OPERATIONS AND PATIENT SERVICES

USER GUIDE

ANTHONY NOLAN

saving the lives of people with blood cancer

If you are a UK Transplant Centre please refer to **Part 1 of this User Guide**

If you are an International Establishment please refer to **Part 2 of this User Guide**

OPERATIONS AND PATIENT SERVICES

USER GUIDE

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UK

ANTHONY NOLAN

saving the lives of people with blood cancer

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DEFINITIONS

1 INTRODUCTION

1.1 Introduction

Anthony Nolan is a charity which saves the lives of people with blood cancer and other blood disorders who need a blood stem cell transplant.

More information about the work and history of Anthony Nolan can be found on the website http://www.anthonynolan.org

The services provided by Anthony Nolan are set out in more detail in this User Guide.

Anthony Nolan complies with the WMDA International Standards for Unrelated Hematopoietic Stem Cell Donor Registries which can be found on the WMDA website (https://wmda.info/). For clarity these also apply to donations by related donors.

1.2 User Guide

This Operations and Patient Services User Guide sets out the procedures to be followed by hospitals in the United Kingdom using Anthony Nolan's services.

This User Guide and the signed service level agreement together form the contract between Anthony Nolan and the Transplant Centre.

This document may be amended by Anthony Nolan from time to time to take account of changes in medical practice, applicable laws or regulations or operational or administrative procedures. Except as set out below, the Transplant Centre shall be bound to comply with such change(s) from the date of notification provided by Anthony Nolan.

Anthony Nolan will give the Transplant Centre twenty (20) Business Days' notice by email of any proposed material change to this User Guide and if the Transplant Centre does not object within such notice period, such change(s) shall be deemed to be agreed by the parties.

1.3 Services Provided by Anthony Nolan

Anthony Nolan:

- recruits potential donors of haematopoietic progenitor cells to the Anthony Nolan register
- manages the Anthony Nolan and NHS Stem Cell Registry
- facilitates the procurement and distribution of haematopoietic cells and lymphocytes
- maintains a bank of Cord Blood Units and a cord blood inventory
- provides international search facilities
- liaises with Transplant Centres, International Establishments and Cord Blood Banks
- provides laboratory testing and histocompatibility services
- undertakes research
- provides a Graft Identification Advisory Service (GIAS)
- provides a Cord Support Programme
- provides cryopreservation services of adult stem cell materials

- provides related donor sample procurement and procurement and distribution of haematopoietic progenitor cells and lymphocytes from related donors. This is currently only available internationally where Anthony Nolan has an arrangement to do this with the relevant international registry or a relevant international hospital
- provides patient information specific to post transplant recovery and late effects
- funds the role of post-transplant clinical nurse specialists (CNS) and clinical psychologists in certain transplant centres in the UK. This ensures access to ongoing support after transplant and improves the post-transplant experience
- provides a volunteer peer support service. This is a telephone service that connects one patient with one peer volunteer who has had a transplant
- provides a return-to-work programme with a vocational rehabilitation company called Working Towards Wellbeing
- provides financial grants to patients who have had a transplant
- organises an annual transplant nurse education day which is specifically aimed at enhancing and informing post-transplant practice and encourages collaboration between UK Transplant Centres
- provides a monthly e-newsletter to UK Transplant Centres to update on patient services and provides current research/audit and education events.

1.4 Anthony Nolan's Operations and Patient Services Division

The Operations and Patient Services Division of Anthony Nolan is made up of several sections, including Donor Services and Transplantation Services. Donor & Transplantation Services coordinates the collection and delivery of blood samples and oversees the provision of haematopoietic progenitor cells and lymphocytes.

1.5 Search and Selection

Search and Selection Co-ordinators within the Anthony Nolan Search Team run computerised searches of UK and international donor registries and Cord Blood Banks to identify suitable unrelated donors and/or Cord Blood Units for a patient.

1.6 Verification and Extended HLA Typing

The Anthony Nolan Search and Selection Co-ordinators and Donor Liaison team arrange for the collection and shipment of blood or saliva samples for the verification and/or extended HLA typing of UK donors, international donors and Cord Blood Units selected by Transplant Centres.

Typing is carried out either at the Anthony Nolan laboratories or at the laboratory nominated by the Transplant Centre.

1.7 Donor Provision and Donor Follow-Up Teams

The Anthony Nolan Donor Provision Team is responsible for the work-up of each Anthony Nolan donor and NHSBT donor selected for transplant. The Welsh Blood Service manages the work-up of WBMDR donors and DKMS UK manages the work-up of DKMS UK donors. Anthony Nolan also liaises with International Establishments to arrange the work-up of international donors and liaises with international Cord Blood Banks to facilitate the import of Cord Blood Units for UK transplants. Working alongside the Anthony Nolan medical team, the physical and emotional wellbeing of UK donors is managed prior to and during donation by the Donor Provision team and post donation by the Anthony Nolan Donor Follow-Up team.

