Minutes of the meeting of the Confidentiality Advisory Group

11 May 2023 via Zoom

Present:

Name	Role
Mr Thomas Boby	CAG Member
Dr Ben Gibbison	CAG Member
Mr Anthony Kane	CAG Member
Ms Clare Sanderson	CAG Alternate Vice Chair
Dr Murat Soncul	CAG Alternate Vice Chair
C. Marc Taylor	CAG Member
Professor James Teo	CAG Member

Also, in attendance:

Name	Position (or reason for attending)
Mr William Lyse	HRA Approvals Administrator
Ms Emma Marshall	HRA Confidentiality Specialist

Mr Dayheem Sedighi	HRA Approvals Administrator
Ms Caroline Watchurst	HRA Confidentiality Advisor

1. Introduction, apologies, and declarations of interest

Apologies – CAG Members Mr Umar Sabat, Dr Stephen Mullin and Ms Rose Payne send their apologies.

CAG Members Dr Ben Gibbison, and Professor James Teo declared that they work at Trusts which are participating sites for the application – 3a. They are not involved with the study, and this was not considered a conflict of interest. Both Members were involved in the development of the recommendation provided by CAG.

2. Support decisions

Secretary of State for Health & Social Care Decisions

The Department of Health & Social Care senior civil servant on behalf of the Secretary of State for Health & Social Care agreed with the advice provided by the CAG in relation to the **06 April 2023** meeting applications.

Health Research Authority (HRA) Decisions

There were no research applications reviewed at the **06 April 2023** meeting.

Minutes:

- 06 April Full CAG Meeting minutes
- March 2023 Sub-committee minutes

3. New Applications – Research

a. 23/CAG/0051 – Retrospective analysis of real-world evidence on the use of glycopyrronium bromide in children under 3 years of age with sialorrhea.

Context

Purpose of application

This research application from Alder Hey Children's NHS Foundation Trust and Proveca Ltd set out the purpose of medical research that seeks to Evaluate the safety and efficacy of using enteral Sialanar® (glycopyrronium bromide) to treat sialorrhoea (excessive drooling) in children under 3 years old, in terms of adverse events, suspected serious adverse events and the associated treatment discontinuation due to such events.

Sialanar® (glycopyrronium bromide) is currently licensed for the treatment of severe drooling in children and adolescents aged 3 years and older with chronic neurological disorders. The existing indication for Sialanar® was based on the position that salivary continence is not normally reached until 15–18 months of age in developmentally normal children. Consequently, drooling is not considered pathological below 3 years of age. Nevertheless, severe drooling is a significant issue for a proportion of children with chronic neurodevelopmental issues below 3 years of age, and it has become apparent that there is significant interest in and use of Sialanar® in children under 3, prescribed off label (use outside of the product license). This study will use retrospective patient data, of children under 3 who have been treated with this drug. It is hoped that a retrospective analysis of this age group, if shown to be an effective treatment, could evidence an expansion of the Sialanar® licence. This would give younger patients easier access to a product to help manage excessive drooling.

The study is limited to the review of existing medical records of participants from birth to 3 years of age treated with glycopyrronium bromide for sialorrhoea, at participating Trusts. ‘s251’ support is requested for the identification of potential participants, who will be identified through review of the available medical records at participating sites by research staff who are not considered direct care team. ‘s251’ support is also requested for the research staff to view medical records during the process of data extraction. Data will be collected for each individual participant for up to 36 months following the commencement of glycopyrronium bromide treatment, or to the age of 3 years whichever is less. ‘s251’ support is requested to allow date of birth and date of death to be uploaded to Redcap (hosted by University of Liverpool), alongside other clinical data, including sex, gestational age, body weight, length at birth, and medical history. Confidential patient information will then be removed by University of Liverpool, prior to analysis being undertaken on an effectively anonymous dataset by Alder Hey Children's NHS Foundation Trust. Any data onwardly disclosed to Proveca Ltd is effectively anonymised.

A recommendation for class 1 and 6 supports was requested to cover access to the relevant unconsented activities as described in the application.

Confidential patient information requested

The following sets out a summary of the specified cohort, listed data sources and key identifiers. Where applicable, full datasets and data flows are provided in the application

form and relevant supporting documentation as this letter represents only a summary of the full detail.

