AIA ASBESTOS INFORMATION ASSOCIATION

20 December 1973

Hearing Clerk
Food and Drug Administration
Room 6-86
5600 Fishers Lane
Rockville, Maryland 20852

Dear Sir:

The following comments are respectfully submitted by the Asbestos Information Association/North America in reference to Department of Health, Education and Welfare: Food and Drug Administration (21 CFR Parts 121, 128, 133), proposed rulemaking on Asbestos Particles in Food and Drugs, as printed in the Federal Register, Vol. 38, No. 188, Friday, September 28, 1973.

The Asbestos Information Association/North America consists of 22 member companies and associations which represent approximately three-quarters of the asbestos mining, milling, manufacturing and importing industries in the United States. The members of the Association are listed on a sheet which has been attached.

The adverse health effects of inhaling large quantities of asbestos fiber over a substantial period of time are documented in technical literature. Some researchers have reported an increased rate of gastrointestinal cancer among some long-term asbestos industry employees. Other researchers have been unable to support an increase in cancer of the GI tract among populations with above normal exposure to asbestos particles. In 1971, the seven-man Panel on Asbestos of the National Academy of Sciences' Committee on Biologic Effects of Atmospheric Pollutants examined all of the relevant data and concluded: "Associations between asbestos exposures and malignancies of the gastrointestinal tract and of other sites have been reported, but the data are still inconclusive". Reviewing the situation two years later, the Advisory Committee on Asbestos Cancers of the International Agency for Research on Cancer

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of the World Health Organization concluded that for some exposed populations, such an increase does exist, but that the excess is relatively small, that further research is needed, and that there is no cancer hazard resulting from the ingestion of "asbestos fibres present in water, beverages, food or in the fluids used for the administration of drugs."

If the human evidence as to a possible relationship between asbestos exposure and an increased risk of gastrointestinal cancer is scanty and contradictory, animal experimentation performed to date is even more so. As is pointed out in the proposed rulemaking, the major feeding (as exposed to injection) experiments of L. M. Swinburn (your reference number 40) and W. E. Smith (your reference number 41) produced no tumors in the gastrointestinal tracts of the animals, even though the amounts of fiber fed to the animals were massive when compared with human occupational exposures known to result in respiratory disease.

These findings have been further confirmed by the work of J. M. G. Davis of the Institute of Occupational Medicine, Edinburgh, Scotland, whose feeding experiments with rats have thus far produced no GI tumors. A 1967 paper by G. M. Bonser and D. B. Clayton ("Feeding of Blue Asbestos to Rats," 1967 Annual Report, British Empire Cancer Campaign for Research, p. 242) likewise reported no tumors in 40 rats fed crocidolite asbestos throughout their lifetime.

Since it has been suggested that mesothelioma might be caused in some instances by a migration of asbestos fibers from other parts of the body, including the gastrointestinal system, it should be pointed out that no mesothelial tumors were found in any of the animals involved in the various feeding experiments.

While some injection experiments have produced site and mesothelial tumors in test animals, the amount of fiber used in each case was so large as to render any attempted translation to human experience completely inappropriate. In addition, the work of M. F. Stanton of the National Cancer Institute ("Some Aetiologic Considerations of Fiber Carcinogenesis," as presented at the World Health Organization Conference on the Biological Effects of Asbestos, Lyon, France, October 2-5, 1972, Paper 43A) and of P. Gross ("The Locus of Pathogenicity of Asbestos Dust," Archives of Environmental Health, Vol. 27, October 1973, p. 240) strongly suggest that injection or implantation cancers in test animals are directly related not only to dose but, even more

importantly, to the size of the fiber used in the experiment. Electron microscope sized fibers did not produce tumors in the test animals. This is extremely relevant to the proposed rulemaking in that the vast majority, if not all, of the asbestos fibers found in air, water, beverages, drugs and food in the United States are in this apparently non-carcinogenic size range.

On the basis of the human and animal studies contained in the literature, one would have to conclude that the relationship between asbestos exposure and an increased risk of gastrointestinal cancer remains tentative. Because of the known respiratory health hazards of asbestos, there has been a tendency among some researchers to ascribe to asbestos sole blame for an excess mortality from any cause experienced by an exposed cohort, even if that cohort was exposed to recognized toxic substances. It is theoretically possible that some other substance or agent is responsible for the excess GI cancer rate found among some asbestos-exposed populations. This would explain why other exposed cohorts have shown no such increase and also why animal feeding experiments have failed to demonstrate an increased risk. Until further research is completed, this possibility cannot be excluded from consideration.

