Medicines & Healthcare products Regulatory Agency

Central Advisory Committee (CAC)

Minutes of the meeting held on 04 October 2021 at 3:00pm via Microsoft Teams

Members attending	
Member	**Role**
Prof Richard Stevens	Chair
Edward Chapman	Lay member
Prof Deborah Saltman AM	Scientific member
Dr Benjamin Cairns	Scientific member
Dr Kate Fleming	Scientific member
Prof Susan Jick	Scientific member
Prof Martin Gulliford	Scientific member
Sonia Patton	Lay member

Apologies	
Member	**Role**
Prof David Fishwick	Scientific member
Prof Li Wei	Scientific member
Prof Umesh Kadam	Scientific member
Prof Jennifer Quint	Scientific member

In attendance	
Attendee	**Role/Post**
Dr Janet Valentine	CPRD Director
Dr Puja Myles	Head of Observational Research
Tarita Murray-Thomas	Senior Researcher
Zara Cuccu	Researcher
Jonathan Lind	Research Applications Manager
Guest Attendees	**Role/Post**
Peter Singleton	Interim Senior RDG Manager
Yemi Macaulay	Research Data Governance Officer

1. Welcome and apologies

The Chair welcomed attendees to the second meeting of the Central Advisory Committee (CAC) and noted apologies. Members were reminded of the Terms of Reference of the Committee.

2. Minutes

The minutes of the CAC meeting held on 26 July 2021 were reviewed and confirmed as an accurate record. There were no outstanding actions.

3. Director's Update (Janet Valentine)

JV provided an update to the CAC on recent developments in the CPRD.

The post-approval amendment feature had been deployed in eRAP. All future applications submitted via eRAP would now have their post-approval amendments processed via this route. Applications dating back to July 2017 would be uploaded to the portal in due course, allowing for amendments to these studies to be submitted via eRAP. JL was thanked for his oversight of this development.

CPRD has created two high fidelity synthetic datasets on CVD and COVID-19. A medium fidelity sample dataset based on the CPRD Aurum database will also be available in autumn 2021. The latter could be used to understand the structure and utility of the primary care data in CPRD Aurum for research, to develop and test analytical tools for use with CPRD Aurum data and to develop machine learning workflows that could be applied to anonymised CPRD Aurum data. This would also be made available as a teaching/training resource. Access to the medium fidelity sample dataset would be available free of charge to users from organisations with a CPRD multi study licence. Requests for access to all synthetic datasets are handled outside of the RDG process, that is, they are not subject to RDG review.

CPRD's pilot journal club initiative in which the wider CPRD user community was invited to attend journal clubs organised by CPRD, has now been routinely adopted by CPRD. This is an opportunity to strengthen the relationship between CPRD and the user community. Routine adoption was in response to positive feedback from the user community. Notification of future journal club sessions will be through the CPRD Research bulletin.

CPRD's GP Questionnaire service is now being implemented electronically as the PROVE (PRoviding Online Verification of EHR) and PROVE Plus services. Short questionnaires (1-3 questions) are implemented under the PROVE service and longer questionnaires (up to 10 questions) will be handled via the PROVE-PLUS service. All studies requesting access to data via GP questionnaires will continue to be reviewed under the RDG process.

The last annual report of the Independent Scientific Advisory Committee (ISAC) is currently being finalised. This will cover a reporting period of 15 months from April 2020 – June 2021 to take account of the period prior to the launch of the new CPRD RDG process. The activity of the ISAC from April 2021 – Jun 2021 will be covered in an Annex to that Report.

4. Secretariat Update (Jonathan Lind)

JL provided an update to the CAC on metrics relating to applications received between 12 July 2021- 1 Oct 2021. 56 new applications were received of which 30 (54%) were triaged as routine for internal review and 26 were triaged as non-routine for ERC review. Approval rate on first submission was about 25%. The high resubmission rate of routine (81%) and non-routine applications (94%) may be due to several factors including ongoing embedding of the new review process and constraints in the use of eRAP. CPRD will monitor review outcomes in the coming months.

JL also notified the CAC that it will soon be possible for all reviewers, including moderators, to view a history of their protocol reviews with the final moderated feedback on eRAP.

