HYLAND
THERAPEUTIC LABORATORIES, INC.

Interoffice correspondence

MAY 19 1978

R. A. DeVreker, Ph.D.

to: D. L. Castaldi

from: A. J. Lazos

subject: Hepatitis Removal
Monthly Summary

date: May 18, 1978

copies: B. Bock
M. Chlebowski
D. Copeland
W. Marguerre
D. O'Connell
R. Russell
R. Taub

Attached is the subject Priority "A" report for the period April 22, 1978, through May 18, 1978.

GRO-C

AJL:ba

Distribution:

General

D. Allen
S. Anderson
R. De Vreker
R. Dutrisac
A. Josephson
M. Rodell
V. Shneider
C. Smiley

Project Team

T. Andary
G. Dolana
S. Holst
R. Keethler
D. McClure
W. Thomas

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WORLDWIDE COURT REPORTERS, INC.

5/18/78

HEPATITIS REMOVAL MONTHLY SUMMARY

I. Progress Since April 1978 — Responsibility

A. Isolation, identification and/or removal of hepatitis from Therapeutic products. — G. Dolana

1. Non-A, non-B hepatitis studies

a. HEMOFIL lot 591D056 has been further evaluated. An ultracentrifuge pellet has been partially purified by rate zonal and density gradient centrifugation. Particles measuring 20-30 nm and 60-80 nm were observed in selected fractions. Immune electron microscopy (IEM) studies showed that antibody appeared to combine with the smaller particle. The antibody used in these studies was of marmoset origin. The marmosets had been infected with the so called "Barker" agent.

b. Additional convalescent serum has been obtained from the non-A, non-B patient who had received HEMOFIL lots 591C004 and 591D001.

c. A liver wedge has been surgically removed from one of the 4 chimps included in the study. The animal selected had received HEMOFIL lot 591D056 and had elevated enzyme 18 days past challenge. The chimp is recovering from the surgery with no complications. A portion of the wedge was hemogenized followed by preparative ultracentrifugation to partially purify any "virus-like" particles. 22 to 28 nm complete and incomplete particles were observed. IEM studies showed that the particles were aggultinated by a selected non-A, non-B convalescent serum. The antibody source used in this study was obtained from the patient who developed non-A, non-B hepatitis after administration of HEMOFIL lot 591D056.

d. Sera from one of the non-A, non-B patients were forwarded to Walter Reed Army Institute

Progress Since April 1978 (cont'd) — Responsibility

of Research for CMV and EB virus antibody studies. The results indicate that the patient had not experienced a recent infection with either of these viruses.

e. The non-A, non-B data obtained to date is being prepared for publication.

B. Studies on determination of pore sizes in molecular exclusion filters utilizing a bacteriophage R17. — T. Andary / G. Dolana

Attempt to ascertain differences between filtration of phage R17 alone and in combination with PROPLEX.

Aliquots of the phage R17 with or without PROPLEX (581D184) were filtered through Pharmaco 30 Å and 50 Å filters. Filtrates and retentates from the filtrations will be analyzed by Dr. Dolana for intact (~25 nm - similar to HBsAg) or fragmented phage. Results of these experiments will indicate, 1) the relative size of the filter pore, 2) the effect of PROPLEX on the filtration of the phage, i.e. does the PROPLEX fragment the phage?

C. Meeting held with R. Russell, Director, Hepatitis Test Marketing, Baxter/Travenol Inc. Discussed Hyland Therapeutics work on non-A, non-B test. Set up ongoing communications. It was agreed that Baxter/Travenol should take advantage of non-A, non-B antigen discovery developments. — A. Lazos

D. Scope of Hepatitis Project redefined based on limited personnel. — Task Force

Recommendations are:

1. Establish an ongoing tracking system on hepatitis testing and removal technology.
2. Continue filter evaluation.
3. Coordinate with Corporate on non-A, non-B test development.

II. Problems or Delays Encountered and Solutions

Problems	Responsibility	Solution
A. Manpower Restraints. Original proposal for removal of hepatitis B infectivity from current and proposed new therapeutic products was presented to the PDC in April, 1977, and rejected. A second proposal, submitted in June, 1977, was approved. Phase I of this proposal was funded for $63,165. On January 19, 1978, additional funding of $78,000 was requested to fund, 1) a collaborative non-A, non-B hepatitis study with the Center for Disease Control, and 2) the services of Dr. Dolana and a Sr. Research Associate. A decision package was submitted in Feb., 1978, to hire the Sr. Research Associate. To date, no decision has been made on funding for the latter two parts of the proposal.	A. Lazos	As mentioned in last month's report, in order to continue with a viable Hepatitis Removal program, the proposal for additional funds and manpower should be approved.

III. Key Milestones and Responsibilities Next Three Months

Milestone	Responsibility	Date
A. Investigation of other potential F-VIII stabilizers which have been proven safe and effective in other therapeutic products.	D. Edgell	Dependent on availability of funds and manpower.
B. Continued evaluation of the efficacy of ion exchange resins and/or molecular filtration in removal of hepatitis infectivity from PROPLEX and other therapeutic products.	T. Andary	Dependent on availability of funds and manpower.

Key Milestones and Responsibilities Next Three Months (cont'd)

	Milestone	Responsibility	Date
C.	Outline plan for removal of hepatitis virus from therapeutic products by Monsanto's polyelectrolyte process.	T. Andary	As soon as S. H provides literat from Corporate.
D.	Results from initial experiments on filtration of phage R17 (with or without PROPLEX) through Pharmaco 30 Å and 50 Å filters.	T. Andary / G. Dolana	5/16/78
E.	Receive strategy guidelines for Corporate development of non-A, non-B test. Coordinate with Ron Russell.	A. Lazos	6/78