Sample Access and Preservation Policy v1

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NICOLA Steering Committee
Centre for Public Health
Institute of Clinical Science B
Grosvenor Road
Belfast
BT12 6BJ

Email: nicola-research@qub.ac.uk

Tel: +44 (0) 2890 978923

Supported by:

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Summary

The **N**orthern **I**reland **CO**hort for the **L**ongitudinal study Of **A**geing (NICOLA) is an omnibus panel study with longitudinal follow-up of a stratified random sample of approximately 8,500 men and women aged 50 years and over in Northern Ireland. The study was designed to be complementary to The Irish Longitudinal Study on Ageing (TILDA) that has been in progress in the Republic of Ireland since 2009 and provides an 'all-Ireland' perspective of the social, behavioural, economic, and environmental aspects of ageing for those living on the island of Ireland. NICOLA has also been designed to complement the English Longitudinal Study of Ageing (ELSA) in order to provide potential for comparisons between the health of older adults in Northern Ireland and England. This places Northern Ireland in the network of existing longitudinal ageing studies such as those mentioned above and including Healthy Ageing in Scotland (HAGIS). A unique aspect of NICOLA is its specific focus on transition points in ageing and the effects of diet on the ageing process. The study also focuses in on other research areas that are of unique relevance to Northern Ireland. Ethical approval for Wave 1 of NICOLA was granted from the School of Medicine, Dentistry and Biomedical Sciences Research Ethics Committee, Queen's University Belfast (QUB, Ethics Reference 12.23).

Baseline data collection (Wave 1) for NICOLA commenced in December 2013, with data collected from 8504 participants via a CAPI (consent obtained from n = 8452). Data was also collected from a physical health assessment (n = 3743), self-completion questionnaire (n = 5042) and food frequency questionnaire. Wave 2 is underway with data collection due to complete early to mid 2019. Follow-up measurements (Wave 3, Wave 4…) will take place every 2 - 3 years over a period of at least 10 years. *Interview and self-completion questionnaires data* (Wave 1) includes: socio-economic and socio-demographic factors (e.g. finances, employment, retirement), self-reported measures on mental, physical, and cognitive health, help and helpers, health and social care utilisation, health behaviours, medication use, social connectedness, social participation, personality measures, and dietary intake. *Health assessment data* (Wave 1) includes: biological samples (blood and urine), multi-omic biomarkers, cardiovascular function, cognitive function, respiratory function, physical activity, visual and retinal function, and anthropometry.

The purpose of this document is to describe in detail the general processes and procedures involved in accessing the NICOLA biological, clinical and multi-omic samples. We aim to encourage and facilitate sample access with all '*bona fide'* researchers as defined by the UK Research and Innovation (UKRI) (https://www.ukri.org/) and welcome proposals from researchers worldwide, either for collaborative projects or for other forms of sample access in order to help advance research knowledge.

By 'bona fide' researcher we mean:
A person with the professional expertise and experience to conduct 'bona fide' research; and a formal relationship with a bona fide research organisation that requires compliance with appropriate research governance and management systems.

By 'bona fide' research organisation we mean:
One that has the capability to lead or participate in high quality, ethical research. It will have a public commitment to adhere to recognised research and information governance good practice. (It is not a requirement that such research is the primary business of that organisation, or that all of the research undertaken by that organisation is published. Nor is it a requirement that the organisation be publicly funded.)

This policy document ultimately aims to help researchers conduct their studies in a transparent and streamlined manner. If your query specifically relates to data generated from completed analysis of biological samples or multi-omic biomarkers, please refer to our separate Data Access Policy Document (available on the researcher section of the NICOLA website) which provides guidelines regarding the use of data from NICOLA.

1. Sample Access Procedure: Overview

1.1. The NICOLA Sample Resource

NICOLA is run as a resource to be used by the research community. The process for accessing samples is the same for all individuals, regardless of research area, institution, location or funding source, provided the proposed research is **not** being carried out for personal or commercial gain.

A Sample Access Committee (SAC) has been established to provide oversight and guidance with any applications requesting access to NICOLA samples and subsequent analysis of samples. Access to biological samples collected within NICOLA is limited as a result of the small volume available. If, however, an extensive range of quality-controlled assays of all samples can be undertaken (e.g. by low-cost typing for molecular samples, by NMR for multiple analytes, or by methods for multiple antibodies) then these assays will be performed and results included within the NICOLA database, thereby increasing access to information derived from biological samples. To develop the sample resources, the NICOLA Steering Committee (NSC) has, in conjunction with ESRC obtained funding for undertaking biological assays and genotyping on samples similar to those performed in the UK Biobank. Further information regarding the biological assays and genotyping laboratory methods used for the analysis of NICOLA samples is available on the NICOLA website. Any further queries regarding samples or laboratory procedures can be addressed by the NICOLA Project Manager (NICOLA@qub.ac.uk). If your query is specifically related to biological samples for molecular analyses please contact Dr Amy Jayne McKnight (via the NICOLA Research Support Office, NICOLA-research@qub.ac.uk).

1.2 Guidance regarding approved use of samples

Ethical approval was obtained for all sample collections. This included consent for future research including genetic studies. Where possible biological samples are stored in multiple aliquots to limit the need for freeze thaw cycles and thereby enable as much analysis as possible. However the number of aliquots varies between sample types. Samples involving Human Tissue (i.e. urine, buffy coat, whole blood) are handled, stored and logged according to standard operating procedures set in place by Research Governance, QUB and which fulfil the requirements laid down by the Human Tissue Authority as defined by the Human Tissue Act 2004 (HT Act).

The samples in the NICOLA biorepository are finite i.e. there are limited stocks available. Given the very limited amount of this depletable resource, access to the samples will be carefully controlled, with guidance from the NICOLA SAC. The NICOLA SAC are responsible for ensuring that samples are used for projects that maximise the amount of data obtained from available samples and that these data are subsequently made available to other researchers. The SAC will facilitate access to stored

samples so that they get the widest possible usage while ensuring that scientific rigour is applied in selecting proposals that will yield data which are i) reliable, ii) informative and iii) novel. Researchers granted access to the samples should maximise the epidemiological strengths of the NICOLA cohort, whilst also recognising limitations of the biorepository (in terms of sampling protocols, processing, storage and availability).

