INTEROFFICE CORRESPONDENCE

DATE May 17, 1983

TO Members of the Ops Committee:

Mr. B. Blomstrom	Mr. N. Martin	Dr. M. Nishida
Mr. L. Coffey	Mr. B. Latham	Mr. R. Olivarez
Dr. T. Drees	Mr. K. Martinez	Mr. B. Thorne
Dr. E. Fedor	Mr. E. Matveld	Mr. I. Yorimire
Mr. J. Gary	Dr. C. McAuley	
Dr. M. Hrinski	Dr. E. Mealey	

cc: C. Davis, J. Roelands, L. Johnson, J. Tufekjian

RE: PMA Biological Section Meeting April 24-27, 1983

The following is a summary of agenda items of interest to Alpha. Please pass this report on to members of your departments to whom this might be of interest.

Biological Purification and Production in Space - Dennis R. Morrison, Ph.D., Lyndon B. Johnson Space Center, NASA

Dr. Morrison gave a long and fascinating speech on experiments being conducted by NASA aboard the space shuttle. The biological purification he spoke of was of either cell products or cells themselves and had been sponsored by McDonnell-Douglas and Ortho Pharmaceuticals Corporation. He discussed the separation by electrophoresis of Anti-Hemophilic Factor in space. He estimated that the cost of such a program would be $4.5 million with a return from all products of $25 million if the space shuttle operated 360 days per year. The procedure used was electrophoresis. He also referred to work sponsored by McDonnell-Douglas on the separation of Albumin by electrophoresis and stated that by next year they would produce a lot of material for clinical trials for FDA approval. He stated that they would use a free-floating satellite which would be serviced by the space shuttle. He emphasized that to accomplish the projects that he was describing we needed a permanent space station with servicing of the satellite. However, it seemed to me that he overlooked the difficulty of taking enough of the source material up to the space station to accomplish what he was describing. Note the yield and purity of the products obtained by these processes are much greater in zero gravity.

AFA 003897

EXHIBIT 120

baby kidney cells, for the production of Urokinase referring to the work that was begun in 19[illegible] by Abbott. NASA has been evaluating micro-carrier beads for cell culture in space. The advantage is that the beads stay suspended and the air in the nutrient medium also stays in the solution. Dr. Morrison emphasized that by all of these methods the increase in production is immense.

The projects that McDonnell-Douglas and Ortho are working on currently is proprietary. He emphasized that NASA does not even need to know the precise nature of the experiments being carried out by commercial firms. NASA is obviously interested in promoting such experiments to support their space shuttle program.

Dr. Morrison participated in other parts of the meeting associated with environmental microbiological control. It was very interesting and rewarding having his input since NASA has some extreme precautions that must be taken in the enclosed environment of the shuttle. This type of technology can be utilized by pharmaceutical firms and for clean rooms, sterile rooms, etc.

PMA Activities - Paul Kaufman, M.D.

Dr. Kaufman noted that Mr. Engman is fond of forming task forces to address issues of interest to PMA member firms and he listed the following ones:

1. The Expert Policy Task Force
2. Tax Policy Task Force (particularly addressing the Puerto Rican tax problems)
3. Product Liability Task Force
4. Patent Term Restoration Task Force
5. Third Party Reimbursement Task Force
6. Patient Drug Information Task Force
7. Animal Welfare Task Force
8. Tamper Resistant Packaging Task Force
9. Drug Diversion Task Force
10. Work Group on Pharmaceutical Product Promotion
11. International Patents and Trade Marks Task Force

Note that they select people from different sections and different companies with expertise on the particular subjects being addressed.

Subcommittee on Diagnostic Products - Mrs. Alice O'Connell

1. Product Field Correction Actions - The Bureau of Devices has recently taken steps to change their system of classifying notices distributed to the field after a product is already in distribution. Examples would be additions to instrument panels, information needed by the consumer but not known at the time of distribution (i.e., discovery of a rare antibody that may be present in antisera and, however, would not ordinarily be considered an interfering substance). In the past the Bureau of Devices has called such notifications recalls which is really quite incorrect. They are now classifying them as device corrective notice changes. It was agreed that we would put this item on the Liason agenda and suggest that the Office of Biologics follow suit for any devices or diagnostic products regulated by them.

2. Monoclonal Antibodies Guidelines - Nothing has been distributed by FDA as yet. It was agreed that this will also be on the Liason Committee Agenda and we will ask about the status of these guidelines.

