NATIONAL OFFICE FOR RESEARCH ETHICS COMMITTEES

National Irish COVID-19 Biobank – REC

RFI meeting minutes

Date*	Start	End	Duration (hrs)	Location
03 July 2023	12:00	16:00	4	Zoom

Attendance

Name	Role
Dr Georgina Flood	Chairperson, NICB-REC
Dr Anne Moore	Deputy Chairperson, NICB-REC
Prof. Kathleen Bennett	Committee Member, NICB-REC
Dr Brian Clark	Committee Member, NICB-REC
Mr John Culliney	Committee Member, NICB-REC
Dr Aisling de Paor	Committee Member, NICB-REC
Ms Joan Jordan	Committee Member, NICB-REC
Dr Sonja Khan	Committee Member, NICB-REC
Dr Patrick Manning	Committee Member, NICB-REC
Prof Shaun O'Keeffe	Committee Member, NICB-REC
Prof. Cathal Seoighe	Committee Member, NICB-REC
Prof Anthony Staines	Committee Member, NICB-REC
Dr Emily Vereker	Head of Office, National Office for RECs
Dr Anne Costello*	Programme Manager, National Office for RECs
Brid Burke	Observer, HRCDC Programme Manager

*Drafted minutes

Apologies**

Name	Role
Prof. Sean Hynes	Committee Member, NICB-REC
Dr Kevin May	Committee Member, NICB-REC
Dr Ciara Staunton	Committee Member, NICB-REC

** All committee members submitted written comments prior to the meeting including those members not available to attend the meeting

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Agenda

- Welcome and notification of apologies.
- Update of phased and partitioned opinion model – Dr Georgina Flood
- Discussion of NICB RFI:
  - 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 Operations, governance and access rights
  - Documents submitted
- Discussion of phased and partitioned ethical opinion model components.
- Confirmation of conditions and recommendations

Decision

Partitioned NICB operations for separate ethical opinions	Ethical Opinion
1. Governance: Governance and oversight	**Favourable with conditions**
2. Participant recruitment: Identification of potential participants; participant facing information and consent protocols.	**Favourable with conditions**
3. Biological samples and data: collection storage, processing, cataloguing, general curation, and security aspects.	**Favourable with conditions**
4. Researcher Access, downstream impact and commercialisation.	**Opinion reserved** subject to new application for full ethical assessment

Deliberations

The Chairperson opened the meeting, welcomed the Committee and noted apologies.

The Committee confirmed that the meeting minutes from both 3 April and 19 April were an accurate reflection of the meeting discussions on those dates.

The Chairperson gave an overview of the agenda highlighting the implementation of a phased and partitioned ethical opinion model as an item for discussion at the conclusion of the RFI discussion.

The Chairperson reminded the NICB-REC members of the importance of the NICB as a national infrastructure. She highlighted the importance of the application of practicality and pragmatism and encouraged an understanding of the biobank's current stage of establishment towards being fully operational. The Chairperson recommended that the coming discussion should strike an appropriate balance between facilitation of biobank operations while retaining the ethical robustness of the biobank, for the public good.

1 Operations, governance and access rights

The Chairperson reminded the members of the items for which further information was requested as follows:

- Governance
- Access
- Standardisation and harmonisation across biobank sites
- Sustainability
- NICB work packages

The following topics were discussed:

Governance

- The Committee considered that biobank governance was generally ethically robust.

Researcher access

- The Committee noted that Access Agreement Templates and Material and Data Transfer Agreement templates have not yet been established and, as such, are not available for ethical assessment at this time. The Committee agreed that access and all associated policies and procedures, including but not limited to material and data transfer agreements and establishment of an independent access committee, should be assessed by means of a new application for full review. This application should be submitted at a time when a sufficient amount of information is available for ethical assessment. A deadline of Q4 2023, as per the milestone timeline submitted by the NICB, was suggested for a new application covering researcher access and associated aspects. The Committee agreed that any favourable opinion issued as part of this process would be contingent on the NICB agreeing to commit to a submission deadline for request of ethical approval for researcher access, inclusive of all required information for this assessment.

  - In coming to this decision it was notable that the biobank is currently in recruitment phase and is not expected to implement access procedures until a sufficient level of samples and data are available. Therefore, it was not unexpected that access policies and procedures were not yet available for ethical review.
  - The committee considered that the PIL/ICF should be transparent such that participants are aware that their samples and data will be distributed to researchers. The reserved opinion on researcher access at this juncture does not impact the requirement for transparency to the participant at recruitment stage.

- The process for REC approval of international research studies wishing to access the biobank was unclear to the committee. It was queried whether International researchers would have access to a local REC in their own country. It was unclear to the committee if there is a mechanism in Ireland for local REC approval of international studies wishing to access the NICB. The committee agreed that a request for this information should be included as part of the Access request ethics application.

Harmonised sample and data retention policy

- A harmonised policy of a 10-year retention period for data and samples, post biobank closure, was considered appropriate. The committee recommended that a plan be developed outlining appropriate storage or destruction of biosamples and data, in the event of biobank closure. The committee suggested that a portion of the current funding should be ringfenced, or that the host Institutions should commit to responsibly managing a closedown, regardless of funding availability, in the event of biobank closure.