It is likely that different researchers will want to conduct a range of overlapping assays on different subsets of study participants (for example, comparing cases of particular conditions versus controls without the particular condition; measurements in samples obtained at baseline and at a repeat visit in a subset to correct for regression dilution). In order to make appropriately efficient, quality controlled use of this limited resource, multiple simultaneous assays in the entire NICOLA cohort would be ideal. Where possible, sub-studies should not routinely reuse the same samples, minimising the likely exhaustion of those samples. Such a strategy would maximise the information available to researchers while minimising sample depletion, and would also facilitate different comparisons since the assay methodology and quality control would be consistent across the whole cohort. Suggestions for particular assays to be included in these multiple-assay schedules will be welcomed, and all assay values will become part of the dataset, thus widening access. In general, however, it is expected that few requests for direct access to aliquots of samples will be agreed by the SAC. As NICOLA has been established as a prospective resource, the participants' samples are expected to be used chiefly (but not solely) to assess the relevance of different exposures assessed at baseline to the subsequent development of disease. This will typically be done by conducting case-control or case-cohort studies of particular health outcomes "nested" within the cohort. Preference will be given to studies that maximise outcomes from each 'thawed sample'. This approach has the advantage that the assays only need to be conducted on samples from relatively small subsets of "informative" participants who develop a particular disease and similar numbers of controls. Decisions about what assays to perform only need to be made when specific hypotheses are clearer (rather than at the time of sample collection), and the range of assays that can be conducted at reasonable cost is much wider. This framework means that assay costs are substantially reduced, depletion of limited samples is minimised, good quality control is facilitated, and scientific return is maximised.

A policy for release of low frequency and rare variants or those with clinical impact is under review. In some cases, the NICOLA team may prefer to conduct the sample analysis in-house in line with researchers needs, and provide the applicant access to data only, however, this will be judged on a case by case basis. Where competition exists for the same set of samples, preference will be given to NICOLA member groups over other requests for applications of similar scientific merit. Safeguards will be maintained to help ensure the anonymity and confidentiality of participants' data and samples. Researchers will enter a legal agreement with NICOLA not to make any attempt to identify participants, and data and/or samples provided to researchers from the Resource will not identify any particular participant (i.e. they will be "anonymised").

1.2.1 Terms of Sample Access

Proposals that request finite samples must satisfy the following criteria to be approved:

- Scientific strength, novelty and potential health or social impact of the proposal must sufficiently justify use of NICOLA cohort samples i.e. the data obtained from the samples will be analysed in conjunction with other data held by NICOLA. Requests to use samples should clearly demonstrate that the proposed study will make use of longitudinal data and cannot be carried out in samples obtained from another source. Use of the samples to investigate associations must be justified on the grounds of potential clinical (or social) relevance, for example

  i) disease diagnosis and pathogenesis

  ii) evidence for public health messages, or clinical guidelines

  iii) clinical or social evidence risk-stratify patients e.g. novel predictors of clinical or social outcomes

  iv) evidence for therapy selection e.g. a biomarker that may predict a better (or worse) response to therapy options.

  v) method harmonisation.

- The analysis proposed does not already exist for the same time point. Samples will not be released for a repeat study where data already exists for NICOLA unless as part of a multi-centre harmonisation study for biomarkers. Requests to repeat or carry out very similar analysis will not be approved unless there are compelling reasons.

- Evidence must be provided to show methodology is appropriate given the processing history of the samples e.g. evidence from published literature or pilot data generated on samples processed in a similar manner. NICOLA samples will not be released for method development unless it is related to method harmonisation.

- The assay test platform should be carried out using gold standard automated methods with proven quality assurance measures in place, preferably NHS accredited or externally audited. The assay should be sensitive enough to detect a signal (<20 % CV as absolute and more desirable <10 %) in a majority of the samples (commensurate with the aims).

- The methodology should include measures to ensure the quality of any remaining sample is not jeopardised and can be used in further assays which can be used on freeze-thawed samples.

- Results generated from any analysis of biological samples must be returned (at an individual result level) to the NICOLA data repository upon completion of the research.

- The volume requested is reasonable and does not seriously deplete the resource. For all assays, the volume of sample consumed by the assay will be judged against the potential benefits of the study, with advice from appropriate experts as required.

- The work proposed is covered by existing ethical approval and is within the scope of the consents obtained for the specific samples.

At least one aliquot of each sample type will be retained for longitudinal studies across NICOLA waves and for future global discovery projects. The exceptions to this are those sample types where only one aliquot was originally produced.

All sample requests for finite biological samples will be subjected to review by the NICOLA SAC to ensure they meet the conditions above and that the amount of material required is acceptable. Please note this means the approval of requests to access NICOLA samples can take up to 12 weeks.

If a request is approved samples will be supplied with the following conditions:

- Researchers will have to pay for access to the sample resource on a cost-recovery basis for their proposed research. These will include a fixed charge for initiating the application review process and for retrieval of samples, and a variable charge depending on how many samples, tests and/or data are required, and any, shipping costs (outward transfer and return). Costs will be provided on a case by case basis depending on the work involved and may be subject to VAT. For contributing members, the level of discount will be dependent on their contribution to NICOLA.

- Where it is possible to use samples which have been thawed and refrozen, samples which have been returned from other projects will be supplied in preference to unused stock if available.

- NICOLA reserve the right to specify where the analysis will be carried out in order to ensure results obtained are comparable to existing data.

- Any samples remaining after analysis must be returned to the NICOLA sample repository

1.3. Requesting access to samples

Researchers wishing to access NICOLA samples may first make an expression of interest either by phone or by email to the NICOLA Project Manager (nicola-research@qub.ac.uk). This may be to find out whether the type and number of samples required are available and to enquire about any charges

that may apply for accessing the samples. Details regarding the subsequent formal process of applying for access to NICOLA samples are provided in Appendix 2.

Researchers are required to take the following steps in order to access the existing NICOLA biological and clinical samples:

Stage 1) *Submission of research proposal form:* An outline of the proposed study should be submitted using the NICOLA research proposal form available within the researcher section of the NICOLA website. This proposal form should clearly state the purpose of requesting the NICOLA samples. The request form should include: contact details of the Principal Investigator (or supervisor for research student), project title, aims / hypothesis, start and the proposed end date of the research, the names of those in the research team, study design (including methods, statistical tests and proposed outcomes), type of samples requested, number of samples requested, volume required (if applicable), concentration required (for DNA only), justification of the samples requested, ability to analyse previously thawed samples, research team (and its expertise), confirmation of ethical approval (if relevant), name, affiliation and role of all persons who will be accessing the samples. The same research proposal form can be used to access data, if required. It is the responsibility of the applicant/researcher to ensure that the study for which the NICOLA samples are being used has the appropriate research ethics approval, research governance and funding approval (if relevant). For multiple projects individual forms must be submitted; one per project.