Even if it is eventually proven that a relationship between asbestos exposure and an increased risk of gastrointestinal cancer does exist, the animal feeding experiments performed to date would have to cast serious doubt on the proposition that the ingestion of asbestos fibers is the cause of this increase.

It should also be pointed out that despite the long-term use of asbestos filters in this country, there is no evidence that anyone in the United States -- or in the world, for that matter -- has ever contracted either GI cancer or mesothelioma from drinking a beverage filtered through an asbestos filter or by being injected with a drug filtered in the same fashion. In fact, the GI cancer rate in the United states is on the decline, and if we were going to see an epidemic of these diseases because of asbestos filter contamination, certainly we would have had some evidence of it before now.

With regard to the question of asbestos-related disease, it must be borne in mind that all of the human groups studied to date have had occupational, para-occupational, neighborhood or household exposures of a magnitude far greater than that which could reasonably be expected to

exist to affect the general public. While precise comparisons are impossible because of different measurement techniques used to quantify asbestos concentrations in the workplace and in ambient air and water (occupational exposures are measured in fibers per cc while ambient exposures are measured in nanograms per cubic meter of air or micrograms per liter of water), rough approximations indicate that even safe occupational exposures are many thousands of times higher than those to which the general public is or has been exposed.

Asbestos is ubiquitous in our environment. It exists naturally in small, though detectable, amounts in serpentine rock formations throughout the world and is constantly being released into the atmosphere through erosion by wind and water. Asbestos is natural to our environment and -- as analysis of dated ice from the polar caps has revealed -- has been for thousands or even millions of years. Man, therefore, evolved into his present form in an atmosphere containing a natural background of asbestos -- both in the air he breathed and in the water he drank. While precise comparisons are impossible, today's atmospheric levels of asbestos, even in urban settings, are still only marginally higher than in the distant past. Most speculation as to the health hazards of the minute amounts of asbestos that have been demonstrated to exist in air, water and in beverages or drugs completely ignores these two most important factors -- the differences in magnitude between occupational and ambient concentrations, and the ubiquitous nature of asbestos in the environment.

To conclude, therefore, as some have done, that because exposure to heavy concentrations of asbestos fiber in the workplace is a recognized health hazard, general public exposure to infinitesimally smaller quantities of the same material must also be a hazard, flies in the face of logic, especially since man has survived such exposures for millions of years. It is reasonable to conclude that the general public is not at risk from infinitesimal quantities of asbestos. Such is the conclusion in the "Report of the Advisory Committee on Asbestos Cancers to the Director of the International Agency for Research on Cancer" (your reference number 52).

On the question of fiber release from asbestos-containing filters into the finished product, it is important once again to comment upon the ubiquitous nature of asbestos in our environment. A number of studies have been undertaken in the United States, Canada, and in the United Kingdom to

determine the so-called "natural background" level of asbestos in ambient air and water. Because of the different analytical techniques employed, the results of the various studies are not 100 percent comparable. However, it would appear that the average background level in water in the U.K. is in the vicinity of $4x10^{-8}$ grams per gallon; and in the United States and Canada, somewhere between 2 and 5 micrograms ($1x10^{-6}$ grams) per gallon. Because of the complexity of the analytical techniques used to measure the asbestos content in water, an error factor of from 400 to 500 percent must be assumed in evaluating the results. The higher background found in North America is probably due to the greater quantity of asbestos-bearing serpentine rock found on the continent -- especially on the Eastern seaboard, where the samples were collected. To place the results in perspective, one microgram per gallon equals one ounce in 2.84 billion gallons.

If these background levels can be considered "normal" for human ingestion, the question must then be raised: how do these levels compare with beverages, drugs, etc. filtered through asbestos-containing filter pads? Research into this aspect of the problem has been conducted by Cunningham and Pontefract (your reference number 43); Nicholson, Maggiore and Selikoff (your reference number 45); Badami and Rickards (unpublished data submitted to FDA on May 1, 1973 by S. Holmes of the Asbestosis Research Council); J. P. Leineweber (unpublished summary of asbestos fiber content in United States commercial beers -- copy attached); Dr. Philip McGrath (FDA memorandum to Dr. Armand Casola); and Dr. J. R. Crout (FDA Preliminary Results of Special Survey).

