NOT FOR PUBLICATION

COMMERCIAL IN CONFIDENCE

COMMITTEE ON SAFETY OF MEDICINES

SUB-COMMITTEE ON BIOLOGICAL PRODUCTS

Minutes of the meeting held on 7 November 1984

Present:

Dr J W G Smith (Chairman)
Professor J G Collee
Professor G C Jenkins
Professor H Keen
Professor J Melling
Dr D P Thomas
Dr D A J Tyrrell
Mr J G Watt
Dr R Mann (Medical Assessor)
Dr J Purves (Pharmaceutical Assessor)
Mr K L Fowler (Secretary)
Mr T J Kirkley
Mr G Wade
Dr D Zutshi

Also Present:

Dr Brinley-Morgan MAFF
Dr A Bristow )
Ms A Ford )
Dr A Meager ) NIBSC
Mrs R Michael)
Dr G C Schild)

1. Confidentiality and announcements

1.1 The Chairman reminded members that the papers and proceedings were confidential and should not be disclosed.

1.2 The Chairman informed the members that Professor Moxon had been appointed to the Sub-Committee to advise on the application for a clinical trial certificate for Rotavirus Vaccine Live (Oral). He explained that Professor Moxon was unfortunately unable to attend the meeting but that he had received Professor Moxon's comments on the application.

2. Apologies for absence

Apologies for absence had been received from Professor Banatvala, Professor Brammar, Dr Lane and Professor Moxon. An apology had also been received from Dr Duncan.

3. Minutes of the meeting held on 5 September 1984

These were agreed and signed by the Chairman as a correct record of the meeting, subject to the correction of two minor typographical errors.

4. Matters arising from the minutes

4.1 The Sub-Committee noted the CSM's advice on applications and a hearing previously seen by the Sub-Committee.

4.2 CT 0002/0127 : Smith, Kline and French : Rotavirus Vaccine Live (Oral)

The Chairman informed members that the CSM had deferred consideration of this application at their September meeting and that it was for further consideration at this meeting.

5. Consideration of applications

The Sub-Committee's recommendations on the applications are at appendicies A-C.

6. Further consideration of an application

CT 0002/0127 : Smith, Kline and French : Rotavirus Vaccine Live (Oral)

The Chairman informed the Sub-Committee that CSM had expressed concern as to whether the evidence of safety of the vaccine was sufficient to justify the clinical trial for a relatively minor infection.

The Chairman informed members that he had received comments on the application from Professor Moxon and Professor Banatvala.

Professor Banatvala, in a letter, pointed out that rotavirus infection is the leading cause of gastroenteritis in children admitted to hospital, responsible for 70 to 80% of such episodes in the winter months. Affected infants were more likely to be dehydrated than those affected by other pathogens. It was an important cause of hospital acquired infection, causing prolongation of hospital stay. Professor Banatvala said that the only hope of control is by vaccination.

Professor Moxon, in a telephone conversation, said that he had experience of the vaccine in trials at Johns Hopkins Hospital. Its quality control was highly satisfactory. The neurovirulence findings were unlikely to be of any significance. He disagreed that the condition was trivial and said that it was highly prevalent and a cause of serious fluid loss and dehydration. He said that 5 per cent of admissions were quite ill, and it was, of course, a serious problem in developing countries. He considered that there was a real need for a vaccine and he saw no reason to object to the proposed study.

In discussion, the Sub-Committee agreed with the points made by Professors Banatvala and Moxon. They noted that the calf rotavirus was ubiquitous and therefore they considered that there was no reason for concern about exposure.

The Sub-Committee commented on a number of other viruses successfully used in vaccines; measles, influenza, mumps and yellow fever, which were neurovirulent in immuno-suppressed monkeys but the findings were of no relevance to the safety of these vaccines. They considered that there was no evidence that animal or human rotaviruses were neurovirulent in animals or man.

The Sub-Committee commented that the vaccine strain showed no difference in its CNS effects from parental virus. Studies in 800 children had been completed, and those on 350 children were known to be in progress, which had shown no signs of neurovirulence.

The Sub-Committee were of the opinion that a clinical trial certificate should be issued.

7. Written Representation

Berofor Nasal Spray : CT 0015/0101 : Boehringer Ingelheim Ltd

On the evidence before them the Sub-Committee considered that:

7.1 The Company's replies to points 1, 2, 3, 5, 6, 7 and 8 of the Section 21(1) letter were satisfactory.

7.2 They would be reassured on point 4 of the Section 21(1) letter if evidence was provided of the absence of monomeric ethylenimine from the product or of the safety of the product if it is present.

7.3 They would be reassured on point 9 of the Section 21(1) letter if the Batch Release procedure was applied, to include the provision of bulks and in-process samples to NIBSC. Access of NIBSC staff to the plasmid may be arranged either for staff visiting the Company Laboratory or by Company Scientists visiting NIBSC, at the discretion of the Licensing Authority.

7.4 The Sub-Committee also made the following remarks:

By the product licence stage:

7.4.1 The sensitivity of the tests for microbial contamination should be established.

7.4.2 Evidence should be provided of the integrity of the plasmid at the end of fermentation cycles in full scale production batches.

7.4.3 Additional information should be provided on the contamination of the product with antibody related and nucleic acid materials.

8. Paper

Committee Papers - Previous application papers.

The Sub-Committee agreed that it may not be necessary to routinely include the previous application papers in current papers but they agreed that this change should be kept under review. They requested that, exceptionally, copies of previous papers be made available for their reference as required.

9. Any other business - AIDS

The Chairman brought to members attention a recent report in MMWR (1984 33, No 42 page 589). This stated that preliminary evidence concerning the effects of heat treatment on the viability of the AIDS virus is strongly supportive of the usefulness of heat treatment in reducing the potential for transmission of the AIDS virus in blood clotting factor concentrate products, and suggests that the use of non-heat treated concentrates should be limited.

Dr Thomas observed that the US licensed products were all, he believed, heated in a dry state.

Members noted these observations and hoped that further evidence would be forthcoming soon.

10. Date and time of next meeting

Wednesday 9 January 1985 at 10.30 am.

GRO-C