Stage 2) Review of research proposal form: Proposal forms will be reviewed by the NICOLA SAC which meet approximately every two months. Each proposal will be reviewed by at least one specialist reviewer for that disease group, one clinician and one basic scientist. All proposals will be reviewed on an individual basis. Consideration of the proposal will be based on four distinct areas: quality, importance, impact, and overall use of this limited resource, with a score out of 10 being given to each proposal (appendix 3). Priority will be given to mega-consortia studies that will generate the most robust research outcomes. Decisions on research proposals will fall into one of the following categories:

(i) approved in principle pending ethics/funding
(ii) approved with no alterations/conditions
(iii) approved with conditions/minor changes required
(iv) approval not granted – requires major changes and/or resubmission required
(v) approval not granted – not supplying samples for this study

The researcher will receive an email informing them of the decision. You may also be directed towards local NICOLA subject leads to discuss your proposed research. In some cases, approval may be refused due to the lack of relevant biological samples. The NICOLA SAC reserves the right to impose additional restrictions as appropriate. Any queries relating to proposal submissions should be directed to NICOLA-research@qub.ac.uk.

Stage 3) Data Induction: The NICOLA Research Support Team will act as liaison and assist you in accessing the required samples. You will also be invited to meet the Data Manager (by Skype if necessary) in order to receive induction into the procedures and policies relating to NICOLA. At the end of the induction you will be requested to read and sign the appropriate Sample Access Agreement and Confidentiality Forms in order to ensure the confidential use of the samples.

Stage 4) Access to samples: For the majority of research studies, NICOLA samples will be analysed 'in-house' in the laboratories located within the Centre for Public Health, QUB. If samples are being analysed externally (outside QUB), then they are provided in accordance with QUB Standard Operating Procedure for Material Transfer http://www.qub.ac.uk/Research/Governance-ethics-and-integrity/FileStore/Filetoupload,914030,en.pdf . In such instances, a MTA request form is completed by a member of the NICOLA SAC, in the first instance, detailing the samples to be transferred. The completed request form is then sent to QUB Information Compliance Team and Research Contracts Team, who in turn are responsible for creating the MTA and seeking signatory authority and approval by both the host organisation (i.e. QUB) and the recipient organisation (external researcher). Samples will not be released until the MTA has been completed and signed by both the recipient organisation and QUB. This procedure applies to both HTA relevant (e.g. urine, buffy coat and whole blood) and non-HTA relevant sample material. Each MTA is unique to the research project being undertaken and will include a project specific appendix detailing the samples NICOLA will supply and the analysis to be completed.

If a researcher is seeking funds for their research from a funding body, the SAC must receive the completed NICOLA research proposal form at least **one month prior** to the submission deadline. It may not be possible to approve those received less than one month before the submission deadline in time for the deadline. It is the responsibility of the researcher to ensure compliance with their funder's terms and conditions with respect to their use of NICOLA samples.

1.3.1 Students accessing samples

Supervisors are ultimately responsible for their MD/PhD, MPhil and undergraduate students in the same way that PIs are responsible for their researchers. We request that any **proposals for student projects are therefore submitted by the supervisor** rather than the student themselves.

1.3.2 Proposal amendments

Amendments to a proposal (after it has been approved) should be addressed using the NICOLA proposal amendment form which can be downloaded from the NICOLA website. The amended form should be submitted to NICOLA-research@qub.ac.uk. A typical amendment could include any of the following:

- Change to the start date or end date

- Change to the researchers accessing the data, additional researchers being added to the proposal
- Change in institution/affiliation
- Any additional data required
- Change in funding source

1.4 Refusal of sample access

Proposals for sample access may be refused by the SAC. Reasons for refusal include the following:

- Lack of availability of samples;
- Applicant not being a *bona fide* researcher as defined by the UKRI
- The proposed work, in the view of the SAC, risks bringing the study into disrepute;
- The proposed work risks disclosure of identifiable information relating to any individual participant;
- In the view of the SAC, there is a conflict of interest in relation to the proposed project.
- The proposed outputs of the project are outside the scope of the NICOLA ethical approval, funders' terms and conditions or QUB policies and procedures.

1.5 Charges for access to existing samples

NICOLA does not provide support for individual projects. Researchers will be expected to pay for access to the sample resource on a cost-recovery basis for their proposed research. Once a proposal has been approved and the applicant informed of the cost these will be non-negotiable. The costs will take into account the retrieval of samples, the number of samples, tests and/or data requested, and any, shipping costs (outward transfer and return). Costs will be determined on a project by project basis depending on the work involved and may be subject to VAT. For contributing members, the level of discount will be dependent on their contribution to NICOLA. Samples will not be provided until an invoice has been settled or a purchase order number is received by our finance department. Charges for accessing samples will be kept under review to ensure that it continues to represent an equitable, balanced and pragmatic approach.

1.6 Management of NICOLA samples

The organisational structure of NICOLA is detailed in Appendix 1.

The NICOLA biological, clinical and genomic samples are governed specifically by the NICOLA Steering Committee (NSC), Sample Access Committee (SAC) and Research Support Team (RST) whose function is detailed below.

1.6.1 NICOLA Steering Committee (NSC)

The NICOLA Steering Committee provides oversight on all research carried out on study participants and on NICOLA data and advises on the best ways of optimising scientific potential. The NSC meets approximately five times per year and is chaired by Professor Frank Kee (NICOLA Scientific Director). Members of the NSC are made up of the various NICOLA work programme leads. Membership of the NSC is subject to change.

Current work programme leads are as follows:

- *Chronic illness, disability, biomarkers: Prof Frank Kee (QUB)*
- *Cognitive health: Bernadette McGuinness (QUB)*
- *Finance: Dr Mark McGovern (QUB) and Dr Chris Watson (QUB)*
- *Genomics: Dr Amy-Jayne McKnight (QUB)*
- *Mental Health & Health Services Research: Prof Michael Donnelly (QUB)*
- *Nutrition: Prof Jayne Woodside (QUB)*
- *Physical activity: Prof Mark Tully (Ulster University)*
- *Socio-economic and socio-demographic health, healthcare utilisation: Prof Dermot O'Reilly (QUB) and Dr Sharon Cruise (QUB)*
- *Social environment: Dr Paula Devine (QUB)*
- *Vision health: Dr Ruth Hogg (QUB)*

1.6.2 NICOLA Sample Access Committee (SAC)

The SAC currently comprises Prof Frank Kee, Prof Dermot O'Reilly, Prof Jayne Woodside, Dr Amy Jayne McKnight, Dr Paula Devine, Dr Charlotte Neville, Mrs Amanda Coulter and Mrs Angela Scott.

