ARMOUR PHARMACEUTICAL COMPANY — INTER-OFFICE MEMORANDUM

DATE: December 9, 1987

TO: Dr. W. Hitchings/Dr. M. Rodell

FROM: M. Graber

CC: C. Brown
F. Feldman
G. Floyd
T. Foster
R. Johnson
G. Lindell
J. Luchese
L. Schnell

SUBJECT: Canadian Health Protection Branch -- Fact Finding Visit

On December 2, 1987, three Canadian Health Protection Branch (HPB) investigators arrived at Armour, Kankakee on a fact finding visit. They were:

Dr. Boucher, Chief, Blood Products Division
Dr. Remis, Epidemiologist (Center for Aids)
Dr. Chaloner-Larsson, Bureau of Biologics

Mr. C. Brown and I hosted the visit in the Personnel Conference Room.

The stated reason for the visit was a study in Vancouver, B.C. of 18 individuals. Six of these patients have seroconverted since May, 1987. These individuals were tested every 6 months since 1985. At least two show clinical signs of infection as well. One individual result has not yet been confirmed. Tests were done by Eliza, Flurescence, and Western Blot methodologies. There was, in addition, one other seroconversion in B.C. and one in Alberta.

In the study of 18 individuals, one item in common for seroconversion was Armour lots. They had other things in common, and two other companies are also implicated. Armour lots were also used by non-seroconverted individuals in the study.

First, Mr. C. Brown explained our lot numbering system. The investigators asked to inspect the batch records for 10 lots of AHF. These lots were:

A41610	B71308
A43510	B71408
B62305	B71508
B67606	B71808
B68907	B74809

All of these lots were 60°C/30 hr. heat treated and were made with 100% HIV screened plasma. They were interested in B71308, especially so when they learned that the 713 pool was split into 3 lyophilizer lots B71308, B71408, and B71508.

Mr. R. Glidden joined us to explain the pooling, clarified bulk, and non-sterile bulk portions of manufacturing procedures. Also discussed was equipment sizing and conditions of mixing bulks. Our process deviation system was described.

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Mr. N. Rabin and Mr. G. Wolfe joined us to discuss filling, stoppering, capping, lyophilization, inspection, and pasteurization. A lengthy description of pasteurization and equipment used to heat and monitor heating of AHF was given. Several heat treatment charts were reviewed, starting with lot B71308.

Mr. J. Finks joined us, bringing plasma receipt records for lot B71308. These were reviewed and many questions were asked about plasma collection. Mr. Finks answered some about the general collection process, labeling requirements, etc., but most were deferred for a conference call with Mr. E. Lindell.

During the afternoon of December 2, Dr. F. Feldman joined us to describe the development of the heat treatment process. Tuckahoe research and CDC information was discussed. Dr. Feldman continued to describe the safety advantages of the Monoclate process and heat treatment. The investigators asked about why in the lab we showed effective log kill but not in manufacturing this time, for which no answer was given. We noted that Armour had voluntarily exchanged heat treated, unscreened AHF in June 1986.

The investigators then reviewed more plasma records, and noted white out on the Plasma Alliance bleed sheet. The remaining manufacturing procedures were reviewed. Dr. Remis asked why in 1986 Armour was using an old April 1985 insert that didn't describe HIV screening. Mr. Brown indicated that the insert was changed with 68°C/72 hr. heat treatment. The 68/72 heat treated AHF was approved by FDA in January 1987. The investigators noted a pencil - draft OoB protocol in lot A43510 record.

On December 3, 1987, the three HPB investigators returned to finish their investigation. They focused more on plasma records and lot B71308.

We started the day with a conference call to Mr. E. Lindell of Plasma Alliance (PA). The following information was given at their queries:

1. PA has a positive HIV test incidence of 0.05% for 1987.

2. PA uses Electronucleonics test kits for HIV and HBsAg. The cut-off used is as specified in each test kit. In 1985, some problems with particular lots of kits occurred, but it was excessively positive results.

3. PA has 18 centers, none deleted since 1985. Three were added since Jan. 1985 -- Kansas City, Witchita, and Tulsa.

4. An explanation of multipact form/bleed sheet used and routing was explained, and how cartons are packed and verified. A brief explanation of how positive HIV units are withdrawn, tagged, and verified.

