

Note of Meeting held at Elstree, 27 June 1969

Present: R.A. Cumming
J. Watt
D. Pendreigh
W.d'A. Maycock
L. Vallet
D. Ellis

SNBPA Blood Products Unit, Edinburgh
Scottish Home and Health Department
Blood Products Laboratory, Elstree

Plastic Bag for Plasma

Mr Vallet reported that he had examined the possibility of reducing the thickness of frozen plasma in the plastic bags from the 3" originally proposed. The minimum possible was 2.5" if the unit volume of 5 L and the proposed shape of the pack were to be retained (the latter being related to (a) arrangements for handling and storing the packs in the new Elstree building (b) the use of a freezing bath based on the Frigidaire model LT 26 -40°C deep freeze).

Dr. Maycock said that the Transfusion Centres at Brentwood and Birmingham liked the new bag system and had reported no serious difficulties.

Mr. Watt gave 1/2" to 1" thickness as the optimum for dielectric thawing with 1 1/4" as the absolute maximum.

In a discussion of alternative bag shapes and thawing arrangements the following points were made by Mr. Watt:

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- (1) that it would be advisable to confirm the availability of the proposed Frigidaire freezer, as there had been difficulty in obtaining this model in Scotland,
- (2) that the system using this freezer had the disadvantage of possible contamination of the plasma with the bath fluid,
- (3) that an alternative type of freezer was used in the food industry, and might be adapted. In this, cooling was by direct expansion of the refrigerant gas in a hollow mould recessed to take the material to be frozen. Mr. Watt thought freezing could be rapid if a refrigeration unit of adequate capacity were used, e.g. 5 L bag, 2" thick frozen and cooled to -30°C in as little as 20 minutes. Cost of Compressor alone might be of order of £250. Mr. Vallet pointed out that -40°C was the minimum temperature to which the plastic, WNC 18, of which the Elstree bag was made, could be exposed, so that the refrigerant temperature would have to be suitably controlled. He also mentioned that a third type of freezer, consisting of 2 refrigerated plates, was under test in Oxford.

Dr. Cumming suggested that by part filling the standard BPL bag when it was used in Scotland it might be possible to reduce the plasma thickness to $1\frac{1}{4}$ " without the necessity of manufacturing two types of bag. This would

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increase costs for bags in Scotland as more bags would be used for a given volume of plasma.

Mr. Watt brought up the possibility of designing a mould for the direct-expansion type of freezer which would take either the Elstree BPL bag or a flatter pack suitable for trial of the dielectric thawing procedure, in Scotland.

It was agreed that the following steps should be taken:

1. that the Scottish unit would undertake the development of a prototype direct-expansion freezer, recessed to take either two Elstree packs of filled dimensions 2 1/2" x 18" x 10", or one larger, flatter pack, occupying double the area, for use in Scotland. The recessed area would thus be a rectangle 2 1/2" x 18" x 21" (extra 1" to allow for a divider). Other requirements to be as follows: (a) Cooling rate of bags should permit re-loading at least once per hour. (b) The unit to be self-contained and movable (on wheels), with air-cooled compressor.

(A second prototype to be made for Elstree would not be developed until the first prototype had been assessed.)

2. that Mr. Vallet would investigate the potentialities of the Oxford-type freezer (made by Grant's).

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Other points confirmed in the course of the discussions:

(a) Plasma packs to have female Luer connectors on the input side.

(Dr. Cumming felt that in the future an increasing amount of plasma might arise as a by-product of special procedures such as platelet preparation, and the plasma bags must have standard connections).

(b) Mr. Vallet to continue with arrangements for bags of revised design, already being discussed with Tavak.

New Products

Mr. Watt reported on experiments aimed at recovering Factor IX from cryoprecipitate supernatant using DEAE-cellulose adsorption. Good yields of Factor IX were obtainable (60% of theoretical). The fraction contained factors II and X but not factor VII or V. There were, however, slight but unexplained temperature rises in pyrogen tests on rabbits. This did not appear to be directly due to pyrogenic substances extracted from the DEAE-cellulose. A 90% clottable fibrinogen could be recovered in the same fractionation scheme.

On the question of the total number of donations now likely to be required for Factor VIII and IX production, Dr. Maycock said he would discuss this problem with Dr. Biggs in the light of experience with cryoprecipitate in the last 2-3 years.

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Dr. Cumming asked how much cryoprecipitate supernatant might be sent to Liberton for fractionation; Dr. Maycock said this could not be predicted at this stage.

The Centritherm (Alfa-Laval Ltd.)

Mr. Watt distributed a duplicated report on trials of this equipment for removal of ethanol from re-dissolved Fraction V.

The following points arose during discussion of this report:

- (1) pH of the solution was not adjusted before passage through the machine (i.e. pH was about 4.8),
- (2) gel filtration analyses were carried out on solutions which had been heated for 10 hours at 60°C after passage through the Centritherm,
- (3) during distillation a "skin" of what appears to be over-concentrated albumin forms on certain areas of the inner surface,
- (4) delicate control of the pressure in the system is required if optimum evaporation rate is to be achieved without frothing; the plant cannot be left to run unattended,
- (5) the operation is 'clean', but not sterile. Carbon seals on the rotating parts cannot be autoclaved. Glass parts are cleaned with chromic acid, stainless steel with "Decon",

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(6) space required: 3' x 5' with access preferably all round but, at least, on 3 sides; water 300 L/hour cold.

It was agreed that approximately 10 kg. of Elstree Fraction V paste should be sent to Edinburgh for ethanol removal in the Centritherm.

Ethanol for Fractionation Use

Mr. Watt reported that a paint-brush had been discovered in a drum of ethanol used in fractionation (a detailed report was distributed) and raised the general question of testing of chemicals and solvents prior to use. No specific conclusions were reached in the ensuing discussion.

On the question of recovery versus disposal of used ethanol it was concluded that differences between the two new units made the decisions on this point independent of each other. At Elstree, site restrictions, staffing questions, and difficulties in ethanol waste disposal had decided the issue in favour of dumping the residues, after suitable denaturation. The sewage disposal situation in the area was such that disposal of the residues from a recovery still would present as big a problem as disposal of the original material.

Mr. Watt was looking into the economics of a recovery process in the Liberton unit.

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Other business

Dr. Maycock mentioned, for information, that a fall in the amount of out-dated blood plasma received by Blood Products Laboratory at Elstree had occurred, following a 'peak' in 1967.

Dr. Cumming raised the question of whether some fractions might be prepared on a regional basis, e.g. a given region receiving back, say Factor VIII prepared from fresh plasma supplied by that region. Dr. Maycock thought that a region's requirements did not necessarily match its capacity to produce the starting material and considered that an overall policy was preferable. This had been the practice in England.

It was decided that the next meeting should be held in Edinburgh in October. It was hoped that it would be possible by then (a) to demonstrate a complete fractionation run on the continuous-flow fractionation system

(b) to have the Edinburgh prototype freezer for bags of plasma in operation.

Mr. Watt would arrange to show the Centritherm in operation.