1.8 Patient Services Team

The Patient Services team provides information and support to UK patients and families before, during and after transplant. The Patient Services team also engages with health professionals to help facilitate long-term quality of life and wellbeing for all transplant patients.

The patient services are provided in several ways:

- Information booklets, leaflets, web pages, blogs, films and podcasts.
- Enquiry service, answering concerns by telephone and email.
- Financial grants. The financial impact of a transplant can be devastating, from loss of income and costs of travelling to hospital, to the impact of side effects. Anthony Nolan gives out small individual grants which go some way to alleviating that pressure.
- Patients and Families Forum, an online discussion board where people share and learn from each other's everyday experience of transplant.
- Post-Transplant Clinical Nurse Specialists (CNS), dedicated to patient wellbeing after transplant. Anthony Nolan specialist nurses provide emotional and practical support and can set up clinics (including late effects clinics).
- Education Days for patients and their families, featuring talks and workshops by health professionals covering issues such the psychological impact of a transplant, research, exercise, diet and finances.

2 PROCEDURE FOR REQUESTING HLA TESTING OF PATIENT OR RELATIVE

2.1 Procedure for a Transplant Centre requesting HLA Testing at the Anthony Nolan Laboratories

If the Transplant Centre requires HLA testing for a patient, the Transplant Centre must send the patient's blood sample, buccal swab or saliva sample to Anthony Nolan with the appropriate completed Histocompatibility Testing Request DOC 2857 form.

2.2 Procedure for a Transplant Centre requesting HLA Testing at the Anthony Nolan Laboratories - for a Donor who is related to the Patient

Anthony Nolan also provides testing services for donors who are related to the patient. If the Transplant Centre is proposing a transplant using a Related Donor, such as a sibling, the Transplant Centre may request that Anthony Nolan carries out HLA testing by sending the relative's blood sample, buccal swab or saliva sample to the Anthony Nolan Laboratories with the appropriate completed Histocompatibility Testing Request DOC2857 form.

2.3 HLA Typing of Blood Samples

Anthony Nolan will perform HLA typing on the patient and donor samples. HLA antibody screening and/or cross-matching can be performed when clinically indicated. Blood samples used for verification typing of patients must not be obtained on the same day as the primary/original samples.

Anthony Nolan will also perform ABO and RhD grouping and IDM testing including: Hbs Ag, HIV, Hepatitis C and Cytomegalovirus (CMV).

2.4 HLA Typing Reports

Anthony Nolan shall issue an HLA typing report and send this to the Transplant Centre by email.

3 THE SEARCH PROCESS

3.1 Search of the Anthony Nolan and NHS Stem Cell Register at the Request of a Transplant Centre

On receipt of a search request from a Transplant Centre, Anthony Nolan shall search the Anthony Nolan and NHS Stem Cell Register for each UK patient. Anthony Nolan shall also search the Anthony Nolan Cord Blood Bank and the NHS Cord Blood Bank for each UK patient unless otherwise instructed by the Transplant Centre. Anthony Nolan will perform a mismatch search if required.

3.2 Worldwide Donor Search - WMDA Search & Match Service

Anthony Nolan shall always use the WMDA Search & Match Service to perform a worldwide search for a suitable donor on behalf of a Transplant Centre.

3.3 Search for a Cord Blood Unit(s) at the Request of a Transplant Centre

Anthony Nolan shall also perform a worldwide Cord Blood Unit(s) search on WMDA Search & Match if the Transplant Centre specifically requires this. The Transplant Centre must provide details of the weight of each patient for whom a Cord Blood Unit(s) search is requested.

3.4 Search Report provided to a Transplant Centre

Anthony Nolan will prepare a search report consisting of the Anthony Nolan and NHS Stem Cell Register donor listings, details of any Anthony Nolan or NHS Cord Blood Unit(s) (if these have been requested by the Transplant Centre), a WMDA Search & Match summary and a covering letter recommending an appropriate course of action.

Anthony Nolan will send this search report to the Transplant Centre by secure email within approximately two business days of the receipt of the search request.

3.5 Search of International Registries at the Request of a Transplant Centre: Request for Further Information – UK Patients

If the initial WMDA Search & Match search produces details of possible matching international donors about which the Transplant Centre would like further information, the Transplant Centre must, by email (or as part of the first search request), request Anthony Nolan to obtain such additional information from the relevant International Establishment. Such additional information shall include, for example, age, gender and Donor ID of the proposed international donor.

3.6 Results of Search of International Registries

Anthony Nolan will send the Transplant Centre, by secure email, if agreed, an initial report on International Donors within three business days of receipt of the request.

The turnaround times of international registries vary so some results may not be available when Anthony Nolan sends out this initial international search report. Anthony Nolan will forward these other results to the Transplant Centre promptly after receiving them.

3.7 Request for Further Details of Cord Blood Unit(s)

If the Transplant Centre wishes to receive further information about a specific Cord Blood Unit listed on the WMDA Search & Match worldwide search results, the Transplant Centre may, by email, instruct Anthony Nolan to request a Cord Blood Unit report from the relevant International Registry or International Cord Blood Bank.