Harmonised Data protection policy

- The Committee acknowledged that all data policies across biobank sites and legal entities will be compliant with GDPR as is set down in law. It was considered, however, that a supplemental guideline/policy for biobank specific aspects of data protection should be devised to ensure standardisation and sufficient data protection in the biobanking context. This policy/guideline should be implemented across all NICB sites.

ISO 20387

- The Committee agreed that ISO20387 accreditation should be encouraged and monitored as an important ethical safeguard.

Sustainability

- The Committee acknowledged that biobank sustainability requires funding. It was recommended that sustainability and funding streams be monitored as the biobank progresses.

Confidentiality

- The Committee acknowledged that all staff working across clinical sites will be HSE staff or would be funded under Section 38 of the Health Act 2004[1]. Therefore, these individuals would be bound by a patient confidentiality agreement as part of their contract. These staff would also be covered by the clinical indemnity scheme. Students in those settings would also be garda vetted and bound by a confidentiality agreement.

[1] Health Act 2004 (irishstatutebook.ie)

2 Biological samples, associated data and research scope

The Chairperson reminded the members of the items for which further information was requested as follows:

- Joint data controllership
- Third party data processors (excluding researchers accessing the biobank)
- Data management
- Auditing
- Data linkage
- Data protection
- Data and biological sample security
- Return of data to the biobank
- Findable Accessible Interoperable and reusable (FAIR) data
- Genetic data
- Biological sample management
- Biobank scope - potential for future broadening of scope

The following topics were discussed.

Joint data controllership

- The Committee considered that joint data controllership arrangements were unclear. In terms of contractual obligations, it was not clear to the committee who has data controller responsibility for what biobank aspects.

Third party data processors

- The Committee considered that information provided on third party data processors was clear and concise.

Data protection and management

- The Committee considered that data management was clear and concise.
- The Committee considered that data protection was clear although further clarity and detail on the legalities surrounding the access agreement would be required to be submitted with a new application for ethical approval of biobank access.
- The Committee considered that information relating to how it would be ensured that data was FAIR, was clear and concise.
- The Committee considered that potential linkage of participant information with the National COVID-19 Immunisation System (COVAX)[2] and the National Virus reference

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

Laboratory (NVRL)[3] databases should be clear in the Patient Information Leaflet and Informed Consent Form (PIL/ICF).

- It was unclear to the Committee how participants would be informed of a breach impacting their data.
- The Committee considered that a computer in St James's Hospital should not be used as an NICB database backup due to the risk of theft and data breach. It was suggested that a cloud-based backup carries considerably lower risk of data breach and should be implemented.
- The Committee discussed the management of clinical information in the context of training of staff who can consistently collect and extract data from handwritten clinical notes of patient encounters, to enter on to REDCap. The committee recommended that it should be ensured that appropriate, consistent and common training in data extraction, should be provided to ensure high integrity of extracted data across sites.

Genetic data

- The Committee acknowledged that the inclusion of genetic data in the biobank is fair, reasonable and necessary. However, it was considered that the legal concerns around genetic discrimination and unauthorised third-party access and misuse, remain a risk. The Committee considered that the access agreement, when submitted, should clearly define what the biological samples, the associated data and any results of genetic analysis could be used for. It was acknowledged that a breach in that binding agreement would be unlawful.
- The Committee acknowledged that genomic data is protected under GDPR so could not be lawfully used by third parties without informed consent however, there remains a risk of security breach. The Committee considered that the two-factor reference number system, with a different reference given to the researcher to that which is held centrally at the biobank, significantly mitigates the risk of reidentification due to data breach.
- The Committee considered that it would be important to have specific and separate informed consent for genomic and genetic analysis. Additionally, information on the risks of misuse should be clear to the participant in the PIL/ICF.
- The Committee recommended that there would be a Biobank Executive Committee (BEC) member with genetic expertise and an appropriate genomic data protection knowledge who, as part of a designated role, would be responsible for genetic data, the associated legalities and the risks involved in processing.

Biological sample management

- Biological sample management was unclear to the Committee. It was considered that the security of samples should be ensured, to mitigate against non-biobank associated university staff inadvertently accessing biobank samples from freezers or Liquid Nitrogen dewars. It was unclear to the Committee whether biobank samples would be kept in shared storage or in locked biobank only freezers/dewars.

Auditing

[3] UCD National Virus Reference Laboratory

- The Committee considered that the information provided on auditing was limited. It was considered that internal audit only is insufficient. The Committee recommended that the NICB implement a system of external auditing within their funding limits.

Participant identification (ID) numbers

- The Committee considered it inappropriate to use participant ID numbers which include a reference to the clinical site where the participant was recruited. The NICB was requested to devise and implement a participant ID mechanism which does not include any information related to the participant or the recruitment site. This ID mechanism should be applied to all NICB participants, with participants already recruited issued with new ID codes.

