



Medicines & Healthcare products
Regulatory Agency

Independent Scientific Advisory Committee

**Summary minutes of the meeting held on Tuesday 17 January 2017 at 11:00am
in R-T-410, 4th Floor, 151 Buckingham Palace Road, Victoria, SW1W 9SZ**

Members attending

Member	Role
Prof Deborah Saltman AM	Chair
Dr Richard Stevens	Deputy Chair and Scientific member
Dr Angelyn Bethel	Scientific member
Dr Krishnan Bhaskaran	Scientific member
Prof Sinead Brophy	Scientific member
Dr Benjamin Cairns	Scientific member
Ms Rosie Cornish	Scientific member
Dr Christopher Edwards	Scientific member
Dr Duncan Edwards	Scientific member
Prof Peter Helms	Scientific member
Prof Umesh Kadam	Scientific member
Dr Evangelos Kontopantelis	Scientific member
Dr Wendy Knibb	Scientific member
Prof Ben Lipsky	Scientific member
Ms Sally Malin	Lay member
Prof Keith Neal	Scientific member
Dr Jennifer Quint	Scientific member
Dr Sara Thomas	Scientific member
Dr Hester Ward	Scientific member
Prof Ian Wong	Scientific member

Apologies

Member	Role
Dr Caroline Jackson	Scientific member
Professor Simon Mitchell	Scientific member
Ms Marcia Saunders	Lay member

On leave

Member	Role
Dr Emily McFadden	Scientific member

In attendance

Attendee	Role/Post
Dr Janet Valentine	CPRD Director
Mr Daniel Brett	ISAC Secretariat
Ms Sonia Coton	CPRD Researcher
Mrs Tarita Murray-Thomas	CPRD Senior Researcher

1. Welcome and apologies

The Chair opened the meeting and welcomed those members in attendance. Ms Rosie Cornish and Dr Evangelos Kontopantelis were welcomed to their first ISAC meeting as newly appointed Scientific Members of the Committee. Mr Daniel Brett and Ms Sonia Coton who were attending from CPRD for the first time were also welcomed.

Apologies were received from Ms Marcia Saunders and Dr Caroline Jackson while Dr Emily McFadden was on leave from Committee duties.

The Chair thanked the three members Professors Umesh Kadam and Benjamin Lipsky, and Dr Simon Mitchell (not present), whose terms of appointment will come to an end on 31 March 2017, for their valuable work as ISAC members.

2. Minutes of the last meetings

The minutes from the 19 October 2016 ISAC meeting were tabled for members' consideration and they would also be shared electronically with Committee members who will be invited to make any comments by email to the Secretariat.

The summary minutes from the 13 July 2016 meeting were awaiting approval and would be reviewed by Members and approved by the Chair between meetings before being uploaded to the website.

Actions: Secretariat to amend minutes from October meeting based on comments from Committee members.

Secretariat to upload summary minutes from July and October 2016 meetings to CPRD website once approved by Committee and Chair.

3. Matters arising

The actions list from the previous meeting was presented by the CPRD Senior Researcher.

3.1 CPRD guidance to researchers regarding ethical approval and ISAC approval

The Deputy Chair raised the issue of studies requiring research ethics approval in addition to ISAC approval. There was a need to clarify wording for researchers about the ethics approval granted to CPRD and how this related to additional ethical approval required by individual studies.

Members concurred that it was not in the remit of the Committee to provide ethical approval for research studies and that ISAC approval did not equate to research ethics committee approval. The Deputy Chair agreed to provide a statement on behalf of CPRD ISAC to be included in the ISAC guidance for applicants on the CPRD website, for use by researchers when writing research manuscripts.

The CPRD Secretariat confirmed that CPRD's MREC approval covered the governance requirements and scope for collection and use of anonymised patient level data and this was only one of CPRD's many safeguards relating to data security, governance and release.

Action: The Deputy Chair to provide a statement on behalf of CPRD ISAC to be included in the ISAC guidance for applicants on ethical approval for studies to be shared with the Committee at the next ISAC meeting.

3.2 ISAC 15 Month Report

The forthcoming ISAC Annual Report 2015/16 would be a 15 Month Report, covering the period January 2015 to March 2016, in order to move to a financial reporting year which was in line with all other Committees of the MHRA. It was noted, as this encompassed a 15 month period, that comparison of metrics from the previous 12 months would not be possible. Members had delegated approval for the Report to the Chair and the Report would be posted on the CPRD website once it had been approved.

3.3 High and low priority ratings for comments in protocol reviews

Members were thanked for consistently applying either high or low priority ratings to the comments they made on protocol submissions. This was an important issue as it helped maintain consistency in protocol reviews.

3.4 Protocol review comments

In relation to resubmissions, it was noted that the onus should be on applicants to reassure the ISAC reviewers that necessary adjustments had been made to the protocol or that the issue raised was considered appropriately. If an issue raised in a review had not been adequately answered the Secretariat could contact the applicants for further clarification.

It was agreed that the issue of when 'approval with comments' was a justified decision would remain as a future item for discussion.

Action: Secretariat to ensure that 'Approval with comments' would be considered for future meetings as an agenda item by the Chair.

3.5 Committee member availability

Members were asked to email the Secretariat with details of when they will not be able to attend ISAC meetings for the subsequent meetings in 2017. Members were also asked to email the Secretariat with details of when they will not be able to review protocols due to being on leave.

