

Independent Scientific Advisory Committee for MHRA database research (ISAC)

Summary Minutes of second meeting held on Wednesday 10th May 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)
Prof. Amrit Hungin
Prof. Paul Little
Ms Barbara Meredith
Dr Sarah Meredith

MHRA¹:

Dr June Raine
Dr John Parkinson
Mr Jeremy Mean
Dr Sarah Davis (Secretariat)
Mr Stephen Fawbert (Secretariat)
Dr Jane Moseley

Apologies:

Prof Ian Harvey

1. Welcome & Apologies

Apologies had been received from Prof Ian Harvey.

The Committee noted that Prof Stephen Evans had decided not to take up his position on ISAC and felt that it would be important to appoint a replacement statistician to the Committee

2. Minutes of the first ISAC meeting.

The draft minutes of the meeting held on 28th February 2006 were adopted.

3. Matters arising from the minutes

The Committee was informed that the agenda for the current meeting covered all the issues arising in the minutes of the first meeting, with the exception of

¹ 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

two items. Firstly, the role of the National Research Register as a public record of successful applications to use GPRD or Yellow Card data for research would be discussed at a future meeting. Secondly, the need to nominate a member to deputise for the Chairman when required was raised; this will be taken forward by the MHRA in discussion with the Chairman.

YELLOW CARD DATA

1. The Yellow Card application process

The Committee supported the application process devised by the Interim Committee on Yellow Card data, but raised some broader issues about the Yellow Card Scheme.

The Committee discussed the process of contacting reporters, and it was agreed that a standard letter would need to be devised, stating clearly why reporters were being contacted. The Committee reminded the MHRA that as the primary purpose of the scheme is safety monitoring, the interest to the public of releasing data needed to be weighed against any impact that contacting professional reporters might have on the doctor:patient relationship. It was agreed the process should be piloted with application 007, and its impact monitored.

Researchers and the MHRA should remember that reporters might have changed jobs and might not be available for follow up, so the MHRA should decide if a time limit needed to be established to determine how far back it would go when deciding which reports would be used in a study where contact with reporters was required.

The Committee discussed the process for contacting patients and whether this should be done through a third party. The MHRA said it would look at the process SEAG used and mirror this if possible.

The Committee sought clarification on Section H of the application form on security, and felt more information should be sought to ensure the data storage and destruction policies are robust. The MHRA said it had already consulted its IT security staff but would also work with other groups such as PIAG to mirror their arrangements if feasible.

The MHRA would give more thought to the publication of research using Yellow Card data, and all successful applications would be highlighted on the MHRA website with links to the research. The same should apply for GPRD data as well.

The Committee also discussed ways applications for Yellow Card data could be promoted.

It was discussed whether patients should always be informed when a health professional completed a report about them. The MHRA said this had been considered in the past but it would consider this again in discussion with the GMC.

2. Requests for Yellow Card data received to date/pending applications

The committee considered the paper provided by the MHRA with examples of the scientific review undertaken by the Interim Committee. The MHRA said it would consider providing ISAC with copies of previous applications where this would inform members of the background to a case.

Application 007 Genetic factors in individual susceptibility to drug induced liver injury

The Application was approved subject to minor amendment.

Application 009

The Committee required further information from the applicant before a decision could be reached on this study.

Rejected applications

The Committee advised the MHRA to reject one application.

3. Data the MHRA proposes to provide to Regional Monitoring Centres

The MHRA explained the historical development of the RMCs and some of the problems this posed in light of the Data Protection Act and new MHRA processes. The MHRA said that it was developing a contract on how Yellow Cards would be followed up by RMCs, and this would include requirements on the storage and destruction of Yellow Cards as they include personal information. The Committee endorsed the proposals on follow up.

The MHRA said it would come back to the Committee at a future meeting with an application from the RMCs on other, non identifiable Yellow Card data they wish to receive to help with promotional, educational and follow up work. The Committee agreed to this approach, and said it would not want information to be provided that RMCs could use to “name and shame” trusts to encourage reporting rates.

The ISAC asked to be kept informed of developments to extend RMC coverage nationwide, and urged the MHRA to include this as part of a long term strategy around promotion and education of the Scheme. The Committee suggested the MHRA engage with other stakeholders such as Royal Colleges and local medical committees.

4. How Yellow Card reporting could be publicised

The Committee said it would also be beneficial to GPs, who are the backbone of the scheme, if the software they use could trigger a Yellow Card when appropriate. Other ways to stimulate reporting would be through CPD of professionals, appointing local champions, engaging with PALS/NICE/lay press and attendance at conferences and scientific meetings. The MHRA

said it was working with its Communications division to develop a strategy to promote the scheme and this input was useful.

