MEMO

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PROTEIN FRACTIONATION CENTRE

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Freeze-drying of 8Y at SRL

Following the recommendations made in JKS's memo of 30th July, Kevin and I have discussed methods of standardising the factor VIII freeze-drying procedures currently being used at SRL.

Kevin has now produced a standard programme to which I have added an expected product temperature profile. During Kevin's absence on leave, I am taking the liberty of circulating this proposal since I think it is important to have a standardised drying procedure before the factor VIII 'fix' goes in.

I hope I am not guilty of any libel in the following discussion, but I know I can rely on Kevin letting me know if I am.

Potentially important variation between freeze-drying cycles can be introduced by existing procedure in any of the following parameters:

1. **During primary drying**

   1.1 Temperature of the condenser coils at the start of the primary dry.

   1.2 Chamber pressure at the start of the primary dry.

   1.3 Product temperature profile during the first 2 hrs of the primary dry (probably caused by 1.2).

2. **During secondary drying**

   2.1 Length of secondary drying time (several days' variation possible).

   2.2 Final chamber pressure (0.01-0.05 mB).

   Standardisation should prevent variations in 1.1, 1.2 and 2.2, and is expected to reduce differences in 1.3. Cycle to cycle variation would therefore be reduced to the near inevitable loading and plant performance aspects (freezing rate, condenser temperature, etc.).

The basis of the proposed cycle is a modified version of the cycle which successfully dried 'fixed factor VIII' in 8Y 45. I will be surprised if this is the best way to dry 8Y, but we are not in a position to recommend improvements at present. Modifications were made mainly on practical and managerial grounds.

The main differences between the proposed cycle and the cycle used for 8Y 45 are as follows:

1. Time shelf temperature held at -50°C reduced from 15 hr to 10 hr.

2. Condenser cooling switched on 1 hr before the end of this period (effectively earlier than in 8Y 45).

3. Pressure controlled at 0.3 mB at the end of this period. Shelf refrigeration switched off by the programme but no positive heating. (Pressure allowed to fall to 0.05 mB before controlling
(4) Secondary drying final pressure increased from 0.03 mB to 0.05 mB.

(5) Secondary drying time at 0.3 mB decreased by 4 hr, and time at final pressure (0.05 mB) increased from 6 hr to 10 hr. Note that the total drying time excluding freezing remains the same at 54 hr.

The reasons for proposing these changes were as follows:

Change 1: To arrange manual operations within normal working hours as far as possible.

Changes 2-4: To standardise automatic operations as far as possible, allowing for 'worst case' plant performance, and the need to prevent triggering hard wired safety devices.

Change 5: Six hours seemed too short!

We hope that the result of these changes will be to minimise and restrict dry to dry variation to the phases hatched in the diagram, and to unforeseen events, plant malfunction, etc.

The product temperature probes currently in use at BPL, which were selected because of their relatively robust construction, are completely incapable of providing a meaningful temperature profile of the product during primary and secondary drying. I will investigate and in the first instance provide a supply of more suitable alternatives. These will certainly be rather more fragile and will require careful handling by all the departments involved (Freeze-drying, CF and Technical Services). Freeze-drying should be prepared to meet the cost of a higher turnover of these probes.

cc. Freeze-drying Working Party.