Confidentiality Advisory Group

Minutes of the meeting of the Precedent Set Review Sub Committee of the Confidentiality Advisory Group held on *09 February 2024* via correspondence.

Present:

Name	Capacity	Items
Dr Tony Calland MBE	CAG Chair	2a, 2b, 2c, 2d
Dr Martin Andrew	CAG Member (Expert)	2a and 2d
Dr Malcolm Booth	CAG Member (Expert)	2b and 2c
Mr David Evans	CAG Member (Expert)	2a and 2d
Mr Anthony Kane	CAG Member (Lay)	2b and 2c

Also in attendance:

Name	Position (or reason for attending)
Mr Dayheem Sedighi	HRA Approvals Administrator
Ms Katy Cassidy	HRA Confidentiality Advisor
Ms Caroline Watchurst	HRA Confidentiality Advisor

1. DECLARATIONS OF INTEREST

There were no declarations of interest.

2. NEW PRECEDENT SET REVIEW APPLICATIONS FOR CAG CONSIDERATION

2.a	**24/CAG/0018**	**Factors predicting serum HLA antibody persistence or decline in kidney transplant**

		patients on the waiting list
	Chief Investigator:	Dr Ying Li
	Sponsor:	NHS Blood and Transplant
	Application type:	Research

The Group reviewed the above application in line with the CAG considerations.

Summary of application

This application from NHS Blood and Transplant (NHSBT) set out the purpose of medical research that aims to identify patient characteristics and factors that may be associated with patient HLA antibody changes. The applicant also aims to develop a machine learning model to predict what happens to kidney transplant waiting list patients' HLA antibodies with time, in order to improve patient management and design of intervention strategies (such as desensitisation). The applicant will classify waiting list patient's antibody dynamics and correlate this with clinical, demographic and other patient characteristics – this linkage will require 's251' support. However, the machine learning element does not require 's251' support, as this will be undertaken on an effectively anonymous dataset.

Human Leukocyte antigen (HLA) specific antibodies are measured prior to kidney transplantation. For a patient having these antibodies against the particular kidney donor, the cross-match will likely be positive (reactive) meaning that transplantation with that donor would be at high risk for rejection: these antibodies prevent transplantation. HLA antibodies can be stimulated by blood transfusion, pregnancy, and transplants. Some patients lose their antibodies fairly quickly (eg within months), whilst others sustain them for years, sometimes decades, and due to a lack of study this is currently unpredictable.

Eligible kidney transplant patients on the waiting list for renal transplant at University Hospitals Birmingham NHS Foundation Trust, will be identified from the NHSBT Histocompatibility & Immunogenetics (H&I) Laboratory Information Management System (LIMS). NHS number, HLA antibodies score, and time of sampling, and a study pseudo-ID will be extracted. This pseudo-ID and NHS number will be disclosed to the WMSDE team (West Midlands Secure Data Environment for Research and Development) at University Hospitals Birmingham NHS Foundation Trust (UHB) for linkage to encoded clinical data, including pregnancy history, transfusion/transplant history, treatment history, vaccination history, using the NHS number. WM SDE will then remove identifiers and provide an anonymous dataset for analysis by the application, within the WM SDE.

Confidential information requested

Cohort	Approximately 2000 kidney transplant patients on the waiting list (active kidney transplant request status) for renal transplant at University Hospitals Birmingham NHS Foundation Trust, who have had a sample taken between 01 January 2015 and 31 December 2021.

Data sources	1. NHS Blood and Transplant (NHSBT) - Histocompatibility & Immunogenetics (H&I) Laboratory Information Management System (LIMS) 2. West Midlands Secure Data Environment for Research and Development (WM SDE) hosted by University Hospitals Birmingham NHS Foundation Trust – Pregnancy history, transfusion/transplant history, treatment history and vaccination history (CAG ref 24/CAG/0025)
Identifiers required for linkage purposes	1. NHS number 2. Pseudo-ID
Identifiers required for analysis purposes	1. N/A – analysis is on effectively anonymous dataset

Main issues considered, discussed and outcomes

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 section 251 of the NHS Act 2006.

Having reviewed the application and considered the risks and benefits involved, the CAG was also assured that the proposed activity was in the public interest.

