INTRODUCTION: NON-CLINICAL MATERIALS

This document provides guidance to organisations seeking access to donated human material for non-therapeutic use.

The primary purpose of NHSBT is to maintain a safe supply of blood, blood components, cells, tissues and organs generously provided to us by altruistic donors for therapeutic transfusion or transplantation purposes.

In fulfilling this primary obligation, and whilst NHSBT makes every effort to ensure that waste is minimised, inevitably there is material which is unsuitable for, or unable to be used in, the clinical/therapeutic supply to hospitals and which would otherwise be discarded by NHSBT.

As part of the wider healthcare community, NHSBT wishes to support work relevant to health, health improvement, education and training and is in a unique position to provide cells, blood components, and tissues for our own non-therapeutic use or for supply in the NHS and to *bona fide* organisations. NHSBT captures broad and generic consent from all donors for use of their materials in:

- *in vitro* diagnostic test validation and laboratory quality control (Controls, Standards and EQA material)
- training and education
- the development and validation of diagnostic reagents
- development and validation of new components, therapeutic products and processing methods
- medical research and development

NHSBT provides appropriately consented materials to approved recipients for approved non-clinical uses through a managed, governed service we call "Non-clinical Issue" (or NCI). This allows NHSBT to balance the wish to support valuable non-clinical work against the potential risk of damage to NHSBT's primary purpose arising from possible adverse donor or wider public reaction.

NHSBT does not sell human material. We are mandated by the Department of Health to recover the costs incurred by us in making donated materials available to approved recipients for approved non-clinical uses. These costs are reviewed annually.

This NCI supply chain **does not** permit the issue of donated material for:

1. Therapeutic application. Requests for clinical spec material or clinical application can be made using this process but supply chains will be set up with a clinical MTA.
2. For use as a tissue culture medium supplement.
3. Culturing cells and DNA for supply and use by other organisations/parties.

If you have any queries on the application process or any of the information contained in this document, please email our NCI Administration Team at nciadmin@nhsbt.nhs.uk

A: NON-CLINICAL MATERIAL REGULATORY REQUIREMENTS

Organisations wishing to store and use human cells or tissue may require a licence from the Human Tissue Authority. Organisations should familiarise themselves with the legislative and licensing requirements and industry best practice for handling and use of human cells and tissue and confirm on the NCI Application Form that they are compliant.

Guidance on licensing from the HTA is available here:
https://www.hta.gov.uk/guidance-professionals/licensing-information

If your study is led from England and involves the NHS in England, you will need to apply for HRA Approval and may also require a review and a favourable opinion from an HRA-recognised Research Ethics Committee (REC). More information can be found here: http://www.hra.nhs.uk/research-community/before-you-apply/determine-which-review-body-approvals-are-required/

Not all research uses require REC approval. However, in order to maintain donor approval for the provision of donations for non-clinical uses, NHSBT has adopted the following provisions which may be over-and-above strict regulatory requirements:

a. Where REC is required, NHSBT will only accept applications for access to materials for research use that are accompanied by HRA-recognised REC favourable opinion,
b. Where REC is not required, NHSBT requires evidence in the form of a hardcopy printout from the HRA online toolkit clearly showing that REC approval is not required for the work you are proposing to undertake.

B: NHSBT POLICY AND KEY CONDITIONS FOR THE PROVISION OF MATERIALS FOR NON-CLINICAL USES

1. Generic consent

- Materials provided for non-clinical use are appropriately consented and supply complies with all statutory and regulatory obligations including (but not limited to) the Human Tissue Act (2004) and associated Codes of Practice and Standards.

- Generic blood and platelet donor consent does not allow donated material to be used in any work involving (i) animal models (ii) genetic analysis that is likely to (or intended to) establish the donor's identity.

- Generic blood and platelet donor consent does include R&D; including genetic analysis where there is no likelihood of the donor being identified by the researcher. R&D must be REC approved where required. Generic consent also covers export, commercial production of healthcare related products, use in education and training, laboratory quality control and activities that support improvements in human health.

