OXFORDSHIRE HEALTH AUTHORITY

OXFORD HAEMOPHILIA CENTRE

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MEMORANDUM

To: All U.K. Haemophilia Centre Directors

TRIALS OF 'HEPATITIS REDUCED' FACTOR VIII - AN UPDATE

Directors will recall the "aide memoire" circulated with paper for the September 1983 annual meeting which described the types of factor VIII concentrate which would be available for clinical trial in 1983-4. We have recently reappraised the situation and there are at present 8 different products in preparation or available for trial. Clinical trials have only been completed on one product, the "Hemofil HT" factor VIII, which is prepared using a 'dry heat' method. The results indicated that there was still a 63% attack rate of non-A, non-B hepatitis on first exposure to this product in patients who have not received factor VIII concentrate previously. These trials are difficult to evaluate as for ethical reasons no control group was used.

The products currently available are:-

(1) Heated products from Armour, Cutter, Travenol and Alpha Therapeutics. The 3 former are 'dry heat' preparations and the latter (Alpha Therapeutics) is a wet heat product.

(2) NHS factor VIII prepared from a specially selected donor panel which is monitored for abnormal LFT's, hepatitis, etc.

(3) Heated NHS factor VIII; one brand is manufactured at the PFC in Edinburgh and will be shortly available. The second, manufactured at Elstree, should be available later this year.

(4) A heated preparation manufactured by Behringwerke, the German Pharmaceutical Company. This is heated at 60°C for a period known to inactivate hepatitis B in the preparation. The problem is that the yield of factor VIII coagulant activity is considerably reduced, so that the cost is likely to be at least 4 fold higher - ?40p per unit. Trials have been carried out in Germany, but no published information is available. At least 30 patients have been studied.

All products except those derived from NHS factor VIII are made from plasma imported from the U.S.A., and, therefore, they carry a putative risk of transmission of AIDS. It is evident that 8 products will be shortly available on the market and, unless these

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are coordinated, there will not be enough patients available to evaluate each product carefully.

We would therefore ask that you take the following action:-

(1) Draw up a list of patients in your Centre who might be suitable for such a trial on the basis of previous blood product exposure, and who are likely to require treatment with factor VIII in the near future.

(2) Notify Miss R.J.D. Spooner at the Oxford Haemophilia Centre of the number of such patients available.

(3) If approached by a Pharmaceutical Company or you are proposing to try one of the NHS products, please let Miss Spooner know what product you intend studying and how many patients will be involved. She will circulate information about all the trials, so that any patients still available who are uncommitted can be used for one of the remaining products, subject to the wish of the local Haemophilia Centre Director.

(4) It is important to ensure that each Company obtains an exemption from a clinical trial certificate from the U.K. Licensing Authority. Studies conducted on a named patient basis carry no protection under the Medicines Act, as the patient's doctor and not the Pharmaceutical Company carries the liability for compensation arising out of unexpected hazards which come to light as part of the trial.

(5) We suggest that the protocol circulated by the Hepatitis Working Party last year should form the basis for the studies. Dr. Craske would be grateful for serial specimens from patients studied to form the basis of a collection for study if markers for non-A, non-B hepatitis become available.

We hope that Directors will collaborate as suggested in this document so that the maximum information about the relative merits of different products will become available with the most economical use of the limited number of patients available.

A.L. Bloom
Chairman, Haemophilia Centre Directors Organisation

John Craske
Chairman, Haemophilia Centre Directors' Hepatitis Working Party

C.R. Rizza
Secretary, Haemophilia Centre Directors Organisation