DATE OF SUMMARY: APRIL 2001

SUMMARY OF THE COMMITTEE ON SAFETY OF MEDICINES MEETING HELD ON 27 MAY 1999

Committee Members:

Present

Professor A M Breckenridge (Chairman)
Professor J C Petrie (Co-Vice Chairman)
Dr M Armitage
Ms H Barnett
Dr R T Calvert
Dr T Chambers
Professor J H Darbyshire
Professor H J Dargie
Professor G W Duff
Dr B K Evans
Professor S J Eykyn
Professor M J S Langman
Dr A V P Mackay
Professor B K Park
Dr R J Taylor
Dr F M Williams
Professor K W Woodhouse

Apologies

Professor E C Gordon-Smith
Professor J M Midgley
Professor R M Murray
Professor I V D Weller (Co-Vice Chairman)

Observers

Dr A Cook (Dept. of Health)
Dr D Salisbury (Dept. of Health)

Mr L R Whitbread (Secretary)
Miss D C Mthimkhulu (Assistant Secretary)

Professional Staff of MCA

Principal Assessor

Dr E Lee (Pharmacovigilance)
Dr A Nicholson (New Drugs)
Dr P Raptopoulos (Abridged)
Dr F Rotblat (Biologicals)

Licensing Division

Dr Linda Anderson (CPS Principal Assessor)
Dr M Barratt-Johnson
Mr T Berridge
Dr S Bowes
Dr S Branch
Dr A French
Mr D Jones
Professor J Lewis
Dr C O'Leary
Dr M Powell
Dr D Rogers
Dr R Shah
Dr J Sims
Dr C Steele
Dr M Thatcher
Dr L Tsang

Post-Licensing Division

Dr C Hawkins
Dr C Hepburn
Dr S Morris
Dr P Tsintis
Dr P Waller

Others

Dr J Dunne	MCA/L
Mr C Gardner	SoL C5
Dr R Hart	MCA/PL
Dr D Jefferys	(Director of Licensing)
Dr S Millican	MCA/PL
Dr J Raine	(Director of Post Licensing)
Dr R Tansley	MCA/PL
Dr J Williams	MCA/PL

Trainees

Dr M Levick	MCA/PL
Dr J Pallett	MCA/PL

NOTE: MCA STAFF MAY BE PRESENT FOR ALL OR PART OF THE MEETING OR FOR SPECIFIC AGENDA ITEMS

Announcements and Apologies

1.1 The Chairman reminded the Committee that the papers and proceedings were confidential and should not be disclosed. Members were also reminded to declare their personal specific, personal non-specific, non-personal specific and non-personal non-specific interests in the agenda items.

1.2 Apologies were received from Professors Gordon-Smith, Murray, Midgley and Weller for the day.

1.3 The Chairman welcomed Drs D Salisbury and A Cook from the Department of Health attending as observers for the MMR paper.

1.4 The Chairman informed the Committee that Professor Sikora had resigned his membership of the Committee.

1.5 The Chairman reminded members that there would be an "*en college*" meeting on 24 June 1999 and asked members to inform him or the Secretary should they have any issues that they wish to be included on the agenda.

1.6 The Chairman informed the Committee that the abridged application Prozac Capsules had been deferred to another meeting to allow for the presence of a gynaecologist for expert advice. [**Note**: see summary for 22 July]

2. **Minutes of the Meeting held on Thursday 29 April 1999**

The minutes were agreed and signed by the Chairman as a true and accurate record of the proceedings.

3. **Matters Arising from the Minutes**

None.

4. **Safety of MMR Vaccine in Relation to suggested concerns about Autism and Crohn's Disease: Pasteur Merieux, Merck Sharpe & Dohme and SmithKline Beecham**

Professor Dargie declared a personal non-specific interest in SmithKline Beecham and left the room. Professor Darbyshire declared a lapsed non-personal non-specific interest in SmithKline Beecham, but this did not debar her from taking part in the proceedings. Professor Langman (Chairman of the Working Party) stated that after the start of the deliberations of the Working Party he became aware that relevant interests which had only included SmithKline Beecham and Pasteur Merieux had later come to include Merck Sharp Dohme – in which he had a personal but non-specific interest. The matter was discussed with ***[see note 1 below]*** and he (Professor Langman) had relinquished his personal interest which then became non-personal non-specific. Working party members were aware of the matters. [**Note**: see also summary of meeting of 22 July]

The Committee were informed of new important information relating to the safety of MMR vaccine, in the form of the report of the MMR Working Party and a publication of an epidemiology study. The Committee considered the report of the Working Party on MMR vaccine. The Working Party had reviewed the reports of parent suspected adverse reactions associated with MMR and MR vaccines as well as the information obtained from medical

practitioners and had concluded that no causal association had been shown between MMR and MR vaccines, autism and Crohn's disease.

Professor Langman, Chairman of the Working Party on MMR vaccine, provided details of the methodology and conclusions of the Working Party. The Committee also considered the findings of an epidemiological study over the period of the introduction of MMR vaccine, conducted in North Thames health region, that reported no causal association between MMR vaccination and autism. It was noted that this paper will be published in the Lancet on 12 June 1999.

The Committee were reassured as to the safety of MMR and MR vaccines, they endorsed the Working Party findings and recommended that this important new information should be communicated to UK health professionals and the public. The Committee agreed that the article on MMR should be published in *"Current Problems in Pharmacovigilance"*, with an accompanying MMR parent leaflet which should involve the Health Education Council who have expertise in this area, and that the Working Party report should be made available to interested parties by post and via the Internet in its entirety.