The relevant Cord Blood Bank shall then be required to provide the Cord Blood Unit reports.

3.8 Repeating Searches

At the request of a Transplant Centre, Anthony Nolan shall re-run a search, for the same patient, after an interval of three months, or a shorter period, which may, in exceptional circumstances, be agreed by Anthony Nolan.

If the Transplant Centre requires further repeat searches (in addition to the initial repeat search referred to above), the Transplant Centre must submit a new repeat search request.

3.9 Cancellation of Search

To cancel a search, the Transplant Centre shall email Anthony Nolan with details of, and the reason for, the cancellation.

3.10 All Communications between Anthony Nolan and the Transplant Centre

In compliance with HTA and WMDA requirements and standards and to ensure traceability and accuracy of information, all communications relating to the services provided by Anthony Nolan concerning the patients, donors and Cord Blood Units must only be channelled through Anthony Nolan.

For changes in staffing, the Transplant Centre must notify Anthony Nolan immediately of the departure of any senior member of staff, including, but not limited to, the Transplant Director, whose absence may adversely affect the running of the programme, and advise of their replacement, whether interim or permanent.

3.11 Communication

Communications regarding search reports shall be by encrypted mail message or other secure means.

3.12 Patients for Whom a Search Is Requested

Each patient for whom a search is requested must be recommended by a physician for a stem cell transplant and must satisfy Anthony Nolan's requirements regarding diagnosis, age and any other factors which Anthony Nolan may, in its discretion, consider relevant.

When considering the diagnosis of a patient, Anthony Nolan will use the recommendations set out in the latest BSBMTCT indications table.
http://bsbmtct.org/indications-table/

If the indication for which the Transplant Centre is requesting a donor is not a standard indication, Anthony Nolan may request further clinical information such as multi-disciplinary team (MDT) outcome from the Transplant Centre.

The Transplant Centre's physicians may exercise their discretion about whether a patient is of a suitable age for a stem cell transplant, provided that such physicians follow the relevant national and international standards and ethically approved protocols.

The Transplant Centre must refer any unusual request to Anthony Nolan and must provide a brief clinical history of the patient with a copy of any supporting information, e.g. relevant publications or consensus expert opinions.

The Transplant Centre may specify whether it requires PBSC or bone marrow derived stem cells, or a Cord Blood Unit(s).

3.13 Procedure for a Transplant Centre requesting a Search for a Donor and/or Cord Blood Unit(s) if the HLA Typing of the Patient is performed at the Anthony Nolan Laboratories

Once Anthony Nolan provides an HLA typing report for a patient, it is then the responsibility of the Transplant Centre to inform Anthony Nolan if a search for a donor and/or Cord Blood Unit(s) is required. There is no need for the Transplant Centre to complete any other search request form.

3.14 Procedure for a Transplant Centre requesting a Search for a Donor and/or Cord Blood Unit(s), if the HLA Typing of the Patient is not performed at the Anthony Nolan Laboratories

If the HLA typing of a patient is carried out at a laboratory other than the Anthony Nolan laboratories, the Transplant Centre must complete a Search Request DOC1685 form and send it via secure email, to the Transplant Centre's specific Anthony Nolan email address.

If there is insufficient information provided on the form, Anthony Nolan will ask the Transplant Centre to provide further details.

The Transplant Centre must send Anthony Nolan the HLA typing report, as described below, for each patient for whom it requests a search.

3.15 Information to be contained in an Email Search Request from a Transplant Centre

All the following information must be contained in an electronic search request from a Transplant Centre:

- Patient's name
- Patient's gender
- Patient's date of birth
- Patient's ethnicity (if available)
- Diagnosis and current status of patient
- HLA typing of Patient (minimum HLA-A, - B and -DRB1)
- Transplant Centre's Patient ID
- Invoice address

If a Cord Blood Unit(s) search is required, the request must also state the patient's weight.

3.16 Checking of Data on Search Requests

Anthony Nolan will check all search requests to ensure that appropriate and adequate data is given before the search is initiated. If any information is illegible or missing, Anthony Nolan will ask the Transplant Centre to resubmit the request including this information.

3.17 HLA Typing Report (which must accompany a Search request by a Transplant Centre if the HLA Typing of the Patient is not performed at the Anthony Nolan Laboratories)

If the HLA typing of the patient is not carried out at the Anthony Nolan laboratories, the Transplant Centre must send Anthony Nolan a HLA Typing Report for the patient, with each search request. The HLA Typing Report must be performed by an accredited laboratory and it is recommended that the HLA typing is performed to high resolution level for HLA-A, B, C, DRB1 and DQB1. This level of typing accelerates the search process.

Low resolution HLA typing slows down the search procedure by identifying donors who, on subsequent analysis, may prove to be mismatches. Many international registries require HLA typing of patients to second field level before the international registry will provide a donor. High resolution patient typing is therefore highly recommended at the beginning of the search process. Information on HLA typing requirements can be found in the Anthony Nolan Histocompatibility Laboratory User Guide DOC455.

