



HYLAND

DIVISION TRAVENOL LABORATORIES, INC.

Post Office Box 2214
3300 Hyland Avenue
Costa Mesa, California 92626
(714) 540-5000

December 21, 1973

Hearing Clerk
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Dear Sir:

As manufacturers of biological products, holding establishment license number 140, we wish to comment on the Proposed Rule concerning Asbestos Particles in Food and Drugs, published at 38 FR 27076 on September 28, 1973.

We would like to point out that:

1. There is no evidence that asbestos in the quantities purported to be present in some parenterally administered drugs has ever caused adverse effects in human recipients, despite the fact that asbestos has been a component of materials used in processing such drugs for many decades. The only evidence of ill effect follows exposure by inhalation and (possibly) by contact and ingestion, and then only following relatively high exposure because of occupation or unusual environment.
2. Asbestos is ubiquitous, as noted in the preamble of the proposal.
3. There is no accepted practical method to demonstrate the presence (or, more important, the absence) of asbestos in parenteral drugs.

We have no objection, however, to attempt to prevent unnecessary exposure to the presently unknown hazard, providing that the quality and efficacy of often life-saving drugs are not impaired in such an attempt. In accordance with this attitude, we have had an active project,

75P-0261

1 11

Hearing Clerk
Food and Drug Administration
December 21, 1973
Page 2

opened in October 1972, to find ways of eliminating asbestos and asbestos-containing materials from all stages of the processing of the injectable products we make. We have no means to demonstrate either the presence or absence of asbestos in our products; therefore the study has been directed solely to the elimination of asbestos-containing materials (filters) so far as possible from all processing steps.

Our injectable products are all derivatives of human plasma and the diluents with which such products as are furnished in dry form are reconstituted for administration. The diluents are all prepared without the use of asbestos or asbestos-containing materials. Asbestos-containing filters have been used for years to achieve the sharp separations of fractions of human plasma proteins needed for purity and physical stability of products and to reach the final product clarity required by present FDA regulations.

Dozens of candidate substitutes for asbestos-containing filter material have been found ineffective in our study. Only in recent months has partial success been achieved. We have been able to use final membrane filtration for all our products, and for some products we have been able to eliminate asbestos-containing filters entirely. However, for other products, we have not yet been able to find an acceptable substitute during the processing.

We should again mention that we have no information as to whether or not the number of asbestos particles, if present, has been reduced by the final membrane filtration.

Although it is not clear, the description of the FDA survey and study in the preamble of the proposal (page 27077, column 3, to page 27078, top of column 1) seems to say that asbestos was demonstrated in many products which were never exposed to asbestos during processing. Thus it may be futile to expect to achieve complete absence of asbestos.

Hearing Clerk
Food and Drug Administration
December 21, 1973
Page 3

The present FDA regulations and requirements for clarity and stability of parenterally-administered human plasma derivatives are based on what has been possible with the use of asbestos-containing filters, not upon any knowledge of harmful effects or lack of effectiveness of preparations less clear or less stable with respect to the formation of insoluble material on aging.

Based upon the above considerations, we feel that the issuance of any regulations such as those in proposed Section 133.3 (j) is premature and should await:

1. Practical methods of demonstrating and quantitating asbestos particles in such biologicals as human plasma derivatives.
2. Knowledge that the present preparations, which may or may not contain very slight trace amounts of asbestos, have any undesirable side effects attributable to asbestos.
3. Knowledge as to whether or not the presently required degree of clarity and physical stability are needed for reasons other than esthetic.

If it should be determined that some kind of regulations in this matter is needed, we have the following comments concerning the proposed form of Section 133.8 (j):

First sentence: This sentence would regulate the filter, not the use of the filter. A better choice of sentence form might be: "Filters which release fibers shall not be used in the manufacture-----."

Second sentence: This directly contradicts the first sentence, saying that such filters may be used under certain circumstances. Further, demonstration that something is not possible is an almost impossible task; the possibility changes with advancement of the art, a matter largely in the hands of the filter manufacturers, not the biological manufacturers, although the latter admittedly can stimulate the former.

XX

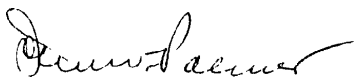
Hearing Clerk
Food and Drug Administration
December 21, 1973
Page 4

Third and fourth sentences; The proposed requirement to furnish evidence that the final (membrane) filter actually reduces the content of asbestos particles seems unreasonable, and we feel it is ample to require that such a filter be used. The demonstration of reduction requires equipment not easily or usually available to a biologics manufacturer, and the reference cited is almost entirely concerned with much larger numbers of particles than might be expected under any condition in a parenteral solution.

This proposed requirement would require proof only that safety or effectiveness is (or might be - a purely subjective conjecture) compromised. It does not consider that clarity and physical stability, which are a part of the present requirements for our products, might be affected with no effect on safety or effectiveness, yet products would not be satisfactory by present release standards.

In summation, we feel that a great deal of information needs to be gathered before regulations such as those proposed for Section 133.8(j) can be considered.

Respectfully,



John W. Palmer, Ph.D.
Vice President and Director of Laboratories

gt

HK



TRANSMITTAL SLIP

TO: Hearing Clerk DATE: 12-21-73

- | | |
|---|--|
| ☐ NOTE AND FILE | ☐ PLEASE REPLY |
| ☐ NOTE AND RETURN | ☐ TAKE APPROPRIATE ACTION |
| ☐ NOTE AND SEE ME | ☐ PER YOUR REQUEST |
| ☐ PLEASE ANSWER | ☐ FOR YOUR SIGNATURE |
| ☐ FOR YOUR APPROVAL | ☐ FOR YOUR INFORMATION |
| ☐ INVESTIGATE AND REPORT | |

COMMENTS:

*This may be a duplicate submission.
We were uncertain as to whether the original
envelope had been addressed to you or
to the Bureau of Biologics through habit.
If this is a duplicate submission, it may be
destroyed.*

J. W. Palmer

SIGNED