

CUTTER BIOLOGICAL

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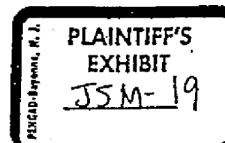
Dear Hemophilia Treater:

As an aspect of our continuing commitment and research activity to produce the best products possible for the hemophilia community, Cutter has conducted collaborate projects with outside investigators in addition to our own independent projects on virus inactivation.

Attached are some preliminary data resulting from several of the above projects. Koate[®]-HT (Heat Treated) is manufactured under controlled conditions at 68°C for 72 hours. The data obtained in a collaborative project with the Center for Disease Control (CDC), Atlanta, GA, adding a certain amount of human Lymphadenopathy Associated Virus (LAV) to Koate and measuring the amount which survives the heat treatment suggests that LAV can be inactivated to a significant extent by the Koate-HT manufacturing process.

Also, the data obtained in a similar collaborative project with Dr. Jay A. Levy of the University of California, San Francisco, adding a certain amount of human AIDS Related Virus to Koate and measuring the amount which survives the heat treatment suggests that AIDS Related Virus (ARV) in AHF concentrates can be significantly inactivated under the conditions of the process for the manufacturing of Koate-HT.

We at Cutter are constantly striving to improve our products, including antihemophilic concentrate products. Based on our belief that Koate-HT provides a true advancement in Factor VIII concentrate manufacture, Cutter is immediately converting manufacture of all Koate to Koate-HT.



MFK 001206

EXHIBIT 23

Your Cutter sales representative will provide further information on this conversion. If you need additional information please contact your Cutter regional sales office (Eastern Region - Charles Stewart **GRO-C**, Western Region - Dave Mahoney **GRO-C**) or our Professional Services Manager 800-227-2720. (In California, call collect 415-420-4181).

Please be assured that we wish to afford every individual with hemophilia the availability of improved coagulation concentrate products.

Sincerely,

GRO-C

Jack Ryan
President

Attachments

MFK 001207

KOATE -HT HUMAN VIRUS INACTIVATION DATA

I. Lymphadenopathy Associated Virus (LAV)

To determine the effect of the Koate®-HT heating process, 68°C for 72 hours, on viruses associated with AIDS transmission, an experiment was carried out jointly with Dr. Steve McDougal of the Center for Disease Control (CDC) in Atlanta, GA. In this study lymphadenopathy associated virus (LAV) was added to an AHF solution which was then apportioned into a number of vials, freeze-dried and heated at 68°C. At various time points samples were removed, reconstituted and tested in live virus by culturing with human lymphocytes, followed by an ELISA type assay which identified the LAV virus. The LAV-spiked AHF concentrate contained 1.6×10^5 virus particles which was reduced to 2.0×10^4 after lyophilization. An assay was carried out at 72 hours of heating at 68°C and showed less than 10^2 particles, which is the lower limit of detection with this assay. This experiment suggests that the heating process inactivated LAV, a retrovirus which has been implicated in AIDS.

	<u>Infectious Particles/ml*</u>
Koate concentrate (liquid)	1.6×10^5
Koate at 68°C for:	
0 time	1.9×10^4
72 hours	$<10^2$

* LAV titrations carried out by Dr. Steve McDougal, Center for Disease Control (CDC), Atlanta, GA

II. AIDS - Related Virus (ARV)

In continuing collaboration with Dr. Jay Levy, University of California, San Francisco, studies were initiated with a lymphocytopathic retrovirus recently isolated from patients with AIDS (Science 225: 840, 1984). This virus, called AIDS-related virus (ARV), was added to Koate concentrates which were freeze dried and then heated at 68°C for 72 hours. The presence of ARV was determined after culturing the concentrates in peripheral mononuclear cells and determining reverse transcriptase activity (RT). In preliminary studies, the data showed that while a high level of RT was detected in duplicate 0 time samples ($0.5 - 1.6 \times 10^6$ CPM), samples which had been heated at 68°C for 72 hours and then cultured showed no significant RT activity. These preliminary results suggest that the heating process employed inactivated the AIDS-related virus. Further studies are underway to more closely define the kinetics of this inactivation.

<u>Koate at 68°C for:</u>	<u>RT* cpm</u>
0 time	$4.86 \times 10^5, 1.6 \times 10^6$
72 hours	$<5 \times 10^3$

* Reverse transcriptase measured in peripheral mononuclear cell cultures 14 days after inoculation.

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