The CAG noted that the use of confidential patient information without consent was discussed with 1 person who was described as a South West Renal Network representative. The Members agreed that despite the breach of confidentiality being minimal, this was insufficient Patient Involvement, and more engagement with relevant patients would be needed. The CAG requested further Patient Involvement was undertaken to discuss the specific issue of use of confidential patient information without consent. Members suggested a video conference with a minimum of 8 renal patients. **(Action 1)**

The CAG noted that the applicant has developed the notification as if it was a letter going to each participant, however the premise of the application is that this is not practicable for the applicant to undertake. The CAG suggested that developing a website notification for NHSBT and UHB, and posters for the relevant renal units would more adequate for the purpose of patient notifications. These should be designed as if the relevant cohort might see them, rather than be designed as if they would be sent directly to them. Therefore, the CAG requested that website notifications and posters should be provided, which entailed information about who the cohort was. The notifications should also state that ‘section 251 support’ was recommended by

the Health Research authority, on advice from the Confidentiality Advisory Group (CAG). The patient notification documents should describe the linkage, and the application specific opt-out described should provide contact details for patients to opt out, but this should not be via the reply slip design currently provided, as it is not envisaged that patients would receive any paper notification. **(Action 2)**

Confidentiality Advisory Group advice: Provisionally supported

The CAG was unable to recommend support to the Health Research Authority for the application based on the information and documentation received so far. The CAG requested the following information before confirming its final recommendation:

Number	Action required	Response from the applicant
1.	Further Patient Involvement needs to be undertaken including the specific issue of use of confidential patient information without consent. Members suggested a video conference with minimum of 8 renal patients.	
2.	Please update the patient notification materials as follow and provide to CAG for review: a. Produce online notifications for NHSBT and UHB, and renal unit posters which clearly describe the cohort, and the linkage. b. Provide the study specific opt-out, which is easily accessible, by including a phone number, email and postal address. c. Add a statement to state that 'section 251 support' was recommended by Health Research authority, on advice from the Confidentiality Advisory Group (CAG).	

The Group delegated authority to confirm its final opinion on the application to the Chair and reviewers.

2.b	**24/CAG/0029**	**Parenting and children's behavioural problems: Micro- and macro-processes at play in the context of intervention**
	Chief Investigator:	Dr Jon Heron
	Sponsor:	University of Bristol (ALSPAC)
	Application type:	Research

The Group reviewed the above application in line with the CAG considerations.

Summary of application

This application from the University of Bristol (ALSPAC) set out the purpose of medical research which aims to understand parent-child behaviour processes across childhood as a function of Mental Health Service referral, contact and use.

One in six school-aged children now have a probable mental health disorder -- up from one in nine three years ago. Services for children and young people's mental health are stretched more than ever before, such that maximising resources is a key priority. The effectiveness of mental-health interventions can be optimised by enhancing our understanding of how an intervention leads to improved outcomes. Parent and child behaviours are primary intervention targets for children's mental health, yet little is known about their assumed mechanistic role. This study aims to address this gap, with specific focus on children's disruptive behaviour as one of the most common reasons for children to receive mental health services.

The applicants seek support to process confidential patient information regarding mental health from GP records, NHS England and Avon and Wiltshire Mental Health Partnership, in line with ALSPAC's existing approval.

ALSPAC wish to:

- Repurpose sensitive data already collected though a previous project specific s251 support within ALSPAC, for this specific project, in order to reduce flow of confidential information,
- And for data not already collected though a previous project specific s251 support, request data from GP providers, NHS England and Avon and Wiltshire Mental Health Partnership using existing processes.

The data will then be combined/anonymised by the ALSPAC team within UKSeRP (managed by the University of Swansea but managed by ALSPAC staff). ALSPAC staff will then make the anonymised combined data available to the researchers within UKSeRP.

Confidential information requested

Cohort	individuals enrolled in ALSPAC (excluding those who have explicitly withdrawn from ALSPAC, declined consent to linkage to their health record, have not received ALSPAC fair processing information or have consented to data linkage)

	13,500 ALSPAC participants have been contacted, of whom over 5,500 have responded. This support is therefore regarding approximately 8000 individuals.
Data sources	1. ALSPAC administrative database (University of Bristol) 2. NHS England a. Hospital Episode Statistics (HES), b. Mental Health Minimum Dataset (MHMD) c. Mental Health and Learning Disabilities Data Set (MHLDDS) d. Mental Health Services Data Set (MHSDS) 3. GP data software providers 4. Avon and Wiltshire Mental Health Partnership NHS Trust
Identifiers required for linkage purposes	1. Study IDs 2. NHS number 3. Date of birth 4. sex 5. postcode For those in the ALSPAC database where linkage has already been undertaken: 1. NHS ID to ALSPAC ID pseudonymised linkage ID number.
Identifiers required for analysis purposes	1. Gender 2. Age at event Effectively anonymous for analysis.
Additional information	Of the 15,000 ALSPAC participants around 5500 consented (or dissented) to data linkage and are not part of this request for support.

