the much longer 20, 30, [or] 40-year tumor induction period that you have got to have in human beings. I think that if that wasn't the case, then all the epidemiological evidence would be showing that chrysotile was the nastiest of the dusts" (Tr. 7/9, p. 36).

Several rulemaking participants (Exs. 84–256, 99, Tr. 7/9, p. 39) expressed the opinion that chrysotile fibers, which are composed of several hundred smaller fibrils, are easily broken apart in the lung as the result of magnesium leaching from the fibers. The magnesium loss reduces the structural strength and length of the fiber, facilitating removal of the fiber by phagocytosis. This process occurs to a lesser extent with the amphiboles, which contain a smaller quantity of magnesium. Although this may explain why chrysotile is more easily cleared from the lung, it also effectively increases the dose, in terms of the number of fibers, that reaches the lung. Dr. Davis explained this possibility:

"Now I believe what happens—and we have evidence of this—is that chrysotile deposited in lung tissue quite rapidly separates out into its individual fibrils. So if you think you have deposited one fiber in the lung tissue, six weeks later you have actually got 100, which potentially at least are the same length, but are very, very much thinner.

Now I think this certainly explains some of the very high harmful potential of chrysotile in our animal experiments. We are actually giving the animals . . . many more fibers even when we are trying to use equal doses [of chrysotile and amphiboles]" (Tr. 7/9.X, pp. 38–39).

To summarize the data on risk differential by asbestos fiber type, human epidemiological studies have suggested that occupational exposure to amphiboles is associated with a greater risk of mesothelioma than is exposure to chrysotile. No clear risk differential for lung cancer or other asbestos-related disease has been demonstrated by epidemiological studies. Animal experiments, however, have indicated that chrysotile is a more potent carcinogen than amphiboles when administered by inhalation or intrapleural injection, thus conflicting with the findings of human epidemiology studies. Rulemaking participants have suggested several reasons for the discrepancy: (1) Exposures to amphiboles in the past were much higher than exposures to chrysotile, (2) chrysotile fibers break up and are more easily cleared from the lung than are amphiboles, effectively reducing the residence time of chrysotile in the human lung, and (3) the break-up of chrysotile fibers into individual fibrils occurs more readily than for amphibole fibers, thus increasing the effective dose of chrysotile in animals. Dr. Davis explained at the hearing that the net effect of these biological mechanisms is unknown:

". . . Is one fiber . . . of amphibole more dangerous than one fiber . . . of chrysotile? There, I . . . [have] to point out that our evidence cannot answer this with certainty. On the one side, you have almost certainly the greater harmful potential of chrysotile and the greater durability of the amphiboles. . . . I could imagine that one fiber of each in human beings will end up roughly the same harmfulness, or that might not be the case. It may be that the greater durability of amphiboles will still give a little bit of an edge. I have no definite data on this, and nobody else has." (Tr. 7/9, p. 65)

OSHA agrees with Dr. Davis that epidemiological and animal evidence, taken together, fail to establish a definitive risk differential for the various types of asbestos fiber. Accordingly, OSHA has, in its Quantitative Risk Assessment (see Section V) and in the establishment of a permissible exposure limit (see Section X) recognized that all types of asbestos fiber have the same fibrogenic and carcinogenic potential.

Evidence for a Differential Risk by Fiber Size and Aspect Ratio: Several studies contained in the rulemaking docket suggest that fiber dimension is an important determinant in asbestos-related disease development. Stanton et al. (Exs. 84–193, 84–195) studied the effects of various sizes of fibrous materials, including all forms of asbestos, implanted in the pleura of rats and found that some fibrous glasses and all asbestos fiber types produced malignant tumors. The most carcinogenic fibers were 0.25 um or less in diameter and greater than 8 um in length. Fibers less than 8 um in length appeared to be engulfed and digested by phagocytes. However, fibers that were 1.5 um or less in diameter and longer than 4 um (an aspect ratio of approximately 3) also showed a higher correlation with carcinogenicity. Wright

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