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December 17, 1973

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

REF: Department of Health, Education and Welfare:
Food and Drug Administration
(21 CFR Parts 121, 128, 133)
Proposed Rule Making on Asbestos Particles
In Foods and Drugs As Printed In
Federal Register, Vol. 38, No. 188
Friday, September 28, 1973

Gentlemen:

We refer to the recent proposal by Commissioner Schmidt printed in the Federal Register, Volume 38, No. 188, Friday, September 28, 1973 in which, at the very end, comments were requested with reference to both the petition, filed by the Center for Science in the Public Interest and the Environmental Defense Fund, as well as Commissioner Schmidt's proposal in rebuttal to same.

We are pleased that comments were requested concerning the petition. My opinion is only substantiated by a potentially dangerous emotionalism designed to create infinitely greater harm to the "Public Interest" than good.

We have noted one unifying characteristic about petitioners such as the Center for Science in the Public Interest. Having embarked upon some crusade, whether real or imagined, they invariably add to the burden without ever acting in a positive sense to contribute to a solution. They spend fortunes to publicize fear and distrust but nary a dime to research and/or demonstrate a truly safe alternative to whatever their current, fashionable diatribe of the moment might be. If their true concern is the "Public Interest" and the "General Welfare", rather than, personal publicity and self-aggrandisement, they ought to put their money where their mouths are in implementing development of a demonstrably better way to go. Otherwise, in my opinion, these groups stand convicted of their own egomania and total absence of sincerity of purpose.

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The scientific community is in the midst of a controversy between those who would regard past history of safe usage as a valid basis for judging the safety or efficacy of foods and drugs and the proponents of the concept that there is no substance that can be regarded safe unless it has been "proven safe" by the application of a variety of animal tests, however novel and uncertain they may be as indicators of the safety of man. As a result of this constant controversy between the two groups who deny, and those who regard experience as a basis to pragmatic assessment of safety, there has been a plethora of sensational stories in the press. We have a whole file drawer full of headlines suggesting that this or that substance may cause cancer, etc. The "evidence" is often based on poorly devised or contrived studies, on unwarranted or unconfirmed conclusions or on speculations extending beyond the limits of the experiments. We understand that Dr. Philip Handler, Director of the National Academy of Sciences refers to such exaggerations as the worst form of pollution, i.e., pollution of the public mind.

In passing on to Commissioner Schmidt's proposal, we would like to address our comments first of all to the actual petition which was filed by the Center for Science in the Public Interest and Environmental Defense Fund jointly, evaluating any comments and also analyzing those references utilized by the petitioners in drawing their brief. At this point it would be best if we stated that this answer to the petitioners' proposal will only be addressed to the subject of cellulose/asbestos filter media and not to the subject of talc.

The petition starts out with a purely irresponsible unscientific conjecture when it states "this petition involves an imminent and wholly unnecessary hazard to public health". We are sure that any responsible individual analyzing this situation would give a great deal more credence to the work done by the Advisory Committee on Asbestos Cancers in their October 1972 meeting in Lyon, France. Statement 7 in the report of the Advisory Committee on Asbestos Cancers, to the Director of the International Agency for Research and Cancer, specifically asks the question "Is their evidence of an increased risk of cancer resulting from asbestos fibers present in water, beverages, food or in the fluids used for the administration of drugs?" The answer on the part of this group was as follows. "Such evidence as there is does not indicate any risk".

The petition states again on the same first page as follows, "The existence of practical alternatives to the use of asbestos filters has also been demonstrated". In totality, this statement is definitely not true. Obviously there can be certain filtration circumstances which would allow a choice of another type of media, but not over the broad spectrum. Saying there are alternatives does not make alternatives. On page 3 of the petition the statement is made "Since there is no level of exposure to asbestos which is known to be safe, any further delay of regulatory action could result in irreparable injury to the public on a massive scale". It is obvious, from such an all encompassing statement, that the true purpose of the Center for Science in the Public

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Interests' petition is not going to stop here. They will wish to ban asbestos in all applications, and we of course know that this is ridiculous and impossible. On page 3 of the asbestos pamphlet put out by the National Academy of Sciences, it is stated that "nearly all the positive evidence of an association between asbestos and human disease has come from occupational groups" specifically pulmonary in background. The Academy also stated on page 6 "Associations between asbestos exposures and malignancies of the gastrointestinal tract and of other sights have been reported, but the data are still inconclusive".

