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DEPARTMENT OF HEALTH, EDUCATION & WELFARE
OFFICE OF THE SECRETARY
WASHINGTON, D.C. 20201

NOV 25 1975

Copy to
Dr Rawlon
Dr Harris
for your early comment
please and any factual answers
to queries in the text which
may be readily available.
H.T.-Y.
24/12/75.

Dr. Henry Yellowlees
Chief Medical Officer
Ministry of Health
Alexander Fleming House
London, S. E. 1, England

? Which of you will act as "contact man"?

Dear Dr. Yellowlees:

I am writing to apprise you of inquiries which have been directed by a Mr. Michael Gillard of Granada Television, London, to members of the staff of our Bureau of Biologics in the Food and Drug Administration regarding U.S. export of plasma derivatives to the United Kingdom, specifically export of Antihemophilic Factor. In addition, there is some specific information which we would appreciate, if you can provide it.

The general gist of Mr. Gillard's inquiries seems to rest on the premise that the American pharmaceutical industry is sending material to the United Kingdom which is so unsafe as to be unacceptable in the U.S. He was apprised of the following facts, which reflect many of his areas of interest:

1. All injectable plasma derivatives manufactured in the U.S. or manufactured outside the country and shipped to the U.S. are subject to licensure as biologics and must be made in licensed facilities in compliance with all of our standards.

2. Plasma derivatives made outside the U.S. and not shipped into the U.S. are not subject to regulation by the Food and Drug Administration, regardless of whether or not the manufacturer is a subsidiary or overseas partner of a U.S. pharmaceutical firm.

3. Source plasma used in manufacturing licensed plasma derivatives, in the U.S. or overseas, must be collected in facilities with U.S.

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licenses. (Mr. Gillard requested a list of the names and addresses of these facilities.) Source plasma collected in the U.S. for export to unlicensed overseas fractionators must be collected and processed in facilities with U.S. licenses. Source plasma collected outside the U.S. and shipped to overseas consignees manufacturing products not licensed by us are not subject to any U.S. regulations.

4. Our hepatitis test requirements, published in 1972 and 1975, apply only to source material. We have not required that final products such as plasma derivatives, which are made from pooled plasma, be tested or be non-reactive for hepatitis B surface antigen (HB_SAg). Only when a manufacturer has chosen to label a final product as tested and non-reactive for HB_SAg have we required the material to be non-reactive, as labeled.

Mr. Gillard indicated that large amounts of Antihemophilic Factor Concentrate are being imported by the United Kingdom and that 70 - 80% comes from the U.S., primarily from Hyland and Abbott. He indicated that lots sent to the United Kingdom in 1975 have been reactive for hepatitis B surface antigen. He was told that this could be the case for lots bearing the U.S. license number of the manufacturer (see item 4 above) unless the manufacturer had chosen to label the final product as tested and found non-reactive. This brings me to several specific questions which I hope you can help us with:

Can you provide us with the identity by manufacturer, lot number, and expiration data of HB_SAg reactive lots of Antihemophilic Factor that have been identified in the United Kingdom and were made by U.S. manufacturers? In addition, we would appreciate the details of the test method used to detect HB_SAg and the results obtained. It would also be important to know whether the labeling carries the U.S. license number, or whether there has been any other type of indication from the companies that the material was manufactured in the U.S. For your information, Hyland does manufacture plasma derivatives in Belgium in facilities which are not licensed by us and therefore not subject to our regulations. Products from this facility, of course, cannot be brought into the U.S. Hyland also has elected to label

their Antihemophilic Factor concentrate lots manufactured in this country, under U.S. license, as tested and non-reactive for HB_sAg since early 1975. Mr. Gillard indicated that one British scientist who is quite familiar with this subject is Professor David Dane in London, and that Professor Dane and others had a lengthy discussion of the subject of HB_sAg reactive lots of Antihemophilic Factor with Hyland representatives last summer.

Mr. Gillard also indicated that there was the feeling in the United Kingdom that the hepatitis warning in the leaflets accompanying Antihemophilic Factor concentrates was not strong enough. We feel that the warning is quite direct and adequate; in fact, it is generally appreciated in the U.S. that every lot of this particular product is probably contaminated with hepatitis B virus. Nevertheless, the benefits achieved by using the product in hemophilia therapy have been considered to outweigh the hepatitis risk, and therefore the commercial concentrates are widely accepted and used in this country. I would appreciate some indications of your views on the labeling and benefit-to-risk considerations associated with these products as well as any questions you may have regarding this matter.

Since the Bureau of Biologics in the Food and Drug Administration is responsible for the regulation of plasma derivatives, I believe it would be helpful if you could identify someone on your side who is interested in this problem to correspond directly with Harry M. Meyer, Jr., M.D., who is Director of the Bureau of Biologics, Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD 20014. I trust we can mutually resolve some of the questions which Mr. Gillard indicated are not only being raised by him, but also by United Kingdom health authorities.

With best wishes.

Sincerely yours,

GRO-C

Theodore Cooper, M.D.
Assistant Secretary for Health