

## Independent Scientific Advisory Committee for MHRA database research (ISAC)

Summary minutes of fourth meeting held on Wednesday 29<sup>th</sup> November, 2006

**Information regarding ongoing deliberations, or that could identify applicants and names of products is withheld under sections 35 (Formulation of policy), 40 (Personal Information), 41 (Information Provided In Confidence) and 43 (Commercial Interests) of the Freedom of Information Act 2000 (FOIA). Further details on successful applications will be published in ISAC annual reports once research using ISAC-approved data has been published - this will also be subject to any relevant exemptions under the FOIA**

### Present:

#### ISAC Members:

Dr Brian Gennery (Chair)  
Dr Jacqueline Cassell  
Dr Martin Gulliford  
Dr David Lovell  
Dr Richard Martin  
Ms Marcia Saunders  
Prof Amrit Hungin<sup>2</sup>  
Prof Paul Little<sup>2</sup>  
Ms Barbara Meredith<sup>2</sup>

#### MHRA<sup>1</sup>:

Dr June Raine  
Dr John Parkinson  
Dr Sarah Davis  
Mr Stephen Fawbert (Secretariat)  
Mrs Tarita Murray-Thomas (Secretariat)  
Professor Sir Alasdair Breckenridge

### Apologies:

Dr Sarah Meredith  
Prof Richard Donnelly  
Dr Corinne de Vries

### **Part One – New members only**

#### 1 **Welcome & Apologies**

- 1.1 New members were welcomed to the Committee by the Chairman. The morning meeting was an induction for new members only and existing members would join after lunch.
- 1.2 Apologies had been received from Prof. Richard Donnelly and Dr Corinne de Vries.

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<sup>1</sup> MHRA staff may be present for all or part of the meeting, or for specific items. GPRD staff are not present when Yellow Card applications are discussed and VRMM staff are not present for GPRD applications

<sup>2</sup> Present for Part 2 only

- 1.3 The Chairman reminded Members 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.

## 2 INTRODUCTION TO ISAC

### 2.1 Terms of Reference

The committee discussed the terms of reference of the Committee that had been agreed in February 2006, to which no amendments were proposed (Tabled Paper 1).

### 2.2 Committee administration and ways of working

- 2.2.1 MHRA explained that there were separate secretariats for GPRD and Yellow Card sections of meetings where applications were discussed. General papers would be covered at the start of meetings, with the Yellow Card Secretary taking the lead on these.

- 2.2.2 The committee were reminded that in addition to the annual declaration of interests, they would need to consider any potential conflicts of interest when reviewing individual protocols. There was a Deputy Chair (Sarah Meredith) where a conflict of interest (e.g. a protocol from his organisation) did not permit the Chairman to participate in the review of a specific protocol.

## 3 GPRD INDUCTION

### 3.1 Introduction and forward look; how the GPRD Group functions within the MHRA; ethical approval for use of GPRD data

The GPRD Group presented an overview of the GPRD, describing the data held within the database and the principles under which it is operated by the GPRD Group within the MHRA. The arrangements in place to control access to and use of the data were described, including Section 60 and ethical approval.

### 3.2 GPRD Protocol review: specific issues

The GPRD Group outlined the procedures for the review of GPRD protocols by ISAC; based on those used previously by SEAG (including the fast track review process which could be requested for studies relating to serious public health issues).

### 3.3 Use of GPRD data by UK academics under the MRC licence

The GPRD Group explained the agreement between the MRC and the GPRD Group which facilitates access to GPRD data for 50 protocols per year by UK academics. The committee was informed that review of

protocols seeking access to GPRD data under the MRC licence would involve the same procedure as used for other protocols, but that they would be required to comment on the suitability of the protocol for funding by the MRC. A modified reviewer's comment form had been prepared for this purpose; this form included the issues members would need to consider when assessing suitability of a protocol for MRC funding.

