



ARMOUR
PHARMACEUTICAL
COMPANY

303 E BROADWAY TARRYTOWN NY 10591 • AREA CODE 914 631 8388
TELEX 420 882 REV MGP & 646 688 INT TARY

June 23, 1986

Ex: 3(1-8)
Wit: J. G. H.
Date: 6-27-86
MILLS & UCHIDA
(206) 292-9063

Attention: Blood Bank Director or Hemophilia Treatment Coordinator

Dear Colleague:

Armour Pharmaceutical Company has an ongoing policy to openly discuss issues associated with the care and treatment of the hemophiliac. One such issue is the potential for Anti-HTLV-III seroconversion subsequent to administration of heat-treated clotting factor concentrates produced from units of plasma collected prior to implementation of Anti-HTLV-III testing.

We have been made aware of three instances in which hemophiliacs have tested positive for Anti-HTLV-III subsequent to the administration of H.T. FACTORATE Antihemophilic Factor (Human), Heat-Treated. However, the circumstances surrounding each case prevent a definite conclusion regarding association of the use of the product with seroconversion.

In one case¹, a patient considered as being a mild hemophiliac received approximately 100,000 AHF activity units of H.T. FACTORATE concentrate and two units of packed red blood cells in conjunction with surgery required due to an automobile accident; questions have also been raised concerning the patient's personal history with regard to other risk factors for Anti-HTLV-III seroconversion. A second case² involved a severe hemophiliac who reportedly received only H.T. FACTORATE concentrate for at least one year prior to seroconverting; previously he had been transfused with quantities of various non-heated products. The third case is that of a mild hemophiliac sporadically treated with cryoprecipitate and non-heated concentrates from 1976 to 1980 who apparently seroconverted after receiving approximately 1,200 AHF activity units of H.T. FACTORATE concentrate in early 1985; however, the initial determination of seronegativity for Anti-HTLV-III was made using unlicensed reagents and purported seropositive ELISA results using these unlicensed reagents were not corroborated by testing with alternate systems. Additionally, several other seronegative patients received the same lot of H.T. FACTORATE concentrate; no change has been noted in their Anti-HTLV-III status.

ARMOUR002948

ARMO0000540_0001

These occurrences of seroconversion are puzzling, in view of the fact that a number of seronegative patients treated with H.T. FACTORATE concentrate have been reported as continuing to remain negative for Anti-HTLV-III.

Confusing circumstances appear to exist with each of these seroconversion incidents and many questions remain as yet unanswered. One major question is the significance of seroconversion and potential causes for its occurrence. Positivity for Anti-HTLV-III can result from exposure to virus, from passive transfer of antibody, or from active immunization subsequent to administration of antigenic material.

In each of the cases of seroconversion, patients received H.T. FACTORATE concentrate that had been manufactured prior to the availability of reagents for Anti-HTLV-III testing of blood and plasma. Testing for this antibody commenced in May, 1985, and all product currently manufactured and distributed by us is derived from plasma shown to be negative for Anti-HTLV-III. Although the incidence of Anti-HTLV-III positive tests in our donor population is low, exclusion of these units from use in production further increases product safety.

Armour Pharmaceutical Company has always considered patient well-being to be its primary concern, and we continue to do so. Consequently, we are making the following recommendations to you, in spite of the lack of clear-cut data and information on the cases described earlier in this letter. We request you to carefully and promptly follow each of these recommendations, which are as follows:

1. Review your inventory of H.T. FACTORATE Antihemophilic Factor (Human), Heat-Treated against the attached list of lot numbers. These are lots currently within their dating period that had been manufactured from plasma collected prior to the availability of Anti-HTLV-III testing reagents. For obvious reasons, those lots beyond their expiration dating period have not been included, and should be discarded.
2. Inform physicians, nurses, coordinators and others involved in hemophilic patient care at your institution that we recommend that lots of H.T. FACTORATE concentrate derived from non-tested plasma not be used. Tell them that an exchange program is underway. We will arrange for you to exchange any inventory of product manufactured from plasma not tested for Anti-HTLV-III at no cost to you.
3. If you have any H.T. FACTORATE concentrate with lot numbers appearing on this list, please call (800) 448-6245 (Pennsylvania call (800) 248-6245). This is a voice message handling system which will then provide you with further instructions.

Please enter either of the following voice mailbox numbers when requested to do so:

GRO-C - Stephen Connelly, or
GRO-C - Spencer Johnson

You will then be given further instructions.