In section 3, in which there is an identification of the petitioners, it is so stated that it is a non-profit corporation composed of Scientists. The word Scientists in itself is impressive but frankly we would question their depth of knowledge in the field of asbestos and related matters. We do not remember seeing any technical papers written and published on the part of anyone from the Center for Science in the Public Interest nor have we seen their names mentioned at worthy meetings such as the meeting in Lyon, France. Certainly the report entitled "Asbestos and You" produced by Messrs. Castleman and Fritsch in February of 1973 cannot be construed by any stretch of the imagination as a clinical or scientific paper. If this effort is the sum total of their credentials it leaves a great deal to be desired. Furthermore, we don't know of any scientific journal which picked up this report for publication.

The Environmental Defense Fund, although composed of responsible individuals, is certainly again sadly lacking in scientific depth for the proper analysis of this subject of asbestos and man.

We now refer to Section 5 of the petition with reference to the evidence of asbestos in foods and drugs. The first sentence in this section states "The presence of asbestos, a known carcinogen, in foods and drugs is well-documented". There are two primary routes of contamination indicated by the petitioners, specifically, filters and talc. First of all, there is no indication on their part as to another primary route, specifically the ubiquitous nature of the asbestos fiber itself. Furthermore, if the presence of asbestos is well documented, let the petitioners so state by whom, and not speak in generalities. Another statement is made in the same paragraph and repeated in a subsequent paragraph that filters are made wholly or partially of asbestos. At this point we wish to state that no one makes a filter wholly of asbestos. Filter pads are generally made of from 5% to 40% asbestos, the balance being organic cellulose.

Still in Section 5, part A, reference is made to the most publicized article in the asbestos bibliography, specifically the paper written by Messrs. Nicholson, Maggiore and Selikoff, entitled "Asbestos Contamination of Parenteral Drugs", published in Science in July 1972. The press picked up the contents of this article and did a fantastic job of what we believe to be quoting out of context. Jack Anderson of the Washington Post must have used parts of this article, as well

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as the U.P., Medical World News, New York Times, Wall Street Journal, etc.

At this time we would like to present with this letter a copy of a letter written to Dr. Selikoff on March 15, 1972 by Mr. John Tuit, President of Columbia Filter Company, Inc., as well as Dr. Selikoff's answering letter of May 9, 1972. Both of these letters refer specifically to this famous article entitled "Asbestos Contamination of Parenteral Drugs". The most interesting part of this correspondence is the last paragraph of Dr. Selikoff's letter of May 9th in which he states "FINALLY, I DON'T BELIEVE THAT THE PAPER CLAIMED THAT WE HAD EVIDENCE THAT ASBESTOS CONTAMINATION AT LEVELS MENTIONED CONSTITUTES A THREAT TO HEALTH. INDEED, I FELT WE MADE CLEAR THAT CANCERS ASSOCIATED WITH ASBESTOS IN HUMANS HAVE SO FAR BEEN OBSERVED ONLY IN OTHER CIRCUMSTANCES, PRESUMABLY AT LEVELS CONSIDERABLY HIGHER THAN THOSE ASSOCIATED WITH PARENTERAL DRUG CONTAMINATION. INDEED, WE CANNOT EVEN GUARANTEE THAT THE ASBESTOS WE HAVE FOUND IN THE PARTICULAR DRUG SAMPLES TESTED BY US CAME FROM ASBESTOS FILTERS IN THE PRODUCTION LINES CONCERNED; IT IS CONCEIVABLE THAT CONTAMINATION OCCURED AT SOME POINT AFTER FILTRATION".

These comments would also apply to Section 6 of the petition dealing with "THE CARCINOGENICITY AND GRAVE DANGERS OF EXPOSURE TO ASBESTOS". Lacking information as to the technique that was used by Nicholson, et al in their paper mentioned above, one cannot evaluate the quantitative aspects. There is no indication of the length of the fibers other than to suggest they were extremely short. There could possibly be an error in the statement on page 5 of their report, under "Quantity" to the effect that the fibrils were 400 angstroms long is an error. This would mean that they are .04 microns long, and since fibrils are .03 microns in diameter, the length is not enough to constitute even a true fiber. If one knew the actual size found in the drug samples, you could then create this sort of dosage and put it into experimental animals and see what the results would be. This is the kind of experimental evidence that is needed to be supplied to the FDA rather than cramming a 50% diet of pure asbestos into a particular animal or injecting a large dosage of pure unidentified type and size asbestos into the animal. At one point, prior to the publication of Nicholson's paper, Dr. Selikoff delivered another paper in 1969 entitled "Inorganic Microparticulates in Parenteral Solutions; Biological Considerations". Interestingly enough the only microparticulate discussed was asbestos, chrysotile specifically. Dr. Selikoff at this meeting was quoted as saying "He had found in the hospital pharmacy's parenterals - from 100,000 to one billion asbestos fibers per vial". He was quoted as stating also that this was "our pharmacy's contribution to the patient's health".

