

TO: *JOHN J. ANDERSON
720 LEITER*

FROM: *GRO-C* 7-16-
Inventor Date

SUBJECT: Disclosure
(Conception of Invention)

WITNESS: *GRO-C* 7-17-
Read & Understood Date

TITLE: *Heat treatment of the
lyophilized plasma proteins*

WITNESS: *GRO-C*
Read & Understood Date

REMEMBER: Whenever you are faced with a problem and you have an idea of how to solve it, it is the time to disclose it - not after the invention is complete, DO IT NOW! By tomorrow, someone else may beat you to it.

Disclosure MUST BE IN INK and is best made by following the consecutive steps listed below:

- | | | |
|--|-------------------|--|
| 1. Date | <u>Mechanical</u> | 5. Drawing |
| 2. Title | | 6. What drawing shows |
| 3. Problem | | 7. How it works |
| 4. Your solution, compared to current practice | | 8. Your signature and two witnesses understand your disclosure |

DISCLOSURE: Problem: The elimination of the hepatitis virus in protein solutions derived from human blood has not been fully realized. Heat treatment of such solutions has not been a wholly satisfactory approach because many of said proteins (eg. AHF) lose much of their biological activity at temperatures required for viral inactivation.

Solution: It is well known that the heat of denaturation of proteins is radically increased if these proteins are not in solution but in freeze-dried form. (They may be stable at 100°C when lyophilized and denature at 60°C in solution). One would expect that freeze-dried viruses would also denature at ~~higher~~ ^{the same} higher temperatures. However, since a hepatitis virus is ~~a~~ ^{an} ~~more~~ ^{ATL} complex and dependent on such structures as a ~~hemagglutinating~~ ^{TSL JLL AL} phospholipid

NOTE: Use both sides of page if necessary

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lipid containing

1. BL JH JH
it may be more susceptible to denaturation at a given temperature than proteins in its surrounding medium when in the freeze-dried state.

We are suggesting that heating freeze-dried blood proteins (suspended before lyophilization in a buffer solution) to an optimal temperature somewhere between 60-200°C might result in plasma products significantly reduced in hepatitis risk.

(Carbohydrates + amino acids added to the suspension medium would be known at elevated temperatures. Adding carbohydrate to a protein solution during heating protects the protein by interfering with the denaturing interaction of the protein and the solution. There is no reason to believe that carbohydrates in the dry state would protect the protein.)
be needed to BL JH JH

(The above suggestion in some ways assumes that the inactivation of hepatitis virus is not dependent on the denaturation of its nucleic acid. Nucleic acids are able to withstand much higher temperatures than proteins.)

(The above suggestion is very difficult to test. This technician does not have the BL JH JH Choty path to knowingly contaminate a \$15,000 lyophilizer with hepatitis

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DISCLOSURE (Name of Inventor)

TITLE: Pasteurization of Dry Lyophilized AHF in Presence of a Carbohydrate

DISCLOSURE: Whenever you are faced with a problem and you have no idea of how to solve it, that is the time to disclose it - not after the invention is complete, but before it is too late, someone else may beat you to it.

Disclosure MUST BE IN INK and is best made by following the consecutive steps listed below

- | | | | | | | | |
|---------|----------|------------|--|------------|-----------------------|-----------------|--|
| 1. Date | 2. Title | 3. Problem | 4. Your solution, compared to current practice | 5. Drawing | 6. What drawing shows | 7. How it works | 8. Your signature and two witnesses who understand your disclosure |
|---------|----------|------------|--|------------|-----------------------|-----------------|--|

DISCLOSURE: Problem: Pasteurization of AHF and other blood proteins has not been realized because of the delicate nature of these proteins and their instability during heating. Pasteurization of lyophilized AHF results in loss of some AHF activity.

Solution: Pasteurize dry, lyophilized AHF in the presence of dry carbohydrate at a level sufficient to stabilize the AHF but not degradation. Thus, a mixture of dry, lyophilized AHF containing from 5% or more carbohydrate can be heated in the dry state at a temperature sufficient to pasteurize the mixture, i.e., about 60-75°C., for a period sufficient to pasteurize the mixture, i.e., about 10 hours, in the absence of glycine.

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