For those of you with rotary dial telephone systems, please call Spencer Johnson collect at **GRO-C**

Armour Pharmaceutical Company believes that the general well-being and health care of the hemophilia patient take the highest priority, and that these actions are warranted in the interests of the patient.

Thank you for your cooperation.

Sincerely,

GRO-C

Michael B. Rodell, Ph.D.
Vice President
Regulatory & Technical Affairs

References

1. G. C. White, II, et al., The Lancet, March 15, 1986, pp. 611-612.
2. W. Vandenberg, et al., The Lancet, April 5, 1986, pp. 803-804.
3. P. Felding, et al., The Lancet, October 12, 1985, pp. 832-833.

H.T. FACTORATE ANTIHEMOPHILIC FACTOR (HUMAN), HEAT-TREATED
Product Manufactured from Plasma Not Tested for Anti-HTLV-III

<u>Lot No.</u>	<u>Exp. Date</u>	<u>Lot No.</u>	<u>Exp. Date</u>
Y80105	June 25, 1986	Y90809	October 6, 1986
Y12506	June 27, 1986	Y91109	October 8, 1986
Y11606	June 27, 1986	Y73703	October 9, 1986
Y11204	June 30, 1986	Y10309	October 9, 1986
Y80005	July 2, 1986	Y14109	October 11, 1986
Y12708	July 3, 1986	Y33709	October 16, 1986
Y12606	July 10, 1986	Y10409	October 17, 1986
Y11706	July 13, 1986	Y92409	October 24, 1986
Y80806	July 19, 1986	Y92609	October 24, 1986
Y85507	August 6, 1986	Y92709	October 24, 1986
Y80605	August 8, 1986	Y10510	October 25, 1986
Y11907	August 10, 1986	Y91709	October 29, 1986
Y14307	August 10, 1986	Y93810	October 29, 1986
Y11807	August 16, 1986	Y11010	October 30, 1986
Y12007	August 16, 1986	Y93410	November 1, 1986
Y12108	August 29, 1986	Y93710	November 1, 1986
Y87308	August 31, 1986	Y94610	November 2, 1986
Y10108	September 4, 1986	Y11110	November 5, 1986
Y85407	September 4, 1986	Y94510	November 5, 1986
Y10009	September 22, 1986	Y94310	November 7, 1986
Y89608	September 25, 1986	Y94710	November 14, 1986
Y89708	September 25, 1986	Y95110	November 15, 1986
Y10209	September 26, 1986	Y93510	November 15, 1986
Y88208	September 27, 1986	Y94810	November 16, 1986
Y90709	October 2, 1986	Y96010	November 16, 1986

ARMOUR002951

ARMO0000540_0004

H.T. FACTORATE ANTIHEMOPHILIC FACTOR (HUMAN), HEAT-TREATED

Product Manufactured from Plasma Not Tested for Anti-HTLV-III (Continued)

<u>Lot No.</u>	<u>Exp. Date</u>	<u>Lot No.</u>	<u>Exp. Date</u>
Y96111	November 16, 1986	Y99412	January 10, 1987
Y95310	November 19, 1986	Y99612	January 10, 1987
Y95410	November 20, 1986	Y13011	January 11, 1987
Y33810	November 21, 1986	Y96211	January 11, 1987
Y95510	December 4, 1986	Y97611	January 12, 1987
Y96611	December 12, 1986	Y99512	January 12, 1987
Y96711	December 12, 1986	Y94110	January 14, 1987
Y97311	December 12, 1986	Y98511	January 16, 1987
Y96511	December 17, 1986	Y97211	January 17, 1987
Y97411	December 17, 1986	Y99812	January 17, 1987
Y97711	December 17, 1986	Y99912	January 18, 1987
Y97811	December 17, 1986	Y97511	January 19, 1987
Y97911	December 17, 1986	Y97011	January 22, 1987
Y98011	December 19, 1986	Y96311	January 22, 1987
Y98411	December 27, 1986	A10601	January 31, 1987
Y98912	January 2, 1987	A13401	February 4, 1987
Y99212	January 7, 1987	A10901	February 6, 1987
Y98311	January 8, 1987	A13201	February 6, 1987
Y97911	January 8, 1987	A12201	February 11, 1987
Y97111	January 9, 1987	A13101	February 11, 1987
Y99712	January 9, 1987	A13301	February 12, 1987
Y96411	January 10, 1987	A13601	February 12, 1987
Y98711	January 10, 1987	A13701	February 12, 1987