3. 510K submissions - The Office of Biologics is still requesting samples of products, labeling, etc. They are going much further than the Office of Devices. This was on the Liason agenda at the last meeting and it was noted that Ortho was finding their position improving at OoB so there will be no further action on this at this time.

4. Additional Standards for Anti-Human Globulin - This item will also be on the Liason agenda since they expected these to be issued in the first quarter of 1993 and they still are not out.

5. A fifth item was added and that is a request for the status of items on regulatory reform. It has now been precisely a year since the meetings were held at OoB in which industry gave input and suggestions for changes in regulations. This will be on the Liason agenda.

Subcommittee on the American Blood Commission - Dr. N. Ashworth

Attached to this memo is a copy of Dr. Ashworth's report. It was also suggested that we should be considering whether it is worth it for PMA to continue to support ABC and it was agreed we will bring up this at a subsequent meeting. For the time being it was agreed that we did not want to be the ones to "pull the plug" on ABC.

[illegible] drawn up by the International Society of Blood Transfusions. Also attached is a copy a Code of Practice on plasma aresis drawn up in respon by the IFPMA. This Code of Practice was submitted by IFPMA to WHO three months ago for their consideration with the suggestion that both ISBT's Code of Ethics and IFPMA's Code of Practice be adopted side by side. Dr. Ashworth and Mr. Petez of IFPMA made this proposal and will follow-up and let us know the results with WHO.

Subcommittee on Plasma Products - Mr. William Shrigley

1) Status report of the Ad Hoc Committee for standardized isoagglutin and test procedures

Members from the various companies have been appointed to this Ad Hoc Committee (Jim Brady of Alpha) and they have exchanged procedures. The next step is to arrange a conference call to put together further action. A status report is expected in early June.

2) Status report of the Ad Hoc Committee for Plasma Protein Fraction

A report was given on the results of the Blood Products Advisory Panel Meeting, March 1-2, in which the panel decided that there was no reason to remove PPF from the market. It was interesting to note that the Cutter people seemed to think that John Hink's presentation was the one that carried the day. I don't agree. It think it was Dr. Mealey's relating the development of PPF to a substitute for plasma.

3) Universal House Standard for AHF

The lot has been produced, samples have been distributed, and results will be discussed at a meeting May 13 at OoB.

4) Anti-Body Test for Human Globulin

Nearly two years ago a petition was submitted by PMA requesting the deletion of the requirement for polio anti-body tests and the substitution of tests for Hepatitis B or Hepatitis A. There has been no response to this by OoB and it was agreed that we would request a response at the Liason meeting.

5) Added to the agenda was the labeling statement regarding AIDS for Factor VIII and Factor IX

During the discussion it was agreed that it could be either a stuffer or a new package insert. It was

change to OoB and then touch base at the time of the Liason meeting and discuss time frames for implementing the change. It was also agreed that the second point will be that we will suggest to OoB that this also be done for blood and blood by products.

Subcommittee on Plasma Procurement - Mr. John Mink

1) Acquired Immune Deficiency Syndrome (AIDS) - After much discussion it was agreed that we would place an item on the Liason agenda asking why blood banks aren't required to do the same as plasmapheresis centers and jointly suggesting that this should be done. The differences in the requirements relate to labelling of plasma collected from a high risk donor and the requirement for examination of lymphadenopathy. We will make this statement as it relates particularly to recovered plasma fresh frozen which can be used in the manufacture of AHF and Factor IX.

There was considerable discussion as to what we would do about individuals who change their story or who, defined at a later date, are from a high risk group. In essence, it was more or less agreed that the actions taken would be 1) to destroy any plasma at the center level, 2) we would not destroy product, 3) Dr. Donahue has made his view known that he would also destroy any units at the plant for political reasons. Note there is some divergence of opinion on this, however, it is apparent that most manufacturers have a policy in place for this. The problem area really relates to donors who have been discovered at a later date to have had AIDS. Dr. Rodell volunteered to call Dennis Donahue and discuss this with him privately, feeling that this was such a political issue that Donahue would not want to discuss it in public.

2) Simian Acquired Immune Deficiency Syndrome (SAIDS) - I reported on the monkey meeting at NIH. This report has already been distributed within Alpha.