This committee are responsible for reviewing and approving proposals for NICOLA which relate to accessing biological, clinical or genetics samples. The committee also provides oversight and guidance with any applications for sample access which raise specific issues.

1.6.3 NICOLA Research Support Team (RST)

The RST is led by the Data Manager who is responsible for maintaining the security of data and ensuring confidential access to data. The Data Manager ensures that the rules of the Data Access Policy are adhered to and that data is managed according to the Data Protection Act 1993 (superseded by General Data Protection Regulation [GDPR] from 25th May 2018) and is effectively protected against access by unauthorised individuals. The Data Manager carries the responsibility for the ongoing quality, integrity, security and accessibility of the data and is responsible for preventing the improper disclosure of information when stored, transmitted, received and archived. The Data Manager functions as a liaison between the Data Access Committee and the staff that carry out the data management tasks. The RST are responsible for managing and curating the research data generated from NICOLA. This includes cleaning NICOLA data received, validating linkages and performing other internal quality and validity checks, preparing documentation about the datasets, handling metadata, securely providing access to

the NICOLA data resource, archiving data, screening output data for statistical disclosure control (appendix 4) and syntax files generated by researchers and incorporating newly derived variables into the original dataset.

2 Types of samples

A wide range of biological, clinical and genomic samples have been collected as part of the NICOLA health assessment (Wave 1). Details of samples are as follows:

Biological Samples
A maximum of 50 mL of blood was taken at baseline (Wave 1) from each participant (where possible) and allocated into the following sample tubes:
Serum: 4 x 5 mL
PAXgene for RNA: 1 x 2.4 mL
Glucose: 1 x 4 mL
Plasma: 4 x 6 mL

Additional samples taken from participants at baseline included:
Blood spot (Protein Saver 903 and Guthrie cards)
DNA and RNA
Urine samples (3 x 1 mL)

2.1 Potentially identifying data

It is important to protect the confidentiality of the NICOLA sample resource, the integrity of the samples and the availability of the samples. Please be aware that if you are generating low frequency variants or clinically actionable variants then this data is potentially identifiable.

3.0 Sample Provision

3.1 Sample Access process

If NICOLA samples are being analysed in-house (i.e. Centre for Public Health laboratories, QUB) a member of the NICOLA SAC will organise laboratory induction, advise you on any specific procedures for accessing the samples, administer the necessary paperwork (such as confidentiality forms) and ultimately provide you with the requested samples. If the samples are being analysed externally, a Material Transfer Agreement (MTA) will have to be set in place between the external organisation and QUB Information Compliance Unit and Research Contracts Team. Once the MTA has been agreed and signed off by both the host organisation (i.e. QUB) and the recipient organisation (i.e. researchers

institution), you will be contacted to confirm a suitable date for the shipping of the requested samples and will also send you a spreadsheet detailing the samples.

3.2 Confidentiality form

Protecting the confidentiality of the study participants is a primary concern of the NSC. This is a particular issue as NICOLA is a regionally based study. The principal investigator and any member of their team who will directly access data generated from sample analysis will be requested to adhere to a number of clauses regarding confidentiality which will be explained during the induction process.

4. Summary of researcher responsibilities

This section summarises the main responsibilities of any researcher wishing to work with the NICOLA samples (biological, clinical or genetic). The same rules apply to *all* researchers regardless of whether they are a member of NICOLA staff, a new collaborator or a long-term collaborator.

4.1. Project proposals

If the NICOLA SAC notices project overlap when approving projects they may suggest possible collaborations but the researcher is under no obligation to act on this: this is a suggestion rather than a pre-requisite of project approval. Once the project is agreed, the NICOLA Steering Committee can publish the title, name(s) and affiliation(s) of the principal investigator(s), the lay summary and the scientific abstract of any research for which access to NICOLA samples and/or data has been granted, and can add information regarding the status of the project.

4.2. Funding

All projects undertaking sample analysis must be appropriately funded. Full details of funding should be documented in the research proposal form.

Please submit your online proposal at least one month prior to any funder's deadline date. Our finance team need sufficient time to be able to provide you with any appropriate costings e.g. cost of sample analysis. We request that any negotiations with funders MUST include the NICOLA SAC at all times.

The researcher must send the SAC a copy of the final submitted grant, the award letter and any other relevant documentation when it is received; once funding is approved, the SAC will arrange a set-up

meeting in order to agree the objectives, timetable and laboratory facilities (if required) required to meet the grant commitments. This will be followed by a 6 monthly update report to ensure the milestones are being met along with further meetings to discuss progress. The PI must make every effort to attend the meetings and submit the required reports. It is the researcher's responsibility to ensure there is no conflict between their funder's terms and conditions and the NICOLA DTA/MTA where applicable.

4.3. Sample access

Researchers must adhere to the NICOLA sample access policy, data access policy and confidentiality form at all times. Researchers must also comply with the terms of the NICOLA DTA/MTA where applicable. Current and future access to the NICOLA resource is at risk if any researcher is found to be breaking these rules. In particular, samples and data generated from sample analysis must NOT be shared with any other researchers. Serious breaches of data access rules will be prosecuted to the full extent of the civic or criminal law.

4.4. Confidentiality/security breaches

Any breaches of sample or data security must be reported immediately to the Operations Management Group (OMG). Examples of sample security breaches include (but are not limited to):-

- Any unauthorised person (i.e. who has not signed a sample access and/or data access agreement for the relevant samples) gaining access to the NICOLA samples;
- Disclosure of sample locations to unauthorised persons;
- Samples being analysed for a different purpose than what was originally stated in the research proposal
- Samples or generated data from the sample analysis being sent or shared with a different party than what was originally stated in the research proposal
- Failure to return all data generated from sample analysis to the NICOLA data manager
- Failure to carry out secure storage and transfer of data generated from sample analysis
- Failure to comply with any of the statements as detailed in the Sample Access and Data Access Confidentiality Agreement.

