The Use of vapour heating as virus inactivation method for FEIBA VH

Vapour heating as the alternative to inactivation in dry heat

Our clinical experience with vapour heated coagulation factor concentrates provided us with evidence for the choice of the most appropriate inactivation method for a FEIBA preparation. In a controlled multicentric study with virginal patients in Italy, preliminary results of the follow-up evaluation showed that neither hepatitis non A/non B nor HTLV-III were transmitted by substitution therapy using factor VII, factor VIII, and factor IX concentrates which had been vapour heated. This result had not been reported in any clinical trial using heat treated concentrates, and has not been reported since.

Rumours of HTLV-III-seroconversion following the use of dry heated products were later confirmed in the Lancet (see enclosures). At the outset of these rumours we pursued most rigorously the idea of vapour heat treatment.

It was thus decided to develop a product specific method for FEIBA by selecting the optimal physical parameters of the vapour heating procedure. Model virus experiments with ICHV (Infectious Canine Hepatitis Virus) showed that virus experimentally added to the preparation in a medium of increased moisture were inactivated much more efficiently than under dry heat conditions (see table 1).

Choice of the moisture content of 7.5 ± 0.5 %

(We regret a typing error in our submission. The actual moisture content should read 7.5 ± 0.5 %)

In a series of studies the influence of different moisture contents on the biological activity of the FEIBA preparation was investigated during vapour heating while the other reaction parameters were kept constant. The results in table 2 show that the FEIB-activity was only reduced to an acceptable extent during a 10 hours treatment at 60°C if the moisture content of the freeze-dried powder was kept at 7.5 %. However, the application of still higher amounts of moisture drastically reduced the FEIB-activity even during much shorter periods of treatment.

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Choice of the temperatures

As shown above, vapour heating for 10 hours at 60°C is an efficient method for virus inactivation. Contrary to Factor VIII, FEIBA allows also short term vapour heating at higher temperatures without producing neoproteins, but with efficient inactivation of HTLV-III during this treatment (see data enclosed in the "Rationale For Using Steam ..." sent to the DHSS earlier this year). Therefore IMMUNO has designed a two step vapour heat treatment for FEIBA including a 1 hour treatment at 80°C.

This last step is meant to provide an additional safety marge for unknown heat-stable viruses.

Table 2

Rate of inactivation of FEIB-activity with freeze-dried FEIBA adjusted to different moisture content

Hours at 60°C	0	0.3	1	3	10	30	Moisture content
FEIB-activity (initial activity set as 1)	1	-	-	-	1	1	0.015 (1.5 %)
	1	-	0.82	0.79	0.77	-	0.075 (7.5 %)
	1	-	0.66	0.58	0.43	-	0.150 (15.0 %)
	1	-	0.34	0.17	0.05	-	0.250 (25.0 %)