Cohort	Participants from birth to 3 years of age treated with glycopyrronium bromide for sialorrhoea Planned sample size of approximately 50-100 patients. Data will go back up to 10 years, starting with the most recent available data.
Data sources	Medical notes from 5 Participating sites: • Alder Hey Children's NHS Foundation Trust • Gateshead Health NHS Foundation Trust • Nottingham University Hospitals NHS Trust • Guy's and St Thomas' NHS Foundation Trust • University Hospitals Bristol & Weston NHS Foundation Trust
Identifiers required for linkage purposes	1. Date of birth 2. Date of death 3. Sex Medical records will be reviewed to extract this data.
Identifiers required for analysis purposes	N/A analysis will be undertaken on a pseudonymised dataset.

Confidentiality Advisory Group advice

The following sets out the Confidentiality Advisory Group advice which formed the basis of the decision by the Health Research Authority.

Public interest

The CAG noted that this activity fell within the definition of medical research and was therefore assured that the application described an appropriate medical purpose within the remit of the section 251 of the NHS Act 2006. The CAG agreed that the application was in the public interest.

Scope

The CAG requested clarification on how the research team identified eligible patients notes. It is stated that medical records would be searched to identify those patients who fit the criteria, however it was not clear if this would involve the screening of all patient notes by the research team in order to do this, or if the direct care team would provide the research team with the relevant list of patients. If it were the first scenario the scope of 's251' support would be required for the research team to review those individuals notes who do not end up being eligible.

The members noted the data flow diagram did not reflect that NHS numbers were no longer collected. The members also commented that the data flow diagram was quite difficult to understand. Therefore, the CAG requested for a revised data flow diagram in line with guidance from the CAG website: Guidance for CAG applicants - Health Research Authority (hra.nhs.uk)

The CAG also requested for the protocol to reflect that NHS numbers were no longer being collected. This revision was not noted as a condition, however, was requested within the next protocol amendment submission.

Practicable alternatives

Members considered whether a practicable alternative to the disclosure of confidential patient information without consent existed in accordance with Section 251 (4) of the NHS Act 2006, taking into account the cost and technology available.

- **Minimising flows of identifiable information**

The CAG notes that the applicant planned to disclose effectively anonymous datasets to Proveca Ltd. However, the CAG noted that because the cohort was so small, and the list of potential conditions these patients may have quite broad, it might be possible for patients to be identified via a combination of data items such as treating hospital, alongside diagnosis. Therefore the Committee wished to remind the applicants to ensure that anonymisation was carried out in line with ICO guidance, to avoid any accidental re-identification with regards to small sample numbers.

- **Feasibility of consent**

The applicant reasons that consent is not a practicable alternative, because the data being collected is retrospective, going back a number of years. As a result, it is possible that children have been discharged and the research site may no longer hold current contact details for the parents. Additionally, it is administratively difficult to contact the parents of patients treated many years ago.

The applicant also reasons that the cohort of patients have complex neurological conditions which in some cases may be life-limiting, and there's a potential to cause parental distress/upset if the applicants were to contact parents of children who are deceased.

The CAG was content that consent was not a practicable alternative.

- **Use of anonymised/pseudonymised data**

Confidential patient information is required to identify eligible patients. Confidential patient information, date of birth and date of death, is also required to be collected and disclosed to the lead site. Full dates are required for accuracy of data in a younger age cohort. Both are modified for analysis.

The CAG was content that using anonymous information was not a practicable alternative.

'Patient Notification' and mechanism for managing dissent

It is part of the CAG responsibility to support public confidence and transparency in the appropriate sharing and use of confidential patient information. Access to patient information without consent is a privilege and it is a general principle of support for reasonable measures to be taken to inform the relevant population of the activity and to provide a right to object and mechanism to respect that objection, where appropriate. This is known as 'patient notification'. This is separate to the local obligation to comply with the principles of the General Data Protection Regulation and Data Protection Act 2018.

A poster has been developed and will be made available in clinical areas where potential participants are seen (eg clinics) giving Parents an opportunity to contact the research team if they do not want their child's data to be included in the study. An study specific opt out is available via the poster. The National Data Opt Out will be respected.

Initially, the CAG discussed whether the notification could be displayed on any appropriate charity websites to try to widen the change that the parents of the cohort might see it. However, this was dismissed as not practicable, as this drug is used for a wide variety of diseases, and therefore there are no outstanding charities that specifically focussed on treating sialorrhoea.

The CAG requested a layered approach to patient notification, for example by providing a QR code or website link which leads on to a website providing additional material. This would contextualise the study further and provide reassurance such as

assuring parents and guardians that this is a medicine licensed for and commonly used in affected children over the age of 3.

