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Note of a Meeting

at Blood Products Laboratory,

Lister Institute, Elstree

Friday, 1 November 1968

Present:	Dr. R.A. Cumming	
	Mr. J.G. Watt	Blood Transfusion Service, Edinburgh
	Dr. I.S. Macdonald	Scottish Home and Health Department
	Dr. W.d'A.Maycock	
	Mr. L. Vallet	Blood Products Laboratory
	Dr. D. Ellis	

1. Progress with new buildings, Edinburgh and Elstree

B.P.L. Edinburgh: Dr. Macdonald said that the present target dates were:-

completion of building - December 1971

completion of commissioning - June 1972

He thought that 2 - 3 months should be added to these dates, so that the building might be expected to be in operation by about September 1972.

Approval in principle for an expenditure of £1·0 million had been given. The present estimate was, however, about £1·4 million. By designing the building to operate at 1,500 L/week, but equipping it to operate initially at 1,000 L/week it was hoped to reduce the estimate to about £1·2 million. It was hoped to submit the cost plan estimate at the end of November.

B.P.L. Elstree: Dr. Maycook reported the present target dates:-

Starting date - February 1969

Completion of building - summer 1970

Completion of commissioning - early 1971

In practice these dates should probably be put back 3 months.

A cost plan estimate of £617,000 had just been submitted: this figure excluded the cost of modifications to the existing building which would have to be undertaken when the extension had been commissioned.

2. Supply of Plasma from R.T.C.s to Elstree and Edinburgh

Containers for plasma and their transport to the ~~B.P.L.~~ CENTRES s were again discussed.

It was confirmed that the containers of plasma should be frozen below -30°C, immediately after filling at the R.T.C.s and delivered frozen to the ~~B.P.L.~~ CENTRES s The main reasons for freezing were:

(a) To reduce to a minimum, or possibly eliminate altogether, the need for bacteriological testing of the large number of containers which would eventually be received by B.P.L.s and, at the same time, to minimize the risk of introducing pyrogenic material into the large pools that would be used in the future. Experience in other countries had shown that plasma stored and transported frozen was a satisfactory material for large scale fractionation.

(b) To preserve unstable substances, such as clotting factors, in specifically collected fresh plasma. Only by using frozen fresh plasma would the B.P.L.s be able to produce adequate amounts of clotting factor concentrates. The use of frozen fresh plasma would also allow B.P.L.s to arrange the preparation of these concentrates independently of R.T.C.s programmes for collecting fresh plasma.

Plastic Containers It was agreed that the containers for frozen plasma should be disposable.

Elstree had developed:-

(i) a bag made from I.C.I. polyethylene lay flat tubular film (WNC 18), capacity about 5·0 litres, which would contain the plasma from about 30 donations of blood and weigh, when full, about 10 lbs. The plastic contained no additives and could be sterilized by gamma radiation.

(ii) an aluminium former in which the filled bag was placed before being frozen.

The freezing chamber (filled with 67% ethanol) of a Frigidaire -40°C cabinet (model No. LT 26) would accommodate 4 loaded formers. The freezing time for 4 bags, simultaneously, from + 25° to - 20°C was not more than 5 hours. After freezing the plastic bags are removed from the formers and placed in cardboard boxes (15 x 10 x 3 1/2 ins.) and stooked in an ordinary large subzero (-25 to -30°C) cabinet.

One -40°C cabinet and one such subzero storage cabinet would be adequate for freezing and storing the plasma from 120 x 5 or 600 donations per week (5 days)

The Elstree bag had been under trial in collaboration with R.T.C. Brentwood. It seemed likely that it would be possible to fill this bag with plasma at least at the same rate as the 80 oz. Winchester can be filled. Dr. Jenkins was working out the technique and apparatus required. It was intended to provide R.T.C.s with complete details of apparatus (e.g. pump and scales) required and a full description of the technique.

Edinburgh had developed a plastic container to hold 4·0 L plasma and measuring 1·9 cms x about 462 cms (18 1/2 ins.) square. The latter dimensions had been selected as they were those of a standard size of radio-frequency electrode. It was intended that this plastic container should be filled <u>in situ</u> in an aluminium box, in which it would then be frozen and transported and stored. It was planned that the boxes, with

their frozen plastic containers, would pass, two abreast, through a tunnel incorporating suitably spaced electrodes; thawing 2 boxes would occupy 5 minutes. The total thawing time for the 250 bags needed for a 1000 L pool would be $\frac{1000 \times 5}{4 \times 2 \times 60}$ or about 10 hours, though it would not be necessary for this to be done in one session.

