Minutes of the meeting of the Sub Committee of the Confidentiality Advisory Group

17 March 2023 via correspondence

Present:

Name	Role	Items
Professor William Bernal	CAG alternative vice-chair	2a
Dr Malcolm Booth	CAG member	2a
Ms Diana Robbins	CAG member	2a

Also in attendance:

Name	Position (or reason for attending)
Ms Caroline Watchurst	HRA Confidentiality Advisor

1. Expressions of interest

There were no conflicts of interest declared.

2.New Precedent Set Review Applications

a. 23/CAG/0036 - Pre-clinical biomarker analyses for Gastrointestinal and Hepato-pancreatobiliary disease: cancers and inflammatory disorders

Context

Purpose of application

This application from University of Nottingham set out the purpose of medical research which aims to investigate biomarkers using a variety of cancerous and inflammatory tissue of the gastrointestinal (GI) and hepato-pancreatobiliary (HPB) tract, to create prognostic, diagnostic, preventative, and predictive models to improve disease outcome and treatment. In the cancer research section, researchers will investigate a range of biomarkers within GI and HPB tumours and their metastases to facilitate diagnosis, prognosis, preventative measures and predictions to therapy. In the inflammatory disease section, researchers will investigate biomarker quality and expressions within GI and HPB inflammatory diseases that may be infective, metabolic, immunological, allergic or drug induced.

GI and HPB diseases, including inflammatory and malignant conditions with associated morbidity and mortality, are common, and cancer in general accounts for 166,533 deaths annually in the UK. There are a number of limitations to the current methods of histopathologic diagnosis. Consequently, the use of biomarkers has become a rapidly expanding field playing a central role in diagnosis and in the selection of tailored anti-cancer therapies. Furthermore, biomarkers are increasingly important to aid with screening, diagnosis, prognosis and predictions to therapy in disease. Hence, research into biomarkers for both cancer and inflammatory diseases is paramount to improve patient diagnosis and prognosis.

The project will use surplus tissue from retrospective diagnostic samples taken as part of standard of care, at Nottingham University Hospitals NHS Trust. Eligible patients will be identified the Data Management Team, who are not considered direct care team, hence the requirement for ‘s251’ support. NHS Trust pathology computer systems will be searched to identify eligible participants, and linked to clinical data surrounding diagnosis from medical records. A pseudonymous ID is added, and confidential patient information removed by the Data Management Team. Subsequently, the tissue

samples from identified participants will only be extracted by clinical colleagues (histopathologists at NUH). Therefore, this element does not require ‘s251’ support.

A key between the pseudonymous ID and identifiable information will be retained within the Trust, by the Data Management Team, for 7 years after the study has ended as per standard procedure under the University of Nottingham sponsor arrangements. Only pseudonymous data will be provided to the research team at the University of Nottingham, who will not have the means to re-identify, and hence the data will be effectively anonymous. Tissue samples will be provided by the Department of Histopathology in Formalin Fixed Paraffin Embedded (FFPE) tissue blocks. The FFPE samples will have been taken during diagnostic surgical procedures and then prepared and stored under the local NHS procedures. Researchers will have access to the anonymised FFPE tissue and digital diagnostic images for analysis. Applicants may need to send anonymised material to different institutes outside of the UK, including Europe and the US for further analysis – this activity does not require ‘s251’ support if appropriately anonymised in line with ICO code of practice, and the applicant has confirmed that this will be the case.

A recommendation for class 1 & 6 support 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	~5000 retrospective patients who have had a procedure to remove tissue from the GI or HPB tract at Nottingham University Hospitals, if there is surplus tissue available after diagnosis has been made. Tissue samples will have originally been taken from patients >5 years ago (between approximately 2000-2016). Microscopy image samples will have originally

	been taken from patients >1 year ago (between approximately 2000-2022).
Data sources	1. The Nottingham University Hospitals NHS Trust a. Histopathology samples/ Microscopy image samples b. histopathologic diagnosis from clinical records
Identifiers required for linkage purposes	1. NHS number 2. Hospital ID 3. Date of birth 4. Date of death
Identifiers required for analysis purposes	1. Gender 2. Ethnicity (this is effectively anonymous to the applicant)

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 Sub-Committee agreed that the public interest in the activity had been appropriately justified.

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.

- **Feasibility of consent**

The applicant reasoned that it would be difficult and extremely time consuming to find details and contact each individual patient for consent. The applicant also reasons that as the samples will have been taken at a time a patient may have been diagnosed with

a disease or cancer, it would cause undue distress to the participants. The CAG commented that undue distress is not usually accepted as a reason for not seeking consenting, however the Members accept the first reason provided, that it would be difficult and time consuming for the direct care team to consent 5000 retrospective patients. Members also commented that consent is also impracticable as many of the patients will have died. The CAG therefore agreed that consent for this project was not a practicable alternative.

