Eli Greene / Carmen Betancourt

MILES

June 29, 1988

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Paul D. Parkman, M.D., Director
Center for Biologics Evaluation and Research
Food and Drug Administration HFN-2
Parklawn Building Room 12A40
5600 Fishers Lane
Rockville, MD 20857

Re: Antihemophilic Factor (Human)

Dear Dr. Parkman:

This letter is to update the FDA on a product exchange in the United Kingdom involving lot 50S021, Antihemophilic Factor (AHF) (Human), dry heat treated. AHF lot 50S021 was manufactured in our Clayton facility March 24, 1987 and expires March 24, 1989. The lot was distributed entirely in the United Kingdom in 21 centers.

On February 11, 1988, we received a preliminary report from the U.K. of possible hepatitis B transmission in six hemophiliac patients who had received lot 50S021. Our investigation of the lot revealed no abnormalities: There were no HBsAg positive donors in the pool; both the pool and final container tests for HBsAg were negative; and a thorough check of our customer service files did not indicate reports of hepatitis B transmission for Factor VIII or Factor IX manufactured from pooled material contained in 50S021.

On March 17, shortly after this initial report but prior to the full investigation of the patient histories, the legal counsel for Miles in the United Kingdom decided, as a precautionary measure, to withdraw the lot from the market and replace it

with another lot of AHF, dry heat treat material. This decision was made in the U.K. based on their knowledge and interpretation of their regulatory requirements.

Once the withdrawal was complete, we still wanted to make ever effort to obtain all the information about the nature of the adverse reactions and requested that Miles' U.S. medical department become involved in the investigation. Dr. Ralph Rousell from our Clinical Department went to the U.K. and met with the reporting physician to thoroughly review the patient's medical histories.

To summarize his findings, all the patients were long-time hemophiliacs ranging in age from 28 to 67, not "boys" as was originally reported. It was also found that three of the six patients receiving lot 50S021 were already seropositive prior to receipt of this particular lot (Patients GRO-A GRO-A and GRO-A ages GRO-A GRO-A and GRO-A respectively). Of the remaining three patients, Patient GRO-A received only lot 50S021 in August 1987 and developed acute hepatitis B in December 1987; no other causative factors could be determined. Patients GRO-A and GRO-A, (both age GRO-A one with von Willebrands disease and the other with mild hemophilia A, also developed acute hepatitis B. Patient GRO-A became jaundiced while patient GRO-A only showed abnormal liver function tests characteristic of hepatitis B. These two patients both received Factor VIII manufactured by Cutter but were also concurrently treated with Factor VIII from another manufacturer licensed in the United Kingdom.

At the completion of the investigation, no clear conclusions could be drawn. In general, the source of hepatitis B was not clear due to the medical histories of these hemophiliacs. Only the hepatitis B contracted by Patient FT appears to be related to lot 50S021.

The vials remaining in the United Kingdom will be destroyed and our investigation is now complete. Since no action was required in the United States with regard to this withdrawal this report is being submitted for your information.

Please call Carol Moore GRO-C if any further information is required.

Sincerely yours,

GRO-C

Moshe M. Sternberg, Ph.D.
Vice President, R&D
Responsible Head, Regulatory Affairs

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