2. Specific consent is required for the use of donated blood and components in any activity using animal models and for all materials in genetic analysis that is likely to establish the donor identity. NHSBT cannot guarantee that there will be material available with specific consent for this use. All requests of this nature for any material supplied by NHSBT will be reviewed by a very senior management team (CARE committee) to decide if this is an

activity we can support (see section E below).

- NHSBT reserves the right to stipulate that specific consent is required for the supply of donated material for any activity and cannot guarantee that specific consent will be achieved.

- Where specific consent is required, NHSBT will require a donor information leaflet to be produced by the applicant to aid and inform the consent-taker in providing specific detail of how donors' donated material/s will be used. CARE will decide the specific information required from applicants on a case by case basis in other scenarios where:
  - Any additional material (e.g. additional blood sample) is requested from the donor and/or
  - The donation is collected *specifically* for a non-transfusion/transplantation use and/or
  - Donor personal details are to be supplied to an external organisation and/or
  - Any additional information requested from the donor (other than year of birth, blood group, gender and CMV status (if known)) and/or
  - The outcome from research or testing may be linked to the individual and may have implications for their health or welfare and/or
  - Specific consent is deemed necessary by a scientific or research ethics committee

Note: applicants should not prepare these as part of the application process; NHSBT will advise what information is required as part of the application review/outcome.

3. The provision of materials for non-clinical use is ancillary to NHSBT's primary purpose. Therefore, materials are supplied by NHSBT on a "best endeavours" basis which does not guarantee the ongoing availability of any materials during any agreement to supply.

4. NHBST will not supply material via NCI which is to be used therapeutically. Material issued via NCI is not for use in establishing cell lines without specific authorisation.

5. Provision of materials is on a contractual basis which controls the supply, restrictions on use, treatment and handling of donations, payment and prohibition on "selling" of blood or blood components.

6. Requests for access to materials are scrutinised under an auditable process by appropriately trained NHSBT staff aware of the relevant regulatory, commercial and donor/public-facing considerations.

7. Recipients of donated materials are responsible for compliance with all regulatory, legal or other obligations arising from the receipt, storage and use of human materials.

8. NHSBT's primary concern is the protection of the clinical supply chain. In considering any application for access to donated materials, NHSBT will balance the wish to support valuable non-clinical work against the potential risk of damage to NHSBT's primary purpose arising from possible adverse donor or public reaction.

9. Costs incurred in making materials available are fully recovered and any surplus is retained by NHSBT for the benefit of the wider Health Service. For the avoidance of

doubt, no charge is made by NHSBT for the donated materials themselves and recipients are similarly prohibited from attaching a value to, or "selling", the donated materials.

10. NHSBT requires that all organisations receiving human cells and tissues for non-clinical use maintain sufficient records of receipt, use, storage and discard to provide a complete audit trail for all human cells and tissues provided. NHSBT reserves the right to audit the records and facilities and interview staff of organisations who receive human cells and/or tissue from us.

11. It is a condition of supply that users accept and sign the NHSBT Material Transfer Agreement (MTA). Materials will not be supplied unless a valid agreement is in place.

12. Material is issued anonymised and unlinked to the original donor. Recipients are prohibited from making any attempt by any means (purposely or inadvertently) to identify or re-identify a donor.

13. All materials must be considered as biohazard and potentially infectious. They must be handled with universal precautions including training and suitable PPE. Whole blood and leukocyte cones are not usually tested/virology-screened before issue for non-clinical work. As these items are issued anonymised, unlinked and before screening results are known, NHSBT is unable to provide results or post donation information about individual products issued.

14. Organisations must not make available in whole or in part any human cells or tissue from material supplied by NHSBT to anyone other than the users named on their application and for the purposes approved on their application and any subsequent agreement. Passing on or making available any product, excess or unused part of any product is expressly forbidden.

15. If your work requires you to pass samples to a third party for external quality assurance, share material, collaborate or share data then this must be made clear on the application form.

16. Full details of the organisation, recipients, use and fate of material must be provided with your application. Where a product is produced containing any donated material, full details of the intended use and availability of the product must be provided in your application. Failure to provide this information in full with your application may result in it being rejected or significantly delayed while we request the information and reassess.