3 Biobank participants and informed consent

The Chairperson reminded the members of the items for which further information was requested as follows:

- Participant sub-groups
- Recruitment
- Withdrawal of participant consent
- Participant decision-making capacity to provide informed consent

The following topics were discussed:

Assisted decision making

- The Committee acknowledged that there are limited supports currently in place for participants who require assisted decision making. The Committee considered that inclusion of individuals who require assisted decision making is important to ensure a complete cohort of participants. In this context the Committee considered that presumption of capacity is the first step. Where participant capacity is in question, there should be a mechanism in place for this to be appropriately managed.
- The Committee understood that recruitment of participants requiring assisted decision making, outside of the emergency department, is not currently envisaged and, as such, is not under ethical review at this time. The Committee recommended that inclusion of participants, requiring assisted decision making, should be considered further by the applicants in future, with submission of an appropriately updated PIL/ICF.

Participant Recruitment

- Recruitment of COVID-19 patients under deferred consent in an emergency setting: The committee considered that the inclusion of this cohort of individuals is crucial to the NICB. The Committee acknowledged that deferred consent in emergency settings is allowable under the health research regulations and considered this approach to be ethically appropriate.
- Recruitment of healthy controls: The Committee considered that, ideally, advertisement for healthy controls from the community would be most appropriate scientifically. However, it is understood that, pragmatically, recruitment of controls from other hospital services and COVID-19 clinics is easiest. It should be noted, however, that biases will be

present when controls are recruited from hospital patients, particularly COVID-19 clinics, only.

- It was not clear to the Committee how the biobank would recruit a sufficient number of appropriate controls for a research study. It was noted, however, that researchers may have appropriate controls available to them and, as such, some researchers may not require controls from the biobank.

Withdrawal of consent

- The Committee noted that the NICB stated that once samples and data have been drawn down by a researcher they cannot be destroyed or deleted when a participant withdraws. In this instance, however, all remaining bio-samples and data stored by the biobank will be destroyed/deleted. The Committee considered this approach to be ethically acceptable. It should be noted, however, that researchers could be asked to cease the use of raw data and destroy unused samples where this will not impact their ongoing research. This is done by the UK biobank.
- The Committee noted that when they wish to withdraw patients are advised, in the PIL/ICF, to contact the site DPO or site PI, the contact details of whom are included at the top of the PIL/ICF. The Committee considered that it should be the point of contact for the site that is contacted, who would then initiate the withdrawal process and inform the DPO.

4 Public engagement, PPI, economic sustainability and commercial value

The Chairperson reminded the members of the items for which further information was requested as follows:

- Intellectual property
- Financial transparency
- NICB team conflicts of interest
- Participant expenses
- Impact
- Commercialisation
- Indemnity
- Public feedback
- Public and patient involvement

The following topics were discussed:

Intellectual Property

- It was advised than an NICB IP protocol/policy be devised in alignment with the National IP protocol.

Financial transparency

- The Committee acknowledged that the NICB it is not a legal entity and therefore it is not obliged to issue financial reports or undergo financial audit. It is, however, the recipient of a HRB funding award. The Committee acknowledged that the HRB has oversight of the NICB award and would require reporting on how those funds are used. The Committee further acknowledged that there would also be financial scrutiny at the host institution level. The Committee considered that this is a sound financial arrangement, and it can be assured the management of biobank funds is transparent.

Conflict of interest

- The Committee considered that the conflict-of-interest policy was adequate.

Participant reimbursement:

- The Committee deliberated over the ethical requirement for participant out of pocket expenses to be reimbursed. It was acknowledged, however, in the context of:
  - the requirements of the biobank,
  - the potential impact of covid research to be supported,
  - the numbers of participants and
  - the optional nature of participants attending visits outside of normal clinic visits,

  that no reimbursement of out-of-pocket expenses is considered ethically acceptable, for this biobank, at this time. The Committee considered, however, that the non-mandatory nature of any extra visits outside of normal clinical visits, and the non-payment of out-of-pocket expenses for these additional visits, should be made clear in the PIL/ICF.

Impact

- The Committee considered that the impact statement included in the response to the RFI did not sufficiently cover the public and patient impact. It was unclear to the committee if the applicants had engaged with the public and/or patient representatives on how research findings might be impactful for them. The Committee considered that the image of the biobank is important, and that wide dissemination of findings was to be encouraged.

Commercialisation

- The Committee noted that no pathway to commercialisation was provided. This information would be requested as part of a researcher access ethics application.

Indemnity

- The Committee considered that sufficient information was provided to confirm full participant indemnity.

Public Feedback

- Ther Committee considered that, supplemental to the condition requiring a participant feedback mechanism in the PIL/ICF, a clear participant feedback process with stated action points was recommended to be developed and implemented.

5 Documents submitted for ethical review

The Chairperson reminded the members of the items for which further information was requested as follows:

- Sample and data access agreements (not submitted)
- PILs and consent forms
- GP notification letter

The following topics were discussed:

Access agreements

- No template access agreement was submitted. The Committee considered that insufficient information was provided to enable an ethical review of researcher access.

