NATIONAL OFFICE FOR RESEARCH ETHICS COMMITTEES

National Irish COVID-19 Biobank – REC

Meeting minutes

Date*	Start	End	Duration (hrs)	Location
03 April 2023	14:00	17:00	3	Zoom
19 April 2023	11:00	13:00	2	Zoom

*The ethical assessment of the NICB application took place over two meeting dates

Attendance

Name	Role	Dates in attendance
Dr Georgina Flood	Chairperson, NICB-REC	03 April 2023, 19 April 2023
Dr Anne Moore	Deputy Chairperson, NICB-REC	03 April 2023, 19 April 2023
Prof. Kathleen Bennett	Committee Member, NICB-REC	03 April 2023,
Dr Brian Clark	Committee Member, NICB-REC	03 April 2023, 19 April 2023
Mr John Culliney	Committee Member, NICB-REC	03 April 2023, 19 April 2023
Dr Aisling de Paor	Committee Member, NICB-REC	03 April 2023,
Prof. Sean Hynes	Committee Member, NICB-REC	03 April 2023, 19 April 2023
Ms Joan Jordan	Committee Member, NICB-REC	03 April 2023, 19 April 2023
Dr Sonja Khan	Committee Member, NICB-REC	03 April 2023, 19 April 2023
Dr Patrick Manning	Committee Member, NICB-REC	03 April 2023, 19 April 2023
Dr Kevin May	Committee Member, NICB-REC	19 April 2023
Prof Shaun O'Keeffe	Committee Member, NICB-REC	03 April 2023, 19 April 2023
Prof. Cathal Seoighe	Committee Member, NICB-REC	03 April 2023, 19 April 2023
Prof Anthony Staines	Committee Member, NICB-REC	03 April 2023, 19 April 2023

Dr Ciara Staunton	Committee Member, NICB-REC	03 April 2023, 19 April 2023
Dr Emily Vereker	Head of Office, National Office for RECs	03 April 2023, 19 April 2023
Dr Anne Costello*	Programme Manager, National Office for RECs	03 April 2023, 19 April 2023

*Drafted minutes

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Agenda

- Welcome and apologies.
- Overview of ethical review process – Dr Georgina Flood
- Discussion of NICB ethics application sections and documents:
  - Application document checklist
  - Operations, governance and access rights
  - Biological samples and associated data
  - Participants and Informed consent
  - Public engagement, PPI, economic sustainability and commercial value
  - Local REC approvals
  - Documents submitted with the NICB ethics application form

Scope of deliberations:

- The NICB-REC is mandated to ethically assesses the NICB in terms of its operations and governance, biological sample and data management, informed consent, public engagement, PPI and commercialisation as a biobanking infrastructure. The scope of the NICB-REC does not extend to the ethical assessment of studies requesting access to the biobank.
- The single, national, ethical opinion delivered by the NICB-REC to the NICB will supersede all local REC opinions delivered to the NICB. This includes local full approvals, partial approvals, unfavourable opinions and/or no local opinion returned.
- A bespoke application form for the NICB was compiled by the National Office in consultation with the NICB-REC. NICB-REC members have specific expertise in biobanking governance, operations and regulatory requirements. The form captured all information required for the ethical review of a multi-site, multi legal entity, national biobanking infrastructure.
- During validation of the submitted NICB ethics application it was confirmed that retrospective samples and data were **not included** as part of the current ethics application. No information could be provided regarding custodianship of retrospective samples and data, or the consent associated with them. The applicants agreed that inclusion of retrospective samples in the NICB would be subject to a future ethical approval request from the NICB to the NICB-REC.

Deliberations

The Chairperson opened the meeting, welcomed the Committee, noted apologies, and gave an overview of the ethical review process and discussion structure as per the meeting agenda.

1 Application Checklist

- The Committee noted that there was documentation requested as part of the application which had not been submitted with the application form. It was agreed that this documentation, or related information, must be submitted prior to an ethics opinion being issued to the NICB. The following documentation was not provided by NICB:
    i. All participant questionnaires including clarification on what questionnaires will be used and when, and what details will be requested from participants and why.
    ii. Letter of invitation to participants.
    iii. Advertisement/recruitment material including links to website information designed to provide information to potential participants.
    iv. Standard operating procedures (SOPs) and flow charts for all harmonised biobank operations.
    v. Biological sample life cycle flow chart.
    vi. Template biological material and data transfer agreement.
    vii. Template access agreement.
    viii. Biological sample and associated data retention policy.
    ix. Staff confidentiality policy.
    x. Non-employee confidentiality policy.
    xi. Security and indemnity certificates for each biobank site.
    xii. Site assessment forms for each site (to include, at a minimum, information on the following: available biobanking related infrastructure at site, human resources at site, staff training available on site, risk mitigation at site [security, power outage, freezer failure etc])

2 Operations, governance and access rights

The following topics were discussed:

Board membership

- The selection and recruitment of the Governance Board, International scientific advisory board and the public and patient involvement advisory board members and the contributed member expertise, were unclear to the Committee. Further information on criteria used and selection process was required.
- It was not clear to the Committee how Board Member conflicts of interest would be managed. Further information was required.

Researcher Access

- The Committee noted that a template access agreement was not provided. The terms, legalities and safeguards of research access were unclear to the Committee. A template access agreement was required to be submitted for review.
- The Committee queried the responsibility of the Biobank Executive Committee in terms of its function as an Access Assessment Committee. It was considered that a clear conflict of interest would arise if PIs involved in the recruitment of biobank participants through their own research studies, were also involved in the evaluation of access requests to those biobanked samples and data. The Committee discussed that an independent Access Assessment Committee would be required as an ethical safeguard.
- The collaboration requirements between the biobank/biobank PI's and third-party researchers accessing biobank samples and data were unclear to the Committee. The Committee queried if third party researchers would feel obliged to form collaborations with the biobank, as opposed to a free and open collaboration. Intellectual Property agreements and any requirements for NICB author accreditation were unclear in this capacity. Further information was required.
- The Committee considered that non-negotiable collaboration agreements may create potential difficulties for international researchers to access the biobank. The Committee acknowledged that non-negotiable elements would be required, however, it was considered that some aspects may be negotiable to ensure international researchers could access the biobank. It was unclear to the Committee how the requirement for local REC approvals would be managed for international studies. Further information was required.
- The Committee considered that an expedited approval process for secondary use of data, to that initially approved by the NICB, may give rise to GDPR concerns and should be managed accordingly.
- The Committee considered that both access requests made, and access requests granted should be publicly available, for transparency.

ISO 20387 accreditation

- The Committee stated that NICB biobank accreditation under ISO 20387 is recommended and should be monitored as an ethical safeguard. A timeline in which to achieve accreditation was requested.

Economic self-sustainability

- The Committee considered that there is an ethical obligation to maximise the societal benefit from the contribution of participants samples and data to the biobank.
- The Committee deliberated on the requirement for a cost recovery plan and queried whether the NICB would be charging researchers for access. Further information was required.

Scope and definition of COVID-19 research

- The Committee acknowledged that COVID-19 has long reaching clinical scope as it effects many organs and different disease areas. As such the Committee considered that the definition of scope as 'COVID-19 research' while broad, is ethically acceptable. The

Committee agreed that any undue limitation of research scope, in this context, may also limit the overall value of this resource.

