Interoffice
Communication

MILES Berkeley, CA

Date February 4, 1987

Copies: L. Ambrus 2/6/87

Subject Response to Prof. Dr. Feltkamp's CCS (A000787)
Concerning Koate HT, Konyne HT, Koate HS

From D. Bowerman

To D. Williams

I have researched the information that Prof. Dr. Feltkamp requested and have prepared the following answers to his questions:

a) Question: When did we change our main production process to heat treatment?

Answer: Qualifying lots were prepared for Koate HT beginning in August of 1983. Qualifying lots were prepared for Konyne HT beginning in June of 1984. Our regular production of these products began around the time our licenses were approved by the OB (Koate HT February 1984; Konyne HT October 1984). Qualifying lots were prepared for Koate HS beginning in December of 1985 through April of 1986. Regular production began around the time our license was approved (April 1986). This license approved Koate HS production for the Berkeley plant only. Complete production change over to Koate HS has been done in the Berkeley plant beginning January 1987. The Clayton plant still continues to produce Koate HT and Konyne HT.

b) Question: When did we deliver the first heat treated batches to the market in the different countries?

Answer:

U.S. -	Koate HS - None Koate HT 2/84 Konyne HT 10/84	Germany -	Koate HS 12/86 Koate HT 2/84 Konyne HT 3/85
Italy -	Koate HS - None Koate HT 5/84 Konyne HT 5/85	U.K. -	Koate HS - None Koate HT 6/85 Konyne HT - None
Japan -	Koate HS - None Koate HT 7/85 Konyne HT 11/85	Spanish -	Koate HS - None Koate HT 10/85 Konyne HT 12/85

c) Question: How long did we sell both products in parallel?

Answer: Koate HT was licensed in February of 1984. Konyne HT was licensed in October of 1984. We sold both non-heat treated and heat treated products in parallel until October of 1985. At that time Cutter notified their customers that non-heat treated products would no longer be available for sale.
Koate HS was licensed in April of 1986. This product has been shipped only to Troponwerke. No lots have been released for any other customers to date. This product will continue to be sold in conjunction with our Koate HT product.

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d) Question: What did we do with the material of the original process which could no longer be used?

Answer: Any non-heat treated Koate and Konyne product that was returned was sent to the Clayton plant where the heat treatment cycle was performed on some of the lots, and others were destroyed. On those lots where the heat treatment cycle was performed, all normal release testing was done against our Koate HT and Konyne HT release specifications, submitted to the OB, and released.

e) Question: What was the relevant wording of our labelling material with respect to possible contamination with the HTLV-virus?

Answer: The exact warning statement which appears on our Koate HT and Konyne HT labeling reads as follows:

> "This product is prepared from large pools of human plasma which contain the causative agents of non-A, non-B Hepatitis, Hepatitis B, and other viral diseases. Each unit of plasma has been tested and found non-reactive for HB_sAg and HTLV-III Antibody by FDA approved tests. The presence of Hepatitis Viruses should be assumed and the hazard of administering this product should be weighed against the medical consequences of witholding treatment."

The exact wording of the warning statement for Koate HS is slightly different. An additional sentence has been added after the sentence describing each individual unit is tested for HB_sAg and HTLV-III Antibody by FDA approved tests. The additional sentence reads:

> ".... Each unit has also been tested for elevated ALT levels. .."

Each individual foreign protocol for Koate HT, Konyne HT, and Koate HS state that "Product prepared from fractionated pooled plasma obtained from donors tested for Hepatitis B Surface Antigen, HTLV III Antibody, ALT, and found negative", except for Japan. The Koate HT and Konyne HT labeling is now being prepared to include the same ALT statement that is found on the Koate HS labeling. This will be submitted to the OB for approval prior to use.

Note: There a still some AHF concentrates in the Berkeley plant which have not been ALT tested. These lots will be sold to the domestic per Marketing's request. These lots, according to Karl Simon will be processed to Koate HT probably by sending the concentrates to Clayton for further processing.

No specific mention of HTLV-virus contamination is present in our labeling.

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f) Question: When did we introduce the testing of our raw plasma for HTLV-antibodies?

Answer: In April of 1985 we introduced HTLV III antibody testing at the plasma centers. All plasma units were being tested for HTLV III antibody by July of 1985 at the plasma centers.

g) Question: Did we have any recall caused by a possible contamination of that kind?

Answer: There has never been a recall of Koate HT, Konyne HT, or Koate HS because of a possible contamination with HTLV-virus. In 1983 there was a recall on some non-heat treated Koate because of a donor who had contracted AIDS after donating. The units from this donor were identified and coagulation products manufactured from plasma pools containing those units were recalled and destroyed. But the heat treated products have never been recalled for this reason.

I hope that these answers will help in the response to Prof. Dr. Feltkamp.

GRO-C: D Bowerman

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