JOINT SUB-COMMITTEE ON ADVERSE REACTIONS TO VACCINATION AND IMMUNISATION

Minutes of the meeting held on Friday 6th October 1989 at 10am in Room 1611/12, Market Towers

Present: Professor J G Collee (Chairman)
Professor J E Banatvala
Dr C Bowie
Dr E Miller
Professor S R Meadow

DH: Dr D M Salisbury (Assessor)
Mrs J F Alderman (Secretary)
Dr S Wood
Dr F Rotblat
Mr P A Whitbourn
Mrs S Thomas
Dr E Rubery

SHHD: Dr O A Thores

1. Confidentiality and Announcements

1.1 The Chairman reminded members of the particular confidentiality of the proceedings of the meeting, as information from companies and patients' clinical details were to be discussed.

1.2 The Chairman welcomed Mrs Alderman, Dr Rubery and Dr Thores.

2. Apologies for Absence

2.1 Apologies had been received from Dr Cavanagh, Dr McGuiness, Dr Fine, Professor Hull, Professor Miller, Professor Breckenridge and Dr Reid.

2.2 Dr Salisbury was asked to write to members pointing out that ARVI depends on representation from its members' wide spread of specialties and knowledge, and their attendance is of real importance to the work of the sub-committee.

3. Minutes of the last meeting

After correction of some typographical errors, the minutes of the meeting held on Friday 3rd March 1989 were signed by the Chairman as a true record of the meeting.

4. Matters arising

4.1 Adverse Reactions Surveillance (item 4.1)- Dr Bowie advised that active surveillance of MMR vaccine in Somerset had just started.

4.2 Anaphylaxis- JCVI has been reassured by the observation that there were no deaths from anaphylaxis following childhood vaccination over 11 years. Dr Salisbury had approached OPCS to see whether any death certificates over the same time period had mentioned anaphylaxis following childhood vaccination. None had. Dr Salisbury was congratulated on taking this initiative. The next issue of the "Green Book" would appear soon after changes had been approved by JCVI in early November. The removal of the text stating that treatment with chlorpheniramine, hydrocortisone and

adrenaline should be "at doctor's discretion" was endorsed by the meeting.

5. Measles, Mumps and Rubella Vaccine

5.1 Vaccine supply and uptake information

It was noted that distribution of supplies gives a reasonable indication of the use of MMR vaccine, and on this basis (which was justified in discussion) 3 years' worth of vaccine had been used in one year. The meeting felt that the present drive and initiative should be encouraged. The experience from the USA is that vaccination at school age is too late to eliminate measles. It was also noted that the SKF vaccine (containing Urabe mumps strain) has nearly all the UK market share. This might be attributed to the fact that the Wellcome product (made by MSD and containing Jeryl-Lynn mumps strain) hurts at the injection site and has a shorter shelf life at room temperature.

5.2 Neurological reactions

5.2.1 Members attending this ARVI meeting included a Professor of Paediatrics, a senior Epidemiologist, a senior Community Medicine Specialist, a Professor of Virology, and other experienced professional with special interests in this field. The details of 19 cases in or relating to the UK were considered, to the end of September 1989, and these had also been checked by a search of the yellow cards. The following agreed criteria were applied to the assessments: likely association=isolation of mumps virus 15-28 days after vaccination, with an appropriate clinical history; possible=clinical history with or without positive CSF cytology and an acceptable time course; negative=no such evidence. The findings were: 3 likely associations, 9 possibles and 7 negative associations with the mumps component of the MMR vaccines in current use in Britain.

5.2.2 These preliminary conclusions are to be reviewed with reference to further information that may be available. It would be important to follow up certain aspects of virological investigations and other observations relating to the local circumstances in some cases. Further information needed to be sought from Professor Anthony on histopathology in the Exeter case, as the reported pathology had not resembled that of vaccine damage or varicella encephalitis.

5.2.3 The risk, assessed on the basis of the numbers of affected cases from whom mumps virus had been isolated (in relation of the assumed numbers of doses of vaccine given) seems to be of the same order as that accepted for polio vaccine, and in the worst analysis considering the likely and possible cases, the risk would be 1 in 200 000, which is still less than that found in Canada.