Operations

Sample and data retention periods

- The NICB requested ethical approval for different biological sample and data retention periods across biobank sites (forever vs 25 years or 10 years). The Committee agreed that diverse and inconsistent retention periods across sites would negatively impact the availability of samples and data. The Committee considered that, as the NICB is a harmonised multi-site infrastructure, there must be consistency and harmonisation regarding the biological sample and retention periods across all NICB sites. The Committee agreed that retention periods need to be standardised across all biobank sites.
- It was unclear to the Committee how biological samples and data would be maintained during the retention period in the event the biobank closed. It was considered that, at recruitment stage, participants must have clarity on the fate of their samples and data in the event of biobank closure.

Work packages

- The Committee noted reference was made to work packages 1 – 5 in appendix 11.3 'NICB Governance' of the protocol however no detail or information was included on these work packages in the application form or submitted documentation. Further information was required.

Technical safeguarding

- Technical safeguarding of biological samples was unclear to the Committee. Further information was required regarding on-site risk mitigation related to power supply, potential freezer failures and or loss of CO_2/nitrogen etc.

Change management

- The Committee queried whether there was an oversight process for change management of harmonised biobank policies and/or processes. It was unclear if a system existed for implementation of new policies and/or making changes to existing policies across all sites. Further information was required.

3 Biological samples, associated data and research scope

The following topics were discussed:

Joint data controllership.

The responsibilities of each joint controller were unclear to the Committee. It was not clear which joint data controller would be responsible for what aspect of data control. For example, it was not clear which joint-data controller would be responsible for ensuring the data protection rights of participants or, which data controller would be responsible for overseeing incidents of data breach should they occur. Further information was required covering these examples and all other data controllership matters which require harmonisation across biobank sites.

Audit

- The Committee deliberated upon the appropriateness of the submitted internal audit plans and noted a lack of external auditing plans. It was unclear to the committee 1) how data would be verified and audited and on what scale this would occur, 2) how data integrity and consistency across participants and sites would be validated, 3) who would be responsible for auditing and would that individual be internal or external, 4) who the audit report would be submitted to and who would be responsible for implementing actions which may arise from the audit. Further information was required to clarify these points.
- The Committee considered that while internal self-audit can be a useful tool there remains a requirement for an external auditing process as an ethical safeguard. Further information was required 1) specifying the process of internal audit and 2) on external audit plans.
- The adequacy of logging of participant data and biological samples was not clear to the Committee. Further information was required.
- The Committee considered that there was a requirement for a harmonised standard operating procedure covering security auditing which would be designed to prevent security and power failure across all biobank sites.
- The Committee considered that 'date of birth' was an unsuitable metric to be used to identify participants recruited at more than one site (duplicates). Further information was required to clarify how participants registered at more than one biobank site would be identified.

Data management and security

Formats and types of data

- The Committee noted that incomplete information on format and types of data to be collected was submitted. The Committee required this information to be completed and submitted.
- An electronic Case Report Form (eCRF) was referenced on pg 29 of the DPIA. It was not clear to the Committee 1) if the eCRF was separate from REDCap, the recruitment log and the sample data base; 2) where it was electronically located, 3) whether it was hosted on a secure platform 4) who has access to it or 5) what information would be captured. Further information was required.

GDPR compliance

- The Committee acknowledged that comprehensive information was provided on data protection via the DPIA. It was, however, not clear to the Committee how the biobank would ensure GDPR compliance. In terms of the principle of data minimisation, the information collected in the data dictionary was considered extensive. The Committee required a rationale for the inclusion of such extensive and detailed data. The Committee considered that summary clarifying the key aspects of how the biobank would ensure GDPR compliance is required?

Data protection and security of data across all sites

- The Committee considered that a harmonised and standardised NICB data protection policy should be developed and implemented across all biobank sites. The Committee

considered that there is an ethical requirement for a harmonised NICB data protection policy, which builds on policies at each site, and includes biobanking specific data protection content relevant to a multisite, multi legal entity biobanking infrastructure.

- The Committee considered that an NICB database backup contained in a computer based in St James hospital was unsuitable as it presented a data protection risk. A suggested that a cloud-based backup would carry considerably lower risk of data breach.. The Committee requested that a robust and secure data backup plan be developed and submitted.

Data extraction

- The Committee considered that extraction of data from paper sources was challenging and carried an associated risk of reduced data integrity. It was unclear to the Committee whether staff extracting data would be sufficiently trained to ensure high integrity of extracted data.

Data handling

- The Committee considered that consistency of data handling across sites would be required to ensure sample and data integrity. No standardised SOPs were submitted. The Committee noted that there are standards by which an organisation such as the biobank can be accredited for handling data. No reference to the HIQA standards of data collection for health and social care[1] was included in the application. This resource has a large amount of useful advice and information on how to handle data[2].

FAIR data

- The Committee noted a reference to FAIR (Findable, Accessible, Interoperable and Reusable) data. However, it was unclear to the Committee how data would be ensured to be FAIR. Further information was required.
- The Committee noted reference to the use of SNOMED[3] however it was unclear to the Committee how SNOMED data would be manged in the context of ensuring data interoperability. Further information was required.

Data linkage

- It was not clear to the Committee whether and how biological samples and data would be linked:
  - with relevant information from the COVID-19 Vaccine (CoVax)[4] database and the National Virus Reference Lab (NVRL)[5].
  - with other data sets external to the NICB and the NICB data,

  and whether any limitations on data linkage to external databases would be applied to mitigate against participant reidentification. Further information was required.

[1] Guidance on a data quality framework for health and social care (hiqa.ie)

[2] Guiding-Principles-Data-Collections.pdf (hiqa.ie)

[3] Home | SNOMED International

[4] COVAX: National COVID-19 Immunisation System | HIQA

[5] UCD National Virus Reference Laboratory

Data breach procedure.

- The Committee considered that a data breach procedure should be harmonised across all biobank sites. As such, a harmonised data breach procedure applicable to and accepted by all biobank sites was required. The Committee considered that the data breach policy should be specific to the NICB as a multisite infrastructure, and not specific to individual biobank sites. It was agreed that it should be clear to participants, when and how they would be notified of a data breach, in accordance with data protection legislation.

Third party data processors

- It was unclear to the Committee whether there would be third-party data processors other than researchers accessing the biobank. Further information on arrangements between, and roles and responsibilities of, any third-party contractors or service providers processing data was required.

Genetic data

- The Committee considered that the risk of participant reidentification, particularly when genetic data is combined with clinical and other data was not clearly addressed. Further information was required.
- The Committee discussed the difficulties associated with anonymisation of genetic data. This discussion was informed by preliminary opinion from European Health Data Space on the issue[6].
- The Committee considered that the increased participant susceptibility to legal concerns including genetic discrimination, risk of unauthorised access and misuse by third parties (insurance companies etc) was not addressed. Further information was required.
- The rationale for non-return of incidental and/or secondary findings was unclear to the Committee The following were discussed as part of these deliberations:
  - International precedents,
  - HSE policy – conditions for return of findings,
  - PPI perspectives – when possible, results should be returned as this is important for trust,
  - Clarity to participants on return or not of findings.
- The Committee considered that the approach to incidental and secondary findings should be kept under review by the NICB and adjusted should law evolve in this area. The Committee advised that participants should be requested to provide consent to be recontacted in the future, in the event that consent to receive incidental or secondary findings could be sought.
- The Committee considered that, in the Patient Information Leaflet and Informed Consent Form (PIL/ICF), a reference to a participant's genetic data being '*unique to you*' was not entirely accurate in the context of familial DNA (similarities and relevance). The

[6] Opinion 05/2014 on Anonymisation Techniques EN (europa.eu)

Committee required a clarification on familial DNA, in this context, to be included in the PIL/ICF.