Main issues considered, discussed and outcomes

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 section 251 of the NHS Act 2006.

Having reviewed the application and considered the risks and benefits involved, the CAG was also assured that the proposed activity was in the public interest.

The Precedent Set Review Sub Committee agreed that this was a well-presented application with no issues.

Confidentiality Advisory Group advice: Fully supported

The CAG agreed that the minimum criteria under the Regulations appeared to have been met, and therefore advised recommending support to the Health Research Authority, subject to compliance with the standard conditions of support.

Conditions of Support:

1. Favourable opinion from a Research Ethics Committee. **Confirmed:** This application activity is covered by main ALSPAC FO (**03 February 2011)**, and addition of this study into main ALSPAC protocol has also been submitted as an amendment to REC (**AM21) Date of FO 20 March 2023**

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. **Confirmed:**

   Due to the number of organisations involved it is the responsibility of ALSPAC, as controller, to ensure that participating organisations 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 an organisation.

2.c	**24/CAG/0030**	**Mapping Neurodevelopmental Trajectories for Adult Psychiatric Disorder: A focus on Autism and Psychosis**
	Chief Investigator:	Professor Anthony David
	Sponsor:	University of Bristol (ALSPAC)
	Application type:	Research

The Group reviewed the above application in line with the CAG considerations.

Summary of application

This application from the University of Bristol (ALSPAC) set out the purpose of medical research which aims to explore the neurological association between autistic traits and psychotic experiences.

This project will investigate neurodevelopmental trajectories for psychiatric disorders, in particular autism and subclinical autistic traits and their overlap with psychosis and psychotic experiences, using longitudinally acquired MRI data from the ALSPAC-MRI-I + II datasets. Analyses will explore the influence of environmental (perinatal and postnatal) and genetic exposures on behaviour. Multi-modal brain imaging scans will be used to illuminate possible interactions between the brain, behaviour, genetics and environmental exposures.

The applicants seek support to process confidential patient information regarding mental health from GP records, NHS England and Avon and Wiltshire Mental Health Partnership, in line with ALSPAC's existing approval.

ALSPAC wish to:

- Repurpose sensitive data already collected though a previous project specific s251 support within ALSPAC, for this specific project, in order to reduce flow of confidential information,
- And for data not already collected though a previous project specific s251 support, request data from GP providers, NHS England and Avon and Wiltshire Mental Health Partnership using existing processes.

The data will then be combined/anonymised by the ALSPAC team within UKSeRP (managed by the University of Swansea but managed by ALSPAC staff). ALSPAC staff will then make the anonymised combined data available to the researchers within UKSeRP.

Confidential information requested

Cohort	individuals enrolled in ALSPAC (excluding those who have explicitly withdrawn from ALSPAC, declined consent to linkage to their health record, have not received ALSPAC fair processing information or have consented to data linkage) 13,500 ALSPAC participants have been contacted, of whom over 5,500 have responded. This support is therefore regarding approximately 8000 individuals.
Data sources	1. ALSPAC administrative database (University of Bristol) 2. NHS England a. Hospital Episode Statistics (HES), b. Mental Health Minimum Dataset (MHMD) c. Mental Health and Learning Disabilities Data Set (MHLDDS) d. Mental Health Services Data Set (MHSDS) 3. GP data software providers

	4. Avon and Wiltshire Mental Health Partnership NHS Trust
Identifiers required for linkage purposes	1. Study IDs 2. NHS number 3. Date of birth 4. sex 5. postcode For those in the ALSPAC database where linkage has already been undertaken: 2. NHS ID to ALSPAC ID pseudonymised linkage ID number.
Identifiers required for analysis purposes	1. Gender 2. Age at event Effectively anonymous for analysis.
Additional information	Of the 15,000 ALSPAC participants around 5500 consented (or dissented) to data linkage and are not part of this request for support.

Main issues considered, discussed and outcomes

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 section 251 of the NHS Act 2006.

Having reviewed the application and considered the risks and benefits involved, the CAG was also assured that the proposed activity was in the public interest.

The Precedent Set Review Sub Committee agreed that this was a well-presented application with no issues.

Confidentiality Advisory Group advice: Fully supported

The CAG agreed that the minimum criteria under the Regulations appeared to have been met, and therefore advised recommending support to the Health Research Authority, subject to compliance with the standard conditions of support.

