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NOTES OF 78 TROUBLE SHOOTING MEETING:

30 NOVEMBER 1989

- Present: R V McIntosh
- A J Dickson
- F Leslie
- M Crowston
- J Sinclair (Part)
- B Cuthbertson
- R J Perry (Part)

Item 1 Product Supply

The product supply "model" will be adapted to show the outcome of sample heating. Batches 243 244 and 245 have passed on sample heating since the last meeting.

The product for release column will contain only those batches which have been assigned to Labelling and Packaging.

27 December 1989 and 3 January 1990 will be deleted as production dates.

Action MC/BC

Item 2. Calibration and Validation of coolant supply

The upstand coolant supply flow rate pattern is very similar when measured under non-operating and operating conditions (Fig 1).

A more detailed analysis than we considered at our last meeting, of simultaneous cryo super temperatures and coolant flow rates (see Fig 2) confirms their close relationship. Establishing the exact nature of the relationship is made difficult by cycling of the coolant temperature (see Fig 2) in addition to flow rate changes.

Having confirmed that coolant flow rate and cryo super temperatures are related it is now necessary to determine whether or not that relationship is evident from 10 minute time points taken throughout the course of thawing and cryo pptn. In this way we can compare current and past coolant control using the stored data on cryo super temperatures at 10 minute intervals.

We already have some data like this (see 14 November 1989 notes) and we will expand these by looking at cryo super temperatures and coolant flow rates during the processing of cryo's of known poor quality (eg 241, 242, 244).

Action AJD

Our aim is to be able to specify:

- 1) A coolant temperature eg.  $-25 \pm 2^{\circ}\text{C}$
- 2) A coolant flow rate eg.  $300 \pm 100\text{mm H}_2\text{O}$  (Barco)

Which will allow us to:

- 3) Limit the cryo super temperature to within a specified range eg.  $+1.5^{\circ}\text{C}$  to  $+3.0^{\circ}\text{C}$ .

Altering the nature of the coolant supply system alone may not be enough to achieve these objectives and improving coolant valves at upstands or introducing some form of automated control at upstands may be necessary.

Different proposals may come from Engineering (maintenance) in their report on coolant supply.

Action RL

Item 3 Cryo quality: Trend analysis

A nearly complete list of data from batch 113 onwards for those items of cryo quality specified at our last meeting has been assembled.

On an initial scan the most obvious trend is to an increasing fibrogen content per unit cryo weight. This is consistent with increased fibrinogen and fibronectin resulting from coolant problems and also with our longer term 'improvement' (decrease) in cryo wt per unit volume of plasma.

However, because the cryo ppte is extracted in a volume related to its weight, the presence of the same or an increased amount of fibrinogen in a smaller cryo wt means that the fibrinogen concentration in the extract will be increased making the Zn pption step less efficient. This may be contributing to the longer term overall decline in Z8 solubility which it is generally considered there has been.

An investigation into retitrating the Zn concentration for optimal precipitation of fibrinogen and/or altering the cryo:buffer extract ratio from the extract is scheduled for R&D.

Action R.M

The cryo quality data will now be analysed following separation into different populations either by relevant processing events/charges (eg. Quickfix; PCU breakdown; non PCU conditioning; new PCU; in-line cryo suspension (etc.)) or by cusum analysis and fitting any resultant populations to process changes.

Action BC

Item 4 UF Performance

Data for UF over the Millipore/Filtron change and over the down time have been assembled (Table 1).

FA Filtron post shutdown V FA Filtron pre shutdown;

FA Filtron pre shutdown V FA Millipore pre shutdown and

All FA Filtron V FA Millipore will be compared.

Action FL

Item 5 Bung Preparation

Some data on moisture content pre and post HT has been collected (Table 2). There is little post shutdown information (when the Huber started) but there is no immediately obvious change in moisture content before and after the onset of recent solubility problems.

However further data are needed.

Action BC

Until further data are available and because it will improve control over moisture content anyway we will continue to use dried bungs in Z8.

Action ND

As a general policy it would be preferred if all 22mm FD bungs were prepared in the same way. R&D will investigate the effect of 'dried' bungs in HT of DEFIX.

Action RVH

Item 6 Final Product Trend Analysis

No data yet.

Action BC

Item 7 Reworks

232 showed 97% recovery when reworked as outlined previously to 232-4. A vial content of 195iu (8th British Conc. Std.) is projected.

No further material will be planned for rework until we have further updated product supply projections and we have post trial HT data on 232-4.

Action RVH

Next Meeting Thursday 7 December 1989 1100 hours Seminar Room