

MEDICINES COMMISSION

MINUTES OF THE MEETING HELD ON 13 MAY 2005 AT MARKET TOWERS, 1 NINE ELMS LANE, LONDON SW8 5NQ

Present

Professor Parveen Kumar (Chairman)
Dr Jeffrey Aronson (Vice Chairman)
Dr Susan Bews*
Professor Joe Collier
Professor Peter Day
Professor Gabrielle Hawksworth*
Professor Veronica James
Professor Ronald Jones
Dr Christine McCartney
Dr Agnes McKnight*
Mr Graeme Millar
Professor Peter Noyce
Professor Stuart Pocock
Mr Clifford Prior*
Professor James Ritter
Professor Philip Routledge
Dr Harriet Scorer
Professor Herbert Sewell
Mr Robert Stevenson
Professor Cameron Swift
Professor Roger Walker
Dr Elizabeth Williamson*

Apologies

Dr Lydia Brown
Professor Edzard Ernst
Professor Gordon Murray

Secretariat

Dr June Raine
Mr Roy Alder
Mr Colin Bennett* (Vet Co-ord)
Mrs Sue Jones (Secretary)
Mrs Lavinia OBrien (Dep Sec)
Mrs Yvonne Muhammad*(Ass Sec)

Legal Adviser

Mr Simon Rogers
Ms Lee Dianda (Observer)

MHRA

Dr Alex Nicholson*
Mr David Brown*
Mr Simon Day*
Mr Richard Woodfield*

MHRA Observers

Dr Linda Anderson*
Dr Alison Daykin*

Invited Expert Advisers

Dr Paul Jarman*
Professor Adrian Williams*

**present for part of meeting only*

1. ANNOUNCEMENTS

1.1 The Chairman welcomed Commissioners to the meeting and reminded those

present that the business and proceedings of the Commission were confidential and not for disclosure to persons or organisations outside. Commissioners were also asked to declare any interests in any of the products and companies concerned with items on the agenda.

1.2 The Commissioners were advised that the final meeting of the Medicines Commission would be on 8/9 September. The MHRA would be hosting a dinner on Thursday 8th and an “end of term” photograph would be taken either that evening or before the meeting was due to start on 9th September.

2. APOLOGIES FOR ABSENCE

2.1 Apologies for absence had been received from the Commissioners indicated above. John FitzGerald of the Secretariat sent his apologies, Colin Bennett would attend the meeting later to present the veterinary paper. Ms Lee Dianda attended the meeting as an observer accompanying the Legal Adviser, Simon Rogers.

3. MINUTES OF PREVIOUS MEETINGS

3.1 The minutes of the meeting held on 11th February 2005 were agreed with minor amendments to the text and signed by the Chairman.

4. MATTERS ARISING

4.1 Para 7.1 - MHRA explained that the programme of events for the period of the UK Presidency of the EU later this year was being developed by the Cabinet Office. MHRA had had some input to the programme and would be involved with 14 scientific meetings whose subject matter included devices, nanotechnology and pharmacovigilance as well as a Heads of European Agencies meeting. The Chief Medical Officer was planning a 3 - 4 day conference on Patient Safety in which the MHRA expected to take a role. In addition, there were three important dossiers that would be progressed through the Council of Ministers while the UK had the Presidency. Commissioners would be alerted once final arrangements for these events had been made so that they could attend if they wished.

5. HEARING - GW Pharma - Sativex and Ducannex Oromucosal Spray PL 18024/0003 – 0004 MC 05/02

5.1 Interests were declared as follows:

Dr Williamson declared a current personal interest relating to a potential rival product and was excluded from the meeting for this item;

Professor Hawksworth declared a non-personal specific interest - after taking legal advice, the Chairman decided that she wanted Professor Hawksworth to remain in the meeting to answer specific questions relating to her particular expertise. Professor Hawksworth was present at, but did not take part in, the hearing. After the hearing she answered questions put to her by other Commissioners and then left the meeting while

the Commission decided its advice;

Professor Jones declared a non-personal, non-specific interest and remained to take a full part in the hearing;

Mr Prior declared an interest as Chief Executive of Rethink, a registered charity.