3) Casual Donor Regulations - Subsequent to their original memo on the requirements for infrequent donors, FDA sent out a letter stating that an RPR test would still be required for such donors and that the consent must be obtained by a professional person. After much discussion it was agreed that we would raise comments at the Liason meeting by stating that we had defined for ourselves an adequately trained professional person as being an RN, LVN, Medical Technologist, Nurse Practitioner, Physician's Assistant, a Center Director, Assistant Center Director, or equivalent.

4) Industry Manual Usage - It was noted after much discussi that OoB will not approv a manual unless it is submitted by a center seeking License or a center seeking changes in its manual. It was agreed that we would go through ABRA and suggest that they go through the proper mechanism to make sure that this manual is submitted by a plasmapheresis center and thereby receives the official approval.

Hepatitis Vaccine for Employees - There was a comparison of the practices of the different manufacturers in offering hepatitis vaccine for their employees at their donor centers. Note that Abbott requires vaccination for employees working with their products, mainly because of the hazards with the core antigen.

Division on Microbiological Control - Harry Joswick, Ph.D.

At the beginning of his division session, Dr. Joswick reported on a very interesting FDA meeting in New Jersey. Mr. Apolone of the New Jersey FDA District stated that purified water systems should have less than 10 organisms per ml. He noted that 8% of lots of non-sterile products were contaminated with gram negative rods. They also noted that some manufacturers in cutting back on energy had reduced the temperature of their purified water loop. FDA believes you should not go below 75°C since legionella will grow at 55-60°C. Mr. Fantasia of the New Jersey District came on strong stating that the quality function is too often interested simply in getting the product out rather than protecting its quality and that the FDA and District intends to get tough on this.

Subcommittee on Sterility Testing - Harold Basch

1) Status and Changes of The USP Chapter on Sterility Testing - It was noted that there will be further changes and it will come out in the pharmacopeial form. However, for the moment, for a repeat test the first stage of the sterility test must be investigated and an explanation found for invalidation of the first stage. However, members of the BioSection present noted that all of Region II of FDA has refused to accept the one and two stage concept. It is apparent that EDRO has not gotten the message from Office of Drugs. It was agreed that Dr. Schmitz will talk to Dr. Jennings of PMA about meeting with FDA on this after the changes appear in the pharmacopeial form. Note that this concept is very important since these inspectors are taking the route that they will not accept the concept of a second stage "retest".

2) Status of Sterile Container - Closure Integrity Test Committee Activities - Note this committee was formed to draft essentially an industry position because FDA

... the closure and container ... of the integ... has been ...gested by the Steering Co...ittee of the Bio-logical Section and in the minutes of the Steering Committee meetings it was agreed that this draft will be circulated among all of the sections of the Science and Technology area of PMA for approval. However, in the mean time it was agreed that we will put this draft on the Liason agenda for discussion with Office of Biologics personnel since they have demanded performance sterility testing in stability protocols.

Subcommittee on Environmental Control and Aseptic Processing - Walt Woodward

1) Discussion of the proposed questionnaire "Current Practices in Use of Chemical Disinfectants in the Pharmaceutical Company". The survey has been completed and will be sent to all attendees. It will be reviewed by the Steering Committee. This should be of considerable interest to us since we have been cited for not rotating disinfectants by the United Kingdom.

2) Proposed Revisions Study to Federal Standard 209B by the General Services Administration - This relates to room classifications of 10, 100, 1,000, 10,000, 100,000. The Institute of Environmental Sciences met in LA last week. This meeting is heavily attended by aero-space and computer people who claim they must have Class 1 or Class 10 Standard. This institute has no set biological controls for the standard. However, IES has said they will set up an Ad Hoc Committee to set up biological controls. IES only defines the parameter, has never said they set up a standard for these classes. However, in an appendix of one of their publications they have set up recommendations so they will delete the appendix. The jist of this is that if the pharmaceutical companies have had to meet aero-space standards which are unrealistic and unneeded in many instances, the standards have been defined as a room without people in it.

A topic from the floor was a note that a notice has come out that an EPA draft for infectious waste management is available. The telephone number to obtain this is (202) 783-3238 (note: Regulatory Affairs will obtain a copy). They are asking for comments on this draft proposal. It is a lengthy document but we are advised to read it and comment carefully. Please note, it has in there suggestions for the disposal of waste from blood and blood by products.

MC:pw
0911R