COMMERCIAL IN CONFIDENCE

NOT FOR PUBLICATION

COMMITTEE ON SAFETY OF MEDICINES

Sub committee on Biologicals.

The Need for Validation of In Vitro Screening Tests for Viral Contamination Of Blood Donations Used in the Manufacture of Blood Products

This paper has been submitted by Dr G Schild and Dr D P Thomas of NIBSC.

Draft Recommendation

The Sub-Committee noted the paper and endorsed its recommenations.

1. All manufacturers applying for new licences for blood products should supply full informationon the screening procedures currently carried out for HIV and HBsAg. Information on the quality assurance and performance evaluation of the kits should be supplied.

2. Ongoing monitoring for current licence holders and for all new licences should be by submission of quality assurance and performance evaluation data with the protocols supplied for the batch release process.

3. The Licensing Authority should write to individual manufacturers and ask them to provide this quality assurance information from a data to be agreed.

THE NEED FOR VALIDATION OF IN VITRO SCREENING TESTS FOR VIRAL CONTAMINATION OF BLOOD DONATIONS USED IN THE MANUFACTURE OF BLOOD PRODUCTS

In June 1986, a letter was sent on behalf of the Committee on Safety of Medicines to all manufacturers of blood products, recommending that in future only blood donations that had been tested for the presence of antibodies to human immunodeficiency virus (HIV) and found negative should be used as source material for manufacture of these products. In October 1985, screening of blood donations for the presence of antibodies to HIV was introduced by the National Blood Transfusion Service (NBTS). Screening of blood donations for hepatitis B surface antigen (HB_sAg) as an index of HBV infection has been a routine procedure for over 10 years.

Some 5-10,000 donors may contribute to a plasma pool from which a blood product is manufactured. A single virus-infected donation may potentially contaminate a large plasma pool and the products derived from it. Consequently, the characteristics of the screening methods for HIV and HB_sAg in terms of their reliability, sensitivity and specificity is of critical importance for the virological aspects of the safety of products prepared from blood donations.

Screening tests for anti-HIV and hepatitis B surface antigen are carried out at the point of blood donation. Testing of the final product has a role in securing freedom from contamination by HIV and HB_sAg, but tests applied to the final product are of limited value in detecting evidence of viral contamination because of the large degree of dilution of individual donations in a pool of several thousand. There are reports of patients being infected with hepatitis B or HIV, despite negative results when the relevant final products were tested.

There is currently no control of the commercial test kits employed for screening of blood used in the preparation of blood products. Such test kits are not licensed under the Medicines Act, and there is currently no independent routine evaluation of test kit samples. A measure of security of the performance of test kits can be provided by the manufacturers' own routine quality control arrangements for each batch of kits. In addition, checking of test performance is normally undertaken by including panels of control sera at the point of use. Supplies Division of the DHSS has influence as a central purchaser, and the PHLS carries out evaluation of the various test kits for HIV antibodies. However, in West Germany and the USA, HB_sAg test kits are licensed by the national control authorities and the performance of samples of kits from each manufactured batch is routinely monitored against licence specifications.

Not all blood products are heated to inactivate viruses, and the safety of the product is heavily dependent on the validity of the screening procedures. There is an urgent need for the Licensing Authority to be more fully informed about the performance, reliability, consistence and quality of the screening tests, usually in the form of test kits, employed by all manufacturers of blood products. It is suggested that the Licensing Authority requests full information on the screening procedures currently carried out by, or on behalf of, all manufacturers of blood products used in the UK. In particular, manufacturers of blood products should be asked to provide the Licensing Authority with complete information on the quality assurance tests and performance evaluation carried out on each batch of the kits or reagents used for the testing of blood donations used in manufacture. Information should also be provided on what standards are used, whether positive and negative controls are used, and what is the sensitivity and specificity of their test kits for relevant viruses. It is

recommended that this information should be provided by manufacturers of blood products as an adjunct to the Licence application and should apply in the first instance to tests for antibody to HIV and for HB_sAg antigen. Ongoing quality control data on individual batches of screening test kits or reagents should be included in batch protocols provided to NIBSC.

The views of the Biological Sub-Committee of the CSM are sought on this matter.

G.C. Schild
NIBSC

D P Thomas
NIBSC

27th April 1987