17. Organisations should be aware that one or more of NHSBT's Regulatory Inspection bodies may require access to the records, staff and facilities of an organisation receiving donated human material.

18. The nature and source of funding for research and development uses must be made clear. NHSBT is mandated to consider the need for explicit informed (specific) consent from donors on a case-by-case basis for material supplied for commercial purposes. Failure to disclose this information or any information relating to commercial activities may result in the request being rejected or accounts terminated.

C: THE APPLICATION PROCESS

It is important to stress that, whilst we aim to support valuable non-clinical work, submission of an application for access to donated materials does not guarantee that an application will be successful and that materials will be provided.

It may also be necessary for you to undertake your own preparatory work (for instance in developing a draft process for obtaining specific consent where required). Undertaking this work also does not guarantee that an application will be successful and that materials will be provided.

NHSBT aims to set up an account within 6-8 weeks of application date. However, non-standard or bespoke account requests may take longer due the nature of the request and the scrutiny required. Requests proposing animal models or genetic analysis can take up to 12 weeks for an initial decision so you should allow sufficient time for this to be undertaken.

D: ACCOUNT REQUEST FORM

Setting up a supply chain begins with submitting a completed NCI account request. Application forms must be clearly legible therefore any application that is not typed, word processed or completed legibly will be rejected. All applications are treated as commercial in confidence. All information relating to NHSBT, including but not limited to information about people, processes, cost recovery, products, services and facilities must be treated as confidential by applicants.

Section 1 captures the essential contact and customer details required for NHSBT to set up and administer an account as well as details of where to send invoices. The expected start date, duration and end of supply date are also required. Where no end date is provided NHSBT will automatically limit this to 2 years.
If you envisage requiring a longer, uninterrupted supply please confirm this with a suitable end date which must not exceed the period for which valid ethical approval and/or HTA licence is in place and this request will be considered by NHSBT.

Section 2 captures details of intended use and any additional information required by us to assess the request.

All questions must be answered and any supporting information (such as REC approval or confirmation from the HRA online toolkit that REC is not required) should be returned with your application.

Where possible, please copy and paste your work/proposal abstract in Section 2.3. If no abstract etc is available, please use this box to describe the work you are undertaking and the uses to which donated materials will be put.

When selecting the "Purpose" (Section 2.1) Please only select research for bona fide research projects as the requirements for research/non-research uses are different and your application will be delayed if information is incorrect or incomplete.

Establishing if your work is research can be aided by the HRA toolkit

http://www.hra-decisiontools.org.uk/research/question1.html

The table requests details of REC approval as well as HTA licence status and requirements. Research users must either provide
(a) evidence that either they have ethical approval in place from an HTA recognised REC or
(b) confirmation of exemption from the HRA (which can be a printed output or screenshot of the decision page).

Please note that where an exemption is being sought, NHSBT can **only** accept evidence from the HRA toolkit and that an assessment by Higher Education Institution Research Ethics Committees (HEI-REC) or other ethics committees is not sufficient.

It is the responsibility of organisations requesting human cells and tissue to ensure that their methods of use and storage are appropriate, are licensed (where necessary) and that there are sufficient records of receipt, use, storage and discard to provide a full audit trail of the use and outcome of all cells provided.

Organisations wishing to use cells across a wide range of projects will need to provide a spreadsheet detailing each of the projects, accompanying your application with the following information:

- Project name/ID
- Project summary so we can understand the use and fate of material supplied
- Material type used in each project
- Tests undertaken
- Details of what happens to/following these results
- Any proposed genetic research
- Details of any third parties accessing material, cells or data

All applicants are required to confirm (in Section 2.2 (e)) that none of the materials supplied by NHSBT will be administered to a person and/or, used in a product which may be administered to a person and/or used as a supplement in a tissue culture medium.

Section 3 requests details of the materials you require which are set out in the accompanying Appendices. Customers can only order materials they are approved for so please ensure you have selected correctly. Requests for access to additional materials will be the subject of a new application.

We ask for indicative figures for volume and frequency of use in order to assess our ability to supply.