[**Note**: see article in *Current Problems in Pharmacovigilance*, volume 25, June 1999 - http://www.mca.gov.uk/mca/csmhome.htm]

5. **Consideration of the Applications - Variation**

The Committee considered and approved an application to vary the terms of the product licence for:

MA 3070/0007:	Hyate:C (Porcine FVIII):	Speywood Biopharm Ltd.

6. **Consideration of the Applications - New Products**

The Committee considered four products. Marketing Authorisations were subsequently granted to each of them. Details as follows:

MA 11723/0288:	Eloxatin Powder for Solution for Infusion - 50 & 100mg vials (Oxaliplatin):	Sanofi Winthrop Limited

Members had no interests to declare.

MA 00011/0245:	Meningitec (Meningococcal Group C Oligosaccharide-Diphtheria CRM $_{197}$ Protein Conjugate):	John Wyeth & Brother

Members had no interests to declare. ***[see note 1 below]*** informed the Committee that the Department of Health is likely to make recommendations for the introduction of a vaccine programme against Meningitis C for children and adolescents, from this autumn.

MA 10949/0327:	Relenza Rotadisk 5mg (Zanamivir):	Glaxo-Wellcome UK Ltd. (T/A Allen & Hanburys)

Dr Evans declared a personal non-specific interest and left the room. Professors Darbyshire, Duff and Park declared non-personal non-specific interests, but this did not debar them from taking part in the proceedings.

M.A. 06009/0001:	Tico Vac (Purified, Formaldehyde-Inactivated Tick Borne Encephalitis [TBE] Virus [Strain Neudorfl] absorbed onto Aluminium Hydroxide):	Immuno AG

Members had no interests to declare. The Committee commented that the clinical Expert Report was informative and well organised.

7. **Consideration of the Applications** - **Abridged Products**

The Committee considered two applications. Members had no interests to declare. Regulatory action continues at the date of this summary on both applications – ***[see note 2 below]***. A third application was deferred to a later meeting (see 1.6 above).

8. **A Phase I Study of the Absorption of Malathion from Headlice Treatments – For Advice (Products: Prioderm, Derbac – M, Suleo – M, Quellada – M)**

The Committee were informed that the MA holder for malathion-containing preparations for lice infestations had completed a Phase I study [**Note**: Clinical Drug Investigation 1999, vol 18 no 2: 105-115], requested by the Committee at its earlier consideration of the safety of malathion containing human medicines, to investigate the extent of systemic absorption of malathion from medicinal products and the effect on plasma and erythrocyte acetyl cholinesterase. The study showed a low level of systemic absorption of malathion and there was no clinically relevant effect on plasma or erythrocyte acetyl cholinesterase.

The Committee expressed concern that an organophosphate was being used as a medicinal product when it is known that many parents use these products for their children repeatedly. The Committee was informed that the product information for all malathion-containing preparations contains a warning against repeated use. It was noted that the study had been carried out in adult volunteers and not in children, who most frequently use these products. However in children down to the newborn, increased absorption was not considered an issue. The Committee agreed that there was no need for any regulatory action.

9. **Sodium Valproate / Obesity & Polycystic Ovary Syndrome** – ***[see note 3 below]***

10. **CPMP: Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Medicinal Products – For Information and Tabled Paper VII - TSE and Medicinal Products: "Response from the Committee on Proprietary Medicinal Products on the Comments from DG XXIV on the Note for Guidance for Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Medicinal Products" (CPMP/BWP/770/99 for information**

The Committee noted this item.

11. **Draft Articles for Current Problems in Pharmacovigilance**

Members were asked to forward any comments to ***[see note 1 below]*** by 27 May 1999 on the following articles:

i. The safety of MMR vaccine

ii. The effect of albumin on mortality

iii. "Third-generation" oral contraceptives and the risk of venous thromboembolism: changes to the product information

iv. Product discontinuation- Parstelin

v. Reporting suspected adverse drug reactions to animal medicines

vi. In Focus – sidenafil

vii. Valproate, obesity and polycystic ovary syndrome

viii. Change in legal status of aspirin 75mg tablets

[**Note**: the proposed article on Valproate, obesity & polycystic ovary syndrome did not appear - see item 9 above and note 3 below]

12. **Review of the Biotechnology Framework and Report**

The Committee noted that its role and that of the Medicines Commission had not changed by the proposals contained in the report.

13. **Trovan and Serious Hepatic Reactions**

The Committee were informed that the CPMP were concerned that cases of hepatotoxicity with trovafloxacin appeared to occur with a greater frequency and severity than for other quinolones. Following a press release on this issue on Tuesday 25 May, an urgent safety variation to improve existing warnings about hepatotoxicity was agreed and a Dear Doctor letter is being sent in countries where trovafloxacin is marketed. The company have been asked to respond to a list of 8 questions by 4 June and a full review of the safety data will be undertaken at the CPMP PhVWP meeting in June. All the various indications will also be reviewed via a working group which is to meet in June. The Committee noted that this centrally authorised product was not yet marketed in the UK.

14. **Adroit Statistics**

The Committee noted this item.

15. **Any Other Business**

None.

16. **Date and Time of Next Meeting**

The next meeting will take place on Wednesday 9 June 1999 at 10.00 a.m.

Note 1: the identity of individuals is being withheld under exemption 12 of the Code of Practice on Access to Government Information

Note 2: information about these applications is being withheld on the grounds that this advice remains confidential as at the date of this summary and publication would be premature while regulatory action continues. The advice will be published in due course. Exemption 10 of the Code of Practice on Access to Government Information applies

Note 3: information about this item is being withheld on the grounds that this advice remains confidential as at the date of this summary and publication would be premature while regulatory action continues. The advice will be published in due course. Exemption 10 of the Code of Practice on Access to Government Information applies