However for future projects of this type, the Members commented that the requirement for 's251' support could be avoided if the routine clinical consent taken at the time of sample storage was revised to include asking the patient for permission for the use of the sample in future research. The Members note that this consent is not an option for this project as the samples used were taken retrospectively. However it is suggested that the routine consent process should be revised to include permission for use of samples in research. This would avoid the requirement for 's251' support for future similar projects.

- **Use of anonymised/pseudonymised data**

Confidential patient information is required to identify eligible patients, link to clinical information, and will be viewed during the extraction of an effectively anonymous dataset for analysis. Analysis will be undertaken on an effectively anonymised dataset. The CAG were content that the use of anonymised data is not a practicable alternative for the activities which require 's251' support.

'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 provided, which will be distributed within appropriate gastrointestinal/HPB clinics on the NUH hospital campus. The poster includes information for patients to opt out of the project specifically if they wish to do so. The National Data Opt Out will be respected. If it is detailed in patients notes that they do not want to take part in research generally, this will also be respected.

The Members were broadly content with this method pf patient notification, but suggested a few changes to the content of the poster. The Members commented that the poster could be written in easier language, so that a lay person could more easily understand. For example, would the average patient understand the title of the poster? '*Had a biopsy or surgery for GI/HPB malignancy or disease over 5 years ago?*' The Members felt that the title, and the subsequent text of the poster should be revised to be clearer and more accessible to the lay person.

The Sub-Committee also commented that it is not accurate to say that, '*All samples and histopathological data will be anonymous*,' without explaining exactly when and how the identifying key will be destroyed. This should be explained.

With regards to contact information for opt out, a phone number and postal address should also be included.

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.

As part of the responses to Confidentiality Advice Team (CAT) queries, the applicant explained that they have contacted Bowel Research UK as part of the People and Research Together (PaRT) network which has over 1600 patients within their group to begin initial scoping of patient and public involvement. However, the applicant has not described if this involved any discussions regarding use of confidential patient information without consent, in the manner that this study proposes.

The applicant has stated that throughout the duration of the study, they will explore multiple GI/HPB conditions, and will be contacting focus groups to have patient input into target areas. This will be through the wider clinical network (MDT and clinicopathological correlation teams) of the Trust. It does not appear that this has yet been undertaken.

The CAG felt that it was not clear from the information provided if any patient and public involvement has been undertaken specifically surrounding the use of confidential patient information without consent. Although it appears from the responses to queries that a large amount of patients may have been involved, the Members were not able to determine what the involvement was. The applicant is to confirm if patients have discussed the use of confidential patient information without consent, for the purposes of this project, prior to ‘s251’ support being provided. If this has not yet been undertaken, the applicant is to undertake further patient and public involvement specifically around this point.

Exit strategy

The exit strategy is anonymisation, on deletion of the key. The project will run for 3 years. At the end of the study, in line with the University of Nottingham Code of Research conduct and Research Ethics, study documents (including the key) will be retained at secure archive facilities for a period of 7 years. ‘s251’ support therefore expected to be required until 2033.

Members noted that the CAG application form stated that the master database – including patient identifiers and re-identification key – will be held by the Chief Investigator (CI) who is a member of the research team at the University. However, it was subsequently confirmed by the CI to the CAT that this is not the case, and that the key will be held securely within the Trust and independently of and outside the research team. The applicant has confirmed that it is only the Data management team who will have access to the key, rather than the research team at the University, however ‘s251’ support is still required for this as the Data management team are not considered direct care team. However, the research team at the University will not have the means to re-identify any individuals. The CAG were content that the exit strategy has been defined, however noted that 10 years does seem a long time for this support to be in place, for this category of precedent set application, and queried whether it would be possible for the key to be retained at the Trust by the direct care team only for the 7 year duration, and thus remove the requirement for ongoing ‘s251’ support.

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. The poster should be revised in line with the advice in this letter, and an updated version provided to CAG. This should include;
    a. the title, and the subsequent text of the poster should be revised to be clearer and more accessible to the lay person.
    b. a more accurate representation of the length of time the key is retained for.
    c. The addition of a phone number and postal address for opt out.

2. Please provide more information about the patient and public involvement undertaken, specifically, if it addressed the use of confidential patient information without consent. Please provide any feedback form patients. If none has been undertaken surrounding this point, please undertake further patient and public involvement to cover this.

3. Please confirm whether it would be possible for the key between identifiers and pseudonym to be retained at the Trust by the direct care team only for the 7 year duration required, and thus remove the requirement for ongoing 's251' support.

4. Please provide the Favourable opinion from a Research Ethics Committee, when available, 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. Favourable opinion from a Research Ethics Committee. **Pending**

2. 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:**

   The NHS England **21/22** DSPT review for **The Nottingham University Hospitals NHS Trust** was confirmed as 'Standards Met' on the NHS England DSPT Tracker (checked 29 March 2023)

Minutes signed off as accurate by correspondence from		
Signed – Officers of CAG		Date
Professor William Bernal, CAG alternate Vice-Chair		*29 March 2023*
Signed – Confidentiality Advice Team		Date
Caroline Watchurst, Confidentiality Advisor		*29 March 2023*