Conditions of Support:

1. Favourable opinion from a Research Ethics Committee. **Confirmed:** This application activity is covered by main ALSPAC FO (**03 February 2011)**, and addition of this study into main ALSPAC protocol has also been submitted as an amendment to REC **(AM14) Date of FO 1 December 2021**

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. **Confirmed:**

   Due to the number of organisations involved it is the responsibility of ALSPAC, as controller, to ensure that participating organisations 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 an organisation.

2.d	**24/CAG/0036**	**Can performing extra tests on non-diagnostic biopsy samples avoid the need for further invasive biopsies in people with suspected cancer of the lung lining?**
	Chief Investigator:	Professor Nick A Maskell (Chief Investigator)
	Sponsor:	University of Bristol Medical School
	Application type:	Research

The Group reviewed the above application in line with the CAG considerations.

Summary of application

This application from the University of Bristol set out the purpose of medical research that seeks to determine whether additional tests on biopsy samples taken from patients with suspected pleural malignancy, who did not receive a diagnosis from an initial biopsy, could have removed the need for further invasive procedures.

Diagnosing pleural malignancy can be challenging. Radiology supports diagnosis but taking a biopsy for diagnosis is the gold standard. Some patients present with fluid around the lining of the lung but malignancies such as pleural mesothelioma (PM) are difficult to identify when this fluid is sampled. Biopsy of the lung lining gives a diagnosis more frequently than fluid, but does not always provide a diagnosis, meaning that a group of patients undergo multiple investigations, with increased risk of complications and delays to treatment initiation. A previous trial, the TARGET trial, had shown that use of PET-CT did not improve diagnostic rates and some repeat biopsies were also non-diagnostic. Advances since the TARGET trial have broadened the panel of tests available for biopsy samples, including tests for markers known as BAP1, p16 and MTAP. If these markers are absent, then a diagnosis of PM can be made. This project aims to evaluate the diagnostic benefit of BAP1, p16 FISH and MTAP in suspected mesothelioma by re-testing the initial non-diagnostic or negative biopsy samples from TARGET trial participants.

Confidential patient information from the TARGET study database at University Hospitals Bristol and Weston NHS Foundation Trust will be disclosed to the North Bristol NHS Trust. North Bristol Trust will disclose confidential patient

information to participating sites to obtain laboratory contact details and patients date of death. North Bristol NHS Trust will then disclose confidential patient information to the relevant NHS pathology laboratories to obtain clinical biopsy samples. The retrieved samples and confidential patient information will then be disclosed to pathology services at North Bristol NHS Trust so further analysis can be undertaken on the samples. The results of the further analysis, along with patient identifiers, will then be disclosed to the research team at North Bristol NHS Trust. A pseudonymised dataset will be used for analysis.

Confidential information requested

Cohort	Patients who participated in the TARGET trial.
Data sources	1. Data from the TARGET study, stored on study database at University Hospitals Bristol and Weston NHS Foundation Trust. 2. Electronic patient records at participating trusts.
Identifiers required for linkage purposes	1. Name 2. NHS Number 3. Hospital ID Number 4. Date of birth 5. Date of death
Identifiers required for analysis purposes	1. Gender
Additional information	The date of birth and date of death will not be included in the dataset used for analysis.

Main issues considered, discussed and outcomes

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 section 251 of the NHS Act 2006.

Having reviewed the application and considered the risks and benefits involved, the CAG was also assured that the proposed activity was in the public interest.

The Precedent Set Review Sub Committee agreed that this was a well-presented application.

The CAG noted that, as most of the participants in the TARGET trial received a terminal diagnosis with a life expectancy of less than 18 months from diagnosis, it was expected that the participants in the trial would now be deceased. Members agreed that a short notice, explaining the research and how to dissent, needed to be posted on the hosting Trust website. **(Condition 1)**

Confidentiality Advisory Group advice: **Conditionally supported**

The CAG agreed that the minimum criteria under the Regulations appeared to have been met, and therefore advised recommending support to the Health Research Authority subject to compliance with the specific and standard conditions of support as set out below.

1. Create an online patient notification material, specific to this project, for the hosting Trust website. please provide back to CAG within one month.

2. Favourable opinion from a Research Ethics Committee. **Confirmed 28 February 2024**

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. **Confirmed:**

   Due to the number of organisations involved it is the responsibility of University of Bristol Medical School, as controller, to ensure that participating organisations 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 an organisation.

   The Group delegated authority to confirm its final opinion on the application to the Chair and reviewers.

Dr Tony Calland MBE	*21 February 2024*
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Signed – Chair	*Date*
Dayheem Sedighi	*20 February 2024*
……	……..
Signed – HRA Approvals Administrator	*Date*