4.5 Data from biological, clinical and genomic samples

We aim to ensure that data generated from the analysis of samples from NICOLA participants are made available as soon as possible after laboratory assays have been carried out and data cleaning is complete. All potential identifiers are removed and disclosure risks are considered such that data may be grouped where appropriate.

4.6 New variables and derived variables

Any new variables or derived variables (such as newly derived variables coming from secondary analyses) created as part of any research project involving analysis of biological, clinical or genetics samples must be lodged with the NICOLA RST after an agreed period of time for archiving and/or merging with the main data resource, along with appropriate documentation detailing laboratory methods (including quality control measures, coefficients of variation for assays, specialist equipment used), and how the respective variables were created and associated syntax/code. The derived variables will be made available to all researchers after those who were responsible for creating the derived variables have published their own work or no later than 24 months after completion of the research analysis (whichever falls sooner); authors must acknowledge the researcher responsible for creating the derived variables in all research outputs. If you fail to complete this request and we receive a specific request from another researcher to access that data, we will contact you. We would then expect you to fulfil the request within 4 weeks. Failure to return data or samples as required to the study or failure to provide the necessary details regarding the creation of the new or derived variables at this point may risk your future access to the resource and may result in any further applications to access NICOLA data and/or samples being suspended until the issue is resolved. If considered appropriate, the NICOLA RST may carry out independent checks and/or validation of the data and results to ensure the continued data integrity and reliability of the study findings.

4.7 Intellectual property

QUB has ownership over the NICOLA resource in its entirety, including any data generated from the analysis of biological, clinical and genetics samples. As such, any requests to access NICOLA samples must be made through the NICOLA SAC. Any data generated as a result of analysis through an approved proposal must remain within the NICOLA resource to encourage ongoing use by the research community.

The Recipient must not share any data or biosamples related to, or derived from, the NICOLA Study with any third party, including (but not limited to) collaborator institutions or commercial organisations.

For the avoidance of doubt the resources provided under this Agreement are not provided for commercial use. However it is acknowledged that its use for research purposes may generate new foreground Intellectual Property. Should the Recipient develop any invention or technology (including any related Intellectual Property) from its use of the resources provided under this Agreement (“Study Inventions”) then it hereby agrees to:

i) Make QUB aware of such Study Inventions promptly upon their disclosure internally to the technology transfer office or similar unit in the Recipient organisation;

ii) Provide QUB with a summary of the intended exploitation strategy for such Study Inventions;

iii) Grant to QUB an irrevocable, perpetual, world-wide, royalty-free licence to use the Study Inventions for the purposes of academic teaching and academic research, including non-commercial research projects funded by a third party; and

iv) In consideration of QUB's valuable contribution to the Study Inventions by its provision of the resources supplied under this Agreement, that should the Study Inventions generate any revenue from its use, exploitation, or commercialisation, then the Recipient hereby agrees that QUB shall be entitled to participate and share in the revenues arising from the Study Inventions. The Recipient agrees that, prior to the exploitation or licensing of any Study Inventions, the Parties shall meet to negotiate and agree an appropriate revenue share and payment terms for and to QUB.

In the event that the Recipient cannot provide an exploitation strategy for Study Inventions (under Clause 4.5 (ii) above), or does not wish to exploit commercially such Study Inventions, then it hereby grants to QUB the option to take assignment of the Study Inventions which QUB may itself, directly or indirectly and without limitation, seek to exploit commercially. Such assignment agreement shall include an appropriate revenue share back to the Recipient, under such terms as the Parties may agree between them at the time of the assignment.

4.8 Publications and dissemination of research data and results

4.8.1 Peer reviewed papers and other research output

All full papers must be sent to the NICOLA RST for approval (email: nicola-research@qub.ac.uk) along with a completed papers checklist (available on the NICOLA website) at least 28 days *prior* to journal submission. This includes any research output being placed in the public domain (for example working papers or non-peer reviewed papers). Conference abstracts do not have to be submitted prior to the conference but must be sent to the Research Support Team prior to being published in conference proceedings or journals. All papers will be read to check that participant confidentiality is protected and to ensure that the paper will not bring the study into disrepute. The RST will also be checking for compliance with the NICOLA publication guidelines (as detailed within the NICOLA papers checklist) including correct insertion and accurate description of NICOLA affiliations, ethical approval and acknowledgments. Researchers will be notified in writing regarding the suitability of each paper for publication (in respect of the above criteria) and if any changes are required to the paper. Further details regarding the process used for screening NICOLA publications are provided in Appendix 5. The RST reserves the right to require that any paper which could potentially breach the confidentiality of any NICOLA participant(s) be withheld from submission for publication. The RST will work with the

authors to overcome such breaches. If the researcher submits such publications regardless, the Steering Committee will attempt to prevent publication. Failure to comply with these guidelines may lead to a restriction in future access to NICOLA data or samples.

The RST may also provide advice and feedback to authors where we feel this may be helpful but their role is not to provide formal peer review. Uptake of any feedback from the RST is solely at the discretion of the authors. Under all circumstances the NICOLA Steering Committee reserve the right to submit letters or papers for publications in response to any paper to explain study procedures or to express a coherent scientific argument. Any appeals against a decision by the RST regarding publication will be directed to the NICOLA Steering Committee.

In some cases, it may be appropriate for members of the NICOLA research team to be invited to be co-authors (and invitees may or may not wish to accept co-authorship). Further details regarding requirements for NICOLA papers along with some accompanying notes are available with the papers checklist. Researchers must inform the NICOLA RST when a paper has been accepted and also send an electronic copy of the final published version to the RST at the following email address: nicola-research@qub.ac.uk.

A list of publications arising from NICOLA will become available on the NICOLA website in due course.

4.8.1.1 Rules on Open Access

4.8.1.1a Papers

NICOLA fully supports the Wellcome Trust and the UKRI policies on open access. In summary, this means that if a) the specific research presented in a paper is wholly or partly funded by the Wellcome Trust or b) any contributing author is wholly or partly funded by the Wellcome Trust (via salary or fellowship/studentship) any publication must be made open access. It is the senior author's responsibility to ensure that any papers published comply with this policy. It is the responsibility of the grant-holder under part a) above or the individual author(s) under part b) above to cover the costs of making a publication open access. Please see the Wellcome Trust website for more information. If your research is wholly or partly funded by the one of the research councils in the UKRI you are required to make your research paper Open Access and by publishing in a compliant journal. Please see the UKRI website for more information. For papers that include authors / co-authors from QUB, a copy of the accepted paper must also be uploaded (by the QUB author) onto PURE, QUB open access institutional repository within 3 months of journal acceptance.