Patient Information leaflet and informed consent form

- The Committee acknowledged that a new, revised adult PIL/ICF was provided with the RFI, which was based on the previous adolescent PIL/ICF. The Committee noted that a requirement for inclusion of 1) data breach information and 2) information on generation of genetic data and associated risk of reidentification had been previously discussed. In this context:
  - The Committee requested that a sentence highlighting the risks of reidentification which are specifically associated with genetic data be included in the PIL/ICF. Additionally, a sentence on the familial nature of genetic data and implications of same was requested to be included in the PIL/ICF.
  - The committee suggested the addition of the wording: *"We will take every measure to protect your data, your identity and your interests, but we cannot always guarantee this. Further information is available at ….".* The Committee requested that this sentence be included under 'How does the NICB protect my privacy?'
- The Committee discussed some of the perennial issues associated with PIL/ICFs generally (including, but not specifically unique to, the PIL/ICFs under review for the NICB). Issues included:
  - Use of the term 'PIL' as a description of the document. This was considered by a PPI committee member to be generally confusing, given the term 'pill' would universally be associated with medication, not documentation.
  - The description of the document as a *'leaflet'* was considered incorrect given the general length of these documents. '*Booklets*' would be a more accurate term.
  - The length of these documents makes it difficult for potential participants to process all of the required information before giving informed consent to be included in a clinical trial/research study/biobank.
  - Walls of text were difficult to read and process generally.

  The committee appreciated, in this context, that, generally, a PIL/ICF cannot be a short leaflet due to the information that is required to be conveyed to potential participants, in order to fulfill the requirement for 'informed' consent.

- The iteration of the adult PIL/ICF provided by the NICB with the RFI response was generally considered by the Committee to be an improvement. It was however, considered that the document was still too dense with somewhat confusing language. The Committee considered that the text could be further simplified, without losing key content, to ensure greater understanding and accessibility of the information in the PIL/ICF.
- The key considerations on the PIL/ICF were discussed as follows:
  - Is it transparent?
  - Is it likely to be understood by the majority of the population?
  - Does the informed consent process allow participants to raise queries in areas they may find difficult to understand in the PIL?
  - Will a researcher/recruiter be in a position to answer these queries?
  - Is there an open conversation component of the informed consent process?

  The Committee members generally agreed that these considerations were positively fulfilled by the current PIL, and the informed consent process, put forward by the applicants.
- The Committee noted that no participant feedback process was available. It was considered that, given the importance of two-way communication between participants and recruiters a general participant feedback mechanism should be included in the PIL/ICF. The committee considered that a clear feedback process with stated action points should be developed and implemented.
- The Committee considered that while various aspects of information are required in the PIL/ICF further detail can be provided or available elsewhere (for example – on the website). The Committee considered that many aspects of the PIL/ICF were overly detailed and the level of information included may be intimidating or off-putting to participants. It was considered that some sections may potentially be shortened highlighting that further/supplemental information is available, and listing where it can be found. This would increase readability and understanding. For instance, the page covering the types of biological samples could be shortened, removing the definitions and signposting further information elsewhere. Further information could take different forms such as supplementary leaflet, conversation with participant recruiter or links to website(s).
- The Committee considered that an introductory sentence should be placed at the start of the PIL/ICF, explaining at a high level why the biobank is needed (without yet referencing the biobank). This sentence could highlight the impact of COVID-19 Pandemic on the global community and the requirement for research to help further understand the virus and improve treatments. An introductory sentence such as this would help to set the scene for the participants reading the PIL/ICF. The first sentence in the section entitled '*What is the purpose of this biobank?*' may be better placed as the first sentence in the invitation section. It is noted that the term '*health research biobank'* is currently used in the first sentence of the PIL/ICF. It would be more accessible for participants to set the scene prior to referencing the biobank or explaining what a biobank is.