E: SPECIFIC CONSENT: GENERAL GUIDANCE

NHSBT's primary concern is the maintenance of safe and sustainable supply of donated materials for therapeutic purposes.

In seeking to protect our supply of donations for clinical purposes, NHSBT's policies and requirements for non-clinical applications may, therefore, be over and above that which is strictly necessary to satisfy regulatory requirements.

NHSBT is mandated to ensure that the use of material for genetic research is in accordance with guidelines issued by the Human Genetics Commission and Human Tissue Authority.

NHSBT donors are not specifically consented for the use of their material in animal models or genetic research that is likely to lead to identification of the Donor.

When NHSBT provides routine, anonymised samples for use in research projects, we will allow the use of DNA/RNA for analysis of gene expression and of specific genes and proteins. All projects must have approval from an ethics review panel or confirmation from the HRA that REC is not required. We will not allow extended genotyping that may lead to the generation of donor-identifiable information on samples without specific consent from the donor.

Applications proposing genetic research requiring specific donor consent and/or work involving the use of animal models will take up to 12 weeks to review and additional time may then be required to establish and agree a process for consent.

Applicants must be able to provide NHSBT with a donor information leaflet detailing:
- the nature of the research being undertaken
- how (and where) animal models are used
- How DNA/RNA analysis will be used
- Where data will be stored and who will have access to it

Any intention to publish results which reference the original source DNA/RNA must be made clear with the application.

In addition, NHSBT may require you to financially contribute to the full costs of setting up bespoke processes e.g. in obtaining consent.

Applicants must be aware that even when all of the above are in place NHSBT cannot commit to approve requests for material to undertake genetic research or work involving animal models. These will be assessed on a case-by-case basis.

F: PAYMENT FOR AND DELIVERY OF MATERIALS

As a public body, NHSBT is required to protect the public's financial interests in the receipt of payment for services delivered. Payment will be expected under the terms set out in the MTA and invoices provided to you. Where the supply will include large-volume provision or individual high-value invoices, NHSBT may require additional payment provisions which may include part-payment up-front before materials are supplied.

NHSBT usually expects customers to collect or arrange for a courier to collect non-clinical material at their own cost.

Occasionally a paid-for delivery service can be offered, and this will be confirmed on completion of your account set-up and is dependent on availability at individual NHSBT supply centres.

FREQUENTLY-ASKED QUESTIONS

Q: How long will it take to set up my account?
A: We aim to set up accounts for standard requests within 8 weeks of receipt of a fully completed request. This is longer for bespoke requests and those involving un-consented uses.

Q: Will I be charged an additional sum for packaging and delivery?
A: Yes, you will be charged for packaging of the materials per order and ad hoc delivery prices are available on request.

Q: Are all blood components tested/virology screened?
A: No, NC13 Whole blood and leukocyte cones are not usually tested/virology-screened before issue for non-clinical work.

Q: I have REC approval for my work. Why does NHSBT also require specific consent for some uses?
A: In addition to compliance with the HTA, the wishes and feeling of our donors and the protection of a safe and sufficient supply of donations for clinical purposes are paramount. Additional steps may therefore be required to ensure that this primary purpose and the interests of donors and the use and fate of their donations are protected.

Q: What is the difference between Research Red Cells and Expired Red Cells?
A. Red Cells have a 'shelf life' of 35 days for clinical uses. Once this is passed, the cells are supplied as 'expired'. Cells that are in date but unsuitable for clinical use (e.g. discoloured) are issued as Research Red Cells

Q.: What volume is in a typical random donor sample and the volume and number of wells in a deep well micro plate?
A.: A donor sample would normally be around 4/5ml per tube. The plates have 0.9ml per well and are 96 well plates.

Q: Which anticoagulant is used?
A: The collection bag that we use contains approximately 66.5 (ml+/- 10%) CPD anticoagulant. Donor samples are supplied in EDTA tubes.

Q: Can you provide the donor consent forms signed upon donation?
A: We can supply the leaflet that is used to inform generic consent but cannot provide individual, signed consent forms.

Q: How Do I contact you?
A: By Email: nciadmin@nhsbt.nhs.uk