

NOT FOR PUBLICATION

COMMERCIAL IN CONFIDENCE

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.