MINUTES OF PEC

FEBRUARY 20, 1986 - FORT WASHINGTON

Participants:

Chairman: Mr. H. H. McDade

R & D: Dr. W. Terry, Dr. J. Tretter, Dr. L. Weerasinghe

U.S. Domestic: Ms. A. Bessler, Mr. S. Connelly, Mr. B. Dovey, Mr. G. Floyd, Mr. T. Foster, Dr. M. Rodell, Mr. J. Sedor, Mr. J. Smith

International: Mr. L. Lucas, Mr. J. Miller, Mr. R. Storm

The initial Plasma Executive Committee of the merged Rorer and Revlon Health Care companies was held at the Fort Washington offices. Mr. H. H. McDade will serve as chairman for the initial meetings. Following is a list of topics and summary comments:

I. Viral Inactivation Review

A. The review of Armour's AHF viral inactivation data has become critical because the plasma community is beginning to have doubts concerning the heretofore unquestioned belief that heat treating inactivates HTLV-III virus.

1. At a congress held in New Castle, U.K., Dr. Peter Jones made the statement that heat treating did not inactivate HTLV-III virus and that four patients developed AIDS.

2. This position was published in the lay press and has resulted in considerable confusion and concern in the international community.

3. Dr. I. M. Nielson subsequently understood that there were five patients and that all belonged to Armour.

(a) Dr. Nielson has two patients who have received Armour Generation II heat treated product and who have abnormal conditions.

(1) Patient #1 has pneumonia but is HTLV-III antibody negative. The patient has received other blood products.

(2) Patient #2 has converted and is HTLV-III positive from Abbott and Electro-nucleonics but not Western Blot. This patient is considered a true false positive.

(b) Ms. Bessler explained to Dr. Nielson that Armour is only aware of two possible patients who may have seroconverted:

(1) Dr. Ten Carte in Holland has a patient who has seroconverted but has not developed AIDS. He does have lymphadenopathy but has received other blood products.

(2) There is a patient in the U.S. who has seroconverted, but he cannot be located by CDC and is a known drug abuser.

(c) Based on this information and discussions with Ten Carte and Bloombeck, a decision was made by the Swedes. They do not believe that the product should be withdrawn and will continue to use it.

(d) Dr. Jones' statement was inaccurate and he has been personally criticized for the remarks.

B. Dr. Terry presented the results of the Meloy heat treating tests.

1. Using the Meloy method in which product is spiked with very high HTLV-III titers and tested under production type circumstances with a very sensitive test, it appears that dry heat treating plasma may not be totally effective.

(a) Plasma from multiple "hot donors" in a pool could surpass the ability of dry heat treating to eliminate sufficient virus.

(b) We are conservatively targeting for five logs as was the published recommendation. Log reduction at varying temperature and timing combinations of heat treating ranged from 3 to 6+ logs.

Decision: Although the data are not absolutely conclusive and absolute comparisons of the methods have yet to be completed, it was decided to upgrade the heating cycle since it appears that higher longer temperature is more effective. Loss of FVIII yield appears to be less than 15% while FIX appears to be slightly more than 20%.

Action: Dr. M. Rodell will review these data with B.O.B. with the purpose of disclosing our latest studies and determining what will be required to get approval for the heat treatment change. He will then proceed with organization of those studies.

Mr. J. Sedor will start the engineering work required to build increased heating baths. It is assumed that manufacturing will not be on the critical path. Conversion timing will depend on B.O.B. approval.

Ms. A. Bessler will review the possible introduction of the Generation III wet heated product with S. Samuels.

2. The Paul Ehrlich Institute has completed the viral inactivation study of FIX and FVIII. Results are as follows:

(a) No detectable levels of Generation I or Generation II 60°, 10 hour.

(b) Moisture content 1-3%

(c) 10^6 log reduction

(d) 28 days 42° lymphocyte culture

Results will be written and in our hands by the week of 24 February. Dr. Terry will review them for accuracy.

3. Dr. Terry considers the Meloy test more sensitive and believes that no product should be used if the plasma donors were not screened for HTLV-III antibody.

Action: Dr. Rodell will review results with B.O.B. since this may well be an industry wide problem. A meeting is to be scheduled for 25 February.

Ms. Bessler will inform Dr. Nielson that some of her lots of product have not been donor screened and ask if she wants to change them.

Mr. J. Sedor will stop shipment of all AHF from unscreened donors.

Mr. G. Floyd will review shipment for three months and document the lots from nonscreened donors.

4. Since this may be an industry wide problem pending B.O.B. response, centers where unscreened donor product may have been delivered will not be contacted until the situation is clear. These include centers in the following countries which may have received product within the last three months:

   (a) Sweden
   (b) U.K.
   (c) Canada
   (d) Puerto Rico
   (e) U.S.

5. A meeting of the P.E.C. will reconvene to review the results of the discussions with the FDA and to take action.

II. MONOCLONAL FVIII

A. Monoclonal FVIII has yielded surprisingly good viral inactivation. The results are primarily due to the process--not heat testing.

B. With the current HTLV-III questions, the monoclonal product appears to have increased potential; however, there are limiting factors.

   1. We can make an additional 3.2 MM units by October 1986 if we are willing to commit the Cryo.

Decision: Japan's order will be considered firm for 1.5 MM units. Commit the cryo and make the units.

   2. Additional funds will have to be committed to develop a launch stock for 1987.

      (a) $600,000 capital
      (b) Cryo
      (c) Matrix and column development

C. 1987 requirements for monoclonal could be 30 MM each for domestic and international. At a minimum, Marketing would like to have 10 MM units for launch 1 January 1987.