- The Committee considered that an informative infographic covering the general biobank process should be included further to the top of the PIL/ICF. The committee suggested that the infographics currently included on page 13 of the adult PIL/ICF are suitable in this context and should be moved up.
- The committee considered that, generally, text should be simplified further to reduce the reading age and comprehension without diluting the information. For example, on page 2 in Section '*Why have I been asked to take part?'* the sentence *"We are inviting people who currently have COVID-19, have recovered from COVID-19 and or have Long COVID to consider participation*" could be simplified to "*We are asking people who have COVID-19 or have recovered from COVID-19 to take part".* Terms like '*academic institutions'* could be replaced with 'universities' for clarity.
- Notwithstanding the fact that the PIL is based on a published template, designed by Committee, with PPI input, the Committee considered that sections could still be shortened to include only the basic required information with further information signposted elsewhere. In this context page three of the adult PIL/ICF was discussed as an example of how this could be done. The Committee suggested that the information on biological samples was unnecessarily detailed and that many participants may not have heard, for example, of Cerebrospinal Fluid, or know what it is. The committee suggested that wording could be simplified and shortened to "*If you consent to take part, the hospital will take some biological samples such as blood and other sample types, the full details of which can be found on the website*" ensuring the information is available on the website or signposted elsewhere.
- The Committee considered the use of the phrase '*next of kin'* to be inappropriate. There is a general community misunderstanding of what the phrase '*next of kin'* means[4]. It is understood that many people believe '*next of kin'* refers to their closest relative only. Further misunderstands include that your '*next of kin'* can make decisions for you even when you have capacity to do so yourself. It is due to this general community misunderstanding of the meaning of the term that the Committee require that the use of the term '*next of kin'* should be discontinued, in favour of a term which can be qualified and is clear to the participant. The Committee suggested the term '*Participant Representative'*, which should be combined with 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 committee request that the term '*next of kin'* is removed and replaced with '*participant representative'* on all PILs. The PPI members on the committee agreed this is an understandable term to use in this context.
- The committee deliberated upon the translation of the PIL/ICF into different languages. It was considered that it would be useful for the PIL/ICF to be available in other languages to safeguard against bias in the recruitment process and ensure a more inclusive, population representative, cohort of participants. Not having different language versions available, however, is not considered to be unethical. This would be a recommendation rather than a condition.

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

GP notification

- The Committee considered that the additional information provided regarding the GP notification was clear.

6 Documentation submitted post validation.

The Chairperson reminded the members of the items for which further information was requested as follows:

- RED Cap code book

The following topics were discussed:

RED Cap code book

- The Committee considered that the REDCap data was extensive and detailed. It was considered that the inclusion of start and end dates for prison terms may lead to identification. The Committee agreed that this information should not be recorded by the biobank. The Committee suggested that duration of prison term(s) could be included instead.

7 Documentation requested as part of the RFI

The documentation requested as part of the RFI was as follows:

i. All participant questionnaires including clarification on what questionnaires would be used and when and what details would 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 SOP 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])

Discussion of documentation requested as part of the RFI

Clinical long covid symptom questionnaires

- The Committee noted that no questionnaires were submitted. The applicants requested permission to access information contained in questionnaires administered as part of routine clinical care, in long COVID clinics. Medical questionnaires which are used to identify symptoms at clinical sites were not provided. It was not clear to the Committee whether or not the same structured symptom information would be collected at each site. The Committee questioned whether 13 different symptom questionnaires may be in use at each of the 13 clinical sites. It was suggested that non-consistent capture of symptom information may lead to disparate medical opinions of what may or may not constitute a relevant symptom to record for each participant. The Committee recommended that the NICB should have sight of the questionnaires used to record long COVID symptoms to ensure a level of consistency in recording of participants long COVID symptoms. This would ensure the integrity and consistency of the participant information recorded, and subsequently made available to researchers. The Committee suggested that it would be prudent for the NICB to ensure, for future prospective collections, that long covid symptoms are collected and recorded in a consistent and standardised way, where possible.

Letter of invitation

- The Committee noted that no participant letter of invitation was submitted. The applicant's clarified that the PIL/ICF serves as the letter of invitation.

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

- The Committee noted that no advertising materials were submitted. The NICB states no current plans to advertise for participants.

Researcher access

- The Committee noted documents related to access (Template Material and Data transfer agreement and researcher access agreement) were not submitted as requested. It was agreed earlier in the deliberations that the Committee will reserve an opinion on all items related to biobank access in lieu of a new application for full ethical review.
- The committee noted that BEC is referenced as the access assessment committee in figure 2, page 13 and in section C, number 15, page 8 of the adult PIL/ICF. The Committee considered that this should be updated to reflect an independent Access Committee will be responsible for evaluating access requests. The Committee agreed that a conflict of interest arises where site leads and PIs (BEC members) who were involved in the collection and storage of particular samples and data, via their own research studies, are involved in the request to access those samples. For this reason, an independent access committee is required to prevent potential access bias.

Harmonised standard operating procedures (SOPs)

- The committee considered the SOPs to be satisfactory. The Committee commented that the readability of the SOPs could be generally improved. It was noted that the Lithium Heparin method SOP manual contained an EDTA protocol in section 7.4, page 32, and recommended that this should be replaced with the relevant Lithium Heparin protocol.

Biological sample life cycle flow chart

- The Committee noted that four charts were submitted covering 1) how samples and data would be collected and stored; 2) How sample and data access is approved and shared; 3) How samples and data are destroyed after use and 4) Sample processing and transport. The Committee considered these charts to be useful and clear visual summaries of biobank processes.

Confidentiality

- The Committee noted that a harmonised staff/non-staff confidentiality policy was not submitted. It was however, noted by the committee that all staff at clinical sites would be covered by contractual confidentiality agreements and the clinical indemnity scheme.

Security and indemnity certificates for each biobank site

- Indemnity certificates for TCD and UCD only were provided.

Site assessment forms for each site.

- A template site assessment form was provided. Site assessments carried out for each site were not provided.

8 Ethical opinion model

The committee discussed and agreed the process through which a partitioned and phased opinion model would be implemented.