4 MATCHING OF PATIENTS AND DONORS

4.1 Matching Programme - Anthony Nolan Laboratories

The matching programme developed by Anthony Nolan includes the HLA–A, -B, -C, -DRB1 and -DQB1 molecular typing data in the sorting algorithm. Where ambiguities exist, resulting in intermediate resolution results, the allele codes developed by the National Marrow Donor Program, USA are utilised to enter data onto the computer (http://bioinformatics.nmdp.org/).

If Anthony Nolan deems this appropriate, Anthony Nolan will extend searches to look for donors with a single mismatch at the HLA-A, -B, -C, -DRB1 or –DQB1 locus.

The standard format for listing donors is younger before older, within the resolution of the donor HLA typing.

Additional information used for matching donors includes ABO and RhD blood group, cytomegalovirus (CMV) status, ethnic group and weight. Most of these factors may be applied as optional filters to reduce a long list of matching donors e.g. a list of CMV negative matching donors only may be requested.

The status of the donor will be clearly indicated on the UK search report. This will highlight any matched donors who are temporarily unavailable, in test for another patient, reserved for another patient or whom have already previously donated. The higher the HLA typing resolution provided on the patient, the more informative a donor listing will be.

4.2 Advice and Responsibility

Anthony Nolan can provide advice on matching donors and patients. The final decision, however, on donor suitability is always the responsibility of the Transplant Centre.

5 VERIFICATION TYPING

5.1 Potential Donor Matches – Verification Typing

On identifying potential donor matches to the patient, further verification testing by a laboratory is necessary to ensure that the donor's initial HLA-typing results and level of matching with the patient are correct and still fulfil the medical requirements for donation.

If the Transplant Centre wishes to request verification typing of a donor, the Transplant Centre shall complete the Verification Typing Request Form DOC1671 and send it to the Transplant Centre's designated Anthony Nolan email address.

Anthony Nolan will contact Anthony Nolan donors and will request other establishments (NHSBT, WBMDR, DKMS UK and international registries, as applicable) to contact their own donors for verification typing samples.

If an Anthony Nolan donor is selected, and a fresh blood sample is needed, Anthony Nolan will discuss donation procedures, health and availability with the Anthony Nolan donor.

Anthony Nolan will inform the Transplant Centre if Anthony Nolan has been unable to contact the donor and shall request new instructions before proceeding further and as set out in section 5.3 -Procedure if Anthony Nolan donor Unavailable.

If an NHSBT donor, a WBMDR donor or a DKMS UK donor is selected by a Transplant Centre, Anthony Nolan will receive the request and will liaise with NHSBT, WBMDR or DKMS UK regarding arrangements for the blood sample shipment.

If an international donor is selected, Anthony Nolan shall, as requested by the Transplant Centre, facilitate shipment of the international donor blood sample to the designated Transplant Centre laboratory for verification typing.

Many international registries require patient high-resolution typing on HLA-A, -B, -C, -DRB1, -DQB1 prior to Donor sample procurement. Therefore, Anthony Nolan strongly recommends providing patient high-resolution typing at the verification testing request stage to avoid delays with donor sample provision.

Once blood procurement arrangements have been made, Anthony Nolan will notify the Transplant Centre of when to expect the blood sample from the donor, together with details of donor availability, medical issues which could affect the donation and the donor's preference of method of donating the stem cells, if known.

5.2 Potential Donor Matches – Extended Typing

If the Transplant Centre requests extended typing of a donor, the Transplant Centre shall complete the Extended Typing Request DOC1672 form and send it to the Transplant Centre's designated Anthony Nolan email address.

The extended typing may be performed on a stored DNA sample, if such sample is available.

If the extended typing of an Anthony Nolan donor is to be performed on stored material, Anthony Nolan will contact the donor to discuss the proposed typing, donation procedures, health and availability.

Anthony Nolan will inform the Transplant Centre if Anthony Nolan has been unable to contact the Donor and shall request new instructions before proceeding further and as set out in section 5.3 -Procedure if Anthony Nolan Donor Unavailable.

If the Transplant Centre requests extended typing of a donor who is not an Anthony Nolan donor (i.e. NHSBT, WBMDR, DKMS UK or international donor) Anthony Nolan will pass the request for extended typing to the appropriate UK registry or international registry but cannot guarantee that such donor will be available to provide a further sample, because the policies of other registries about providing further samples vary.

Anthony Nolan shall endeavour to keep the Transplant Centre informed about the progress of the extended typing and will pass on the results of extended typing which it receives from other UK registries or from international registries to the Transplant Centre as soon as Anthony Nolan receives the results itself.

5.3 Procedure if Anthony Nolan Donor Unavailable

If an Anthony Nolan donor does not respond within seven calendar days, Anthony Nolan will contact the Transplant Centre to establish whether to continue with the request. The Transplant Centre will be required to confirm its decision by email.

The request will expire should an Anthony Nolan donor still not have contacted Anthony Nolan within 28 days from the original request. Anthony Nolan will contact the Transplant Centre to establish whether to continue with the request.