Action: S. Connelly and L. Lucas will review forecasts, prices and vial unit sizes. By 5 March, full D and S plans will be placed on manufacturing.

G. Floyd will review capacity and work schedules to develop a maximum output proposal.

D. Clinical results have been reviewed by Dr. Terry.

1. The 01 protocol (half life and recovery) has been completed and half life appears to be roughly one third to one half more than expected--15 hrs vs 8 hrs for other products.

2. 02 (mouse antibody protocol). The same six patients have continued and are being reviewed for antibody development. Results indicate that there is no difference in antibody levels at one month. There are, however, antibodies in a high percentage of untreated patients.

3. 03 virgin patient U.S. study. Investigators want to see 02 results for 2.5 months before starting. By mid-May, these U.S. 03 studies should start.

4. 03 virgin patient European study. The start was delayed by CTX approval. We assume all details will be resolved confirmed by the investigators meeting on March 5.

5. All of our virgin patient studies will begin too late to be formally presented at the World Hemophilia Foundation Meeting in Milan. Dr. Terry will speak on the monoclonal program and marketing will seed the audience with investigators.

E. Monoclonal trademark activities were summarized by L. Lucas. International has elected to file the mark MONOCLATE in U.K., Germany, and Japan. If we are able to force a registration in those markets, we will register throughout the major markets.

1. Counsel has advised us that it will be difficult, but the desirability of a universal Armour mark is such that we have elected to proceed.

2. The back-up mark is FACTORATE MONO C which is likely to register.

III. 1986 K3 Plant Production Plans

A. While the original plan assumed 1.0 million liters of FFP from Plasma Alliance, it appears that 1.2 million liters is possible.

1. Current collection and bonus programs are yielding unsuspected results.

2. Cost per liter of plasma is approximately $53.

B. The current plan is attached:

C. J. Sedor questioned the desirability of continuing collection in excess of requirements and asked for approval to sell plasma on the open market.

Action: H. H. McDade will contact I. Regier to determine if plasma could be converted and sold to Fujuralino on a profitable basis.

L. S. Lucas will contact Woelm to determine if their 70,000 L contract is firm. Germany has made commitments to purchase plasma for 170 DM per liter. If possible, we will stop the purchase and take product from Plasma Alliance. Current plasma collection costs are approximately $53/liter.

IV. Industry Meeting on ALT and Anti-HBc Testing

A. Dr. Rodell reported that the FDA Blood Products Advisory Committee met on February 13 concerning ALT and anti-HBc testing.

B. In Dr. Rodell's opinion, it is likely that the advisory committee will recommend and that B.O.B. will accept a requirement for ALT testing, but not anti-HBc. No date was specified for the requirement to take effect but Dr. Rodell will follow the situation closely.

V. Plasma Executive Committee Meetings

The next meeting will be scheduled for mid-April.

Action: L. S. Lucas will schedule the meeting.

GRO-C

L. S. Lucas

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	1985	1986			
AHF GI (MMU'S)	ACTUAL	BUDGET	D&S	COMMITTED FORECAST	DIFFERENCE D&S/FCST
DOMESTIC	141.0	139.0	142.0	142.0	-
EXPORT	9.0	10.0	9.4	10.0	(.6)
U.K.	20.3	18.8	15.6	18.8	(3.2)
CHILE	.6	.5	.1	.5	(.4)
SOUTH AFRICA	.4	-	-	-	-
OPEN	-	17.0	-	-	-
TOTAL	171.3	185.3	167.1	171.3	(4.2)
BEHRING AHF (MMU'S)	-	-	-	5.0	(5.0)
CRYO TO BEHRINGWERKE (KGS)	301.0	900.0	646.0	900.0	(254.0)
AHF GII (MMU'S)					
DOMESTIC	2.5	5.0	2.5	2.5	-
GERMANY	29.3	29.1	22.7	29.3	(6.6)
SWEDEN H.T.	5.3	-	3.9	5.7	(1.8)
U.K.	.4	-	-	-	-
JAPAN	1.8	-	.2	-	.2
SPAIN	.5	-	-	-	-
OPEN	-	5.9	-	-	-
TOTAL	39.8	40.0	29.3	37.5	(8.2)
ALBUMIN					
DOMESTIC 5% MIU	512	510	556	556	-
DOMESTIC 25% MIU	1194	1190	1232	1232	-
DOMESTIC PPF MIU	238	265	295	295	-
PUERTO RICO MIU	7	15	12	12	-
U.K. SOL MIU	29	42	86	86	-
SINGAPORE SOL MIU	5	4	11	11	-
CHILE SOL MIU	1	1	-	-	-
JAPAN SOL MIU	-	69	-	-	-
TOTAL	1986	2096	2192	2192	-
NSA POWDER					
EXPORT POWDER KG	0	1000	0	0	-
JAPAN POWDER KG	1976	2000	4000	4000	-
TOTAL	1976	3000	4000	4000	-
ISG					
DOMESTIC SOL. KG	419	450	429	450	(21)
EXPORT PWD. KG	310	400	50	400	(350)
JAPAN PWD. KG	428	200	200	200	-
GERMANY PWD. KG	404	200	200	200	-
TOTAL	1561	1250	879	1250	(371)

REM/DWB:ca
2/7/86

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CIVIL ACTION NO. 85-170 OR 85-699

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1985 REQUIREMENTS MOVED TO 1ST QUARTER 1986

PRODUCT	D&S
NSA POWDER	
EXPORT/SCLAVO POWDER KG	500
AHF GI (MMU)	
EXPORT/CANADA MMU	.8
AHF GII (MMU)	
SPAIN MMU	.4

DWB:ca
2/7/86

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CIVIL ACTION NO. 85-178 OR 85-699
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