9 Conditions

Ther following conditions of favourable outcomes in partitioned areas were agreed:

Governance and oversight

The NICB-REC favourable ethical on '*Governance and oversight*' was subject to the following conditions:

- PPI: The NICB Governance board must include a member or members who can represent the views of the patient and public community.
- Academic sites: The protocol appendix references five academic biobank hubs however six academic hubs are references in the application. Please update this figure.

Identification of potential participants; participant facing information and consent protocols

The NICB-REC favourable ethical opinion on 'Identification of potential participants; participant facing information and consent protocols' was subject to the following conditions:

The Committee request the following edits to all six Patient Information Leaflets and Informed Consent Form(s) (PIL/ICF):

- PIL simplification: It is acknowledged that the PIL is based on a published template, designed by committee with Public and Patient Involvement (PPI) input. Aspects of the

PIL are, however, overly detailed and technical. It is considered that the level of information included may be intimidating or off-putting to participants. The Committee acknowledge that while various aspects of information are required in the PIL/ICF, the sections could be shortened with further, supplemental detail available, and signposted, elsewhere (for example, on the NICB website). The Committee request that the content of the PIL/ICF is simplified further where possible to ensure comprehension for all participants, without diluting the information. Examples of edits are included below:

  - Information on biological samples is technical. Participants may not have an understanding of the term '*Cerebrospinal Fluid*'. It is suggested that wording could be explained further or, simplified "*If you consent to take part, the hospital will take some biological samples such as blood and other sample types, the full details of which can be found on the website*". Ensuring the information is available on the website or signposted elsewhere.
  - Terms like '*academic institutions'* could be replaced with '*universities*' for clarity.

- Introduction: An introductory sentence, setting the scene for the biobank should be placed at the start of the PIL/ICF, explaining at a high level the importance of a national COVID-19 biobank. This sentence should highlight the impact of the COVID-19 Pandemic on the global community and the requirement for research to help further understand the virus and improve treatments. The first sentence in the section entitled '*What is the purpose of this biobank?*' may be better placed as the first sentence in the invitation section. It is noted that the term '*health research biobank'* is currently used in the first sentence of the PIL. It would be more accessible for participants to set the scene prior to referencing the biobank or explaining what a biobank is.
  - Suggested first sentence: "*The COVID-19 pandemic has had a major impact on our society. Research will help further understand the virus and improve treatments*. *You are invited….* "
- Biobank processes: An informative infographic covering the general biobank processes around how biological samples and data are collected, stored, and accessed should be included to the top of the PIL/ICF. The infographics currently included on page 13 of the adult PIL/ICF are suitable in this context and should be moved up, closer to the top of the document.
- Site contact details: The assigned site team member contact details should be included in the PIL/ICF if this individual is not the site PI.
- Findings: A statement that incidental or secondary findings will not be returned to the participants should be included in the PIL/ICF and clearly explained. Further details such as the rationale behind non-return of incidental or secondary findings should be available elsewhere (eg NICB website), or included in the PIL/ICF as appropriate.
- Familial genetics: PIL/ICF page 4 section 2; The term genome is '*unique to you'*, while true, is misleading given the similarities between familial DNA. This wording may distract from familial relevance and should be rephrased, with an explanation in the PIL/ICF that there may be implications of genetic findings for family members.
- Genetic data: There is an inherent risk of reidentification associated with genetic data. The Committee acknowledged that the inclusion of genetic data in these activities is fair, reasonable, and necessary. However, the risks of reidentification should be made clear to

the participant. A sentence highlighting the risks of reidentification which are specifically associated with genetic data should be included in the PIL/ICF.

- GDPR: A sentence should be included in the PIL/ICF notifying the participant that processing of identifiable data will be carried out in accordance with GDPR requirements. Further information on GDPR compliance should be signposted and available elsewhere eg information such as data use limitation and data minimisation principles etc could be available on the NICB website.
- Data breach: information on the risk of data breach should be set out in the PIL/ICF. The committee suggest the following example of additional wording: *"We will take every measure to protect your data, your identity and your interests, but we cannot always guarantee this. Further information is available at …."*. Further information should be made available on the NICB website.
- Linkage with COVAX and NVRL databases: Further clarity is required in the PIL/ICF. The following wording is suggested: "*Your hospital may, in future, wish to access your information held in the National COVID-19 Immunisation System database (COVAX) or National Virus Reference Lab database*"
- Data privacy: The PIL/ICF should reference the release of personal information to the courts if requested. The following wording is suggested: "*We will keep your data private unless required to be released under court order*".
- Participant reimbursement: The non-mandatory nature of extra visits outside of normal clinical visits, and the non-payment of out-of-pocket expenses for these additional visits, should be made clear to the participant in the PIL/ICF.
- Participant feedback process: Given the importance of two-way communication between participants and biobank recruiters, a general participant feedback mechanism should be included in the PIL/ICF. Suggested wording is as follows: "*If you would like to submit feedback on any part of this process, please contact the site PI*".
- Use of the phrase '*next of kin'*: The term '*next of kin'* is required to be removed from all Patient facing documentation and information and replaced with the term '*participant representative'*. The NICB-REC agreed this is an understandable term to use in this context.
  - Rationale: There is a general community misunderstanding of what the phrase '*next of kin'* means. Many people incorrectly believe it refers to their closest relative only and that '*next of kin'* [5] has the authority to make decisions, even when an individual has functional capacity to do so. A phrase which can be qualified and, as such, is clear to the participant should instead be used. The term '*Participant Representative'* is considered appropriate. It should be combined with information on the individual's relationship to the participant (family, friend, carer or GP), and assurances that the individual understands and can represent the will and preference of the participant. It should be very clear that a 'participant representative' can only assent for the