4. Chair's Report

There had been a large number of protocol submissions since the last meeting many of which had been on similar research themes. Members were thanked for their work in reviewing these protocols, particularly where reviewers had been sent more than two protocols during the same month.

5. CPRD Director's Report

The CPRD Director updated the Committee on staffing changes in the ISAC Secretariat since the last meeting. A CPRD Research Applications Officer, had joined in November 2016 with duties including day-to-day administration of the ISAC. A new Head of Observational Research had also been recruited and would join in April 2017. The Observational Research team has recruited a number of positions and now comprised six Senior Researchers, three Researchers and two Research Assistants.

5.1 National Data Guardian Review on Data Security, Consent and Opt-Outs

The Government would shortly be publishing their response to the public consultation on the National Data Guardian (NDG) Review on Data Security, Consent and Opt-Outs. CPRD would input into the development of the resulting policy to ensure factors affecting CPRD were considered in the agreed consent model.

5.2 CPRD GP engagement and data flows

Data from a number of pilot GP practices who used EMIS GP software had now been received in a format that would support future data linkage and other CPRD services. From March 2017, the intention was for CPRD to roll this capability out to all EMIS CPRD contributing practices. GP practices using EMIS had been able to contribute to CPRD in the past, but their data had been received on a quarterly basis and could not be linked to other data sets. This was an important development for CPRD as half of GP practices in the UK were using EMIS software.

The most important priority for CPRD was to grow the number of GP practices that contribute data to CPRD and a new GP engagement team had been established and was working towards this aim.

5.3 Data mining and machine learning

There had been increasing numbers of ISAC applications to use CPRD data to undertake research using machine learning, data mining and artificial intelligence methodology. This was an area that required consideration by the MHRA as protecting the integrity of the CPRD database for pharmacovigilance research was paramount. In developing a new policy on permitted use of the data, CPRD would work together with the ISAC seeking their guidance about wider use of such methodology within the CPRD data asset.

5.4 Understanding Patient Data initiative

A new independent initiative 'Understanding Patient Data' had been established to support better conversations about uses of health and care information with healthcare professionals. CPRD had offered to share case studies and any other information that would be of value promoting the benefits of data sharing.

5.5 e-ISAC

Initial work was underway scoping requirements for an electronic application form (e-ISAC) and the Committee would be updated when plans were more advanced.

6. ISAC Secretariat Report

Mrs Murray-Thomas presented a progress report on protocol processing for the year to date. It was noted that the number of studies including a health services research component had risen significantly since the last year.

7. ISAC Audit

A paper summarising the purpose of the ISAC Audit and the activities which had taken place to date was presented. Members discussed a number of issues including the methodology used to conduct the audit, validity of auditing compliance to guidance that was not in place when protocols were approved and the possible negative impacts on researchers and public trust from releasing data that was potentially flawed or misleadingly indicated wrong-doing. Five options were presented for discussion by the Committee:

- a) To publish the ISAC Audit findings in its current state.
- b) To discuss the ISAC Audit findings at a CPRD User Group Meeting.
- c) To summarise the ISAC Audit findings in the ISAC Annual Report.
- d) To expand the ISAC Audit to compare data from more recent years to the data that was examined from the first stage of the Audit already.
- e) To not publish the results of the ISAC Audit.

Members unanimously agreed to recommend that the findings of the audit should not be published as a scientific paper. Members agreed that the results of the audit would in its present form be unlikely to be acceptable for publication because of a number of deficiencies in its design and the changes made to the advice for applications to use CPRD data over the period of review. Members also did not favour publishing the findings in the Annual Report or comparing the preliminary data with outputs from more recent years.

It was agreed that audit findings would be presented at a CPRD User Group meeting. This would provide a suitable forum to explain the original purpose of the exercise within the context of any methodological short-comings and provide an opportunity to gather feedback from researchers on how a future audit could add value. The ISAC 15 Month Report 2015/16 would include text stating that the findings of the ISAC audit would be presented at a future User Group meeting.

The Deputy Chair was asked to chair a sub-committee charged with presenting the ISAC Audit findings at a CPRD User Group meeting.

Actions: Secretariat to include a statement relating to the audit in the forthcoming 15 Month Report.

The Deputy Chair to chair a sub-committee to present the ISAC Audit findings at a CPRD User Group meeting.

8. Primary Care expertise on study teams – guidance to applicants

A paper on the current guidance on the importance of naming an individual with experience of UK primary care practice as an applicant on the protocol was presented. It was recommended that applicants be advised to provide evidence that a UK-based GP or group of GPs had been involved in the development of the protocol.

It was agreed that applicants do not need to name a UK-based GP as an applicant per se, provided they could demonstrate an up-to-date knowledge and understanding of how primary care practice works in the UK.

It was further agreed that ISAC would update guidance to applicants on this issue and that a line would be added to the application form asking how the applicants meet the criteria. The reviewer comments back to applicants would take this criterion into account as relevant.

Action: A statement on behalf of CPRD ISAC to be included in the ISAC guidance for applicants on Primary Care expertise on study teams to be shared with the Committee at the next ISAC meeting.

9. Protocols for discussion – Data Mining and Machine Learning

The Committee discussed two protocols that had been highlighted as of interest from over the last few months.

10. Next meeting

The next ISAC meeting will be held on 25 April 2017 in room R-T-503 at 151 Buckingham Palace Road, Victoria, SW1W 9SZ.