- If the Transplant Centre wishes to continue, email confirmation will be accepted
- If the Transplant Centre wishes to cancel, email confirmation will be required to confirm formal cancellation of the request.

5.4 Cancellation of Typing or Blood Sample Procurement

The blood sample request can be cancelled by the Transplant Centre at any point. The request will remain open until written confirmation has been received to confirm the decision to cancel.

A Transplant Centre may cancel requests for further typing, or for blood sample procurement or blood sample shipment, at any time.

Anthony Nolan requires at least two business days' notice to allow time for the donor to be contacted and the procurement of the blood sample from the donor to be cancelled.

If notice of cancellation is received by Anthony Nolan when the typing, sample procurement or sample shipment has begun, the Transplant Centre shall still be required to pay the full charge for such typing or sample.

5.5 Virology Screening for Donors

If an Anthony Nolan donor who has been selected for verification typing has not been tested for virology within the last three months, Anthony Nolan will perform virology screening (Hep B, Hep C, HIV, CMV and blood grouping) on newly obtained (fresh) blood samples.

NHSBT, WBMDR and DKMS UK have their own procedures. Virology tests of International donors are usually part of the standard verification typing request.

5.6 Typing Results

For verification typing performed in Anthony Nolan laboratories (where Anthony Nolan has a separate agreement in place with the Transplant Centre for GIAS), Anthony Nolan will email the tissue typing report to the Transplant Centre's designated laboratory approximately seven business days after Anthony Nolan receives the blood sample.

For verification typing performed in the Transplant Centre's designated laboratories, the Transplant Centre must arrange for this laboratory to return the donor typing results to Anthony Nolan as soon as possible, by fax or email, indicating whether the donor should be released or reserved.

Where applicable, UK and international donor registries will report the typing results to Anthony Nolan via EMDIS.

5.7 Release of Donors

If the Transplant Centre does not instruct Anthony Nolan to reserve a UK donor, Anthony Nolan, NHSBT, WBMDR and DKMS UK will hold the donor for 60 days after the date on which the verification typing samples were shipped and then release the UK donor. In the case of an international donor, if the Transplant Centre does not instruct Anthony Nolan to reserve such a donor, Anthony Nolan will give instructions to the international registry to release the international donor within 60 days.

5.8 Concurrent Verification Typing Sample and Work-up Request for an Anthony NolanDonor

Transplant Centres can request concurrent verification typing/work-ups for urgent patient cases where there is insufficient time to perform the verification typing of the donor separately to work-up. Anthony Nolan will process concurrent verification typing/work-ups for Anthony Nolan donors who have not yet been typed in the Laboratory associated with the patient's Transplant Centre. In such cases, the Transplant Centre must provide high resolution verification typing results of the donor to Anthony Nolan prior to the patient starting conditioning, or before the donor begins G-SCF, whichever happens first, along with a written statement confirming that they have reviewed the verification typing results of the donor and wish to proceed with the work-up.

5.9 Reporting of Discrepancies in HLA Typing Results

The Transplant Centre must report all discrepancies in HLA typing results to Anthony Nolan as soon as possible.

6 GRAFT IDENTIFICATION ADVISORY SERVICE

6.1 Graft Identification Advisory Service (GIAS)

GIAS is a Histocompatibility and Immunogenetics service provided by Anthony Nolan to Transplant Centres to support the selection of unrelated donors and/or Cord Blood Unit(s) for verification and extended typing in a time efficient and cost-effective way.

GIAS will be provided by Anthony Nolan if it has been indicated by Anthony Nolan as a service provided in the separate signed service level agreement referred to in section 1.2 of this User Guide.

6.2 Search

If the Anthony Nolan laboratories are not providing HLA testing, Anthony Nolan will initiate a search as soon as the search request, which gives details of the patient's HLA typing, has been received.

If the Anthony Nolan laboratories are providing HLA typing, Anthony Nolan will initiate a search as soon as the patient's typing has been completed. Alternatively, if preferred by the Transplant Centre, once typing is completed Anthony Nolan will wait on instructions from the Transplant Centre to run a search.

Anthony Nolan will extend the standard search to any additional level, including mismatching, International and a Cord Blood Unit(s) search where agreed with the Transplant Centre.

6.3 Search Results and Recommendations

If the Transplant Centre requires only a search of the Anthony Nolan and NHS Stem Cell Register, Anthony Nolan will endeavour to send the results of the search within two business days of receipt of the search request.

If extended searches are required, Anthony Nolan will endeavour to send the results of such searches within three business days of receipt of the search request together with Anthony Nolan's recommendations for donor or Cord Blood Unit(s) selection. The timing of results of searches of international registries is beyond the control of Anthony Nolan and may take longer than three business days and Anthony Nolan cannot accept responsibility for any delay in these circumstances. When Anthony Nolan receives the results of the searches, it will forward the results to the Transplant Centre within one business day of receipt.