- The Committee considered that court requests for access to biobanked genetic data for the purposes of the judiciary should be clear in the PIL/ICF.

Biological sample and associated data life cycle

- The Committee considered that there was a lack of clarity on the sample and data biobank life cycle, from recruitment to researcher access. Further information was required.

Material transfer agreement (MTA)

- No MTA template was provided for ethical review. The Committee discussed that an MTA when provided should contain a requirement to refer to the NICB in publications. An MTA should also that note that the applicable law is Ireland, and any disputes should be resolved in the Irish courts. The Committee required the submission of an MTA template.

Return of data to the biobank

- The Committee queried
  - whether there was a process for linkage of returned data from researchers, with the associated biological samples and
  - whether there was an associated timeline for return of data from researchers;
  - how the integrity of returned data would be ensured if it is returned from a research lab and, as such, is not clinically validated and
  - whether the data would be partitioned into returned vs original medical data.

  Further information was required.

Participant identification (ID) codes

- The Committee considered that there was inappropriate references to the biobank and to the participant recruitment site within the participant ID code. The use of ambiguous ID codes was considered to be an ethical requirement. The Committee noted that HIQA has guidelines on devising data identifiers which are based on international best practice[7]. GS1 barcodes, for example, are non-identifiable. The Committee requested revision and submission of a participant ID reference strategy which would ensure no participant data is revealed by the reference used for their samples and data.

Participant category breakdown

- The Committee noted an expected participant recruitment of 8000 participants. The expected category breakdown was not provided: IE – Acute COVID, Long COVID, Controls, Minors etc. The Committee considered that selection bias in recruitment may impact the usefulness of all data collected in a public health impact capacity. Further information was required on 1) the breakdown of participant groups, 2) rationale for the breakdown and, 3) expected participant numbers in each sub-group.

[7] Recommendations for a Unique Health Identifier for Individuals in Ireland | HIQA

- It was unclear to the Committee how healthy controls would be recruited and from where. Further information was required.

Security, standardisation and protection of biological samples across sites.

- Harmonised SOPs were not provided. The Committee considered that harmonisation of standard operating procedures across all biobank sites was required as an ethical safeguard.
- The Committee considered that a backup storage procedure would be required for biological samples. The Committee commented that best practice should be implemented, such as splitting resources across sites, providing a mirrored resource of biological samples for risk mitigation purposes to prevent sample loss. The Committee required submission of a robust and secure backup protocol for biological samples.
- The location of the biological sample data base and log, and how the information kept therein would be linked to REDCap, was unclear to the Committee. Further information was required.
- The Committee required details on the process to oversee the amounts of biological samples being released and how and under what circumstances access to biological samples would be prioritised, given the finite amounts that would be available to access. The Committee requested that consideration should be given to this in the terms of the access agreement. Further information, as well as an access agreement template, was required.
- On-site risk mitigation related to power outage, freezer failures, and/or loss of CO2/nitrogen etc was unclear to the Committee. Further information was required.

Biobank Scope – potential for future broadening of scope

- It was unclear to the Committee whether the NICB team had considered the possibility of the future of the biobank in terms of evolving scope and whether there were any future plans to develop the NICB as a biobank for other diseases. The Committee deliberated on the impact on the informed consent of participants, should the biobank expand in scope in the future. Further information was required including a strategy on how informed consent would be managed in the event of an expansion of biobank research scope.

4 Biobank participants and informed consent

The following topics were discussed:

Accessibility

- The Committee considered that the accessibility of participant facing material could be improved by use of simplified language.

Genetic information

- The Committee considered that the familial impacts of genetic data were unclear to participants in PIL/ICF.

Decentralisation of sample collection

- It was unclear to the Committee whether or not the applicants had considered the potential for decentralisation of sample collection. The Committee queried whether the NICB had prospects for the facilitation of samples to be taken from participants in their own home. The Committee acknowledged that the cost implications of this may be prohibitive reducing feasibility.

Vulnerable groups and assisted decision making

- The participation and management of vulnerable groups and those with diminished capacity to provide informed consent was unclear to the Committee. It was confirmed by the applicants during validation of the ethics application that participants requiring assisted decision making in accordance with the assisted decision-making act are not under review as part of the current application. This participant group may be included in a future submission.
- The Committee considered that there should be no unnecessary challenges made to a participant's capacity to provide informed consent. Some participants may have diminished capacity, but still have decision-making capacity to provide informed consent. The Committee commented that it was unclear whether participants with any level of diminished capacity would be included in the biobank. Further information was required clarifying 1) how the decision-making capacity of participants would be assessed to ensure informed consent could be provided and 2) what supports, accommodations and safeguards would be provided to ensure no unnecessary challenges would be made to an individual's decision-making capacity to provide consent and 3) how the principle of presumption of capacity[8] would be adhered to.
- In the event a participant was found to have diminished decision-making capacity after consent has been provided, it was unclear to the Committee what safeguards would be in place to ensure that their will and preference would continue to be asserted.
- The Committee noted that a section of the application form pertaining to participant diminished capacity was not filled in. The Committee required that section 3.3.1 (Will all participants have the decision-making capacity to give informed consent?) of the application form be filled in and submitted.

Recruitment & consent

- The Committee was unclear as to the informed consent protocol for the recruitment of unconscious participants in the context of those who do not have decision-making capacity at the time of recruitment (eg acute COVID-19 patients admitted to Hospital Accident and Emergency departments). Further information was required.
- The strategy for recruitment of healthy control participants was unclear to the Committee. Further information was required.
- It was not clear to the Committee how much consideration time would be given to the participant between the relevant information and the PIL/ICF being given to the them and the logging of their informed consent. Further information was required.
- With regard to the requirement for informed consent and the importance of participant understanding, it was unclear to the Committee how the informational needs of the

[8] Legislation | Decision Support Service

participant, and their level of understanding of the PIL, would be assessed by the recruiter. The Committee suggested that a video which shows the participants what is involved in the consent process would be useful. It was agreed that this would diversify how information is provided and would facilitate absorption of important information by different people enabling participants to make more informed decisions. Different people take in information in different ways. The Committee agreed that this should be considered by the applicants.

- The Committee considered that the potential for judiciary access to biobanked data upon court request should be clear to participants at the time of recruitment.

Participant withdrawal

- The process for withdrawal of participation from the biobank was not clear to the Committee. Further information was required on:
  - how it would be ensured that data and samples would be destroyed when the participant had confirmed that they wish no further use of their samples and data.
  - how the withdrawal of participants would be communicated to researchers who had been given access to the participant's samples and data.
  - the process the researcher must follow in this instance.

