Norman,
You may find this chronology helpful.

HYLAND THERAPEUTICS DIVISION
TRAVENOL LABORATORIES, INC.

Interoffice correspondence

GRO-C

to: J. M. Noel -- Less

date: August 23, 1985

from: M. Eras -- GO GRO-C

copies:

subject: Outline of Product Safety Work

Plasma Sourcing

We have committed that we will not use plasma from high risk sources, such as:

prisons or

geographic areas which are considered to be high risk, i.e. San Francisco, Hollywood and New York City.

We do not obtain plasma from third world countries.

Lesotho, S. Africa was closed in 1976 (our only African plasma center).

The Mexico City plant (which used Mexican sourced plasma) was closed in 1981.

Puerto Rico was closed in 1980.

Plasma Screening

Donor Education/Self-Exclusion

Donors were given educational material on AIDS and requested to exclude themselves from the donor pool if they fell into one of the high risk categories in 1/83.

Donor screening by center personnel

Questions designed to uncover symptoms of AIDS were added to medical history questions in 1/83.

Physical exam was revised to look for specific symptoms of AIDS (enlarged lymph glands, etc.) in 5/83.

Routinely review of weight records for unexplained weight loss begun in 6/83.

Donor center personnel education to look for signs of AIDS, begun 1/83 and is a continuing program.

High risk individuals added to permanently defered donor list

High risk individuals or close contacts of high risk individuals added to the permanently defered donor list in 1/83.

HTLV-III screening begun 4/8/85, + donors permanently defered.

Plasma from + donors is destroyed.

High risk and + donors are permanently excluded from donating.

Product Treatment

The Centers for Disease Control and the National Hemophilia Foundation believe that current heat treatments inactivate HTLV-III virus. The NHF is recommending that hemophiliacs use heat treated products when they are available because they are safer.

Where a treated product has been licensed, we do not distribute the unheated product.

Introduction of Heat treated coagulation products by Hyland

Treated HEMOFIL 3/83

Treated PROPLEX SX 10/84

Approval for treated PROPLEX pending, expected in ~~9/85~~ 2/86 GRO-C 1/21/86

Approval for treated AUTOPLEX pending, expected 1986

FOR TRAVENOL USE ONLY

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Product produced by ethanol fractionation (PROPLEX, AUTOPLEX, GAMMAGARD)

Montagnier showed inactivation of HTLV-III virus with 25% ethanol.

Wallbank (U. of Manitoba) refutes this, saying that in human plasma 25% ethanol is not a high enough concentration to destroy the virus.

Our work with human source plasma does not support Wallbank's conclusion. Preliminary data shows rapid inactivation of HTLV-III virus in human plasma following addition of 20% ethanol. Further work is planned.

Product produced from ethanol fractionation which is then heat treated (NSA, PPF, ISG)

Our experience with protein solutions is that hepatitis virus is destroyed by heating in final containers at 60°C. This has been documented for about 40 years. In addition, there have been no known cases of hepatitis from Hyland NSA or PPF. We have not had any reported cases of hepatitis from ISG. HTLV-III has been shown to be far more labile than hepatitis virus, therefore, we assume that HTLV-III virus is inactivated by normal manufacturing methods for these products. Further, there have been no reports of AIDS contracted from these products.

Results

Our experience with hemophiliacs showed no seroconversion for HTLV-III antibody in patients given only treated Factor VIII concentrate (HEMOFIL T)

Morbidity and Mortality Weekly Report (5/3/85) reports a decline in cases of AIDS for hemophiliacs, contrary to the experience with AIDS cases in general. This is observed without yet seeing the effect of HTLV-III screening of plasma which began in April/March of this year.

Final Container Testing

We have no intention of testing final containers for HTLV-III antibody, since we do not know that the antibody and antigen would fractionate together.

We test source plasma for antibody

1) Because it is the only test we have and
2) people who have antibodies to HTLV-III have been exposed to the virus and may be infective. These persons are excluded from the plasma pool. In addition, because detectable levels of antibody sometimes develop after the person has become infected, we destroy all previous bleeds as well.