UK BTS/NIBSC

Ad hoc meeting on tests for viral contamination in blood products, held on Tuesday, 28 June 1988 at 2.30pm at NIBSC.

Present:

Dr J H Napier	Acting Chairman (WG Microbiology)	RTC Cardiff
Dr D R Bangham	Secretary	NIBSC
Dr T W Barrowcliffe		NIBSC
Dr B Cutherbertson		PFC Edinburgh
Dr J Garrett		NIBSC
Dr P Minor		NIBSC
Dr J Smith		PFL Oxford
Dr D P Thomas		NIBSC

Papers available included:

- Specification for the validation of virus inactivation procedures used during the manufacture of clotting factor concentrates. Draft May 1988 - B Cuthbertson for WG.PF.
- Report of a meeting held at NIBSC 30.3.88 on contamination of blood products with viruses: detection and validation of inactivation procedures. (Dr D P Thomas)
- Factors to consider in the study of inactivation or removal of viruses from therapeutic products (D R Bangham)

1 The meeting was arranged with virologists at NIBSC to review the draft papers of the BTS/NIBSC Liaison proposed guidelines concerning the measures to remove/inactivate virus in the preparation of blood products and the validation of those measures. The paper mainly under consideration was the May draft listed above, which refers to bulk plasma for production of clotting factor products.

2 Outline of production methods

Such products are derived from large pools of 1-2000 litres, or more. These large pools are made by adding successive batches of 200-500 donations, after they have been crushed and thawed and centrifuged to remove cryoprecipitate. The supernatant from a (defined) large pool is then fractionated with cold ethanol to produce the two main products albumin (which is then pasterized) and immunoglobulin products. The cryoprecipitate bulk is further fractionated (eg by chromatography) to make Factor VIII and Factor IX products; the residual albumin and immunoglobulins are added back to the 'cryosupernatant' for further extraction.

Points agreed included:

- The main protection against virus contamination rests in the measures taken to select donors and screen the individual donations. Detection of contamination after addition of a single plasma to a large volume pool was statistically much less probable.
- The size of each bulk plasma pool must be identified during manufacture, and a sample of it sent to NIBSC for additional tests for HIV and hepatitis viruses.

- The validation of a purification process should include at least one step shown to effect at least 10^5 reduction of the titre of the spiked virus, and show that the combined overall procedure effects a reduction of about 10^8.
- The several factors which can influence estimates of virus reduction/inactivation will be mentioned in the introductory preamble.
- The tests should rely on estimates of residual active particles, not on indirect assay systems such as estimates of enzyme activity.
- Dr Cuthbertson will revise the document in the light of the discussion and send it to those who attended this meeting for approval.

Tests for HBsAg

- No specifications for a detection limit can be made until a national working standard could be produced for use in all 20 RT centres;
- Estimates of the number of ampoules needed are being made - about a million donations/year need to be tested;
- No progress can be made until satisfactory premises for filling and freeze drying the material becomes available: this is being considered at NIBSC. Dr Morag Ferguson (NIBSC) will be responsible for setting up such a standard.

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