Medicines & Healthcare products Regulatory Agency

Central Advisory Committee (CAC)

Minutes of the meeting held on 17 Oct 2022 at 3:00pm via Microsoft Teams

Members attending	
Member	**Role**
Prof Li Wei	Chair
Prof Susan Jick	Scientific member
Dr Benjamin Cairns	Scientific member
Prof Martin Gulliford	Scientific member
Dr Kate Fleming	Scientific member
Prof Umesh Kadam	Scientific member

Apologies	
Member	**Role**
Mr Edward Chapman	Lay member
Prof David Fishwick	Scientific member (retired)
Mrs Sonia Patton	Lay member
Prof Richard Stevens	Scientific member
Prof Deborah Saltman AM	Scientific member
Prof Jennifer Quint	Scientific member

In attendance	
Attendee	**Role/Post**
Dr Puja Myles	Director of CPRD
Tarita Murray-Thomas	Senior Researcher
Jonathan Lind	Research Applications Manager
Tarryn Gourley	Research Applications Officer

1. Welcome and apologies

The Chair welcomed attendees to the fifth meeting of the Central Advisory Committee (CAC) and noted apologies. Members were informed of changes in membership of the CAC. The Chair thanked Professor David Fishwick for his contributions to the Committee and wished him the best for his retirement. Professor Evan Kontopantelis and Dr Achim Wolf were also thanked for their service as ERC members. Professor Richard Martin, who has replaced Professor Fishwick as ERC 6 Chair, and Dr Arlene Gallagher, who has replaced Dr Wolf from ERC 9, were welcomed.

Members were reminded of the Terms of Reference of the Committee. The Chair explained that the purpose of the meeting was to feedback on members' experience of paired ERC meetings, as agreed at the last CAC meeting and provide oversight of protocol triage via the triage calibration exercises.

2. Minutes

The minutes of the CAC meeting held on 17 May 2022 were reviewed and confirmed as an accurate record. There were no outstanding actions.

3. Director's Update (Puja Myles)

PM provided an update to the CAC on recent developments in Clinical Practice Research Datalink (CPRD).

PM informed the CAC that she has now been appointed CPRD Director and that her former post of Head of Observational Research would soon be advertised.

Members were informed of CPRD's key priorities for the next three years - transitioning to a new trusted research environment (TRE) model of data access, ensuring better tools to enhance data utility, working to increase transparency and public engagement, and expanding services such as the ethnicity record. PM noted that CPRD is currently on target to meet the 27% UK population coverage of CPRD by the end of the financial year 2022/2023.

PM also provided an overview of developments in CPRD primary care databases, including optimisations to CPRD Aurum (data from EMIS) and the progress on TPP data testing (data from SystmOne). An overview of new linkages was provided. This included: the Intensive Care National Audit and Research Centre (ICNARC) data on COVID-19 intensive care admissions; the CPRD Aurum Pregnancy Register; and CPRD Aurum Mother-Baby Link.

Members were notified of data governance updates. CPRD has received a refreshed approval from the Research Ethics Committee (REC). Members were also informed of the successful NHS Digital audit of CPRD's disclosure risk measures and client audit procedure and that the CPRD website now included a summary of client audits that had been conducted.

PM informed members that work continues on the CPRD Trusted Research Environment (TRE). There is a functioning minimal viable product which includes synthetic CPRD Aurum data and statistical software packages such as R, Python and Stata. The next iteration should be ready by March 2023 for a select number of researchers to pilot. There is parallel work to review existing policies and processes to ensure that they will support the transition to the new TRE model of data access.

4. Secretariat Update (Jonathan Lind)

JL provided an update to the CAC on metrics relating to applications received between 11 May 2022 - 12 Oct 2022. 133 new applications were received of which 55 (41%) were triaged as routine for internal review and 78 (59%) were triaged as non-routine for ERC review.
For studies triaged as routine that were reviewed, 17 (31%) were approved on first submission and 36 (65%) required resubmission. For studies triaged as non-routine that were reviewed, 6 (8%) were approved on first submission and 56 (72%) required resubmission. CPRD will monitor the difference in required resubmissions between applications triaged as routine and non-routine. Overall review times are just under 8 working days for routinely triaged studies, whilst external reviews average just under 11 working days. This is in keeping with timeframe commitments for protocol reviews. The move to the online eRAP system has not had any notable impact on review times.

JL noted that CPRD is keen to hear any feedback from reviewers and moderators to understand which protocol sections are being failed most often and the reasons behind this. Any feedback received will support the continued development of the guidance, with an eye to bringing down the number of resubmissions.

JL also addressed common issues experienced by applicants. Firstly, JL reminded Members that discretionary comments should be phrased as suggestions, rather than instructions, which

can be actioned as post-approval amendments rather than at the resubmission stage. Unclear phrasing is leading to many applicants assuming they must make changes before resubmitting. Secondly, JL reminded Members that when a particular section is failed, all related sections must also be failed. There is a plan to automate this in future.

JL provided an overview of eRAP updates. The biggest developments were feasibility studies and linked data requests transitioning to eRAP.