## **4 YELLOW CARD INDUCTION**

### **4.1 The Yellow Card database**

The MHRA gave a presentation on the history of the Yellow Card Scheme, reporting rates and reporting methods. The presentation also included information on signal detection processes and the Electronic Transmission of ADR reports within the EU. Members would have the opportunity to go on a tour of VRMM division at a future meeting and the MHRA's pharmacovigilance software would be demonstrated.

### **4.2 The Independent Review of Access to the Yellow Card Scheme and the Yellow Card application process**

4.2.1 The MHRA gave a presentation on the 2004 Independent Review chaired by Dr Jeremy Metters. The presentation also included information on the data categories the Interim Committee on Yellow Card data had devised in line with Data Protection (DP) and Freedom of Information (FOI) requirements and the application form and guidance notes. A list of applications received to date was tabled (Tabled paper 2).

4.2.2 The Committee requested further discussion on impact analysis at a future meeting.

4.2.3 The Committee asked the MHRA to consider whether there should be a statement on Yellow Cards informing reporters that Yellow Card data could be used for research, and whether they should have the option of opting out of this. This would be considered when forms were revised.

## **Close of Part One, followed by lunch with the MHRA Chairman**

### **Part 2 – All members**

## **5 Welcome, Apologies and announcements**

5.1 Existing ISAC members joined the second part of the meeting, to discuss routine ISAC business. Dr Sarah Meredith had sent her apologies.

5.2 The Chairman informed members that Professor Ian Harvey had resigned from the Committee due to other commitments. The Chairman

would continue in office until the end of 2007, when a replacement would be sought.

- 5.3 The Chairman reminded Members 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.
- 5.4 It was agreed that the membership of ISAC should be divided into two teams to review GPRD protocols, to improve the efficiency of the reviewing process. Each team would consist of 6 members with Dr David Lovell serving on both teams to evaluate the statistical components of all protocols.

*Team 1*

Dr Jacqueline Cassell  
Dr Corinne De Vries  
Prof Pali Hungin  
Dr Richard Martin  
Ms Barbara Meredith  
Dr David Lovell

*Team 2*

Prof Richard Donnelly  
Dr Martin Gulliford  
Prof Paul Little  
Dr Sarah Meredith  
Ms Marcia Saunders  
Dr David Lovell

- 5.5 It was proposed that all new members should have a period of training to familiarise themselves with the reviewing process. To this end, it was suggested that a sample of previously reviewed GPRD protocols and their corresponding feedback be circulated to new members for scrutiny. GPRD protocols actively under review were also to be forwarded to new members until 31/12/2006. This would provide opportunities for practice until the Team system became operational on 01/01/2007. During the training period, new members would provide anonymised comments without a decision on protocols under review.
- 5.6 Yellow Card applications would continue to be reviewed at committee meetings, with a Yellow Card Centre Head invited to attend as expert for the day at each meeting.

**6 Minutes of the third ISAC meeting**

The minutes of the meeting held on Monday 17<sup>th</sup> July 2006 (Paper 1) were agreed as a true record subject to minor amendment of paragraph 8.

**7 Matters arising from the minutes**

The Committee was informed that the agenda for the current meeting covered all the issues arising in the minutes with three exceptions. The MHRA was still taking forward issues around promotion of the Yellow Card Scheme, IT security of applicants and retention of data by researchers.

**GENERAL PAPERS**

**8 Publication of information on ISAC approved protocols**

- 8.1 The MHRA presented Paper 2 on different approaches that could be adopted when publishing summary minutes further to the Committee's concerns in July that there could be serious commercial and public health implications of releasing information on pending applications.
- 8.2 The Committee endorsed the proposed model for publishing summary minutes and approved summary minutes of the May meeting to be placed on the MHRA website.
- 8.3 The Committee noted the current proposals for the first ISAC annual report, scheduled for summer 2007 and fully endorsed the recommendation that applicants are urged to place their research on the National Research Register where appropriate. Guidance and communications with researchers would need to be updated.