  Further information clarifying these points was required.
- It was unclear to the Committee if the process for withdrawal of assent would be equivalent to that of withdrawal of consent. Further information was required.
- Informed consent is required, under GDPR, for the anonymisation process of a withdrawn participant's data. It was unclear to the Committee when the required informed consent for anonymisation of data upon withdrawal would be sought. Further information was required.
- The Committee considered that it should be made clear to the participant, upon withdrawal, that when genetic data is anonymised there remains a risk of reidentification.
- It was unclear to the Committee whether participant re-identification at the relevant biobank site would be required for participant withdrawal. Further information was required.

5 Public engagement, patient and public involvement (PPI), economic sustainability and commercial value

The following topics were discussed:

Ethical considerations on economic sustainability to ensure future improved population health.

- The Committee considered that, to ensure public health benefit, economic sustainability of the biobank was an important ethical safeguard. In this context clarity was required on financial transparency and publishing of annual accounts.

- The Committee discussed cost recovery in the context of economic sustainability and queried whether the biobank would be charging researchers for access. Further information on an access charging schedule was required.
- It was unclear to the Committee if the biobank would ringfence costs for biological sample and data maintenance, to be used in the event of biobank closure. Further information was required.

Ethical considerations regarding best use of participant samples and data towards translational research and improved medicinal products in the interest of population health.

- In the interest of ethical public health beneficence, the Committee questioned how or if intellectual property rights would be managed in the context of potentially valuable research outputs from the use of the biobank.
- The Committee considered that a clear pathway to impact via commercialisation was required. It was agreed that transparency on commercialisation would be important, given a propensity for participant sensitivity regarding how the use of their samples and data in research may lead to commercialisation. The Committee considered that it would be important to highlight to the participants, the requirement of commercialisation as an integral part of the research process. Commercialisation facilitates the development of new medicinal products in the context of translation of research evidence to the bedside to improve patient care. Additionally, safeguards against misuse of data (selling etc) in the commercial sector should be in place and transparent to the participants. A detailed pathway to commercialisation was required.
- The Committee considered that the pathway from research evidence to translation to the bedside was unclear. The impact of the biobank was not sufficiently clear as described in sections 4.1.1 (*How will the impact of the biobank on society, health and social care research and innovation be measured, reported and disseminated to the public and participants during the life of the biobank?)* and 4.3.1 (*Please describe the anticipated societal and population health impact of the biobank*) of the application form.
  - The Committee required further information describing the anticipated impact the biobank may have on society, health and social care research and innovation and how this impact would be reported and disseminated to the public and participants during the life of the biobank. Additionally, the Committee required specific information addressing potential advances in health care and benefits to the public.
  - The Committee understood that long term impact in this capacity can be difficult to accurately anticipate however, it was considered that surrogate outcome measures expected during the timeline between the conduct of the research and the resulting public health impact could be measured. These outcome measures may initially include participant numbers, types of biological samples, access requests and approvals. As research progresses outcome measures may include research articles, patents, contribution to public policy etc as part of the expected pathway to commercialisation, leading to, for example, new medicinal products, vaccines, diagnostics and interventions which impact patient care ultimately improving public health. The Committee required further information on how the impact of the biobank would be measured.

Public feedback

- The Committee considered that a public feedback process would be an important ethical safeguard to ensure participants have a clear mechanism for discussing any issues with the biobank team. It was unclear to the Committee whether a public feedback mechanism would be developed and implemented. Further information was required.

Inclusion of PPI in the access assessment process

- The Committee considered that PPI is an important aspect of all parts of the research process and should be included at all stages of biobank governance. It was not clear to the Committee whether PPI representation would be included in the access assessment and decision process. Further information was required.

Participant indemnity

- The Committee considered that the applicants' statement that the clinical indemnity scheme (CIS) '*should*' cover claims was insufficient. The CIS will cover expenses for pay out, but not representation. Therefore, there is additional expenses not covered by this scheme. Additionally, the CIS only covers PIs who are consultants employed by the HSE. Further information was required to clarify 1) how it would be ensured that all indemnity costs would be covered and 2) whether participants would be required to inform their private health insurance provider about their participation in the biobank. The Committee considered that the risk of any potential claims involving private health insurance should be made clear to the participants.

Re-imbursement of expenses to participants

- Re-imbursement of expenses to participants who are requested to donate biological samples outside of normal clinic visits was unclear. The Committee required further information clarifying whether and how participants would be re-imbursed for their expenses in this instance. For example, reasonable travel expenses, parking and potentially childcare if it would be required specifically to enable inclusion of a specific participant subgroup which may otherwise be underrepresented.

6 Local REC approvals

- The Committee noted that there were disparate opinions from local RECs on the ethics associated with the governance and operations of the NICB. For eg different sample and data retention periods ranging from 10 years to 25 years to forever at different sites - and associated issues.
- It was clarified that the single national ethical opinion NICB-REC ethical opinion delivered by the NICB-REC to the NICB would supersede, from the date of its issue, all local REC opinions including local full approvals, partial approval, unfavourable opinions and/or no local opinion returned.

7 Documents submitted for ethical assessment[9]

Documents submitted for ethical review were as follows:

- NICB Protocol - the following was discussed:
  - The Committee considered that the protocol lacked clarity on the joint data controllership arrangements in the context of the specific roles and responsibilities of each joint controller.
  - The Committee considered that biological sample management across databases was unclear in the protocol (sample log vs recruitment log vs REDCap).
  - The Committee noted reference to an electronic case report form (eCRF) in the protocol. It was unclear to the Committee if the eCRF was separate to REDCap.
  - The Committee considered that the data verification process was unclear. Further information was required.
  - The Committee considered that the participant ID codes as outlined in the protocol were inappropriate due to the inclusion of a biobank site reference within the ID code.
  - The Committee noted the applicants made reference to work packages in the protocol, however, no detail on these work packages was provided. Further information was required.
- PI CVs
  - The Committee considered each of the NICB Co-Director CV's to be appropriate.
- Governance structure document - the following was discussed:
  - It was unclear to the Committee how the individuals on the Governance board were chosen/found or rationale for inclusion. Further information was required.
  - The Committee considered that there was an ethical requirement for a separate and independent Access Request Committee to prevent conflicts of interest.
  - The process for recruitment to the ISAB and PPIAB was unclear to the Committee. Further information was required regarding member roles and member expertise.
  - In the context of harmonised change management across all biobank sites, it was unclear to the Committee if there was a harmonised process to put in place new NICB policies or make changes to existing NICB policies. Implementation of new policies or changes to existing policies across biobank sites was unclear. Further information was required.
- DPIA - the following was discussed:
  - The Committee noted that not all site DPOs provided comments on the DPIA.
- Sample and data access policy – the following was discussed:

[9] The information contained within the documents submitted for ethical assessment also fed into previous discussions based on the structured NICB-REC ethics application form sections. Therefore, some discussion information may be duplicated in this section.

- The Committee considered that local ethical approval may not be possible in all circumstances. It was unclear to the Committee how the required local ethical approval for international studies would be managed. Further information was required.
- The Committee noted that the researcher access agreement template was not submitted for ethical review. This document is required to enable an ethical assessment of research access.
- The Committee considered that many local Research Ethics Committees would not ethically assess a research study until access to samples and data has been confirmed. It was unclear to the Committee whether researcher access would be subject to ethical approval or if ethical approval would be required prior to access being requested. Clarification was required.
- It was unclear to the Committee if there would be prioritisation of access dependent on the use of samples and the potential volume of generated data to returned to the biobank by the researchers – (eg various omics) which would be then available to future researchers, increasing the research value. Further information was required.

