Bayer

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Dr. R. D. Andrews,
Senior Medical Officer,
Department of Health and Social Security,
Medicines Division,
Finsbury Square House,
33/37a Finsbury Square,
London EC2A 1PP.

Your ref/date Date 11 May 1976 Our ref JB/jm Haywards Heath

Dear Dr. Andrews,

Anti-Haemophilic Factor (Human) Koate - PL/0010/0061

I am now in a position to supply you with the outstanding information for Koate which you requested in your letter of 11th March, 1976. I do not know whether you have yet received from the U.S. Bureau of Biologics the data concerning the calibration of the U.S. Factor 8 standard against the International Standard, which I informed you about in my letter of 23rd April, 1976. I have been assured by Cutter that there should be no problem.

In addition, we have the following comments to make on the points raised in your letter:

1. In-house standard

The current in-house standard, Lot 1588-77, was prepared from plasma obtained from 16 normal donors. The plasma was collected by plasmapheresis in a licensed plasmapheresis centre using sodium citrate anticoagulant. Following collection, each unit of plasma was transported in crushed ice to Cutter's laboratory and assayed for Factor VIII levels. The 16 individual units, each containing approximately 250 ml of plasma, were pooled and thoroughly mixed. Following mixing, the plasma was filled via automatic filling equipment into clean sterile 6 ml vials. The fill volume was 2.25 ml per vial. Approximately 1500 vials were filled. Following filling the plasma was frozen and lyophilized. The vials were then labelled and stored at -70°C or colder. The process, from collection of the plasma to lyophilization required four hours. The filling operation was performed at 5°C.

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Accelerated degradation tests have not been conducted. Since the standard is stored at -70°C or less there is no reason to question the stability. It is felt that the accelerated degradation studies would yield no meaningful data with regard to stability of the standard.

2. Batch to batch reproducibility

The three protocols which we sent to you with our letter of 27th February, 1976 represented consecutively produced and released lots of Koate even though the batch numbers were not sequential. However, to avoid confusion we are sending an additional protocol for bulk lot MO 46571. This, together with the protocols previously sent for lots MO 46569 and MO 46570, provides information on 3 consecutively produced lots which are sequentially numbered as well.

3. Labelling

If we are still required to put statements on our labelling regarding the limits of citrate, fibrinogen, sodium and chloride, we will place the following limits on the vial carton and we would submit a sample of the new labelling as soon as it was produced.

Citrate	Not more than 55 mMoles/L
Fibrinogen	Not more than 0.25 gm/10 ml
Sodium	Not more than 200 mEq/L
Chloride	Not more than 200 mEq/L

I trust that this information answers the question of the Committee and that we shall soon obtain a Product Licence.

Yours sincerely,

GRO-C

Mrs. J. M. Boult, B.Pharm MPS
Registration Officer.