## **GPRD DATA**

### **9 GPRD External linkage**

GPRD proposed a strategy for improving research validity and utility in GPRD. The strategy focused on the concept of external data linkage and the need for trusted third parties to facilitate the process. The Committee fully endorsed the proposal as presented.

### **10 Data Mining in GPRD**

It was likely that researchers would approach the Committee for approval to undertake data mining in GPRD in the near future. ISAC discussed the pros and cons of this methodology but felt that the main concern was not about data mining as a process in itself but rather about how the findings of such an exercise were reported in the literature. The Committee considered that protocols seeking approval for data mining should be dealt with on a case-by-case basis rather than using a blanket approach. An expert on the science of data mining should be invited to a future committee meeting to provide further insights on the process and implications of use in GPRD.

### **11 MRC Initiative Update**

11.1 A summary of the numbers and types of MRC protocols submitted for review by ISAC was tabled. In 2006, MRC protocols accounted for about 30% of all reviewed protocols. GPRD informed the committee of the MRC research day organised by GPRD in August 2006 for both potential and current users under the initiative.

11.2 Professor Little had been asked by the Health Services Board (HSPHRB) to monitor the type and quality of research applying for data under the terms and conditions of the MRC licence. GPRD would keep Prof Little informed of progress on the initiative.

### **12 Ethical Issues: Protocol: 06\_075**

GPRD presented Paper 3 on protocol 06\_075, which had been approved electronically but raised some issues that warranted further discussion at the meeting, such as what constituted good medical practice in the switching of

medication in primary care. There was some discussion about whether a more 'sensitive' approach could be used with patients including writing to inform them that switching had taken place or been recommended. It was suggested that it might be useful to hold an annual symposium where issues of such a nature could be discussed and the finding from studies such as that described in protocol 06\_075 presented for added insight.

### **13 Contribution of GPRD data to meta-analysis on NSAIDs**

13.1 ISAC expressed support for the international collaboration outlined in Paper 4 but raised a number of issues about the homogeneity/heterogeneity of the other studies to be pooled in the analysis, the quality of recording of important variables in these studies and the ability to reduce bias and control for confounding factors in the analysis.

13.2 In light of the above, the Committee requested that a detailed protocol of the proposed analysis be submitted for further consideration prior to the transfer of the GPRD dataset to Canada. Additionally, further information was requested on the quality and size of the other datasets to be pooled, the variables to be used (and their definitions) and the key variables to be combined to look for an effect.

## **YELLOW CARD DATA**

### **14 Procedures for contacting patients through Yellow Card reporters**

14.1 MHRA presented an outline procedure for communications between the MHRA and healthcare professionals who had submitted a Yellow Card, where the Yellow Card might be of interest to a specific research project. This process would be initiated when a researcher wished to obtain additional information from a reporter and/or the patient who was the subject of a report.

14.2 The MHRA would always make initial contact with the reporter. The researcher would receive relevant contact details, in order to request the additional information directly, only when the MHRA had received consent from the patient to release this information. Paper 5 included a draft letter for use by the MHRA when making initial contact with reporters, together with a draft information leaflet on the use of Yellow Card data in research to accompany the letter. Plans to consult on the proposed procedure and associated documentation with relevant professional bodies were welcomed by the Committee. Members were asked to provide specific comments on the draft letter and leaflet in writing to the MHRA after the meeting.

14.3 The Committee reminded the MHRA that patients may not be aware that the suspected reaction had been reported on a Yellow Card and that this may make reporters reluctant to discuss the proposed research with the patient in question. It was therefore important that any communications with patients were handled sensitively, and further thought should be

given to whether contact between reporter and patient should be face to face (as envisaged by Metters) or in writing.

**15 Any other business**

15.1 Meeting dates for 2007 had been published (Paper 6)

**16 Date of next meeting**

The next meeting would be held on Friday 16<sup>th</sup> February 2007 at 10.30am in Market Towers.

GPRD/VRMM  
December 2006