- Participant information leaflets and informed consent forms (PIL/ICFs). The following was discussed:
  - The Committee agreed there was a requirement to simplify the language used in the PIL/ICFs. It was considered that PIL/ICFs should be tailored to the average reading age of the target cohort. (General population vs adolescent/child). The Committee suggested that the young adult PIL/ICF may be more appropriately used as the main adult information form. It was recommended that adult PIL/ICF should be written for the average reading age of the population, which is 12 years old with 12 to 14 being the ideal average for adults. The Committee acknowledged that the average reading age for young adults would be lower than the adult cohort and, as such, the language levels should be as low as possible and should potentially be combined with audio/visual aids. The Committee considered that the level of information should also be adjusted to be more inclusive for younger cohorts. The Committee recommended that the applicant team should consult with the National Literacy Agency (NALA[10]) to review all PIL/ICFs.
  - The Committee queried whether a child would be given an opportunity to re-assent when they turn 13. Further information regarding whether the 13 – 17 years assent form was intended for recruitment use only was required.

  - The Committee considered that the use of the term '*Next of Kin'* should be discontinued due to a common misunderstanding[11] of its meaning[12]. The Committee suggested the term '*designated representative'* (with the understanding that this term has no basis in law) may be most appropriate in combination with information on the

[10] Home - NALA

[11] Opinion: Áine Flynn, Director of the Decision Support Service: '*It's often wrongly assumed next of kin will have authority to make decisions for us*'

[12] The Myth of 'Next of Kin' | Decision Support Service

individual's relationship to the participant (family, friend or GP) and assurances that the individual understands and can represent the will and preference of the participant. The role of the '*designated representative'* in the assent process should be clear. The Committee required that this be clear on all forms which include a section for '*designated representative'*.

- The Committee considered that there was a requirement for consent forms to be stored as long as participant biological samples and data. Further information was required.
- The Committee considered that for inclusivity, the Parental consent form should include reference to 'guardian' as well as 'mum' and 'dad'.
- The Committee considered that a summary PIL may be useful whereby participants can read and understand it without being overwhelmed with information from the outset. Upon reading the summary PIL the participant should be aware that they can request the full information document if they so wish. The Committee suggested that information could also be signposted online.
- The Committee noted that no translated versions of the PIL/ICFs would be available to participants who do not speak English. The Committee suggested that translated version PIL/ICFs should be considered to ensure inclusiveness of participation and a cohort of participants representative of the population.
- The Committee queried whether translations of key documents would be available in common languages other than English. If not, the Committee required further information on how potential recruitment bias resulting in lack of diversity in the participant cohort would be managed.
- The Committee considered that, in PIL/ICF, a reference to a participant's genetic data being '*unique to you*' was not entirely accurate in the context of familial DNA (similarities and relevance). The Committee required a clarification on familial DNA, in this context, to be included in the PIL/ICF.
- The Committee acknowledged the complexity involved in compiling a PIL/ICF which includes all relevant information and yet is accessible.

- General Practitioner (GP) notification letter. The following was discussed:
  - It was unclear to the Committee if the participant's GP would be contacted as standard. Further information was required.
  - The involvement of, and request of information from, GPs was discussed in the context of how GPs might engage, or not, with additional work associated with their private patients being involved as participants of the biobank. In this context the Committee required further information on the following:
    - NICB considerations on how receptive GPs may or may not be to additional work associated with patients being involved as participants of the biobank;
    - Would the GP be expected to collate and send patient data to the biobank?
    - Would the GP require consent from the patient to release their information?
    - Would GPs charge participants for this work?

- The Committee queried whether there is a GP organisation which could be engaged with by the NICB to make sure all parties understand data portability rights of the participants and to enable facilitation of this process.

Documents submitted post application validation were as follows:

- Template collaboration agreements – The template collaboration agreements relate to arrangements made internally between NICB sites. No ethical issues were identified.
- Inter institutional agreement with the funding body (HRB) – no ethically related comments were required.
- Standard operating procedure (SOP) name list – SOPs were not submitted.
  - The Committee require the submission of a harmonised set of SOPs used across all biobank sites. Harmonised SOPs are an ethical safeguard to ensure consistency in participant sample and data management and processing.
- REDCap code book. The following was discussed:
  - The Committee queried the appropriateness of the recording of participants sensitive data such as prison stays and homelessness.
  - The Committee noted that there was no clear structure to the information requested from the participants in terms of usability or usefulness for the purposes of COVID-19 research. Rationale and justification were required on the extensive participant data captured in the REDCap code book.
  - It was unclear to the Committee if REDCap takes software usage statistics or not. This speaks to security of data. Further information was required.
- Biobank Executive Committee (BEC) terms of reference
  - The Committee considered that more detailed information regarding the scope of the BEC and terms of reference could have been provided.
- Governance Committee Terms of reference – The Committee considered that further information regarding the Governance committee members and their roles was required.
- Security environment summary: The following was discussed:
  - The Committee considered that appropriate and secure backup plans were required for both biological samples and data.
  - The Committee considered that there was a requirement for a standardised data breach protocol as previously discussed. Furthermore, the means through which participants would be notified of a breach involving their data was unclear to the Committee.

Decision

The Committee agreed that a request for further information (RFI) would be issued to the NICB (Appendix I). A decision letter outlining the requests for further information would be prepared by the National Office, approved by the NICB-REC Chairperson, and then issued to the NICB. The Committee agreed a submission deadline of five weeks and an NICB-REC ethical assessment period of two weeks. It was agreed that the NICB-REC would re-convene

to discuss all further information provided by the NICB on a date to be confirmed. It was also agreed that the ethical assessment of the further information would include a written component with Committee members submitting comments prior to the RFI meeting.

The Committee confirmed that it would bring forward all agreed provisional conditions (appendix II) for discussion/confirmation at the RFI meeting.

Meeting close

At the conclusion of the discussion the Committee members thanked the Chairperson for the highly efficient facilitation and structure of the discussion process which was found to be collegiate and effective.

The Chairperson thanked the members and closed the meeting.

NATIONAL OFFICE FOR RESEARCH ETHICS COMMITTEES

Appendix 1 – Request for further information (RFI) issued to NICB 10 May 2023

1 Application Checklist - RFI

- The following documents were requested:

  xiii. All participant questionnaires including clarification on what questionnaires will be used and when, and what details will be requested from participants and why.

  xiv. Letter of invitation to participants.

  xv. Advertisement/recruitment material including links to website information designed to provide information to potential participants.

  xvi. Standard operating procedures (SOPs) and SOP flow charts for all harmonised Biobank operations.

  xvii. Biological sample life cycle flow chart.

  xviii. Template biological material and data transfer agreement.

  xix. Template access agreement.

  xx. Biological sample and associated data retention policy.

  xxi. Staff confidentiality policy.

  xxii. Non-employee confidentiality policy.

  xxiii. Security and indemnity certificates for each biobank site.

  xxiv. Site assessment forms for each site (to include, at a minimum, information on the following: available biobanking related infrastructure at site, human resources at site, staff training available on site, risk mitigation at site [security, power outage, freezer failure etc])

2 Operations, governance and access rights - RFI.

Governance

- The Committee requested information on the criteria for appointing members to the Governance board, including a rationale for inclusion of each member and how potential conflict is managed and independency is ensured.
- The Committee requested information on the criteria for appointing the individuals to the International scientific advisory board (ISAB) and Public-patient involvement advisory board (PPIAB). Information on the process for appointment, member roles, and what expertise each member contributes was requested.

