TABLED QUESTIONS/ANSWERS

U.K. HAEMOPHILIA CENTRE DIRECTORS MEETING

10TH OCTOBER 1986

1. **What specific information caused the withdrawal?**

: On 29th September we received a telephone report of two U.K. sero-conversions potentially associated with Armour I.P./H.T. FACTORATE product.

: On the same day we contacted the D.H.S.S. Subsequently, we met them on 3rd October and 6th October.

: The conclusion reached at the 6th October meeting was that Armour would relinquish our Product Licences for FACTORATE I.P. and H.P. products.

Other factors in addition to the two sero-conversions reported on 29th September were as follows:-

1. Armour previously reported three sero-conversions possibly related to FACTORATE I.P./H.T.

2. Neither the D.H.S.S. nor the U.S. F.D.A. had any other reports of sero-conversion associated with heat treated product.

3. Armour's heat treating cycle uses a lower temperature and shorter time than other U.K. Factor VIII products.

2. **Please inform us if any of these cases are inter-related by batch numbers?**

: All cases were multiply treated but,

: Apparently the only batch relationship is a single common batch used by each of the most recently reported cases.

: We have no indication that there is a batch relationship to the potential problem.

3. **Was there donor testing of the batch or batches?**

: In all cases, the product associated was manufactured from plasma collected prior to the availability of HIV antibody screening procedures.

: These procedures were implemented by Armour in April 1985 and phased in January-June 1986.

: All five patients involved have been previously treated with unheated product produced from unscreened plasma.

4. **Please inform us if in any case of sero-conversion a donor or donors with AIDS, AIDS related disease or HIV antibody positivity has subsequently been traced?**

   : In two of the five previously described cases, a single plasma pool is known to have contained donations from one individual who subsequently developed AIDS. These two cases were not the two most recently reported.

   : ARC has not been related to any donor or batch.

   : With regard to HIV positivity, we have yet to complete the review. It is not possible to follow up donors who voluntarily leave the panel and, although we can trace by donor, it is an enormously time consuming exercise.

   : Because the material was unscreened, we assume that a small number of donors were positive. Initial positive tests were 0.25%. Currently donors testing positive represent 0.05%

5. **Are the two cases of sero-conversion associated with batches of FACTORATE withdrawn in earlier communication from Armour this year?**

   : Yes, the FACTORATE was manufactured prior to HIV antibody screening of donors.

6. **If so, why are current donor-tested batches being withdrawn?**

   : I believe that we answered this question in the first one. We agreed to relinquish our Product Licences (after discussion with the D.H.S.S.).

7. **Alternatively, why weren't all batches withdrawn at the previous communication?**

   : We examined those data at that time. Our experts, independant authorities, the D.H.S.S. and the U.S. F.D.A. unanimously concluded that those data were insufficient to warrant product withdrawal.

   : No case of sero-conversion has been associated with screened plasma.

   : Yesterday, the F.D.A. took the same decision again.

   : We will go through a rapid but exhaustive review, and if we were to determine further evidence to suggest that the product <u>was</u> unsafe, we would remove it worldwide.

8. **Please give full clinical and laboratory data on each of the cases known to have sero-converted on Armour material, in this and other Countries?**

   : First, we do not know that patients sero-converted <u>as a result</u> of Armour product, but they were being treated with Armour product when they sero-converted.

: Two of the cases have been described in The Lancet. Those are the cases of Vandenberg et.al. and White et.al. We can provide references upon request.

: The three remaining cases from the U.K. are yet to be completely documented and are priviledged information from the Physicians involved. Under these circumstances, at this stage, we can disclose no more information than what has been said.

9. **Have cases of HIV sero-conversion or NANB occured due to administration of current donor-tested/heat treated material, anywhere in the world?**

: None has been reported to our knowledge.

10. **Please would the Company comment on the implied suggestion in its statements that the product might only have been unsafe because donors who had not been HIV antibody tested were implicated?**

Surely, this has little relevance because the method of viral inactivation used must have failed and the failure will not be affected by testing?

: Again, we accept the association between Armour heat-treated FACTORATE and these two sero-conversions, although this is still a step removed from allowing us to demonstrate causation.

: Secondly, we believe that the initial viral load in any plasma pool is of particular relevance.

: In laboratory conditions, it is possible to spike plasma to such high titres that no currently available process will totally inactivate the challenge.

: Virology experts have calculated what amount of AIDS virus could exist in the pooled plasma donations for each batch of our product. Our laboratory experiments demonstrate that our manufacturing process destroys in excess of that amount.

11. **What method of heat-treatment, what temperature?**

: Armour heat-treats in a dry state at 60°C for 30 hours without the addition of stabilising agents.

12. **Is there any laboratory data which suggests that heat-treatment as used by Armour may not be effective in removing HIV?**

: No, on the contrary, three studies have demonstrated that our manufacturing process inactivates virus in amounts in excess of the theoretical maximum expected viral challenge.

: I emphasise that I am referring to the entire manufacturing process. Recently completed work in our Meloy Laboratories indicates, for example, that additional purification steps inactivates additional virus.

13. **Why was no statement made by the Company after the first reports earlier in the year?**

: Dr. Peter Harris, our Medical and Technical Director in the U.K. issued a letter to all users in March 1986.

: In that letter, he invited contact should anyone be concerned about Armour products as a result of reports in the literature concerning sero-conversion after using heat-treated product.

: He also included Armour's viral inactivation data and information on donor screening.