Our standard recommendations include three donors to be requested for verification and/or extended typing together with three back-up donors if available, and if required, up to 10 Cord Blood Units on which unit reports shall be requested by Anthony Nolan (if previously agreed with the Transplant Centre) from the relevant Cord Blood Bank. An additional list of the top three UK only donors will also be provided, if suitably matched UK donors are available, for all adult unrelated donor searches. Anthony Nolan will make its recommendations based on the patient information and matching requirements (selection algorithm) supplied by the Transplant Centre and shall apply Anthony Nolan expertise. The number and composition of recommendations can be tailored to suit the individual Transplant Centre's requirements.

6.4 Verification Typing or Extended Typing Requests

Requests for verification typing after a search has been run will be made in accordance with pre agreed arrangements with each Transplant Centre.

Any typing requests automatically made will be noted in the covering letter sent by Anthony Nolan to the Transplant Centre with the search results and recommendations. Should these typing requests not be required, the Transplant Centre must contact the designated Search and Selection Co-ordinator to stop the request for verification typing and extended typing. This request to stop such requests must be confirmed in writing via email and be made within three business days of the search results being issued. A cancellation charge may be incurred by the Transplant Centre if cancellation is received after this period.

6.5 Back-Up List

Where there is a GIAS agreement in place with the Transplant Centre, Anthony Nolan will immediately proceed to the verification and/or extended typing of another donor or Cord Blood Unit(s) taken from the back-up list of donor or Cord Blood Units should the initially selected donor or Cord Blood Unit(s) be unavailable, or where there is an unacceptable mismatch. Where there is no agreement in place, Anthony Nolan will advise the Transplant Centre and await further instructions.

6.6 Reporting

Once a week Anthony Nolan will email an updated GIAS spread sheet to the Transplant Centre. This will include current information about arrangements for shipping samples, the progress of the donor's extended typing and the progress of the typing of the patient's siblings or other relative, if applicable.

7 FACILITATING A WORK-UP FOR THE COLLECTION OF PBSC OR BONE MARROW FROM AUK DONOR

7.1 Requesting a work-up of a UK Donor for a PBSC or Bone Marrow Collection

A Transplant Centre which requires PBSC or bone marrow from a donor on the Anthony Nolan and NHS Stem Cell Register must send Anthony Nolan a Formal Request for Blood Stem Cell Collection (First Transplants Only) DOC3842 and a formal laboratory HLA typing report for both patient and donor.

The Transplant Centre must complete each section of each form. Any gaps may delay processing the request.

When completing the Formal Request for Blood Stem Cell Collection (First Transplants Only) DOC3842 form, the Transplant Centre should insert '1' next to the preferred stem cell source, and '2' if the other stem cell source will also definitely be accepted. The Transplant Centre should insert '0' if the other source is not an option (i.e. the Transplant Centre will prefer to use another donor if the selected donor will not donate via option 1, the preferred stem cell source).

Unless otherwise instructed by the Transplant Centre on the relevant prescription form:

- PBSC collections will be diluted with autologous plasma to get an approximate final concentration of less than 200x106ml TNC (Total Nucleated Cell)
- Bone marrow will be diluted with ACD (acid-citrate-dextrose) at a dilution of 1:7 vol ACD/vol BM (bone marrow).

If the Transplant Centre requires different dilutions, the Transplant Centre must specify this on the relevant prescription form.

Anthony Nolan or the applicable registry will test for the following infectious disease markers as part of the donor's medical: anti-HIV1, anti-HIV2, p24 antigen, anti-HTLV 1 and 2, HIV-RNA, anti-HBc, HBsAg, HBV-DNA, anti-HCV, HCV-RNA, HEV RNA, anti-CMV IgG and IgM, anti-toxoplasmosis IgG and IgM, Treponema Palladium serology, VZV IgG, EBV (anti-VCA IgG and IgM).

If any additional tests are required at the point of work-up, the Transplant Centre will need to contact their co-ordinator requesting additional pre-collection blood samples from the donor.

7.2 Confirmation and checking of Work-Up Request

Anthony Nolan will confirm receipt of each work-up request by email to the Transplant Centre within one business day.

Anthony Nolan will check all work-up requests for an Anthony Nolan donor to ensure that the appropriate (HLA-matched) donor has been selected for the patient, by verifying initial donor eligibility based on HLA requirements, age, previous medical and social history, and information provided by the donor. Anthony Nolan will also check that the patient's criteria (age, diagnosis, disease status) and transplant protocol comply with Anthony Nolan's standards.

Anthony Nolan will notify the Transplant Centre by fax or email of the name of the Donor Provision Co-ordinator responsible for the patient's work-up request.

7.3 Anthony Nolan's Contact with the Donor

For each Anthony Nolan donor, Anthony Nolan will notify the donor by telephone immediately.

For each Anthony Nolan donor, Anthony Nolan shall check with the selected donor that they are still willing to proceed and is available on the dates requested by the Transplant Centre.

If a request is received by Anthony Nolan for a WBMDR donor, Anthony Nolan will forward the request to WBMDR. The WBMDR will then be responsible for contacting its donor and taking them through the work-up process. The WBMDR will be in direct contact with the UK Transplant Centre and will copy Anthony Nolan into all communications.