- Information regarding the oversight process to put in place a new policy or make a change to an existing policy was requested.

Access

- Clarity was required on whether it would be possible for researchers accessing the biobank to conduct their research project, using biobank samples and data, with no collaborative links to the PIs in the biobank. The Committee required clarity regarding any obligation on researchers accessing the biobank to collaborate vs free and open collaboration. Answers to the following questions were requested:
  - What are the terms and conditions set out in the access agreements, regarding Intellectual Property Rights?
  - What is the NICB's policy and expectations on author accreditation for published academic articles, which reference the NICB as a resource? Specifically, is it envisaged that individual members associated with the NICB, and/or the NICB as the biobanking infrastructure, will receive accreditation?
- The Committee requested information regarding the NICB policy on international researchers requesting access to the biobank and how the requirement for local REC approvals for those international studies would be managed.
- A separate and independent 'Access Committee' is required, to ensure impartiality in terms of NICB access requests granted. This Access Committee should be separate from the BEC. In accordance with best practice an Access Committee should be independent and have sufficient skills to make a decision (including expertise in law, ethics & PPI). A plan for 1) the establishment of an independent access Assessment Committee, 2) a terms of reference document for the Access Committee, and 3) information on member roles, criteria for appointment and member contribution was requested.

Standardisation and harmonisation across biobank sites

- The Committee requested that the applicants to submit a standardised strategy for data and sample retention which would be implemented across all biobank sites.
- The Committee requested a plan for retention and/or destruction of biological samples and data on the ceasing of the biobank and a timeframe for that retention and/or destruction plan.
- The Committee requested information regarding on-site risk mitigation as the technical safeguarding of biological samples was unclear. eg information related to power supply which may result in freezer failures and or loss of CO2/nitrogen etc.
- A proposed timeline for accreditation of the NICB under ISO 20387 was requested.

Sustainability

- The Committee requested the submission of an economic self-sustainability and cost recovery plan including an access costing structure.

NICB work packages

- The Committee requested information on work packages 1 to 5 as referenced in appendix 11.3 '*NICB Governance'* of the protocol, as no explanation or information was provided on these work packages in the application form.

3 Biological samples, associated data and research scope - RFI

Joint data controllership

- The Committee requested clarity on joint-data controllership arrangements, roles and responsibilities. Specifically, information regarding agreements/arrangements in place, which outline what party/controller is responsible for what aspect of data processing was required.

Third party data processors (excluding researchers accessing the biobank)

- The information provided implied that there will be no third-party data processors. i.e. there would be no third party contractors or service providers processing data. Clarification on third party data processors in this context was requested, including what arrangements would be in place, and setting out roles and responsibilities.

Data management

- In terms of the principle of data minimisation, the information collected in the data dictionary was considered extensive. The Committee required a rationale for the inclusion of such extensive and detailed data.
- Further information on the electronic Case Report Form (eCRF) as referenced on pg 29 of the DPIA was requested as follows:
  - Is the eCRF separate from REDCap, the recruitment log and the sample data base?
  - What secure platform is it hosted on it? where is it located? who has access to it?
  - What information is captured?
- The Committee commented that extraction of information from paper-based sources can be challenging. Further information was requested as follows:
  - how are data extracted from paper-based sources?
  - who will extract data from paper? and
  - who will enter the data on the system?

  With data being collected at different sites, it was unclear how data handling would be standardised to ensure consistency. Information on standardisation and integrity of data handling was requested.
- Information of all data formats to be handled, as per section 2.2.3 of the application form, was requested.

Auditing

- Information on auditing was requested as follows:
  - How will data be verified and audited?
  - On what scale will data be verified and audited?
  - How will data integrity and consistency across participants and sites be validated?
  - Who is responsible and is that individual internal or external?
  - Who is the audit report is submitted to?

  - Who is responsible for implementing actions that may arise from the audit?

- Relating to the responses to a) above, information was requested regarding the implementation of an auditing process to ensure both the data and logging of biological samples is adequate.
- Information on auditing of biological samples was requested. How often will biological stock levels and biological sample integrity be monitored?
- The Committee commented that '*date of birth'* is not a unique identifier. The applicants were requested to outline a robust strategy to ensure that duplicate participants across biobank sites are identified and managed appropriately.
- The Committee requested submission of a harmonised standard operating procedure covering auditing designed to prevent security and power failure across all biobank sites. This SOP should include who is responsible, whether that individual is internal or external and who the audit report is submitted to.

Data linkage

- The Committee requested information regarding how biological samples and data will be linked:
    i. with relevant information from the COVID-19 Vaccine (CoVax) database and the National Virus Reference Lab (NVRL).
    ii. with other data sets external to the NICB and the NICB data,
- The Committee requested information on whether there are any limitations on linking further data sets at a later point in time as the NICB matures, to mitigate against participant reidentification.

Data protection

- Notwithstanding the information provided the Committee requested a short, but specific summary outlining how the biobank will ensure GDPR compliance. In this context the applicants were asked to outline, in the summary, the role of the lead DPO.
- The Committee requested that a harmonised and standardised NICB data protection policy is developed and implemented across all biobank sites. The data protection policy should be specific to the NICB as a multisite biobanking infrastructure, and not necessarily specific to individual biobank sites.
- The Committee requested further information regarding the risk of participant re-identification. It was requested that the information provided should specifically address how personal details and information combined with genetic data may result in re-identification, and how this risk would be mitigated.

Data and biological sample security

- Management of data breach: The Committee requested that a harmonised and standardised NICB data breach policy be developed and implemented across all biobank sites. The data breach policy should be specific to the NICB as a multisite infrastructure. It should be clear to participants, when and how they would be notified of a data breach, in accordance with data protection legislation.
- The back up of the NICB database on a computer based in St James hospital was considered unsuitable from a security perspective. A suggested alternative backup was

an offsite server which provides both physical and digital security. The Committee requested that a robust and secure data backup plan be developed and submitted.

- Identifier references proposed were considered to be problematic as they reveal information including the biobank and the recruitment site. The Committee requested revision and submission of a sample reference strategy which would ensure no participant data is revealed by the reference used for their samples and data.

Return of data to the biobank

- The Committee requested further information regarding:
    i. the process for linkage of returned data from researchers, with the associated biological samples and,
    ii. the associated timeline for return of data from researchers.
- Information regarding how the integrity of returned data would be ensured if it is returned from a research lab and, as such, is not clinically validated.
- Whether the data would be partitioned into returned vs original medical data was queried.

Findable Accessible Interoperable and reusable (FAIR) data

- Reference to FAIR[13] (Findable, Accessible, Interoperable and Reusable) data was noted. The Committee requested detailed information regarding how the applicants will ensure data is FAIR.
- The Committee requested clarity on how SNOMED will contribute to interoperability and how non-SNOMED data would be managed in this context.