5.2.4 Special consideration was given, at the request of SHHD, to a case from Glasgow of July 1989. This was a fiscal case and as such was higly confidential. Doubts were expressed about the cause of death of this child, and while it was not possible to give a clear judgement, it was felt that there was unlikely to have been a causal relationship with the vaccine and that this was an unusual case. The letter from Dr Stephenson had left the matter open, and it would be reasonable to ask for further information as to the family's circumstances, social history, the child's and the family's previous medical history, and for a detailed account of the viral investigation and timecourse in light of the negative virology. The existence of bronchopneumonia of 12-24 hours duration needed to be clarified in the face of the other evidence of sudden death, and anxiet

was expressed over the retinal haemorrhages. This was difficult to relate to meningoencephalitis in a child of this age. It would be reasonable to ask Dr Doyle to expand on the view that the cerebral changes were similar to those reported in the paper by Hart and Earle that was cited, especially as the CSF was normal.

5.2.5 Dr Doyle's report had mentioned that the lesions were not destructive and were thought to be minimal. Expert opinion should be sought as to whether minimal cerebral lesions were judged to be compatible with significant effects.

5.2.6 The meeting's further sadness was expressed over the press reports, which could have harmful implications and unneccessarily damage public confidence in vaccines.

5.2.7 Two drafts for suggested statements were tabled and examined, and amendments to the SHHD version were agreed. The amended version is at annex A. Any statement would be issued only with the prior approval of CSM and JCVI, who would be guided by SHHD with reference to the fiscal proceedings.

5.3 Oral report of meeting with NIBSC

NIBSC are now able to sequence mumps virus, to distinguish between wild and vaccine-related strains, and to distinguish between Urabe and Jeryl-Lynn vaccine strains. Dr Minor would obtain further samples using saliva from patients with symptoms of wild disease and from those with post-vaccine parotitis. NIBSC were thanked for this most significant advance.

5.4 Death of child:report

The meeting was provided with the details of a child from Clacton who had died 12 days after MMR vaccination. No evidence of either death from meningoencephalitis or from MMR related conditions was found. An echovirus had been identified.

5.5 Material from manufacturers

A summary of the Canadian experience and a paper from Germany were examined, and the paucity of data from the US was noted. The help of SKF was appreciated, and a letter from Professor Collee/Dr Salisbury would be sent.

5.6 Publications on MMR

Copies of various manuscripts currently in the press had been made available to members. These were of great use at this stage of the sub-committee's deliberations.

6. Extract from Meyler's Side Effects of Drugs, 11th edition, 1988; Immunobiological Preparations, Dittman S

Dr Salisbury was thanked for this updated extract.

7. Any other business

7.1 Dr Bowie commented that there should be ongoing evaluation of MMR-related neurological events so that the fullest information is available to set against instances such as those discussed at this meeting.

7.2 The meeting thanked Professor Collee and expressed gratitude for his courtesy and efficiency as ARVI Chairman.

8. Date of next meeting

Friday 23rd March 1990, at 10am.

FOR SHHD

ANNEX A

IN CONFIDENCE

REPORT OF DEATH OF 16 MONTH OLD CHILD

In July 1989 a 16 month old child was found seriously ill by his parents and subsequently died. The cause of death was certified as "not ascertained" although there was evidence of bronchopneumonia and aspiration of gastric contents.

The child had received MMR vaccine five days before his death and had apparently been well following vaccination. However, post mortem examination revealed evidence of minimal brain changes of a non specific nature and the possibility was raised that these might have been vaccine-related.

The case was therefore reported to the Subcommittee on Adverse Reactions to Vaccination and Immunisations (ARVI), a group of experts who advise both the Committee on Safety of Medicines (CSM) and the Joint Committee on Vaccination and Immunisation (JCVI). ARVI have considered all available clinical and biological data carefully and do not consider that there is evidence to support a link between MMR vaccine and the cause of death.

25/6