To further demonstrate the twisting of reasonable analysis, I refer you still to Section 6, page 11, in which the petitioners state "Although, in the limited studies to date, no excessive tumors have been observed in the gastrointestinal tract of animals fed asbestos, other animal tests have confirmed the carcinogenic properties of asbestos".

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This reference comes primarily from page 7 of the asbestos pamphlet, published by the National Academy of Sciences, dealing with asbestos dust introduced into the chest cavity. Interestingly enough they changed one word in their usage of page 7 by substituting the word "experience" in place of the original word used on page 7, specifically inhalation. It was obvious that the word inhalation would not work as well as the word experience, especially when they ended the same sentence referring to ingestion or injection of foods or drugs containing asbestos.

While the petitioners admit that asbestos fibers are virtually ubiquitous, they apparently ignore the fact that this could also be a primary source of asbestos fibers in all products, including food and drugs. We are told that glacial ice of ancient age also reveals the same ubiquitous nature of asbestos fiber.

Finally, to summarize my comments with reference to the petition and the petitioners, they have indicated that they wish the use of asbestos/cellulose filters prohibited "until such time as it has been conclusively shown that asbestos is not carcinogenic when ingested". This approach would appear to be not American in legal nature but Continental law. If this be the case then just about everything should be banned, including coffee, sugar, etc.

Returning now to what the FDA has done with reference to this matter to date, we are extremely impressed with the speed with which the FDA asbestos task forces have accumulated and digested all the available information they could find concerning asbestos. The first contact we had with the FDA with reference to asbestos filters was in March of 1972 as the result of a telephone call. Subsequently we have provided as much background information and bibliography as we could, and have had two meetings with each of the task forces in Rockville as well as in Washington itself. Frankly, as manufacturers of cellulose/asbestos filter media, we realize we would be at a great disadvantage in participating in the scientific areas of this matter.

We have been seriously handicapped in our relations with our own customers in the food and drug fields, primarily because the only contacts with the FDA and the various industries concerning this matter were of a rather forbidding nature. For example, we refer you to the four attachments, specifically Dr. Sam Gibson's letter of June 27, 1972, Dr. Harry Meyer's letter of May 23, 1973, Mr. Pat Adamo's letter of January 26, 1973 and the circular letter from the Alcohol Tax and Firearms Bureau dated October 18, 1972 with reference to foreign substances in bottled alcoholic beverages. The food and drug industries have become somewhat "gun-shy" with reference to edicts or regulations promulgated by various government agencies such as the FDA. Therefore, when letters of this type are received and there is no other general information to the public concerning the matter, everyone starts fearing

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the worst. The FDA's evaluation of the subject of asbestos filters has been going on for almost two years and there has been a dearth of any favorable comments emanating from Washington. As a result there has been a great deal of damage to our industry, because of the total uncertainty of the matter, and the lack of communication to allay fears until a final decision is made. A check of your records will indicate that our particular industry has been totally cooperative with the FDA and totally honest. When the original subject of the use of our type of cellulose/asbestos media was brought up, you will find from your records that other industries fearing a government problem tried to avoid the subject and hide their heads in the sand, so to speak. We, in turn, have been totally forthright and cooperative.

We would now like to return to Commissioner Schmidt's proposal with reference to asbestos/cellulose filter media and to discuss methodology at this point. First of all, most of the major experimental studies on inhalation were done to simulate previous occupational inhalation, which would be the proper approach. However, we seriously doubt if the several studies performed to investigate the effect of asbestos in foods and drugs were conducted on a proper scale of exposure. I would wonder if it is possible to extract the fibrous material from a standard dosage of pharmaceuticals and utilize this as an injection in your tests. It certainly would be a great deal closer to the true situation than 10 mg of unidentified asbestos injected into animals.

I understand there is a technique of tritium labeling asbestos fibers. I believe this has been done on asbestos material for injection into experimental animals for subsequent tracing of the test material within the animal organism. I am now wondering if this could also be done on an ingested basis.

Mr. Philip McGrath's report to Dr. Armand Casola on electron microscopy evaluation of effluent passed through an asbestos filter pad was fascinating but not surprising to us in our particular industry.