5. Oversight of Routine/Non-Routine Protocol Triage (Chair / Tarita Murray-Thomas)

CAC members were asked to provide feedback on CPRD's administration of the protocol triage calibration exercise circulated prior to the meeting. Members were asked to comment on the calibration process such as assigning CAC members into calibration groups, the format/structure of the calibration proforma, time assigned for the calibration exercise etc.

Members agreed that the exercise was straightforward but requested more time to complete and discuss the ratings within their teams. Members asked for the proforma to be updated to include a clear mechanism to capture group feedback.

In terms of the actual exercise, members felt that having greater visibility of the evaluation process used by CPRD to reach triage decisions would be useful and that working through one or more examples collaboratively with CPRD may add greater value to the calibration process. In terms of the completed responses from the exercise submitted prior to the meeting, TMT reported that agreement between CPRD triage and CAC triage was about 60%. Members noted that the goal of the calibration exercise was not necessarily to achieve consensus on ratings but to ensure that there was appropriate oversight of the triage process and an understanding of how the triage decisions were made. Members felt that discussion at the meetings should focus on specific cases-studies.

Potential areas for discussion at the future meetings include studies with a focus on clinical effectiveness, equity in health care, and studies triaged as being of major public health importance/implications.

6. When to request an IG review (Peter Singleton and Yemi Macaulay)

PS presented on key information governance (IG) risks that should be assessed as part of the RDG process. CAC members asked for clarification on whether applications were screened by CPRD for IG risks prior to the review process, and if so, to what extent were reviewers expected to assess applications for IG risks. CAC members were advised that information governance risks could be identified at any stage in the application process - application validation, protocol triage or during the protocol review process. Where an IG risk was identified at an earlier stage in the application process (validation or protocol triage), this would be flagged on eRAP. While it was anticipated that nearly all IG risks would have been flagged by internal reviewers, CAC members were reminded that they also had a role in ensuring that no risks had been missed especially if these related to novel methodologies or obscure clinical topics. The CPRD IG team has drafted guidance to support reviewers in evaluating information risks during protocol review. This will be circulated shortly for use by reviewers and discussed at the next meeting.

7. Approaches to ERC Moderation (Chair/Tarita Murray-Thomas)

The CAC Chair presented 3 options proposed by CPRD to undertake calibration of ERC moderated feedback at future meetings. These included:

i. Peer review of all ERC moderated feedback by pairing ERC Chairs on a rotating quarterly basis. Calibration would take place outside of CAC meetings
ii. CAC review of select ERC moderated feedback – nominated by ERC. Calibration would take place during CAC meetings
iii. CAC review of select ERC moderated feedback – nominated by CPRD. Calibration would take place during CAC meetings

Additional options put forward by CAC members were also considered, including: the use of an open and explorative approach in which ERC members nominate protocols for discussion at the meeting; working collaboratively outside of the meeting to calibrate feedback; and calibration during the CAC meeting focusing on a single protocol identified at the protocol triage stage. However, some members expressed concerns about the demands on time to meet outside of the CAC meeting. It was agreed that calibration should be undertaken during meetings and that ERC Chairs and CPRD should each nominate one protocol for discussion at the meetings.

BC asked whether CPRD had any plans to actively engage with ERC reviewers about calibration of feedback for e.g., whether there were any plans for joint ERC meetings. PM advised that annual training was planned for all ERC reviewers as part of the wider quality assurance process. ERC Chairs to ascertain from team member whether there was an interest in meeting other ERC teams outside the annual calibration meeting.

8. Agenda for Next Meeting (Chair)

The Chair noted that the following items were on the agenda for the next CAC meeting:

- Minutes of the previous meeting
- Secretariat update
- Oversight of protocol triage
- Oversight of ERC moderation

9. AOB (Chair)

None

10. Summary and Close (Chair / Tarita Murray-Thomas)

Agenda item	Action	Date to be completed by
6	CPRD IG team to circulation IG guidance to reviewers and obtain feedback at the CAC meeting in Jan 2022.	Jan 2022
7	CPRD to canvass and book the next CAC meeting in Jan 2022	Nov 2021
7	CPRD to canvass and book group training session for all CAC and ERC members	Jan 2022