If a request is received by Anthony Nolan for an NHSBT donor, Anthony Nolan will contact NHSBT to inform them of the request. NHSBT will then contact its donor, inform them of the request and obtain their consent to pass their contact details to Anthony Nolan. Anthony Nolan will then proceed with the work-up as it would for an Anthony Nolan donor. All communication about the work-up will be with Anthony Nolan.

If a request is received by Anthony Nolan for a DKMS UK donor, Anthony Nolan will contact DKMS UK to inform them of the request. DKMS UK will be responsible for contacting its donor and taking them through the work-up process. All communication about the work-up will be with Anthony Nolan. However, if the request is for a subsequent donation for a DKMS UK donor and Anthony Nolan facilitated the original work-up then Anthony Nolan shall proceed with the work-up as it would for an Anthony Nolan donor.

7.4 Procedure if Donor is Unavailable

If the donor does not respond to the various forms of communication within a period of 48 hours, Anthony Nolan will inform the Transplant Centre of the potential delay.

If the donor is not available on the requested dates, this information, with alternative dates proposed by the donor, will immediately be relayed to the requesting Transplant Centre.

7.5 Preferred Method of Donation

Anthony Nolan will make the donor fully aware of the options regarding the two methods of haematopoietic progenitor cell (HPC) donation, PBSC and bone marrow. Anthony Nolan will tell the donor the Transplant Centre's preferred method of donation, but Anthony Nolan will not at any point put pressure on the donor to select the preferred method.

If the donor's chosen method of donation is not the Transplant Centre's preferred option, Anthony Nolan will notify the Transplant Centre accordingly to find out whether this is an acceptable option for the Transplant Centre, and whether or not it is still willing to proceed with the donor. If confirmed by the Transplant Centre, Anthony Nolan will then proceed with making the arrangements for donation. If the donor's chosen method of donation is not an option for the Transplant Centre, Anthony Nolan will not persuade or pressure the donor into changing their mind.

7.6 Booking the Medical, Counselling, Consenting and Collection Procedure at the Collection Centre

When the dates for the donation and transplantation have been agreed by the donor and the Transplant Centre, Anthony Nolan will book a full medical for the donor at one of Anthony Nolan's contracted Collection Centres to ensure that the donor is medically fit to donate.

Anthony Nolan will arrange all the logistics of the medical examination and the donation, including all necessary travel arrangements and the reimbursement of any out-of-pocket expenses, including subsistence, for an accompanying relative or friend. Anthony Nolan will arrange the following appointments, and will notify the Transplant Centre of the confirmed dates for:

- the donor's medical examination, consenting and counselling for the donation procedure (if pre-collection samples are required by the Transplant Centre, Anthony Nolan will endeavour that this examination does not take place on a Friday, but this cannot be guaranteed)
- the estimated date on which the results of the donor's clearance will be received
- if the method of donation is PBSC, the dates of the G-CSF injections
- the date(s) of the donation
- the date and time for expected delivery of the donated PBSC or bone marrow.

The Transplant Centre must complete and return the Confirmation of Work-Up Schedule DOC4256 form.

7.7 No Donor / Patient Contact (Unrelated Donors)

Unrelated donors will never donate in the same hospital as the hospital in which the patient is being treated. Unrelated donors will never be attended by a physician who is involved in the care of the patient.

7.8 Donor Clearance

When the donor's full medical report has been received, an Anthony Nolan Medical Officer will confirm that the donor is suitable and able to proceed with donation and complete the Donor Clearance form. The Transplant Centre shall sign and return this form to Anthony Nolan to confirm that the Transplant Centre accepts the donor, the dates, and the proposed collection regime. Any medical issues discovered during the donor medical that do not impact upon the donor's fitness to donate (donor suitability) but which may have implications for the patient (donor eligibility) will be communicated via the Donor Clearance form so that the Transplant Centre can confirm it is happy to proceed with the donor.

7.9 Procedure if a Donor Fails Medical

If any tests or examination results are not within the accepted range, such results will be reviewed immediately by Anthony Nolan. If any condition is uncovered which prevents the donor from donating, Anthony Nolan will immediately notify the Transplant Centre that the donor will not donate. Anthony Nolan will not give the Transplant Centre any details of the reasons why the donor has failed their medical.

On occasion, the Anthony Nolan Medical Officer may decide that further medical investigations are required before a final decision on the donor's suitability to donate can be made by Anthony Nolan.

The Anthony Nolan Donor Provision Co-ordinator will inform the Transplant Centre in writing that the donor requires further testing before a decision regarding the donor's suitability to donate can be given.

Details of the further testing will not be given to the Transplant Centre but the expected date on which the results will be available will be given for the proposed transplant date, to be changed if necessary and/or other appropriate actions to be taken.

The Transplant Centre will be notified of any donor results that could be clinically important to the patient's care.