Rethink has run public and political campaigns on the risks of cannabis and its links to psychosis; Mr Prior had personally appeared in the media and on public platforms. Mr Prior had also had a conversation about these issues in a brief meeting with a senior member of GW Pharma at a conference. The Commission debated for sometime whether Mr Prior should remain or not because of his connection with the Rethink campaign. The Commission agreed that, although Mr Prior's interest did not relate directly to this application, public perception might be that there was a risk of bias and so he was excluded from the meeting for this item.

In addition, *Professor Routledge* declared that he was acting as principal investigator in a study into the properties of THC, but that the study was not funded by the pharmaceutical industry. He was advised that no interest need be formally declared.

5.2 Dr Paul Jarman attended the morning session of the meeting in the capacity of Expert Adviser for the Commission's pre-hearing discussion. Professor Adrian Williams attended as Expert Adviser for the hearing and the post-hearing discussion. Their roles were to advise the Commission on the detail and aspects of the clinical management of patients with Multiple Sclerosis (MS). They did not have any interests in GW Pharma or the product and did not give specific advice to the Commission in relation to the application or product, other than to suggest issues which the Commission may wish to raise with the company. They did not take part in the hearing.

5.3 The MHRA Examiners presented their assessment of the company's application and the Commission had the opportunity to ask questions. The Commission also had the opportunity to ask Dr Jarman questions relating to the clinical management of patients with MS. At the invitation of the Commission, Dr Jarman gave an overview of the prevalence and clinical course of multiple sclerosis, with its differing patterns of progression, leading to varying degrees of disability. He outlined the options for symptomatic treatments and disease-modifying drugs, and referred to the need for additional treatment options. He described spasticity as a clinical sign and outlined the associated symptoms of which patients may complain, including pain or discomfort, stiffness, weakness or spasms. He referred to the assessment of spasticity and commented on the limitations of the Ashworth scale (including its insensitivity and inter-observer variability) and the need for other ways of assessing spasticity.

5.4 The Commission discussed at length the evidence it had before it and reviewed questions it wished to ask the company when they made their presentation.

5.5 The morning's deliberations started at about 10.30am and lasted for around 2.5 hours. Just before 1 pm the company asked if they could take a lunch break before the hearing commenced. They were asked to return at 2 pm. There was a break between 1.10 pm and 2 pm.

5.6 The company's presentation began just after 2pm. Prior to this, the Chairman had informed them: that the hearing would be taped and a copy of the tape provided to them at a later date; who would be present, their respective roles (including the Expert Adviser); and the Commissioners who had been excluded from the proceedings because of interests. The company explained that one of its experts had been unable to attend (Professor Lynne Turner-Stokes) and two others (Professor Derick Wade and Professor Christine Collin) were unable to stay for the afternoon owing to prior commitments but that their parts of the presentation would be covered by the remaining members of their team.

5.7 The presentation began with short presentations by the Chief Executives of the MS Trust and MS Society before the company presentation. The company representatives and experts then gave the main presentation and the Commission had the opportunity to ask questions and seek clarification on a number of issues. Following the oral hearing, the Commission discussed the issues further and unanimously agreed its findings and advice. The Commission carefully considered the oral and written evidence before it and agreed to advise the Licensing Authority that it should refuse to grant the Marketing Authorisations applied for. In reaching its advice the Commission considered all the scientific data and arguments presented, and concluded that the evidence of efficacy was insufficient to support granting marketing authorisations. *The Commission's detailed findings are withheld under section 43 of the Freedom of Information Act* This part of the meeting was concluded at 5.45 pm.