The CAG additionally requested revisions to the poster, requesting for the generic medication name to be used in addition to the scientific name, and for an explanation of the specific breaches of confidence requiring CAG review and 'section 251' support.

Furthermore, the CAG requested for the study specific opt-out to appear first within the notification. It should state that opt-out via this method was not necessary if participants had already applied the National Data Opt-Out. Also, the poster should not provide a link to the National Data Opt-Out, only reference that it will be respected.

Lastly, the CAG requested for all these revisions to the poster, and any further website notification to be reviewed by a patient and public involvement group.

Patient and Public Involvement and Engagement

Meaningful engagement with patients, service users and the public is considered to be an important factor for the CAG in terms of contributing to public interest considerations as to whether the unconsented activity should go ahead.

The study was discussed with the University of Liverpool public and patient involvement group (PPI) on Wednesday 15th March 2023. 8 Parents attended this meeting and were given an overview of the proposed study, how data will be protected and asked for their comments regarding the plan not to seek study specific consent due to the retrospective nature of the study. All Parents agreed that this was an appropriate course of action and would have been happy for their child's data to be included should they have met the inclusion criteria. This seems to indicate support for the use of data without consent.

The CAG was satisfied with the engagement from the patient and public involvement group. However, as previously stated, requested for continued engagement to occur with regards to the patient notification materials.

Exit strategy

's251' support is also required until date of birth and date of death is deleted from the eCRF by University of Liverpool. The applicant has answered as part of query responses that University of Liverpool will delete these data once the database has been locked for analysis and the Sponsor has approved deletion, but has not given an indication of any potential time point for this.

In addition, a key will be retained at each site to enable re-identification of individuals if required for any potential Regulatory data queries or audits. This will be retained for 10 years and retained by each participating site. ‘s251’ support is therefore required for 10 years, until the keys are deleted.

The CAG therefore requested clarity on an estimated time point for when the University of Liverpool would delete the date of death and date of birth from the electronic case report form (ECRF).

Furthermore, the CAG requested a justification on why the key needed to be retained for 10 years.

Confidentiality Advisory Group advice conclusion

The CAG agreed that there was a public interest in this activity, were supportive in principle of this activity proceeding, and therefore recommended to the Health Research Authority that the activity be provisionally supported. However, further information and actions would be required prior to confirming that the minimum criteria and established principles of support have been adequately addressed.

In order to complete the processing of this application, please respond back to all of the request for further information, and actions required to meet the specific conditions of support where indicated, within one month.

Request for further information

1. Please clarify how the research team identify which patients are eligible, and if ‘s251’ support is required for any screening of additional patients in the process.
2. Please provide an updated data flow diagram, in line with advice in this letter.
3. Please confirm that any effectively anonymous data will be anonymised in line with ICO guidance, especially with regards to small numbers.
4. Please update the patient notification materials in line with advice in this letter and provide to CAG for review.
5. Please provide clarity on an estimated time point for when the University of Liverpool would delete the date of death and date of birth from the electronic case report form (eCRF).
6. Please justify why the key needs to be retained for 10 years.

7. Please provide favourable opinion of the REC, as per standard condition of support below.

Specific conditions of support (provisional)

The following sets out the provisional specific conditions of support. These may change in the final outcome letter depending on the responses to queries.

1. Please reflect within the protocol that NHS numbers are no longer collected. Please submit this updated protocol within the next protocol amendment submission.

2. Favourable opinion from a Research Ethics Committee. **Pending**

3. Confirmation provided from the DSPT Team at NHS England to the CAG that the relevant Data Security and Protection Toolkit (DSPT) submission(s) has achieved the 'Standards Met' threshold. See section below titled 'security assurance requirements' for further information. **Confirmed:**

   Due to the number of organisations involved it is the responsibility of Alder Hey Children's NHS Foundation Trust and Proveca Ltd, as controllers, to ensure that participating Trusts meet the minimum required standard in complying with DSPTs, and take remedial action if they become aware of any that fall below this, or where any concerns are raised about a Trust.

4. Office Report

Members were reminded that the office report had been sent to them and that any queries could be followed up with the CAT team.

5. Any other business

The Chair thanked Members for their attendance and the meeting was closed.

Signed – Chair	Date
Ms Clare Sanderson, CAG Alternate Vice-Chair	*18 May 2023*
Signed – Confidentiality Advice Team	Date
Mr William Lyse, HRA Approvals Administrator	*12 May 2023*