We also read with interest the "Special Survey on Asbestos Particles in Parenteral Drugs", by Dr. J. Richard Crout. This survey would indicate to me that the level of asbestos in these solutions was apparently no higher than the environmental level involved. It certainly cannot be attributed definitely to the use of asbestos/cellulose filter media.

We refer you to page 27078 of paragraph 2 in which it is stated "The precise effect of asbestos pad filtration on removal of pyrogens is not completely known at the present time". There has been a more recent paper on this subject which was not included in your bibliography, written by a Dr. Wellhaeuser and Dr. Schmidt in Germany. We are enclosing a copy of same for your use. Our purpose in doing so is to counter your statement by saying that a great deal is known about

pyrogens and how they can be eliminated by adsorptive filtration. From this article you will see that the free pyrogens can only be removed by asbestos filter pads. Although we supplied Dr. Armand Casola with six printed articles on pyrogens, only one of them appears as item 46 in the bibliography on page 27079. Possibly some of the other articles that we supplied would add more to the matter of pyrogen retention and the knowledge thereof.

Returning to the actual proposal of Commissioner Schmidt concerning article 133.8 - Production and Controlled Procedures, let us please tell you first of all that the idea of utilizing an after-filter following the use of asbestos/cellulose filter pads is not new. Prior to 1937, there had been no truly effective way of filtering intravenous solutions to achieve non-pyrogenicity on a production basis. The use of cellulose/asbestos filter pads allowed for the processing of large quantities of solutions such as sodium citrate, dextrose, heparin, blood, plasma as well as all the antibiotics which came along during World War II.

There were practical difficulties encountered during this trial work and the most serious difficulty noted was the presence of shreds and particles in the filtrate. While the injection of solutions containing these particles into numerous experimental animals caused no detectable symptoms, their presence was none the less objectionable. After 16 months of evaluation for a suitable after-filter, the difficulty was overcome by the use of an aloxite fiber eliminator located between the asbestos/cellulose filter media and the collecting chamber. Among some of the rejected after-filters were Jena, Chamberland and Berkefeld filters.

While we are pleased that Commissioner Schmidt is planning on taking no action with reference to ingested products, we do take exception to some of the terminology utilized in reference to the use of asbestos/cellulose filter media on parenterals.

Specifically we do not like the terminology stating "no asbestos-containing filter may be used unless it is not possible to manufacture a drug without the use of such a filter". It would be far more lucid and reasonable if the proposal so stated that "when an asbestos-containing filter is utilized, a suitable after-filter must also be utilized to retain fibers."

We believe there should be no specific reference to the use of a membrane and we do not see the reason why you would want to limit yourself to this specific item. Any regulations made by the FDA will have to be lived with for years. There are other appropriate after filter media that should meet the recommended standards you have indicated and which might be far more feasible for various producers to utilize. We are quite sure that you will be receiving comments direct from manufacturers of such material. For example, there are available certain commercial grades of lint free filter paper that have been tested by such independent laboratories as United States Testing Company, Inc., and the results of such tests have indicated total removal at 430 magnification.

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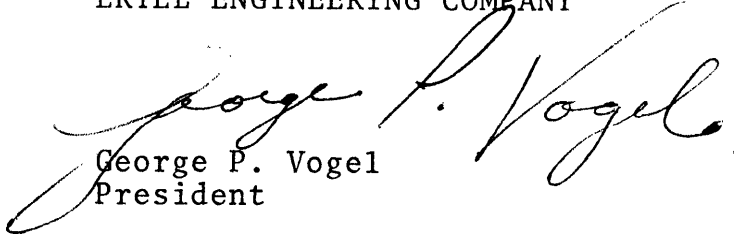
We believe that if the FDA rules that regulation is required, said regulation should read "Parenteral solutions filtered by asbestos-containing filter media are not to be considered as contaminated. But when such asbestos-containing filter media is used, the exercise of good housekeeping and production procedures requires the use of secondary filtration for the removal of possibly migrating fibers."

We find valid and totally sensible Commissioner Schmidt's further proposal "Use of an asbestos-containing filter without subsequent use of an additional non-asbestos-containing membrane filter is permissible only upon submission of proof, etc."

Frankly, we do not envy those in the FDA who have to make final decisions to this type. The integrity of a group such as the FDA must be unimpeachable and therefore we can see that it is expedient that you not be stampeded into making an ill-advised ruling with which we will all have to live with for many years to come. Certainly the Delaney Amendment, while in principle is excellent, is not in keeping with today's scientific sophistication.

Sincerely yours,

ERTEL ENGINEERING COMPANY



George P. Vogel
President

GPV:am

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