Please note that secondary analyses of NICOLA data that is not funded by the Wellcome Trust nor has any contributing author supported by the Wellcome Trust does not need to comply with the Wellcome Trust policy, however, NICOLA would encourage this wherever possible.

4.8.1.1b Data – individual journal policy

A number of journals request that datasets used in a publication are deposited in publicly available resources. Our data management policy does not permit this beyond summative data or data that will be deposited in the UK Data Archive and Dementias Platform UK (DPUK).

4.8.1.1c Data – individual funder policy

It has also come to our attention that some funders are also requesting that data be made publicly available. Our data management policy does not permit this beyond the data that will be deposited in the UK Data Archive.

4.8.2 Theses

We request that an electronic copy of any theses that use NICOLA data is provided to us as soon as possible after a degree is awarded. Please note that any images within an electronic thesis require copyright approval.

4.8.3 Reports and other publications

We request that an electronic copy of any reports and other publications that use NICOLA data is provided to us as soon as possible.

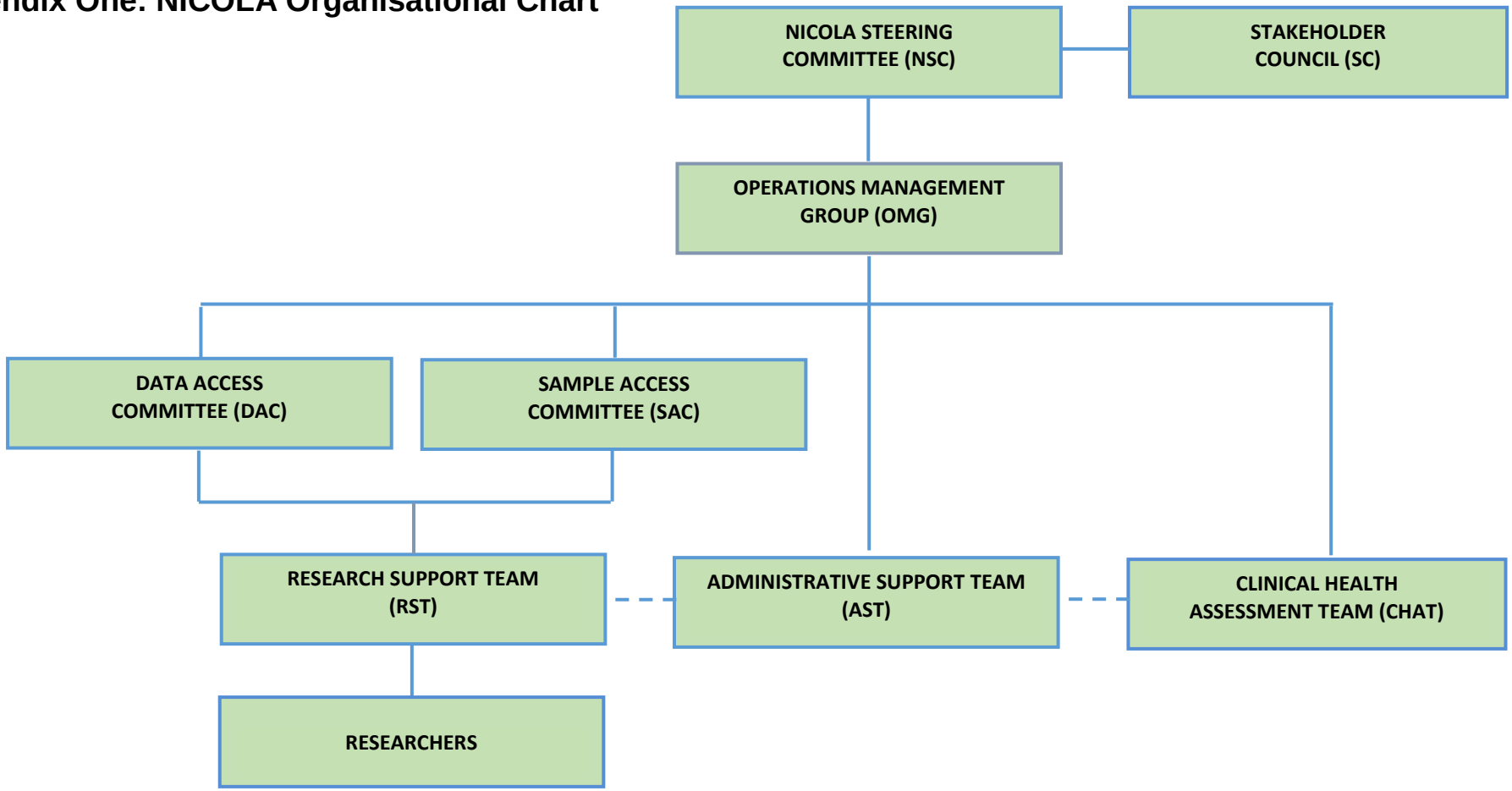
4.8.4 Conference Proceedings

Conference abstracts do not have to be submitted to the NICOLA RST prior to the conference but must be sent to the RST prior to being published in conference proceedings or journals.