H.T. FACTORATE ANTISEMPHILIC FACTOR (HUMAN), PLASMA-TREATED

Product Manufactured from Plasma Not Tested for Anti-HTLV-III (Continued)

<u>Lot No.</u>	<u>Exp. Date</u>	<u>Lot No.</u>	<u>Exp. Date</u>
A13901	February 18, 1987	A17802	March 10, 1987
A15001	February 20, 1987	A16802	March 11, 1987
A10801	February 20, 1987	A17202	March 11, 1987
A14701	February 21, 1987	A17402	March 11, 1987
A15101	February 21, 1987	A17502	March 11, 1987
A15201	February 21, 1987	A17602	March 11, 1987
A16501	February 21, 1987	A18802	March 11, 1987
A14601	February 26, 1987	A17902	March 12, 1987
A14801	February 26, 1987	A18702	March 15, 1987
A14901	February 26, 1987	A18902	March 15, 1987
A13801	February 27, 1987	A18502	March 18, 1987
A15301	February 27, 1987	A18402	March 19, 1987
A15801	February 27, 1987	A19102	March 19, 1987
A15901	February 28, 1987	A106203	March 22, 1987
A15601	March 2, 1987	A19202	March 25, 1987
A16902	March 4, 1987	A19503	March 26, 1987
A15501	March 5, 1987	A19903	March 26, 1987
A16202	March 5, 1987	A17702	March 28, 1987
A16301	March 6, 1987	A19703	April 1, 1987
A16702	March 6, 1987	A19803	April 1, 1987
A17302	March 6, 1987	A105903	April 1, 1987
A17002	March 7, 1987	A20203	April 4, 1987
A33602	March 8, 1987		

H.T. FACTRATE ANTIHEMOPHILIC FACTOR (HUMAN), HEAT-TREATED

Product Manufactured from Plasma Not Tested for Anti-HTLV-III (Continued)

<u>Lot No.</u>	<u>Exp. Date</u>	<u>Lot No.</u>	<u>Exp. Date</u>
A20403	April 8, 1987	A23304	May 14, 1987
A20803	April 8, 1987	A23204	May 15, 1987
A20103	April 9, 1987	A23904	May 15, 1987
A20603	April 9, 1987	A24304	May 16, 1987
A20903	April 12, 1987	A24704	May 16, 1987
A21103	April 12, 1987	A24004	May 20, 1987
A20003	April 16, 1987	A24504	May 22, 1987
A21603	April 16, 1987	A24104	May 22, 1987
A21503	April 17, 1987	A24804	May 23, 1987
A21303	April 18, 1987	A24404	May 24, 1987
A22203	April 18, 1987	A25705	May 29, 1987
A21403	April 23, 1987	A25505	May 30, 1987
A21703	April 23, 1987	A34005	May 30, 1987
A21803	April 23, 1987	A25104	May 31, 1987
A22704	April 25, 1987	A25905	June 3, 1987
A22904	April 25, 1987	A26205	June 4, 1987
A22504	April 26, 1987	A25605	June 5, 1987
A23104	April 30, 1987	A25805	June 5, 1987
A22604	May 3, 1987	A21904	June 6, 1987
A23004	May 8, 1987	A25004	June 6, 1987
A22303	May 8, 1987	A26605	June 15, 1987
A22103	May 10, 1987	A26705	June 19, 1987
A23404	May 10, 1987	A26805	June 19, 1987
A23804	May 13, 1987	A106505	June 20, 1987
A23704	May 14, 1987	A27305	June 21, 1987

ARMOUR002954

ARMO0000540_0007

H.T. FACTORATE ANTIHEMOPHILIC FACTOR (HUMAN), HEAT TREATED

Product Manufactured from Plasma Not Tested for Anti-HTLV-III (Continued)

<u>Lot No.</u>	<u>Exp. Date</u>
A27705	June 21, 1987
A27005	June 25, 1987
A28005	June 25, 1987
A28506	June 28, 1987
A23906	July 24, 1987
A31507	August 8, 1987
A33207	August 26, 1987
A34107	August 26, 1987
Y33908	August 27, 1987
A35208	September 5, 1987
A106708	September 12, 1987
A35308	September 19, 1987
A30106	September 25, 1987
A106609	October 1, 1987
A106809	October 29, 1987