[5] This view is in line with the views of the Decision Support Services: https://decisionsupportservice.ie/news-events/myth-next-kin

participant in instances where the participant cannot consent for themselves due to diminished capacity.

- Independent Access committee: The Biobank Executive Committee (BEC) is referenced as the access assessment committee in figure 2, page 13 and in section C, number 15, page 8 of the PIL/ICF. The PIL/ICF should be updated to reflect that an independent Access Committee will be responsible for evaluating access requests. A conflict of interest arises where site leads and PIs (BEC members) who were involved in the collection and storage of particular samples and data, via their own research studies, are involved in the request to access those samples.
- Guardian option: The parental consent form should include a guardian option in addition to options for *'mum'* and *'dad'*.

Biological sample and data collection, storage, processing, cataloguing, general curation, and security.

The NICB-REC favourable ethical opinion on 'biological sample and data collection, storage, processing, cataloguing, general curation, and security' was subject to the following conditions:

- The NICB database backup: A static desktop located in James' Hospital cannot be used as a backup system due to the risk of theft and subsequent data breach. An alternative backup system is required. It is suggested that a cloud-based backup would carry considerably lower risk of data breach and should be implemented.
- Biological sample management: Clear information is required on security of samples to mitigate against non-biobank associated university staff inadvertently accessing biobank samples from freezers or liquid nitrogen dewars. Will biobank samples be kept in shared storage or in locked, biobank access only, freezers and/or liquid nitrogen tanks?
  - The NICB-REC requires a stated commitment to, the security of biological samples at all sites.
- Prison term information. The inclusion of start and end dates for participant prison terms may contribute to participant reidentification. This information should not be recorded by the biobank. It is suggested that duration of prison term(s) should be included instead.
- Participant ID numbers: It is considered inappropriate to use ID numbers which include a reference to the clinical site where the participant is recruited. The NICB is requested to devise and implement a participant ID mechanism which does not include any information related to the participant or the recruitment site. This ID mechanism should be applied to all NICB participants, with participants already recruited issued with new ID codes.

Other conditions

- The NICB must commit to submitting a new application requesting ethical approval for researcher access downstream impact and commercialisation and all associated processes (point 4 of governance and operational breakdown on page two of this letter) by Q4 2023. A bespoke ethical application form requesting the required information for an ethical assessment of research access processes will be made available to the NICB for this new application.

- The NICB must commit to progress towards ISO 20387 accreditation as soon as practically possible. This is a reporting requirement in the 6-monthly progress report.
- The NICB must commit to the development of a plan for the eventuality of the NICB terminating operations. This should include a strategy for appropriate storage and/or destruction of biological samples and data in the event of the NICB closure. This is a reporting requirement in the 6-monthly progress report.
- The NICB must commit to development of a harmonised, biobank data specific, data protection policy for all sites. This is a reporting requirement in the 6-monthly progress report.
- The NICB is requested to update all patient facing information, including information available on the website, to reflect all requested updates outlined in the conditions above.

10 Recommendations

The NICB-REC made the recommendations listed below. These recommendations are not conditions of the favourable opinions listed above, however the Committee agreed that information on the progress of these recommendations would be requested as part of the 6-monthly progress report and/or as part of a new application for full NICB-REC ethical assessment of researcher access and all associated processes. Recommendations were as follows:

- Training: It was recommended that staff be trained in the extraction of data from paper sources. This would be particularly important for extraction of long COVID symptoms from participant questionnaires at long COVID clinics to ensure consistent collection and extraction of data from handwritten clinical notes.
- Clinical long COVID symptom questionnaires: Medical questionnaires which are used to identify long COVID symptoms at clinical sites were not provided. The information from these symptom questionnaires form part of the participant's medical record. It was not clear to the committee if the same structured symptom information would be collected at each site. It was recommended that the NICB should have sight of the questionnaires used to record long COVID symptoms to ensure a level of consistency in recording of participants long COVID symptoms. This would ensure the integrity and consistency of the participant information recorded, and subsequently available to researchers. It is recommended that it would be prudent for the NICB to ensure, for future prospective collections that long COVID symptoms are collected and recorded in a consistent and standardised way, where possible.
- Audit: An independent auditing plan was recommended to be developed and implemented as soon as possible, within the current funding limits of the NICB.
- Feedback process: Supplemental to the condition requiring a participant feedback mechanism in the PIL/ICF, a clear participant feedback process with stated action points was recommended to be developed and implemented.
- Findings: It was recommended that the approach to return (or non-return) of incidental and secondary findings be kept under review. Non-return of incidental and secondary findings to participants was considered appropriate at this time, however the Committee

suggested that this policy should be kept under review and adjusted should law evolve in this area.

