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TO: M.M. Mozen

DATE: November 30, 1983

FROM: M.B. Doblin, R.E. Louie

COPIES TO: M.M. Sternberg
P. Ng
G. Mitra
K. Lembach

SUBJECT: Development of Virus-Free Plasma Products

A crash program directed towards the development of virus-free plasma products was started several months ago, when concern about the utility of copper phenanthroline as an inactivating agent developed. The use of heat treatment alone as a means of achieving the desired objective has not been completely successful. Those model viruses with known properties of thermo-resistance also survived under the constraints of time and temperature imposed by requirements for preservation of product activity. A review of the appropriate literature has provided a list of chemical agents known to be virucidal under a variety of conditions (i.e. relative to time, temperature and concentration of the compound). The table lists these chemicals without qualification:

Anionic detergents	Glutaraldehyde
Cationic detergents	Ethyl ethyleneimine
Non-ionic detergents	Tri-n-butyl phosphate
Urea	Benzimidazole
2-mercaptoethanol	Benzene
Alcohols	Ethylene chloride
Acetone	Tri-chloroethylene
Ether	Ethyl trimethyl ammonium bromide
Chloroform	Bromelain
Beta propiolactone	Saponin
Formaldehyde	Lipases
Paraldehyde	Phenol

It is obvious that the list is even more extensive than it appears, since the members within groups such as the detergents have not been specified. While the list is by no means comprehensive, it shows that many candidates exist, although a number would be rejected out-of-hand for various reasons (incompatibility, toxicity, etc.)

One way to deal with this problem would be by team effort. A qualified group could be formed to select a number of chemicals which can be certified safe for human use or, at the very least, would not be present in non-physiological concentrations in the final product.

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The list of acceptable chemicals would then be given to members of the Biochemical Research Department to determine the maximum conditions of time, temperature and concentration under which the particular plasma product could be treated without significant reduction in biological activity.

Once these parameters have been identified, then members of microbiology research would carry our inactivation studies with a diverse group of viruses to determine the range and extent of effectiveness of the various chemicals.

Clearly, it is unreasonable to expect one compound to be universally effective. If the ultimate target was limited to Hepatitis B virus, the problem would not be so difficult, in view of the recent report on the inactivation of this virus by chloroform. Since the putative AIDS agent(s), as well as non-A non-B hepatitis, must also be considered, then efforts should be directed towards incorporating at least two types of compounds, one effective against lipid-containing viruses and the other active against non-lipid containing viruses.

These laboratory studies would then be followed by trials in chimps to prove the effectiveness of the compounds against Hepatitis viruses.

In summary, it is proposed that a multidisciplinary team effort be undertaken to develop virus-free plasma products.

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MD:RFL:jmo

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