6. Papers

6.1 Appointments to the Veterinary Products Committee

6.1.1 Dr Bews left the meeting for this item.

6.1.2 The Medicines Commission considered the short-listing and recommendations made by the Sift Panel for membership of the Veterinary Products Committee with effect from 1 January 2006. The Commission noted that for some posts, no suitable alternatives had been identified. It agreed recommendations to be made to Ministers. *The details of the recommendations are withheld under section 40 of the Freedom of Information Act.*

6.2 Proposals to restrict the use of *Senecio* species in unlicensed medicines

6.2.1 Written representations relating to the proposals to restrict the use of *Senecio* species in unlicensed medicines, except those for external use, had been referred to the Commission under section 62(5) of the Medicines Act 1968. The Commission was asked to consider those responses and to report its findings and conclusions.

6.2.2 A traditional Chinese medicine (TCM) known as Qianbai Biyan Pian, which traditionally contains the toxic plant *Senecio scandens*, was supplied in the UK in 2002. Species of plants within this genus contain unsaturated pyrrolizidine alkaloids (PAs),

known to be hepatotoxic to humans. Medicinal products containing them therefore represent a clear risk of harm.

6.2.3 The use of one *Senecio* species - *S.jacobaea* - is currently restricted in unlicensed medicines by a long-standing piece of legislation, the Medicines (Retail or Supply of Herbal Remedies) Order 1977. However, use of *Senecio scandens*, which is now thought to be available in the UK, and other *Senecio* species is not. Despite a voluntary agreement in March 2002 with the herbal sector to withdraw all unlicensed medicines containing *Senecio* species, the MHRA has continued to receive reports of supply from TCM outlets of Qianbai Biyan Pian to consumers in the UK. To date, the MHRA has received 10 reports of supply of TCMs containing *Senecio* species.

6.2.4 The MHRA launched a public consultation (MLX 296) in January 2004, giving options for proposals to restrict *Senecio* species in unlicensed medicines other than for external use; in particular, the MHRA proposed that Ministers make an order under section 62 of the Medicines Act 1968 prohibiting the sale or supply of unlicensed medicines consisting or, containing, *Senecio* species. The Medicines Commission considered the options put forward in the consultation document, and considered the replies to that consultation. The Commission noted that the Chinese Government had raised the possibility that a medicine containing *Senecio* could be prepared in such a way that it was free of unsaturated pyrrolizidine alkaloids, thereby mitigating safety concerns. The Commission noted that the proposed order under section 62 would apply only to *Senecio* in medicines. It recommended that, after consideration by Ministers, the Food Standards Agency should be informed of the Commission's advice.

6.2.5 The Commission noted that it would remain open for an applicant for a marketing authorisation or - in future - a registration under the Directive on Traditional Herbal Medicinal Products - to demonstrate the safety of a particular product containing *Senecio* species. Currently there was no systematic framework for manufacturing and quality control in relation to the UK regime for unlicensed herbal medicines. There was practical evidence of variable manufacturing standards in the sector. It was, therefore, not currently realistic to adopt a regulatory option for unlicensed medicines based on an assurance that the *Senecio* species used would be free of unsaturated pyrrolizidine alkaloids.

6.2.6 The Medicines Commission found that of the options falling short of a prohibition on supply, none would ensure safe use of unlicensed medicines containing *Senecio* species. The Commission concluded that, in the interests of safety, it agreed with the final proposal to prohibit the sale, supply or import of unlicensed medicines containing any *Senecio* species except those for external use.

6.3 Publication of the Health Select Committee Report into the influence of the pharmaceutical industry

6.3.1 The Commission was invited to give its advice on the report of the Health Select Committee into the influence of the pharmaceutical industry. The Vice Chairman agreed to consider the recommendations of the report against the Commission's earlier written submission to the committee and to bring any gaps to the attention of Commissioners to address. He agreed to co-ordinate the response and submit it to MHRA for inclusion in the consideration of the Government's response to the report.

7. Any other business

7.1 Commissioners were asked to let the Secretariat have any comments on the remaining papers on the agenda as soon as possible.

8. Date of Next Meeting

8.1 15th July 2005.