5. The PA look-back procedure on HIV+ units was discussed.

6. PA uses an ALT cut-off of 76.

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7. No profile of donors testing positive for HIV has been constructed.

8. A description of PA laboratory testing operations was given.

9. Mr. Lindell estimated that if a pool used 3000 units, around 700 donors would be in the pool.

10. PA participated in CAP panel. All lab technicians are certified. Mr. Lindell stated and later confirmed that no lab employee was fired for incompetence during the years 1985, 1986, and 1987 to date.

11. No excessively negative runs of HIV tests have been noted.

12. No PA plasma centers are in inner cities, three have probably predominately college students -- Minneapolis, West Lafayette, and Knoxville.

13. Core testing is not done by PA

In addition, written responses to the following were promised by Mr. Lindell.

1. Incidence of HIV positive tests by month and plasma center for 1986 and 1987.

2. A donor profile description and a copy of ABBRA profile description.

3. Threshold or action limits for excessive positive or negative rate of HIV test results and the review cycle.

After the telephone call, in my office, we again went to the Personnel Conference Room. We were joined by Mr. N. Rabin to answer questions on the Kaye recorder sheet for lot 435. Questions as to why thermocouples (TC) malfunction, how Armour knows it, and what we do about it were asked. We showed the investigators our Q.C. evaluation procedure C-130. The investigators suggested that a 24 hour circular chart is not appropriate for a 30 hour or longer heat cycle due to overlap of pen tracings.

We were then joined by Mr. Finks with more plasma records. He was asked to bring in the look-back notification letters Armour receives from PA. These were reviewed for common donors to those represented in lot B71308. The following items were found in the look-back review.

	Donor	Unit	Shipment	R/R No.	Use in Lot	Reason for Look-Back
1.	4-35103	173231	46-A7-48	142886	A71308	HIV positive
2.	3-33621			142916	A71308	History of high risk
3.	21-36860			142590	A71308	History of high risk
4.	5-68642	182249		142875	A71308	HIV positive

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Mr. Lindell determined that Unit 1 was tested on 9/4/86 and was positive 2 of 3 tests. Unit 2 was an admitted homosexual, and Unit 3 was a spouse of an HIV positive test.

During the look-back review, the investigators noted that a bound book should be used to note all positive units pulled from receipts of plasma and for confirming the destruction of them. Mr. Finks noted that since October 1986 a copy of the destruction notice is placed in the plasma shipment packet. The investigators also noted we do not note in any batch record that a donor used in the pool had subsequently had an HIV positive unit.

Dr. Boucher went for an abbreviated tour of Q.C. Chemistry and Microbiology labs and AHF and Building 16 areas.

Another conference call was made to Mr. Lindell at PA. He explained the screening criteria used and retest procedure used. Mr. Brown provided a list of PA plasma centers (Attachment A).

The following questions were left with a request for a written response:

1. Describe, for each occurrence, the reason for withdrawn units in plasma records.

2. For the donors subsequently showing HIV positive, please provide as many details as possible, including (a) why there was a gap in donations, (b) what were the absorbance (or whatever) readings for each and every HIV test on the donors, (c) what the test cut-off was, (d) the age and sex of the individuals, (e) any information as to subsequent testing activity on the individual, i.e., who referenced to, etc.

3. For 3 shipments not reviewed, provide a summary of information on them similar to that collected by the investigators while here.

4. Trace anyone in these lots (10 lots) to determine if they have ever tested positive by reviewing look-back records.

5. Provide information on how plasma is scheduled and why lots would be pooled by blood type.

We obtained a photocopy of information they recorded from our plasma records (Attachment B). The investigators noted that the records were easily followed and seemed complete. There was traceability of plasma, although sometimes somewhat difficult. Our understanding of the pasteurizing tanks was good. Although no citation or letter of observations will be issued, Dr. Boucher noted that the HPB will talk to Armour's Regulatory and Medical people after they receive all of our information.

GRO-C

Max Graber
Manager
Quality Assurance

MG/dp
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