14

REVLON HEALTH CARE — INTEROFFICE MEMORANDUM

DATE: March 6, 1986 — C.C.

TO: *Distribution List

FROM: Michael B. Rodell, Ph.D.

SUBJECT: SUMMARY OF AHF MEETING - FEBRUARY 27, 1986

A meeting was held at Fort Washington on the above date in order to discuss issues associated with possible seroconversion for Anti-HTLV-111 in several hemophiliacs being treated with FACTORATE-H.T. concentrates. Participating in that meeting were those shown on the distribution list, although Dr. Terry did so via telephone.

During the course of the Plasma Executive Committee (PEC) meeting held on February 21, 1986, we became aware of the following circumstances:

1. Dr. Gil White (University of North Carolina - Chapel Hill) and his associates are preparing to report on a mild-to-moderate hemophiliac who received approximately 100,000 activity units of AHF and two bags of red cells to support surgery necessitated by an automobile accident. Several weeks after surgery, the patient appeared to have seroconverted; this event is the subject of reports previously issued by me on February 10, 1986 and December 30, 1985 (copies attached). Anita Bessler and Dr. Karl Hansen spoke with Dr. White on February 25, 1986; a summary of that conversation is also attached.

2. Dr. Ten Cate (Netherlands) has informed our European sales organization that he has a severe hemophiliac who, according to him, has received only FACTORATE-H.T. concentrates since January, 1984; prior to that time he had been treated with a variety of non-treated concentrates and cryoprecipitate. In January, 1985 the patient was Anti-HTLV-111 positive; samples drawn in the Spring and Autumn of 1984 were negative. The patient complained of fatigue and slight fever; he also had an unexplained lymphadenopathy. In the following months, complaints subsided and the lymphadenopathy disappeared.

3. Dr. Peter Jones issued a statement during a hemophilia conference held in Newcastle, England in early February that four hemophiliacs (one in Holland and three in the U.S.) have "been infected" after using heat treated concentrate. This comment caused a considerable amount of concern on the part of the U.K. Department of Health and Social Services (DHSS), as well as in Eastbourne.

EXHIBIT GRO-C 3 9/13/95

Pltfs Ex 19 for Id. 10/31/91 SW, CSR 1 of 3

Rx-3527-C EXHIBIT 93

712853

208025

4. Dr. William Terry presented data generated by members of his organization at Meloy, indicating that the heat treatment procedure currently employed by us (60°C-30 hours) was not totally effective in eliminating added HTLV-111 from FACTORATE Concentrates. Furthermore, more rigorous conditions applied to Generation I (intermediate purity) FACTORATE concentrate also resulted in residual detectable levels of HTLV-111, although current as well as experimental conditions all were capable of inactivating virus in quantities equal to or greater than $10^5$ organisms/ml.

5. Dr. Terry became aware, during ensuing comments, that testing of units of Source Plasma for the presence of Anti-HTLV-111 had been implemented in April-May, 1985. However, significant quantities of FACTORATE concentrates derived from plasma collected prior to testing began are currently in inventory and in distribution. It was his opinion that this material should be withdrawn from the market.

Following considerable discussion, it was agreed that I would arrange a meeting with Dr. David Aronson (OBRR, FDA) to review the Meloy inactivation data with him, and attempt to elicit an opinion from him as to the adequacy of our process and any concerns he may have regarding continued use of concentrates derived from plasma not tested for Anti-HTLV-111. I met with Dr. Aronson on February 25, 1986, and was accompanied by Dr. Charles Swartz of the R&D Division. Dr. Aronson made the following comments to us:

1. He has previously seen disparate HTLV-111 inactivation data, which, in his opinion, more likely is due to variables in testing sensitivity. He believes that the Meloy data, demonstrating elimination of at least $10^5$ organisms/ml. in Generation 1 product is satisfactory, and that our current heat treatment process is adequate relative to HTLV-111. As for Generation 11 product, he is willing to await the results of the retest currently being undertaken.

2. Dr. Aronson's major concern is not with HTLV-111 transmission; rather, he continues to encourage us to evaluate more rigorous heat treatment in order to reduce the potential for non-A, non-B hepatitis transmission.

3. In his opinion, heat-treated product currently on the market, derived from plasma not tested for Anti-HTLV-111, need not be withdrawn from distribution.

I also asked Dr. Aronson if he were aware of any instances of seroconversion for Anti-HTLV-111; he stated that the only case he knew of was the one reported by Dr. White at North Carolina. I told him we had reports of a patient in Holland and another patient in England, and that I would report further to him on these cases after my return from the U.K. Immediately after meeting with Dr. Aronson, I summarized the discussion in a telephone conversation with Mr. Cawthorn, Mr. Dovey, Mr. Smith, Dr. Tretter, and Mr. Sedor.

71251

19-2

The follow-up meeting on February 27, 1986 was held in order to review the entire situation and to make a decision as to what, if any, action should be taken regarding existing product derived from untested (for Anti-HTLV-III) plasma. All facts were reviewed, Dr. Aronson's opinion was stated, and the views of each participant were adequately stated. After several hours of discussion, Dr. Tretter commented that the issue was confined to the fact that several hemophiliacs had converted to being positive for Anti-HTLV-III, but that this seroconversion was without any clinical indication of illness. Dr. Terry stated that, although this was certainly true, the use of final product derived from untested plasma presented an undefinable potential additional risk to patients, albeit a very small one.

The concensus attained at that meeting was to initiate the following steps, in order to provide the hemophilia community with product reflecting as much added margin of safety as possible:

1. The distribution of product derived from plasma not tested for Anti-HTLV-III would be stopped, unless absolutely no adequate supplies of material produced from tested plasma were available.

2. When adequate supplies of new product are in inventory, an exchange program will be undertaken. At that time, customers will be advised to exchange their existing supplies for product derived from tested plasma.

GRO-C

Michael B. Rodell, Ph.D.

MBR:ag

*Distribution List
Ms. A. Bessler
Mr. R. Cawthorn
Mr. B. Dovey
Dr. K. Hansen
Mr. J. Miller
Mr. S. Samuels
Mr. J. Sedor
Mr. J. Smith
Dr. W. Terry

71285

19-3