5. Proposals to pair ERCs (Jonathan Lind)

JL reminded members that, following the last CAC meeting, the committee agreed to proposed pairing of ERCs in order help facilitate learning and calibration. CAC members were asked to provide feedback on the ERC pairings and whether any additional support was needed from CPRD to facilitate the pairings.

Member responses suggested that no meetings had taken place between the pairs and that support from CPRD may be needed to organise meetings. It was agreed that CPRD would looks for ways to facilitate the meetings and this item would be kept on the agenda.

6. Oversight of Routine/Non-Routine Triage (Chair)

CAC members were asked to provide feedback on the triage proforma exercise circulated prior to the meeting. Group Chairs provided summaries on whether their group agreed or disagreed with CPRD's triage rating for a selection of protocols, which were reviewed between 01 August 2022 and 09 September 2022. TMT noted that there was 72.8% total agreement between CPRD rating and CAC rating of protocols as routine and non-routine.

TMT noted that comments arising from CAC protocol triage calibration teams provided important insights that may help to shape guidance on application of the triage criteria.

KF reported that there was slight disagreement in Group 1 over what are considered standard or non-standard methodologies. In Group 2, MG noted that perhaps the criteria of public health importance could benefit from being narrowed down, as a lot of studies could currently be considered non-routine based on the criteria. LW noted that there was general agreement within Group 3 and that differences could be explained through the different interpretations of the criteria by individuals.

In subsequent discussion, SJ noted that understanding the objective of each criterion, for example the risk or concern, was really useful in discerning the appropriate triage route of a protocol. PM noted that protocols could also be triaged as non-standard for reasons of public confidence. There would be further discussion of the triage criteria at the next CAC meeting.

7. ERC Review Moderation (Chair)

CAC members were reminded that one of the Committee's responsibilities is to facilitate calibration of reviews across the ERCs for consistency. This is important to ensure that there is consistent application of the reviewer guidelines and issuing of feedback to applicants. At the last meeting, members agreed to discuss one protocol nominated by a CAC member and one protocol nominated by CPRD.

KF presented a protocol that was escalated for CAC review and members discussed issues relating to the review of studies with concerns over problematic definitions of study

populations. Members agreed that the RDG process provided applicants ample opportunity to respond to concerns before a decision to reject a protocol is reached.

8. RDG 1-Year Review Update (Tarita Murray-Thomas)

TMT informed Members that a draft report, following the 1-year review of the RDG process, would be reviewed by the CPRD Senior Management Team and would inform a range of stakeholders including the MHRA Patient Safety and Engagement Committee, internal/ERC reviewers, and applicants. TMT informed members of some of the findings of the report.

One of these areas was the protocol reviewing workload - between 01 June 2022 – 31 May 2022,181 (58%) of new research applications were reviewed by ERCs and 131 (42%) were reviewed by CPRD. The ERC workload exceeded that expected by CPRD as this was projected to be about 30% of all applications per annum.
TMT also pointed to the high number of protocols reviewed and rated as resubmission required during the review period (138/231). Recommendations to improve the quality of applications received by ERCs included expanding validation checks to include problem areas and further development of the CPRD RDG reporting interface.

Information governance (IG) reviews was another area addressed in the report. Recommendations in this area included: CPRD producing information governance guidance for applicants to help them to also consider information governance risks during the protocol development stage, providing more IG focused training, hosting IG review guidance on the electronic research application portal eRAP) and routinely providing automated IG advice with every feedback.

TMT highlighted that protocol moderation was working well and that CPRD was considering whether having more GPs on ERCs or in the ad hoc pool would benefit the review process. TMT announced that to accommodate CAC discussion around problematic issues or specific items of interest to the CAC, a standing item on the agenda for CAC meetings would be created with immediate effect.

Members noted that the RDG process was a very efficient process and that improvements to the eRAP system had streamlined work for reviewers and moderators.

9. Publication and public health benefit: Discussion (Tarita Murray-Thomas)

Members discussed concerns about proposed research studies that do not include plans to disseminate /publish findings. For example, research conducted in part fulfilment of academic degrees, with no plans to publish beyond the dissertation. Members suggested that academics could use their own judgment on whether to publish. There was no consensus on how findings of research not published could benefit public health. PM noted that from a CPRD perspective, as long as clear public benefit was demonstrated in the application and findings made available to facilitate this, there was no requirement for publication in a peer-reviewed academic journal.

10. Mortality in CPRD Aurum (Martin Gulliford)

MG advised the Committee of work undertaken in his team suggesting issues in the recording of death data in CPRD Aurum and discussed how this may affect studies using CPRD Aurum data. Members discussed potential reasons for the lower mortality found in CPRD Aurum, as compared to national estimates. CPRD committed to looking into this further after the meeting.

11. AOB (Chair)

No other business was raised.

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

Agenda item	Action	Date to be completed by
N/A	CPRD to canvass CAC members for dates and book the next CAC meeting in February/March 2023	Jan 2023
5	Feedback on ERC pairs	Next CAC meeting, TBA
8	Create CAC standing item for members	Next CAC meeting, TBA