Genetic data

- Information provided on genetic data was considered to be inadequate. The applicants stated that genetic data would possibly be shared with academic researchers and commercial companies worldwide. This potentially gives rise to legal concerns including genetic discrimination, risk of unauthorised access and misuse by third parties (insurance companies etc). The Committee requested detailed information to clarify how genetic data, specifically, would be managed and how the risk associated with sharing of genetic data would be mitigated.

Biological sample management

- Security, standardisation and protection of the integrity and fidelity of biological samples across all biobank sites was required. The Committee requested standardised SOPs to be submitted. In addition, the Committee requested information on how compliance of NICB harmonised SOPs would be ensured across biobank sites.
- The Committee considered that a backup storage procedure would be required for biological samples. The Committee commented that best practice should be implemented, such as splitting resources across sites, providing a mirrored resource of biological samples for risk mitigation purposes to prevent sample loss. The Committee requested submission of a robust and secure backup protocol for biological samples.

[13] FAIR Principles - GO FAIR (go-fair.org)

- The Committee requested information regarding the location of the biological sample data base and log and information on how it is linked to REDCap.
- The Committee requested details on the process to oversee the amounts of biological samples being released and how and under what circumstances access to biological samples would be prioritised, given the finite amounts that will be available to access. The Committee requested that consideration should be given to this in the terms of the access agreement.

Participant sub-groups

- The Committee noted there were 8000 expected but unspecified participants. The Committee requested information on expected participant sub-groups including:
    i. the breakdown of participant groups,
    ii. rationale for this breakdown, and
    iii. expected participant numbers in each sub-group.
- The Committee requested detailed information regarding how healthy controls would be recruited and from where.

Biobank scope – potential for future broadening of scope

- The Committee requested information on the proposed future of the biobank in terms of evolving scope and any future plans to develop the NICB as a biobank for other diseases.
- The Committee requested detailed information on how potential expansion of biobank research scope would impact the informed consent of participants. A strategy on how this would be managed was also requested.

4 Biobank participants and informed consent - RFI

Recruitment

- The Committee requested clarity on how much time, generally, would be given to prospective participants to review and consider the information set out in the participant information leaflet and consent form, prior to informed consent being sought.
- The Committee requested that the applicants fill in and submit section 3.3.1 (Will all participants have the decision-making capacity to give informed consent?) of the application form in the context of unconscious participants who do not have decision-making capacity at the time of recruitment.

Withdrawal of participant consent

- The Committee requested clarification on the process associated with participants withdrawing from the biobank. It was requested that this clarification should specifically include information on:
    - how it would be ensured that data and samples would be destroyed when the participant had confirmed that they wish no further use of their samples and data.
    - how the withdrawal of participants would be communicated to researchers who had been given access to the participant's samples and data.
    - the process the researcher must follow in this instance.

Confirmation was requested that the above points would also apply to participant assent.

- The Committee requested information on whether participant re-identification at the relevant biobank site would be required for participant withdrawal.

Participant decision-making capacity to provide informed consent

- The Committee requested information on the following:
    i. How the decision-making capacity of participants would be assessed to ensure informed consent could be provided.
    ii. What supports, accommodations and safeguards would be provided to ensure no unnecessary challenges are made to an individual's decision-making capacity to provide consent.
- Some participants may have diminished capacity, but still have decision-making capacity to provide informed consent. In this context, the applicants were asked 'how will the principle of presumption of capacity be adhered to?'
- The applicants were asked - If a participant is found to have diminished decision-making capacity after consent has been provided what safeguards are in place to ensure the will and preference of the participants will continue to be asserted?

5 Public engagement, Patient and Public involvement (PPI), economic sustainability and commercial value - RFI

Intellectual property

- To understand the how the biobank as a publicly funded national infrastructure aims to ensure impact and benefit for public good through research and innovation, the Committee requested information on the biobank's policy regarding intellectual property management of research outputs derived from the biobank resources. This information speaks to the overarching ethical use of public funds and participant samples and data to improve public and patient health.

Financial transparency

- The Committee requested information on financial transparency and publishing of annual accounts.
- The Committee requested information on an access charging schedule.
- The Committee requested information on how, or if the biobank intends to reach financial self-sufficiency.

NICB Team conflicts of interest

- The Committee noted that there are no conflicts of interest stated in the application form. Clarity was requested on how future conflicts of interest among the NICB team and Co-Directors would be managed, should this arise. A conflict-of-interest policy for the NICB was requested.

Participant expenses

- Re-imbursement of expenses to participants who are requested to donate biological samples outside of normal clinic visits was unclear. The Committee requested clarity on whether and how participants would be re-imbursed for their expenses in this instance. Additionally, the Committee requested submission of a timeline and process for expense reimbursement to participants.

Impact

- The impact of the biobank was not sufficiently clear as described in sections 4.1.1 (*How will the* impact *of the biobank on society, health and social care research and innovation be measured, reported and disseminated to the public and participants during the life of the biobank?)* and 4.3.1 (*Please describe the anticipated societal and population health impact of the biobank*) of the application form.

    i. The Committee requested information describing the anticipated impact the biobank should have on society, health and social care research and innovation and how this impact would be reported and disseminated to the public and participants during the life of the biobank. Additionally, the Committee requested specific information addressing potential advances in health care and benefits to the public.

    ii. The Committee understood that long term impact in this capacity can be difficult to accurately anticipate however, surrogate outcome measures expected during the timeline between the conduct of the research and the resulting public health impact could be measured. These outcome measures may initially include participant numbers, types of biological samples, access requests and approvals. As research progresses outcome measures may include research articles, patents, contribution to public policy etc as part of the expected pathway to commercialisation, leading to, for example, new medicinal products, vaccines, diagnostics and interventions which impact patient care ultimately improving public health. The Committee requested information on how the impact of the biobank would be measured.

Commercialisation

- The Committee considered that transparency on commercialisation is important given a propensity for participant sensitivity regarding how the use of their samples and data in research may lead to commercialisation. The Committee considered that it would be important to highlight to the participant the requirement of commercialisation as an integral part of the research process, which facilitates the development of new medicinal products and their translation to the bedside to improve patient care. The Committee requested information:

    i. on a detailed pathway to commercialisation, and

    ii. on the safeguards in place against misuse of data (selling etc) in the commercial sector.

Indemnity

- In the application form the applicants stated '*the clinical Indemnity scheme 'should' cover claims*'. The Committee requested that the applicants clarify how it will be ensured that all participant indemnity costs are covered.

- The Committee requested clarification as to whether participants would be required to inform their private health insurance provider about their participation in the biobank.

Public feedback

- The Committee requested information on a public feedback and complaints process and how it would be managed.

Public and Patient Involvement (PPI)

- The Committee requested clarity on the inclusion of PPI in the access request process.

6 Local REC approvals – No RFI

7 Documentation - RFI

Sample and data access policy

- The Committee requested the submission of a sample access agreement template.
- The Committee requested clarity as to whether studies requesting access to the biobank would be required to have ethical approval in place before an access request is made or after access is granted.
- Where access is requested prior to ethical approval being sought for the research study, the Committee queried whether access would be dependent on the ethical approval of the study.
- The Committee requested information on whether there would be prioritisation of access, dependent on the nature of the research project and the potential volume of useful data to be returned to the biobank (and made available to future researchers).