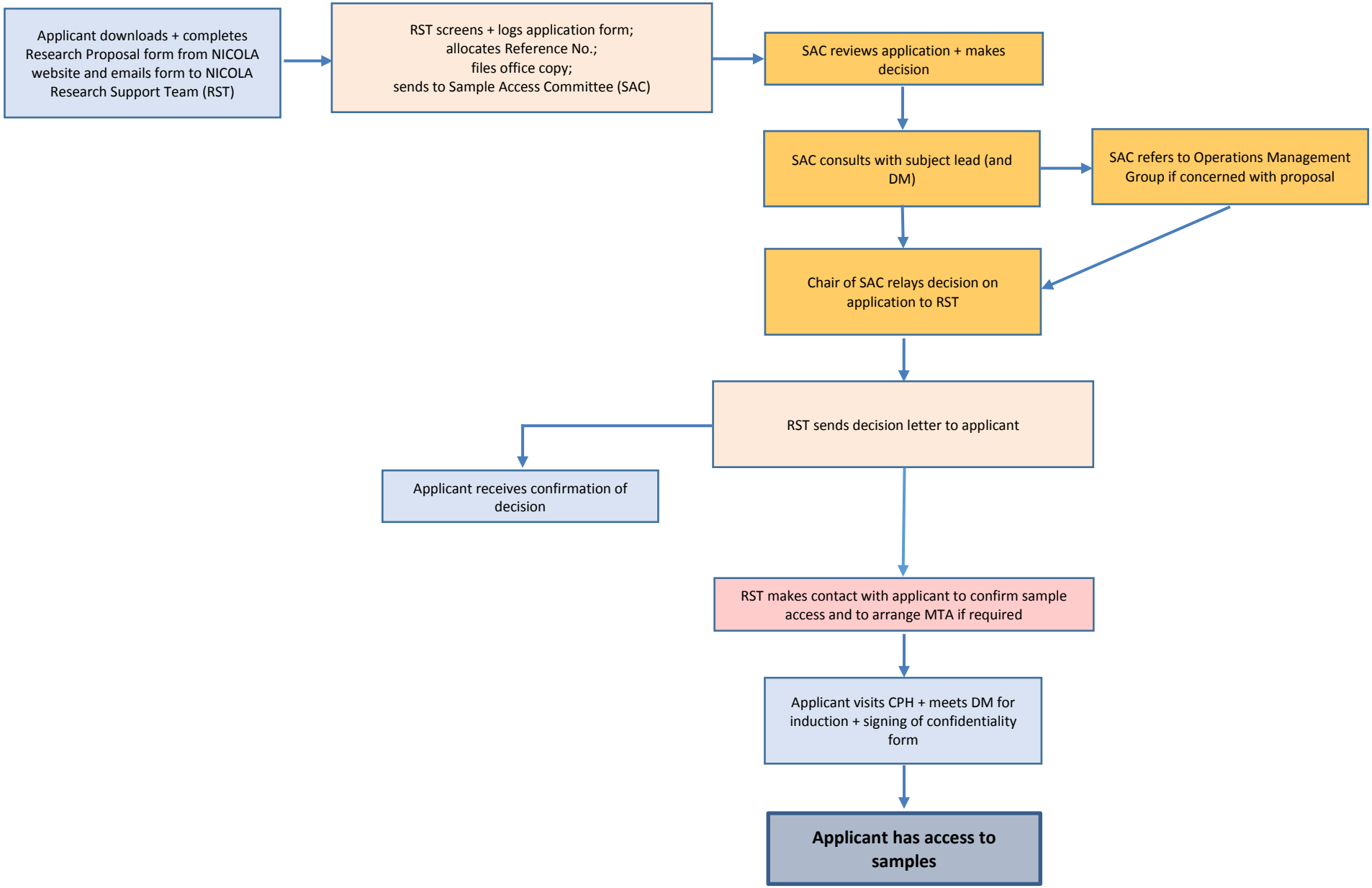
4.9 The Media

All press releases on research arising from the study must be written in conjunction with the NICOLA RST and under the guidance of QUB communications team. We reserve the right to publish press releases on certain articles and expect the lead author of the article to agree the press release with the NICOLA RST and to be available to deal with media enquiries and interviews. We may also ask authors to prepare a précis of important papers and/or lay-summaries to include in reports to funders and future applications for core funding.

Appendix One: NICOLA Organisational Chart



Appendix Two: Flowchart showing the process of applying for access to NICOLA samples (applicant version)



Appendix Three: NICOLA Sample Research Proposal Review Form

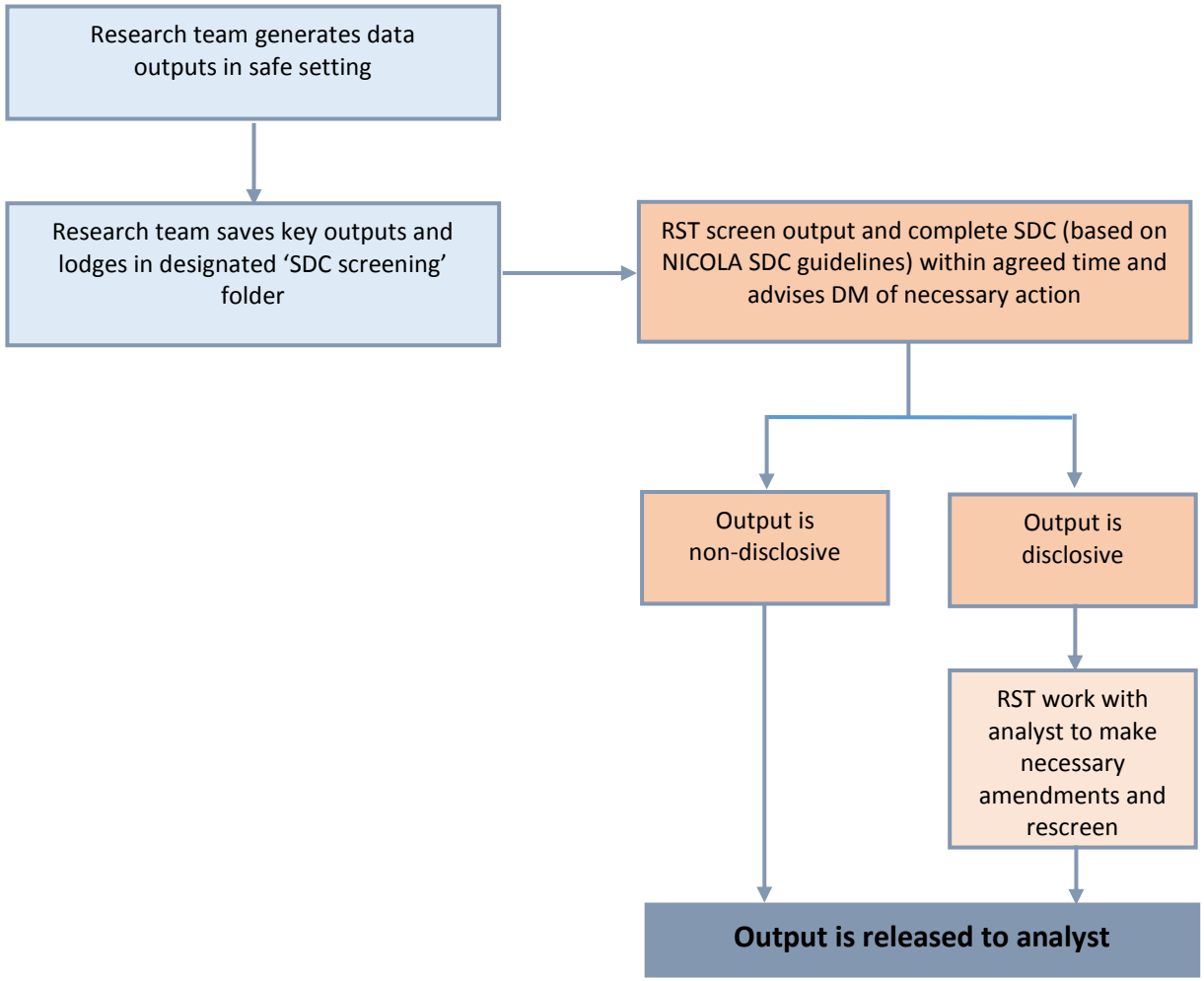
SCORE	INDICATORS
Excellent quality research	
10	Exceptional
9	Excellent research which is (or will be) be at the forefront internationally. Addresses very important medical or scientific questions. Likely to have a high impact on medical practice, or on the relevant scientific field.
Good quality research	
8	Good, bordering on excellent
7	Good quality research which is internationally competitive and at the forefront of UK work. Important research which will be highly productive, and likely to have a significant impact on medical practice, if applicable.
6	Good quality research, on the border between national and international standing.
5	Good quality research which is at least nationally competitive. Addresses reasonably important questions and will be productive. Good prospects of making some impact on medical practice, or on the relevant scientific field. Any significant concerns about the research approach can be corrected, easily.
Potentially useful study	
4	Potentially useful, bordering on good quality research.
3	Research plans which contain some good ideas or opportunities, but which are very unlikely to be productive and/or successful. Major improvements would be needed to make the proposal competitive.
Unacceptable	
2	Potentially useful in some aspects, bordering on unacceptable in others.
1	Serious scientific or ethical concerns. Should not be approved.

