ASBESTOSIS RESEARCH COUNCIL

P.O. BOX NO. 40,
ROCHDALE,
ENGLAND OL12 7EQ
TEL. 47422

SHs/MG

3rd December, 1973

The Hearing Clerk,
Food and Drug Administration,
Room 6-86,
5600 Fishers Lane,
Rockville,
Maryland 20852
U.S.A.

Dear Sir,

Department of Health, Education and Welfare
Food and Drug Administration
(21 CFR Parts 121, 128, 133)
Asbestos Particles in Food and Drugs
Notice of Proposed Rulemaking

In accordance with the provision made therein, I wish respectfully to submit a number of comments on the above notice, printed in the Federal Register, Vol.38, No. 188 on Friday 28th September 1973, as follows:-

1. I was privileged to discuss the general question of the use of asbestos-containing filters in the preparation of foods and parenteral drugs with officers of the Food and Drug Administration at two meetings on Tuesday 1st May, 1973. A meeting under the Chairmanship of Dr. Robert Schaffner was held at the Bureau of Foods in Washington and a meeting under the Chairmanship of Dr. Armand Casola was held at the Bureau of Drugs in Rockville. At these meetings I tabled a number of documents, including in particular a report on the work of Dr. L.M. Swinburne (your reference No. 40) and a report on "The Estimation of Asbestos in Liquids" by Badami and Rickards. This latter report was confidential at the time, but is now ready for submission to "Nature" for publication with only minor modifications. It gives the results of a British study on the measurement of the small quantities of asbestos present in drinking water, beverages and parenteral drugs, and compares them with results quoted in two published papers (Cunningham and Pontefract - your reference No. 43a and Nicholson et al - your reference No. 45). The report stresses

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the need to work with reasonable quantities of liquid and to run a sufficient number of blank tests to allow for contamination and to assess the background levels. The results show that the asbestos content of water, beverages and drugs from filtration or other sources is extremely small.

2. Two more recent reports, issued by the Food and Drug Administration, are of considerable interest in indicating that asbestos filters do not add asbestos fibre to the filtered liquid. The first, from Mr. Philip McGrath to Dr. Armand Casola, and dated 10th July 1973, shows that an asbestos filter, far from adding to the contamination, almost eliminates asbestos from a liquid which has been deliberately heavily loaded with the material.

3. The second report, from Dr. J. Richard Crout to the Acting Director, Bureau of Drugs describes a survey of the products of fourteen manufacturers of parenteral drugs. This report calls for particular comment on a number of counts. I have no strong criticism of the analytical procedure, but considerable doubt must be cast on the accuracy of the results when very small volumes (e.g. 1 ml) of liquid are involved. Further, the small range of values (0-27) for asbestos fibres seen under the optical microscope from the wide range (1-1000 ml) of liquid volumes handled suggests strongly that the fibres actually observed are due to background contamination in the laboratory. All the samples tested by electron microscopy, whether or not an asbestos filter had been used, gave a positive indication of asbestos in the filtered material. This is further evidence that the asbestos filter is not the source of contamination, bearing out the statement in the rule-making document that "Asbestos fibres thus are ubiquitous in air, water and a large percentage of the earth's crust".

4. Turning to biological evidence on the migration of asbestos following injection or ingestion and its effects, the rule-making document rightly draws attention to the fact that the major studies have been concerned with inhalation. Of the few non-inhalation studies, that of Schmahl (your reference No. 48) describes the development, not of mesotheliomes, but of sarcomas, in his animals. This type of tumour is not regarded as of asbestos origin. The latest work of Roe and his colleagues (your reference No. 51) on the sub-cutaneous injection of large doses of crocidolite asbestos in mice has shown only a limited migration of fibres, with "no evidence of massive or selective spread to subserosal tissues in the thorax or abdomen". The authors further comment "One disturbing feature of the present experiment was the occurrence of what appeared to be asbestos fibres in tissues from some of the untreated control mice", thus providing further evidence of the ubiquity of asbestos.

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5. On 18th-20th November 1973, a Conference jointly organised by the National Institute of Environmental Health and Safety and the Environmental Protection Agency, was held in Durham, North Carolina to discuss the biological effects of ingested asbestos. Although I was not present, I understand that the meeting added little to the knowledge on this subject and that few presentations had the slightest bearing on it. Dr. J.M.G. Davis described his experiments currently in progress on the ingestion of asbestos by rats, indicating that so far he had seen no signs of gut damage or of asbestos penetration. Dr. I.G. Webster reported that he had given a single dose of crocidolite to one baboon and claimed to have found gut penetration from an analysis of tissue. Some of those present wondered, however, whether the asbestos had in fact penetrated or was still on the surface of the gut wall. Dr. R. Pontefract gave a further report on his published work (your reference No. 44), which had already been widely criticised because of the method used to introduce the asbestos into the animal. Dr. G.E. Westlake, who published a paper eight years ago (your reference No. 42) describing feeding experiments on rats which had resulted in tumours in three animals after three months, reported to the conference that his remaining fifty-seven rats had survived for their full life term and no further tumours had been found. In short, the conference showed that genuine feeding experiments had generally given negative results for penetration. Tumours and tissue damage had only occurred where the mode of entry of the asbestos had been artificial.

6. Turning to the subject of talc used in the preparation of food or drugs, I agree that most commercial talcs contain amphibole or chrysotile asbestos fibres, or both, to some degree and it is no doubt desirable to estimate the quantities present. The method proposed for this in the rule-making document appears to be the best that can be devised for general use, but, where possible, supporting evidence should always be sought by X-ray diffraction, electron microscopy, or other appropriate analytical techniques. I am intrigued by the proposal to call for talc at least 99·9 per cent free of amphibole fibres and at least 99·99 per cent free of chrysotile fibres, implying that the latter type may be the more hazardous. If the fear lies in the possibility of tissue penetration or damage, then it is well known that, because of the physical properties of the fibres, this is more likely to happen with amphiboles than with chrysotile, not that there is much evidence except in the case of lung tissue.

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In the light of the above comments, I would sum up my views on the subject as follows:-

(a) There is still no firm evidence that the introduction into the body of asbestos by ingestion or sub-cutaneous injection in the small amounts normally encountered is hazardous.

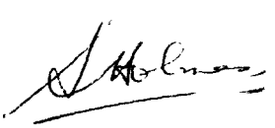
(b) There is no evidence that the use of asbestos filters contributes substantially to the asbestos present in beverages and parenteral drugs. There is indeed evidence that filtration through asbestos may remove some of the fibres already present from other sources.

(c) In view of (a) and (b) above, and the recognised value of asbestos filters in imparting clarity to potable liquids by the removal of bacteria, it is gratifying to note that the Food and Drug Administration does not propose any control or prohibition on the use of asbestos filters in the processing of beverages or food.

(d) Again in view of (a) and (b) above, and bearing in mind the generally accepted role of asbestos filters in removing pyrogens from parenteral drugs, there would appear to be no need to restrict their use as proposed in clause 133.8(j), provided that a membrane after-filter is used to act as the best possible, although not absolute, barrier against the very small amounts of asbestos present in the drug from whatever source. Indeed, it would appear from the Crout report that this is standard practice in the industry.

I forward these observations in the sincere hope that they may be given consideration by the Food and Drug Administration in drawing up its rules.

Yours faithfully,



S. Holmes B.Sc., Ph.D., F.Inst.P.