NOT FOR PUBLICATION

COMMERCIAL IN CONFIDENCE

The Safety of Immunoglobulins

1. The CSM at its January meeting endorsed the decision of the Biologicals Sub-Committee. (Minutes appended).

A letter has been sent (28.2.86) to all licence holders for immunoglobulins asking them to apply for variations to their product licences to cover the following points in the minutes.

1.1 All immunoglobulin preparations should as soon as possible and not later than 1 July 1986 for intravenous and 31 December 1986 for intramuscular be prepared only from donors shown to be HTLVIII antibody negative.

1.2 Manufacturers should provide evidence of the capacity of their process to inactivate viruses by 1 July 1986 in respect of intravenous, and 31 December 1986 in respect of intramuscular immunoglobulin preparations.

They have also been informed that no preparations containing HTLVIII antibodies will be released.

It is anticipated that all companies (with the possible exception of Sandoz) will be able to comply with Point 1 immediately. All companies have virus inactivation studies in house. No reports of seroconversion after immunoglobulins have been received or noted since the last meeting of the EAGA.

2. A meeting was held at NIBSC on 7 February to discuss "Virological Aspects of the Safety of Blood Products". The views of the CSM were upheld, and it was decided to form an informal working group to review developments in this field. Objectives which have been suggested for this group are:

2.1 to provide a forum for the exchange of technical and scientific information pertaining to the safety of blood and blood products especially in relation to virus contamination and the evaluation of the capacity of manufacturing procedures to inactivate and/or eliminate viruses.

2.2 to consider the need for and pursue collaborative research work in relationship to the prevention of transmission of LAV/HTLV-III and NANB hepatitis by blood products and the evaluation and further development of testing methods for blood donations and products, and

2.3 to consider the need for ongoing surveillance of recipients of blood products for evidence of viral infection.

BPL Elstree, PFC Edinburgh, NIBSC and Medicines Division DHSS will be represented on this group.

GRO-C

4 March 1986

DR F ROTBLAT

csm|86|1st Meeting

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COMMITTEE ON SAFETY OF MEDICINES

BIOLOGICALS SUB-COMMITTEE

THE SAFETY OF IMMUNOGLOBULIN PREPARATIONS

This paper was reviewed by the Biologicals Sub-Committee.

1. **New evidence was considered concerning the safety of immunoglobulin** preparations with respect to transmission of infection.

   1.1 Some batches of immunoglobulins have been found to contain antibodies to HTLVIII. This is not an unexpected finding as most preparations available at present are derived from donations not screened to exclude antibody positive donors.

   1.2 At least one report suggests that HTLVIII virus may not be inactivated or eliminated by the version of the Cohn cold ethanol fractionation process used to prepare immunoglobulins, in the study (Prince et al).

   The Sub-Committee felt that the relationship of these laboratory findings to manufactured material was tenuous, especially in view of the fact that other studies have shown good evidence that the cold ethanol process is effective in this context. However manufacturing processes using ethanol fractionation vary considerably.

   1.3 HTLVIII like agents have been isolated from one patient treated with an intravenous preparation (Sandoglobulin) for hypogammaglobulinaemia. The patient is apparently suffering from AIDS and no other risk factors have yet been identified.

   The virological evidence in this patient is however not clear cut and it is possible that the virus is not a true AIDS virus and did not derive from the therapeutic use of the immunoglobulin.

   HTLVIII like virus has also been isolated on two occasions from a second patient who had received BPL and Gammimmune (Miles) intravenous immunoglobulins. This patient has previously contracted non-A, non-B hepatitis, probably from the BPL batch.

2. The Sub-Committee was aware of the long safety record of intramuscular **immunoglobulins with respect to the transmission of infection. In particular there has been no evidence of transmission of HTLVIII infection by intramuscular immunoglobulins, despite their extensive use and preparation from sources that will have included HTLVIII infected donors.**

   The safety of intravenous immunoglobulins is possibly less certain. There have been only a few documented incidents of transmission of NANB hepatitis and, until the case referred to above, no reported cases suggestive of HTLVIII transmission.

3. The Sub-Committee noted that immunoglobulin preparations are of considerable clinical value and in some circumstances life-saving.

4. The Sub-Committee recommended on the evidence considered that no new licensing action to withdraw or restrict supplies should be taken in respect of intravenous or intramuscular immunoglobulin preparations.

However

4.1 All immunoglobulin preparations should as soon as possible and not later than 1 July 1986 for intravenous and 31 December 1986 for intramuscular, be prepared only from donors shown to be HTLVIII antibody negative.

4.2 **As from now no preparations containing HTLVIII antibody in the plasma pools, bulks, or final product should be released for use.**

4.3 **Manufacturers should provide evidence of the capacity of their process to inactivate viruses by 1 July 1986 in respect of** intravenous, and 31 December 1986 in respect of intramuscular immunoglobulin preparations.

4.4 The Sub-Committee considered that at present there was insufficient evidence to justify changing the indications for use of immunoglobulin.

5. The Sub-Committee recommended that close surveillance should be maintained of the development of any new virological, epidemiological or clinical data.