Transport of Frozen Plastic Containers Experience gained at Elstree and Brentwood and experience in Scotland indicated that the frozen plastic containers could be transported without thawing, if they were packed in insulated containers with a charge of CO_2 snow. A Jablo box would accommodate 2 Elstree bags

It was clear that a larger specifically designed insulated box would be required.

It was agreed that, if at all possible, there should be a single standard plastic bag. Mr. Watt took six Elstree bags for radio-frequency thawing tests. Dr Maycock arranged to send Mr. Watt one aluminium former as used at Elstree.

It was agreed that a meeting should be held when Dr. Jenkins had completed his filling trials of the Elstree bags and devised an "ideal" filling technique.

It was also agreed that a prototype insulated container for transporting frozen plastic bags should be designed and built, after the bag design for both centres had been agreed.

3. Plasma Protein Fraction

Production Assuming that new extension, Elstree, began to operate in 1971, it was possible that a considerable part of the change-over from dried plasma to PPF would have been accomplished by autumn 1972, when the B.P.L. Edinburgh might be coming into operation. It was hoped that PPF for England and Wales would then be provided as follows:

	Initially	Spare capacity
B.P.L. Elstree	62,000	28,000
B.P.L. Edinburgh	28,000	13,800
	90,000 bottles	41,800 bottles

(bottles containing 400 ml 4·5 g per cent protein)

Depending on the reception given PPF, it might be that Elstree would have to operate towards capacity before Edinburgh was ready. It was confirmed that the Edinburgh laboratory, when commissioned, would be able to fractionate 28,000 bottles PPF p.a., from plasma forwarded from England; the laboratory would not, however, have the spare capacity noted above until additional equipment had been obtained to bring its fractionation capacity to 1,500 L/week. PPF produced in Glasgow for England would be sent direct to Supply Dept for redistribution.

The meeting agreed that the proposed total capacity of about 130,000 bottles PPF p.a. seemed reasonable for the estimated needs of England and Wales during the next 10 years.

Specification Tests on pilot batches prepared at Elstree showed that PPS containing 85 to 87% albumin, measured after heating, was less stable to mechanical treatment and liable to form precipitates.

Data from both Elstree and Edinburgh indicated that an increase in the purity of the albumin in PPS resulted in a decrease in the proportion of aggregated protein observed after heating.

After further discussion it was agreed that the albumin content of PPF prepared at Elstree and Edinburgh should be in the range 90 to 95 per cent.

4. Uniformity of Containers and "Units" of issue

It was agreed that:

(a) as a general principle, Elstree and Edinburgh should use the same type and sizes of containers and the same "unit" or "units" of issue of any given plasma fraction.

(b) PPF should be bottled in 400 ml vols ($4{\cdot}5 \pm 0{\cdot}2$g per cent protein solution) in the lightweight disposable bottle being developed by Supplies Division, Ministry of Health. It was mentioned that Elstree was considering issuing PPF in appropriately designed 10-bottle cartons, which would be used by United Glass to deliver the empty bottles to B.P.L.

(c) Normal Immunoglobulin should continue to be issued as a 15 g per cent solution in 250 mg and 750 mg doses in the rubber capped vials at present used by Elstree and Edinburgh.

(d) Further discussion was desirable concerning the "units" of issue of anti-haemophilic globulin, Christmas Factor and specific immunoglobulins.

5. Costing

It was agreed that, eventually, the cost of preparing plasma fractions for the Department of Health and Social Security at B.P.U. Edinburgh would have to be calculated and appropriate charges made.

6. Ethanol Content of Certain Fractions

It was reported that ethanol varying from 0·10 to 0·43% w/v had been detected in 9 batches of frozen immunoglobulin and from 0·025 to 0·10% w/v in 13 batches of Elstree immunoglobulin.

Mr. Watt reported that, using an Alfa Laval Centritherm evaporator to remove ethanol, he found residual ethanol as follows:

30 g per cent immunoglobulin solution: ethanol 0·016 mg %

5 g per cent albumin solution: ethanol 0·005 - 010 mg %

He also reported that, using three different methods, reconstituted dried plasma had been found to contain 5 to 10 mg per cent ethanol.

7. Next meeting: It was agreed that another meeting should be held in February.