- BEC: It was recommended that there should be a Biobank Executive Committee member with genetic expertise as well as appropriate genetic data protection knowledge who would be responsible, with a designated role, for genetic data, the legalities and the associated risks.
- Translation of PIL/ICF: It was recommended that the PIL/ICF be made available in, for example, the three main commonly used languages in Ireland, to safeguard against bias in the recruitment process and ensure a more inclusive, population representative, cohort of participants. The Committee suggests this could be potentially implemented digitally, with PIL/ICF translations available on the website. Additionally, where prospective participants require a translated PIL/ICF in their native language, it was recommended that the NICB should aim to accommodate this request.
- IP protocol: Given the public funding investment in the NICB national infrastructure, it was recommended than an Intellectual Property protocol/policy be developed as appropriate for the NICB, and in alignment with the National IP protocol.
- Video to support recruitment and informed consent: The Committee recommended the development of a video which illustrates to potential participants what is involved as a participant in the biobank, to facilitate the informed consent process. This would diversify how information is provided and would facilitate absorption of important information by different people enabling potential participants to make more informed decisions. The Committee suggested that a video could be included on the website.
- Participants that lack decision-making capacity: The committee understood that recruitment of participants that lack decision-making capacity, outside of emergency care scenarios, is not currently envisaged. Inclusion of all individuals who lack decision making capacity is important to ensure a complete cohort of participants that have experienced COVID-19. It was recommended that inclusion of participants that lack decision-making capacity, is considered further in future, with an appropriately updated PIL and accommodations provided for their participation.
- Recruitment of healthy ‘control’ participants: It was understood that recruitment of ‘control’ participants from COVID-19 clinics and potentially other hospital services is most pragmatic. However, the committee commented that biases will be present when control participants are hospital patients only. The committee recommend that it would be most appropriate for ‘control’ participants to be recruited from the general community also. The NICB-REC strongly recommended that the NICB develop an implementable plan to select and recruit control participants from the community to minimise risk of bias.
- SOPs: Lithium Heparin method SOP contains an EDTA protocol in section 7.4, page 32. The committee recommended that this SOP is updated appropriately for correctness.
- Termination of NICB: A commitment to develop and implement a resourced and responsible closedown plan is included above as a condition. It was further recommended that a portion of the current funding should be ringfenced, or that the Host Institutions commit to responsibly managing a solvent closedown, regardless of funding availability, in the event of biobank closure.

Meeting close

At the conclusion of the discussion, the Committee agreed that the National Office would compile the outcome letter which would be circulated to NICB-REC members and approved by the Chairperson prior to issue to the NICB.

The committee members thanked the Chairperson, Dr Georgina Flood, for her highly efficient facilitation of the meeting discussion. The members also thanked the National Office Programme Manager, Dr Anne Costello, for highly efficient management of the ethical review process.

The Chairperson thanked the members and closed the meeting.

NATIONAL OFFICE FOR RESEARCH ETHICS COMMITTEES

Appendix One – Phased and Partitioned Ethical Opinion Model

Ethical Opinion model

The biobanking experts on the Committee (Dr Brian Clark, Dr Ciara Staunton, Prof Sean Hughes and Dr Sonja Khan), were involved in the development of a phased and partitioned ethical opinion model which was then discussed with, and endorsed by, all members of the NICB-REC as part of the RFI meeting.

The implementation of a 'phased and partitioned ethical opinion model' enabled the NICB-REC to facilitate NICB operations in a time expedient and ethically robust way. It also allowed an iterative ethical review process corresponding to the NICB's expected milestones towards being fully operational. The opinion model enabled an ethical opinion to be delivered on aspects of NICB operations where all required information was available for ethical review. It also enabled the NICB-REC to reserve an ethical opinion on aspects of biobank operations which are yet to be fully established (and for which the required information was unavailable for ethical review). A phased and partitioned opinion model allowed for the issue of an ethical opinion on different aspects of biobank operations by:

- The issuing of a **favourable opinion** on aspects of NICB operations found to be ethically robust,
- The issuing an opinion of **favourable subject to conditions** on aspects of NICB operations found to be ethically robust subject to the fulfilment of conditions, or
- **Reserving an opinion** on aspects for which insufficient information is available to enable an ethical assessment. All biobank operational aspects receiving an opinion reserved outcome are subject to submission of a new application for full ethical assessment.

The breakdown of biobank elements which received separate opinions under the phased and partitioned opinion model are as follows:

- **Governance**: Governance and oversight
- **Participant recruitment**: Identification of potential participants; participant facing information and consent protocols.
- **Biological sample and data**: collection, storage, processing, cataloguing, general curation, and security aspects.
- **Researcher Access**, downstream impact and commercialisation.