GPRD DATA

11. Improving procedures for GPRD protocol review

Following concerns about the higher than expected volume of protocols received since the introduction of ISAC, the MHRA presented proposals which aimed to reduce ISAC's workload by improving the quality of GPRD protocols submitted for review and introducing the concept of proportionality into the review process.

The Committee discussed draft instructions for applicants on protocol content, which would be enforced in order to ensure that protocols cover all issues expected by ISAC and therefore potentially reduce number of protocols which for which resubmission was requested as a result of a failure to discuss important issues. The Committee agreed that such guidance would be helpful and gave comments on the draft guidance. Issues relating to quality which had been encountered in protocol review to date were discussed, in particular, the need for power calculations/feasibility counts to be included, and the appropriateness of imposing age restrictions for inclusion in proposed research.

The Committee discussed a method which would involve the objective assessment of protocols on receipt and subsequent referral for proportionate review by ISAC, based on the applicant's prior experience with GPRD and experience within UK primary care. Although this was felt to be a potentially useful approach, the Committee felt that the current size of ISAC precluded this approach. It was suggested that the MHRA should give further consideration to increasing the size of the Committee. A revised procedure for the review of revised/resubmitted protocols was also adopted, in which the Chairman would evaluate whether the applicants had adequately addressed those issues raised during initial ISAC review, referring the revised protocol for wider review only where the applicant's response was considered unsatisfactory. A new approach to handling and resolving disparate views of members on an individual protocol was also proposed and adopted by the Committee.

The Committee agreed to review the instructions on protocol content once these have been updated in line with the discussions at the meeting. MHRA will also update the GPRD application form to include checklist to enforce the protocol content instructions. These instructions will be publicised and implemented once the revised version and updated application form have been agreed by the Committee.

12. Research governance arrangements for GPRD

The Committee was informed that Trent MREC had granted ethical approval for the release of GPRD data by the MHRA for use in observational research.

Study-specific MREC approval would be required only where the MHRA is providing GPRD data for use in research which includes patient involvement (e.g. completion of questionnaires) or linkage to other data sets; additionally, ISAC can recommend that study-specific ethics approval is sought if they have any other concerns in relation to an individual protocol.

Since MREC approval is prospective, the approval granted to the GPRD Group in 2006 will not cover the data provided to EPIC in the past. Applicants using GPRD data sourced from EPIC will therefore be advised that they need to consult their data provider as to their arrangements for obtaining ethical approval for the proposed research.

The Committee was also informed that the MHRA had recently appointed a Caldicott Guardian, who had reviewed and given approval for all relevant GPRD Group procedures relating to the handling of data.

13. Patient involvement in GPRD research

The Committee discussed the involvement of patients in GPRD research. Given the nature of the database, it was felt that patient involvement might be best focussed on the interpretation of the data and results of studies using this data. For instance, researchers might propose to investigate the quality of care for diabetic patients based on records of prescribing of antidiabetic drugs in the GPRD, whereas the patient view might be that issues such as the exchange between the patient and the GP are more appropriate measures of quality of care.

It was agreed that further discussion on this issue would be held at a future meeting, to include examples identified by members from protocols reviewed in the interim period.

14. Requests for GPRD data to be discussed

Since 1st March 2006, a total of 33 new protocols for research using GPRD data had been submitted for review by ISAC. In order to resolve disparate comments on protocols raised by members during electronic review, a total of five protocols were referred to the ISAC meeting for further discussion.

The Committee considered 5 applications. They advised that 4 applicants should be asked to submit a revised protocol and advised the MHRA to reject one application.

GENERAL PAPERS

15. Blinding of applications

The MHRA presented a proposal for the blinding of research applications/proposals being reviewed by ISAC. This would involve removal of information which would potentially identify applicants (either directly or indirectly); however, information on the experience/expertise available within

the research team would need to be gathered for GPRD protocols where the committee needed to evaluate whether applicants have sufficient expertise to carry out the proposed research.

The Committee agreed that blinding of protocols/applications should be piloted for 6 months for GPRD protocols only, following which the impact of this approach would be reviewed. The Committee agreed to review a revised application form which will include questions on the experience/expertise within the project team prior to implementation of blinding; the pilot will commence at the same time as the implementation of instructions on GPRD protocol content (see 11.).

16. IT security and Freedom of Information

The Committee welcomed the update provided and said the paper had answered any questions they had. The MHRA said it would return to the committee at a later date on the issue of destruction of Yellow Card data provided to applicants.

17. Any other business

No issues were raised.

18. Date of next meeting

It was agreed that the next meeting would be held on Monday 17th July 2006 in Market Towers.

GPRD/VRMM
June 2006