NICOLA Project Number	
Quality	
Importance	
Impact	
Overall use of the NICOLA sample resource	
Total score (out of 10)	
Comments	

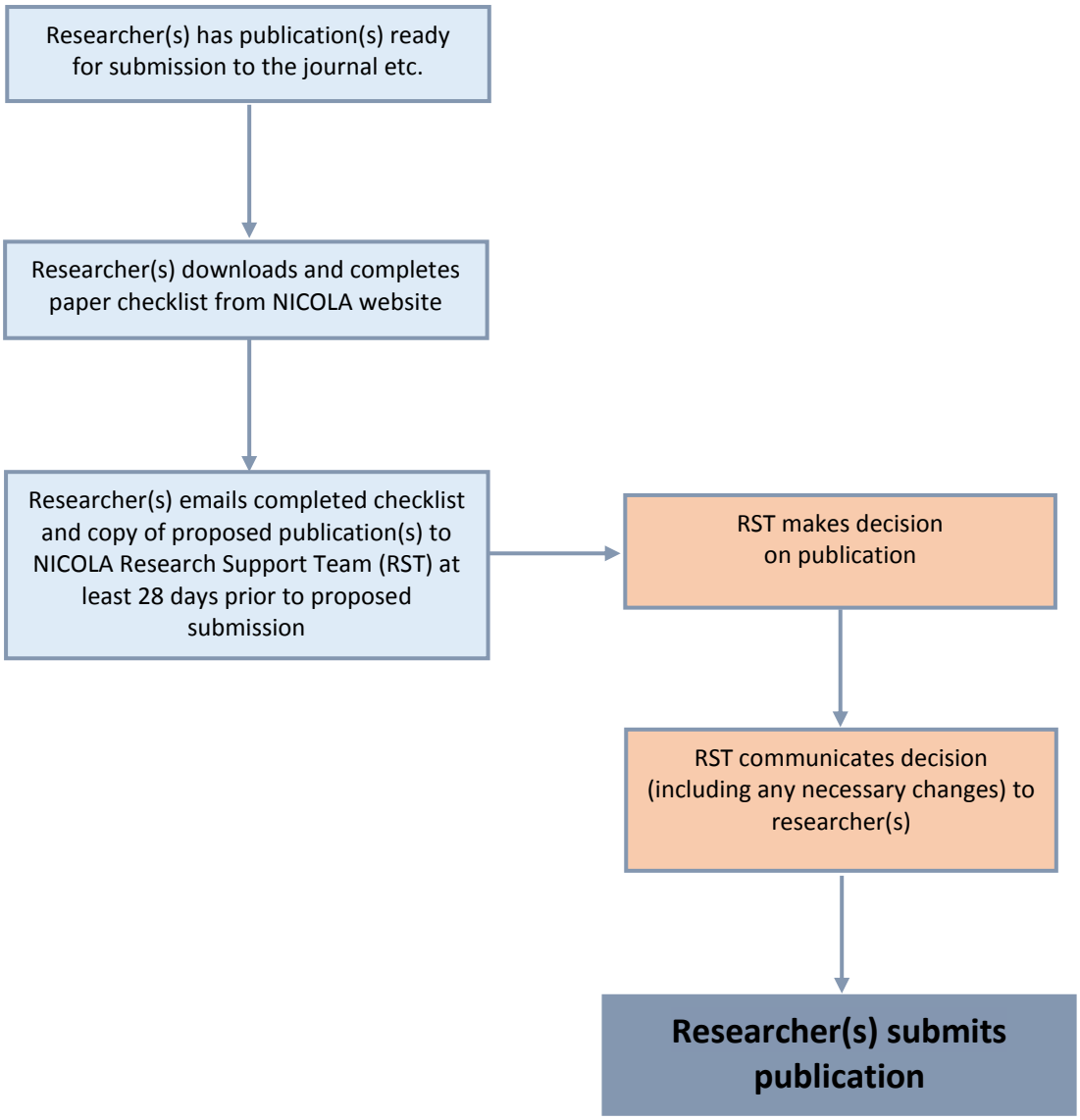
Signed: ……...

Date: ……...

Appendix Four: Flowchart showing the process for Statistical Disclosure Control (SDC) screening of NICOLA outputs created in the safe setting



Appendix Five: Flowchart showing the process for the screening of NICOLA publications



Appendix Six: Policy updates

This appendix will detail the changes made to this Sample Access policy since the release of v1.0 on 09/10/2018