HYLAND
DIVISION TRAVENOL LABORATORIES, INC.

Interoffice correspondence

to: Distribution

from: L. Kriley

subject: Project Decision Council Booklet

date: October 29, 1979

copies: J. Daniel
P. Geraghty
G. Harding
R. Kinley
M. Rodell
T. Stagnaro

Attached is a copy of the subject booklet which contains updates on the following projects:

1. AHF Hepatitis Risk Removal
2. Proplex Hepatitis Risk Removal
3. Intermediate Grade Hemofil
4. Alpha IV_1 Paste Sourcing
5. PPF Quality Improvement
6. IVGG U.S. Licensure
7. 5%/250 ML Albumin DIN Project

They were to be reviewed at the P.D.C. meeting that was scheduled for October 26, 1979.

GRO-C: Lee Kriley

LK/kj

Distribution

C. Brooks
D. Castaldi
R. De Vreker
S. Holst
G. Phelps
H. Termeer
W. Thomas

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BAJ 014334

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Hepatitis B and non-A, non-B Hepatitis Infectivity-Free Hemofil

Project Update

Research effort on this project has been initiated but progress has been limited by the unplanned dedication of personnel to the Autoplex project and because of the delay in the approval of required additional staff that was indicated in the June 15th PDC presentation. Several lots of regular potency and high potency Hemofil have been heat treated by Research and partial characterization of these lots has been completed. These results are inconclusive relative to Hepatitis inactivation because virology tests have not been performed on these lots.

Virology evaluation of these lots has not been possible because the personnel required to perform this work were included in the decision package that was just approved on October 3rd. However, because of the relocation of the Research Group within the Costa Mesa facility, the virology laboratory is not scheduled to be available for use until mid-November. The gamma radiation treatment of Hemofil has been arranged by Research. The net impact of these factors per Dr. Thomas is that the project is two months behind the critical path schedule that was presented at the PDC meeting in June.

Protein Development is continuing to develop ultrafiltration for the production of Hemofil but the possible removal of Hepatitis risk cannot be evaluated until the virology laboratory in Research is staffed and operational.

A significant development within this project which is supplementary to the original PDC presentation is the plan to license Hemofil in Germany with the only claim being that it has been heat treated. Compared to Behringwerke's regimen of treating their product at 60° for ten hours, Hemofil will be treated at 60° for either 24 or 72 hours. All clinical studies will be done with material for which virology data is not available so they will have to be redone later if heat treatment proves to be effective in the removal of the Hepatitis risk. Arrangements for the production of clinical materials in Lessines and for the performance of the clinicals in Europe should be finalized by Dr. Thomas within three weeks. The following is a summary of the current estimated schedule of activities for this aspect of this project and a basic activities flow chart is included as attachment 1.

Activities	Responsible Individual	Schedule
Heat treat 7 lots of Hemofil	W. Thomas	10/22 to 11/5
Reestablish high potency Hemofil product specifications for heat treated material	W. Thomas	10/22 to 11/5
Coordinate the availability of an incubator for Lessines	W. Thomas	10/22 to 1/2/80
Initiate heat treated Hemofil stability studies	W. Thomas	10/22 - continuing
Conduct Morton Grove dog cardiovascular and guinea pig toxicology studies	W. Thomas	3 weeks after receip of material at Morton Grove
Coordinate plan for European production and studies	W. Thomas	10/22 to 11/14
Initiate limited safety and Factor VIII recovery study	Drs. Van Essche and Dolkart	2/1/80 to 2/21
Summarize study data and prepare and submit IND	Drs. Van Essche and Dolkart	2/21 to 2/28
Initiate full clinical studies	Drs. Van Essche and Dolkart	4/1 - continuing

None of the other information contained in the June 15th PDC presentation has changed.

Attachment 1

BAJ 014337

MDL BAX038503
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Hepatitis B and non-A, non-B Hepatitis Infectivity-Free Proplex

Project Update

Only preliminary research effort has been initiated on this project. Because of the commitment of manpower to higher priority projects, i.e. Autoplex and Hepatitis-Free Hemofil, and because of the delay in the approval of required additional staff that was requested in the June 15th PDC presentation, this project is effectively four months behind schedule per Dr. Thomas. The revised schedule for license submission to the Bureau of Biologics is March 1, 1981. The other aspects of this project remain as presented on June 15, 1979.

Intermediate Grade Hemofil

Project Update

The significant need for this product continues to exist and heavy emphasis has been given to this project by Protein Development. Production documentation for all three fill volumes has been written and is being finalized, and packaging and filling documentation has been written for the 250 B.W.S. A.U. product.

Except for the use of the Development Lab for Autoplex production, this project would be two weeks ahead of schedule. However, it is now approximately five weeks behind schedule and the three pilot lots that were scheduled to be completed by September 30th are now scheduled to be completed by November 7th. These lots will be produced in the GMP mode and will be primarily used for stability studies with approximately 200 bottles from each lot being available for other uses such as commercial sale. With this filtration size they will be able in Protein Development to assess any potential problems in production.

Guy DeCaritat has indicated that shipment of the first commercial lot to Lessines by January 20, 1980 will fit well into their schedule because this is when they expect to have packaging components and sterile water from Ammill-Phoenix, a new sterile water supplier, available.

It now appears that the product can be produced and sold under existing Hyland Hemofil licenses in both the U.S.A. and the U.K. Initial market evaluations in the U.K. by T.I.S. indicate that this product should be well received. The 250 B.W.S. A.U. Intermediate Grade Hemofil product will be packaged in a separate 10-pack box and the other components that are routinely sold with Hemofil in Europe will be distributed in a separate box. The packaging designs of the 500 and 750 B.W.S. A.U. presentations and the label copy are to be finalized this week.

This project is proceeding as planned with the exception of the delay that was encountered because of Autoplex production.

PPF PARTICULATE - UPDATE

CONTENTS

PPF PARTICULATE - UPDATE

I. SUMMARY

A. 9/19/79 PDC decided to emphasize Aerosil method development (Section II).

B. BUREAU OF BIOLOGICS MEETING in October with Dr. Rodell, D. Castaldi, and S. Holst resulted in:

1. Favorable initial BuBio reaction to Aerosil method.

2. Outline of BuBio data requirements for Aerosil method submission (contained in S. Holst's draft protocol, Section III).

C. BUREAU OF BIOLOGICS REQUIREMENTS, major elements:

1. 5 Consecutive Pilot Lots for submission.

2. Residual Silica, quantity and morphology (size).

3. Aerosil Effect on PPF Composition. Determine any change.

4. Safety.

a. In Vitro.
b. In Vivo (animal).

D. SILICA SOURCING.

1. Research is currently testing different brands of silica.

2. Protein Development is developing a protocol for incoming raw material silica lots acceptance, as silica lots may vary in adsorption capability.

E. WORKER SAFETY. Protein Development has provided J. Hines with silica data and information sources, and has requested a recommendation on necessary measures.

F. DRAFT PROJECT COMPLETION PROTOCOL (Section III) is due to be reviewed by Protein Development on 10/26/79. Manhour/cost figures and a schedule can be developed when this protocol is finalized.