Patient information leaflets and informed consent forms (PIL/ICFs)

- The Committee recommended consultation with the National Literacy agency (NaLA) to review all PILs and consent/assent forms.
- The Committee noted that the adolescent PIL may be more appropriate to be used as the Adult PIL given the average adult reading age of 12 – 14 years. The Committee requested that the adult PIL is simplified in line with the national average reading age for adults. It was considered that all PILs should be edited to reflect the average reading age for the relevant cohort.
- The Committee requested that the use of the term '*next of kin'* be discontinued due to a common misunderstanding[14] of its meaning[15]. The Committee suggested the term '*designated representative'* (with the understanding that this term has no basis in law) may be most appropriate in combination with information on the individual's relationship to the participant (family, friend or GP) and assurances that the individual understands and can represent the will and preference of the participant. The role of the '*designated*

[14] Opinion: 'It's often wrongly assumed next of kin will have authority to make decisions for us' (thejournal.ie)

[15] The Myth of 'Next of Kin' | Decision Support Service

representative' in the assent process should be clear. The Committee requested that this is clear on all forms which include a section for '*designated representative'*.

- The Committee requested information on whether a child would be given an opportunity to re-assent when they turn 13. Clarity on whether the 13 – 17 years assent form was intended for recruitment use only was requested.
- The Committee requested information on how it would be ensured that all assent and consent forms would be maintained for as long as the samples and data.
- The Committee requested information on whether translations of key documents would be available in common languages other than English. If not, it was requested that information was provided on how potential recruitment bias resulting in lack of diversity in the participant cohort would be managed.

GP notification letter

- The involvement of, and request of information from, GPs was discussed in the context of how GPs might engage, or not, with additional work associated with their private patients being involved as participants of the biobank. In this context the Committee requested information on the following:
    i. Will the participant's GP be contacted as standard practice?
    ii. Has it been considered that GP's may charge participants for this work?
    iii. Has a cost reimbursement for time involved been considered to encourage GPs to engage with this process?
    iv. GP data will not be pseudonymised, how will the biobank manage this?
    v. How will the NICB ensure all parties are aware of patient/participant data portability rights and enable facilitation of this process?

SOP list

- The Committee required the submission of all harmonised operational SOPs as referenced above under required documentation and elsewhere. Additionally, the Committee requested information regarding how these SOPs would be actioned across all biobank sites and how compliance to NICB SOPs would be assured and audited at each site. Furthermore, the Committee requested submission of a process covering the revision, review and updating SOPs as necessary.

RED Cap code book

- The Committee queried the appropriateness of recording sensitive data such as prison stays and homelessness. The Committee requested a rationale for the inclusion of this information.
- The Committee requested that the applicants clarify whether REDCap takes software usage statistics, as this has potential to lead to information leak.
- The Committee considered that selection bias in recruitment may impact the usefulness of all data collected in a public health impact capacity. The Committee requested information on how this had been considered by the applicants.

NATIONAL OFFICE FOR RESEARCH ETHICS COMMITTEES

Appendix II – Provisional conditions

Provisional conditions are identified requirements for which no further information is required or requested. While no specific further information is requested relating to these items the Committee agreed provisional conditions would be subject to confirmation post RFI process.

1 Application Checklist

- No provisional conditions

2 Operations, governance and access rights.

- Access requests are required to be assessed by an independent Access Committee as an ethical safeguard. The NICB should provide terms of reference and a plan for the set-up of an independent Access Committee.
- An expedited approval process for secondary use of data, to that initially approved by the NICB, may give rise to GDPR concerns. Any requests from researchers to use data or biological samples for secondary processes, not requested at the time of initial access, should be assessed and managed according to best practise. Any expedited process, in this regard, should ensure a level of ethical safeguarding equivalent to the initial access review.
- Both access requests made, and access requests granted should be published for transparency.

3 Biological samples, associated data and research scope

- The PIL/ICF should include permission to contact for future consent, should the biobank expand to support research in areas other than COVID-19.
- The PIL/ICF should be clear regarding non-return of incidental or secondary findings and should include the rationale as to why incidental or secondary findings will not be returned to the participant.
- The NICB should keep its approach to incidental and secondary findings under review. This should be adjusted should law evolve in this area. Participants will need to consent to be recontacted for consent to receive incidental or secondary findings in the future. This information should be included in the PIL/ICF.
- The material transfer agreement, when submitted, should contain a requirement to refer to the NICB in publications.
- The material transfer agreement, when submitted should note that the applicable law is Ireland, and any disputes should be resolved in the Irish courts.

- A Cloud backup system is required as an ethical safeguard, instead of a backup saved on computer located at St James hospital. A computer-based backup poses a significant data breach risk.
- The reference in the PIL/ICF section 2.7.2 – stating that your genome is *'unique to you'* may distract from relative relevance of familiar DNA and should be removed or rephrased explaining that there are implications of genetic findings for family members.

4 Biobank participants and informed consent.

- It should be ensured that when consent is being taken that it is a two-way conversation, and that the participant fully understands the information provided.
- The applicants should request that the NALA review the PIL/ICFs and that the PIL/ICFs are revised according to the NALA recommendations.
- The Committee suggested that a video which shows the participants what is involved in the consent process would be useful. It was agreed that this would diversify how information is provided and would facilitate absorption of important information by different people and would enables more people to make more informed decisions. Different people take in information in different ways, and this should be considered by the applicants.
- The Committee considered that the young adult PIL/ICF may be more appropriately used as the main adult information form. It is recommended that PILs should be written for the average reading age of the population, which is 12 years old; 12 to 14 being the ideal for adults. The average reading age for young adults would be lower and should potentially be combined with audio/visual aids. Language level should be as low as possible, and the level of information also needs to be adjusted and be more inclusive for younger cohorts.
- The PIL/ICF should include information regarding release of information to the courts if requested. Suggested wording: "*We will keep your data private unless ordered by a court to give it up*".
- PIL/ICF section 2.7.2 statement that your genome is '*unique to you'* is misleading given the similarities between familial DNA. This may distract from relative relevance and should be rephrased or removed.
- The parental consent form should include a *'guardian'* option in addition to options for '*mum*' and '*dad'*.

5 Public engagement, PPI, economic sustainability, and commercial value

- The costs of a biobank wind down should be clarified in terms of staff retention until the biobank is fully dispersed/dissolved: In the event of the biobank is wound down the Committee request assurances that funding will be ringfenced to ensure staff retention until the biobank is fully dispersed/dissolved to ensure an ethically appropriate and full dispatch of samples and data in this instance.

6 Local REC approvals

- For NICB-REC reference only - No associated provisional conditions

7 Documentation

- The Committee considered that a summary PIL may be useful whereby participants can read and understand it without being overwhelmed with information from the outset. Upon reading the participants could request the full information document if they so wish. Information could also be signposted online.
- The protocol appendix references five academic biobank hubs however six academic hubs are references in the application. This figure should be updated.
- The committee considered that the sample and data flow diagram in the PIL/ICF should be revised to increase clarity.