The results of the Cunningham et al, Badami et al, and Leineweber studies all showed the asbestos fiber content of the various soft drinks, beers, wines and parenteral drugs tested to be no more than, or in many cases, less than the natural background level of asbestos that one would expect to find. Badami and Leineweber could find no correlation between the use of asbestos-containing filter pads and an increase of asbestos fiber in the finished product. Only Nicholson et al found levels of asbestos in parenteral drugs higher than would be considered normal.

Of special interest with regard to the proposed rulemaking are the reports of McGrath and Crout. While only preliminary in nature, the Crout survey shows that the use of asbestos-containing filters bears no relationship to the

presence of asbestos fibers in the finished product. In this respect, it confirms the studies of Badami and Leineweber, and throws considerable doubt on the proposition that the elimination of asbestos filters for parenteral drugs would result in any reduction in asbestos content of the finished product. In fact, the McGrath survey could lead to the conclusion that asbestos filters should be required for all filtration systems, since, to quote the McGrath memorandum, "Filtration through an asbestos filter demonstrated the remarkable capacity of this device to reduce the amount of asbestos in a given sample". It would be highly ironic, in light of the controversy that this subject has generated, if it turned out that the best method for the reduction of natural background levels of asbestos in base liquids would be the use of an asbestos filter!

To summarize briefly:

1. The evidence for a relationship between asbestos exposure and an increased risk of gastrointestinal cancer is inconclusive.

2. If such a relationship could be established, the evidence to date casts serious doubt on the proposition that the ingestion of asbestos fibers causes either gastrointestinal cancer or mesothelioma.

3. The size range of fiber most commonly found in beverages, drugs, etc. does not appear to be carcinogenic.

4. Asbestos is ubiquitous in our environment and has been for millions of years.

5. With the exception of the Nicholson et al study, which has been the object of serious criticism, none of the studies done to date shows an unnatural level of asbestos fibers in the finished product.

6. No correlation has been demonstrated between the use of asbestos filters and the presence of excess asbestos fibers in the finished products.

7. It is unlikely that the elimination of asbestos filters for parenteral drugs will result in a reduction in the asbestos content of the drugs.

8. The levels of asbestos found in beverages, drugs, etc. have not been shown to be hazardous to human health.

On the basis of the above, the following comments and recommendations are offered:

1. The FDA acted properly in not placing restrictions of any type on the use of asbestos filters in the food and beverage processing industries. This decision should not be altered.

2. In light of (a) the available medical evidence (b) the proven value of asbestos filters in removing pyrogens from parenteral drugs, and (c) the unlikelihood that asbestos filters contribute significantly, if at all, to the asbestos content of the final product, it is our recommendation that the FDA delete from Section 133.8 (j) of the proposed regulations that portion prohibiting the use of asbestos filters "unless it is not possible to manufacture that drug or drug ingredient without the use of such a filter".

3. Applying the "prudent person" approach, we support the precautionary measure of requiring a non-asbestos-containing after-filter whenever an asbestos filter is used for filtering parenteral drugs, even though it is highly unlikely that this is necessary either from the public health or drug purity standpoint.

4. Because of the extreme complexity of the technology involved and the possibility of substantial error, we further recommend that the requirement for proof of reduction be eliminated from the proposed regulation. Since the sampling method as described in the NIOSH document is useful only for detecting light-sized fibers, and not those in the EM range, which constitute the vast majority of all asbestos fibers likely to be found in a parenteral drug, the method is in-appropriate and misleading for evaluating the asbestos burden of a particular drug. In addition, it would appear from the studies described above that the asbestos content of the pre-filtered solution is more important in determining the content of the final product than whether or not an asbestos filter with or without an after-filter is used.

5. We support that portion of Section 133.8 (j) with regard to the use of an asbestos-containing filter without an after-filter.

We believe these recommendations will provide the public with the health protection as required in the proposed regulations. In addition, the elimination of the sampling requirement and of that portion of the regulations prohibiting the use of an asbestos filter unless it is not possible to manufacture the drug in any other fashion, will considerably ease FDA's administrative enforcement of the standards. It would be much simpler for an FDA inspector to merely check to see that an after-filter was being used to assure compliance with the regulations than it would be to set up some type of permit system that could create confusion and serve neither the FDA nor the companies involved in the joint interest of best public service.

The Association appreciates the opportunity to submit this letter and requests that the recommendations and comments herein be given fullest consideration in the development of final standards on the use of asbestos-containing filters by the Food and Drug Administration.

Sincerely yours,

R. H. Mereness
Executive Director

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Attachments: Summary of Asbestos Fiber Content in Commercial Beers, J. P. Leineweber

Member list Asbestos Information Association/ North America