HIGHLY CONFIDENTIAL

MEETING AT BPL

Wednesday, 15th December 1982

Present: Professor A. Bloom
Dr. C. Rizza
Dr. H. Gunson
Dr. J. Craske
Dr. J. Cash
Dr. R. Lane
Dr. M. Harvey
Dr. J. Smith

Agenda

The implications for the Haemophilia and Blood Transfusion Services of Commercial Introduction of "Hepatitis-Safe" Factor VIII and IX.

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1. Commercial Consideration

Factor VIII concentrates occupy 13% of the gross operating turnover of blood products. Factor VIII therefore lies fourth to albumins, specific immunoglobulins and normal immunoglobulin which collectively occupy 86% of the market. Factor IX, with all other products, occupies less than 1% of the market.

N.B. Reduction of use in [illegible] many

Price instability in the world market on blood products has introduced many bizarre effects, particularly in Europe. The price battle for Factor VIII intermediate concentrate in the UK is an example. Intense competition and unacceptably low prices is alleged to have resulted in the withdrawal of Hyland Hemophil II from the UK market and the threatened possibility of a second major company withdrawal in 1983. Companies preparing field for price increases e.g. Safe-product

The withdrawal of standard intermediate concentrate allows certain logical predictions:

(1) Residual monopoly of standard concentrates allows lack of competition to move the price upwards.

(2) A clear-field entry for commercial "Hepatitis-Safe" Factor VIII, which by nature of its "special-product" status (unproven) can command a price structure more in keeping with market expectations.

(3) Through loss of yield in production of "Hepatitis-Safe" products, "special status" is augmented by scarcity value since there must be a shrinkage in world availability of the new concentrates.

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2. UK Options in Production

(1) Expansion in output to meet UK demand

(2) Evaluation of "hepatitis-safe" status - incurred penalties - economic considerations ? Protein status of products vs VIII:C status e.g. continued injection of 'heat' aggregated protein.

(3) Evaluation of acceptable methodology into hepatitis inactivation and acceleration into production.

3. Current Commercial Approach to UK Users

The random approach now being adopted by commercial manufacturers to haemophilia directors in UK to study "H-S VIII" has many severe disadvantages for the NHS and gives little or no payback to the UK in return for opportunistic and non-contractual use of the special potential of the UK Haemophilia Service as a collective entity.

(1) Legal/Regulatory basis

(a) Only importation of HSVIII HSIX for use in named-patients is permissible

(b) For Clinical Trial - import licence is needed and no exemption would be offered

(2) Product Status

HSVIII and HSIX are the end-products of new processes for which formal licensing is ultimately required. Under 1(a) above, the manufacturer is not obliged to reveal any data on process or product at the early stages of development and trial in patients. Under 1(b) above, the manufacturer would be required to set out to the Regulatory Authority all required details on process, final product and tests of quality control, batch-to-batch reproducibility, toxicity test data and interim basis for claims of improved safety and efficacy.

N.B. In the final analysis, the licence application will be judged, amongst other factors, on process but particularly on evidence of safety and efficacy. It is essential to know that process and product used to demonstrate inactivation of virus in products at an early stage of product development (prior to trial) is the same, or as good as, the process to be used in normal manufacture. It is essential to bear in mind that the virus inactivation process may carry significant (and undeclared) yield penalties and that primate-based batch control is unlikely to support QC data in regular production. The true basis for claims of safety in regular production lies with on-going prospective studies in humans.

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3. Efficacy and Safety of HSVIII and HSIX

The above statement defines the need for centralised, fully controlled prospective trials of "HS" materials, best operated through a properly executed National Clinical Trial lodged with the Regulatory Authority.

End results will carry a level of significance of value to user and producer. Information beneficial to the UK will be optimised.

Manufacturers entering the trial should undertake to make positive contributions of data and financial support in return for a properly conducted trial in a well-documented community of haemophiliacs.
[It is realised that overseas producers do not have access to trial facilities of equivalent quality and veracity elsewhere.]

4. Proposals

(a) That random exploitation of the haemophilia service by commercial organisations for the study of "hepatitis-safe" products should be discouraged.

(b) That the Haemophilia Services should create a formal basis for controlled clinical trial of alleged "hepatitis-safe" products in line with the requirements of Medicines Act.

(c) That the Haemophilia Services, PHLS and NBTS should combine resources in a manner likely to advance economic treatment of NHS haemophiliacs with safe products.

R. S. LANE,
Director, BPL.
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