Immuno Ltd

Arctic House, Rye Lane, Dunton Green,
Nr Sevenoaks, Kent TN14 5HB

Telephone: Sevenoaks (0732) 458101
Telex: 95413

27th September 1983
NB/BMC

Dr. H. Eibl

Dr. O.F. Schwarz

Dr. K. Anderle

Mrs. I. Diernhofer

We have now been informed that the Committee on Safety of Medicines are unable, on grounds of efficacy and quality, to recommend the Licensing Authority to issue a Product Licence for Feiba.

You will notice that they have not included, "on grounds of safety", so we will not be prevented from continuing to sell on a doctor/named patient basis.

You will be further pleased to know that apart from a minor detail, they have accepted the additional data on the manufacturing process so that is one big hurdle passed.

The items remaining are the following:

3.2. The Committee considered that inadequate evidence of efficacy had been provided for Haemophilia A patients with Factor VIII inhibitors and agreed that point 2 of the Section 21(1) letter had not been answered. This said "Adequate evidence of efficacy should be provided for Haemophilia A patients with Factor VIII inhibitors".

I will endeavour to pin them down on exactly what is wanted, but this may also mean a visit to the professional staff by Dr. Eibl Dr. Anderle and myself.

3.4. The Committee were reassured by the additional data supplied by the Company on the manufacturing process with the exception that full details of the ethylene oxide sterilisation procedures for all components should be provided. They agreed that if this was done, point 4.i. of the Section 21(1) letter had been cleared. This said "We should provide complete data on the manufacturing process".

We have ascertained that the problem here is twofold:

.../2

(a) The failure of Sherwood in Ireland to answer a letter from the Medicines Division asking for details of their ethylene oxide sterilisation procedures, including tests for and limits for residues. We have written to Sherwood in Ireland asking them to expedite a reply concerning syringes, filter needle and transfer needle.

(b) We must ask you for full details from Transcoda on similar lines as above concerning the aeration needle.

3.6. The Committee were not reassured by the additional details of the Immuno house standard for lyophilised inhibitor plasma and agreed that point 4.iii of the Section 21(1) letter had not been answered. This said, "Additional information should be provided on the details of the Immuno house standard for lyophilised inhibitor plasma". The answer you provided was "Only plasma of one individual donor is used. The inhibitor titre ranges between 20 - 100 Bethesda units".

We believe this has been interpreted as meaning we rely on one single individual and, therefore, they have asked for clinical details of the donor and an explanation of what you would do in the event of losing this donor. It is more likely that what you really meant was that you used single donor plasma, (not pooled), which could be obtained from any one of a number of donors, provided they were in the inhibitor range.

However, can you please confirm this and provide any more information along the following lines:

(a) Actual methods for determining the Bethesda units in the house standard

(b) The reason for defining a Feiba unit as follows: "One Feiba unit is defined as the FEIB activity shortening the activated PTT of a high titre Factor VIII inhibitor plasma, (Immuno House Standard), to 50% of the blank value".

(c) Confirmation that the method used does result in a product the batches of which are reproducible as far as uniformity of potency is concerned.

(d) They do not, it would seem, understand how the test is done and this can perhaps be made clearer. It is perhaps confusing to describe the selected inhibitor plasma as Immuno House Standard and in the next sentence say it can be any where between 20 and 100 units. We believe they are puzzled as to whether or not the test is a true one because they think some further activation of the Feiba sample under test occurs during the incubation stage of the PTT test because of the presence of kaolin.

We ought to stress the fact that we are measuring the difference between the test sample and a blank value on every occasion.

We hope to obtain even further clarification of this point in about two weeks time.

.../3

3.7. The Committee were not reassured by the product particulars, labels and data sheet provided by the Company and agreed that point 4.iv. of the Section 21(1) letter had not been answered. They said "Additional information should be provided on product particulars, labels and data sheet".

We have secured clarification and they mean they need us to stipulate:

(a) Origin of all components in Kit

(b) The ethylene oxide answers in 3.4 a and b above.

(c) A statement that labels and data sheet have already been provided.

Yours sincerely,
for IMMUNO LTD.

GRO-C

Managing Director