7.10 Procedure if the Cell Count Collected from the Donor is Low

If the cell count of the PBSC collected from the donor is less than 1x 10^6 CD34+ cells/kg patient weight after two days of apheresis, Anthony Nolan will discuss the situation with the Transplant Centre.

Provided that the CD34+ cell dose per kg patient weight exceeds 1x10^6, arrangements for further haematopoietic progenitor cell (HPC) collection will not be made unless the patient fails to engraft and unless there are concerns about loss of viability, e.g. the cells are being cryopreserved or there are valid clinical concerns about engraftment from the Transplant Centre.

7.11 Postponements and Cancellations of Donations

Anthony Nolan will immediately notify the Transplant Centre, both by telephone and by email, of all postponements and cancellations of the scheduled donation. The Transplant Centre must provide a 24-hour telephone number for this purpose.

In rescheduling a donation, if the last virology testing was performed on a donor sample taken more than 30 days prior to the donation date, Anthony Nolan will ensure that repeat virology testing is performed.

If the transplant has been postponed by more than 60 days, Anthony Nolan will arrange for virology, haematology, and biochemistry tests to be repeated. These tests will be carried out at Anthony Nolan's designated Collection Centre.

If the transplant has been delayed by more than six months, Anthony Nolan will arrange a repeat full medical examination of the donor.

The Transplant Centre must immediately notify Anthony Nolan of any postponement or cancellation by completing the Notification of Change (Cancellation or Postponement) DOC2258 form.

The form must be emailed to Anthony Nolan. The cancellation or postponement request cannot be processed until this form is received by Anthony Nolan.

If these cancellations or postponements require urgent action by Anthony Nolan and occur outside office hours, the Transplant Centre must call the Anthony Nolan emergency telephone number: +44 7710 599 161.

8 FACILITATING A WORK-UP FOR THE COLLECTION OFPBSC OR BONE MARROW FROM AN INTERNATIONAL DONOR, AT THE REQUEST OF A TRANSPLANT CENTRE

8.1 Sending a Request Form for an International Donor

A Transplant Centre which requires PBSC or bone marrow from an international donor must send Anthony Nolan the following forms:

- Formal Request for Blood Stem Cell Collection DOC3842 and formal laboratory HLA typing reports for both patient and donor.

The Transplant Centre must complete each section of each form. If there are any gaps, this may delay processing the request.

When completing the Formal Request for Blood Stem Cell Collection DOC3842 form or the Related Donors – Formal Request for Blood Stem Cell Collection DOC3983 form, the Transplant Centre should insert '1' next to the preferred stem cell source, and '2' if the other stem cell source will also definitely be accepted. The Transplant Centre should insert '0' if the other source is not an option (i.e. the Transplant Centre will prefer to use another donor if the selected donor will not donate via option 1, the preferred stem cell source).

8.2 NMDP or Gift of Life Donors

If the donor is an NMDP donor or a Gift of Life donor, the Transplant Centre will send Anthony Nolan the request forms, as set out in section 8.1 of this User Guide, together with a high-resolution HLA report for both patient and donor. Any request being sent without high resolution typing available will be delayed unless otherwise instructed by the Transplant Centre on the relevant prescription form.

- PBSC collections will be diluted with autologous plasma to get an approximate final concentration of less than 200x106ml TNC (Total Nucleated Cell).
- Bone Marrow will be diluted with ACD at a dilution of 1:7 vol ACD/vol B.

8.3 Confirmation and Checking of Work-Up Requests

Anthony Nolan will confirm receipt of each work-up request by fax or email to the Transplant Centre within one business day.

If Anthony Nolan is providing a GIAS service, Anthony Nolan will check all work-up requests for an international donor to ensure that the appropriate (HLA-matched) donor has been selected for the patient, by verifying initial donor eligibility based on HLA requirements.

Anthony Nolan will also check that the patient's criteria (age, diagnosis, disease status) and transplant protocol comply with the relevant international registry's standards (where known).

If Anthony Nolan is not providing GIAS services, Anthony Nolan will not provide any of the checks referred to in this section.

8.4 Contact with International Registry

Anthony Nolan will forward each request for an international donor to the respective international registry. The international registry will then proceed to contact the international donor and will confirm availability and dates. Anthony Nolan will notify the Transplant Centre by email of the name of the Anthony Nolan Donor Provision Co-ordinator who will be responsible for the patient's work-up request.

With each request Anthony Nolan will also send the External Registry Virology Checklist (HPC) DOC3092 form to the international registry. The international registry will complete this to confirm the infectious disease markers that will be tested at the international donor's medical. Anthony Nolan will forward this to the Transplant Centre for review. If any additional tests are required, the Transplant Centre will need to contact their co-ordinator requesting additional pre-collection blood samples from the international donor. Anthony Nolan will forward this on to the international registry.

The time frame for confirmation of dates and availability of an international donor will vary but Anthony Nolan will maintain contact with the international registry and Transplant Centre to ensure that all information is received at the appropriate times to allow the transplant to proceed on schedule. Anthony Nolan will forward information to the Transplant Centre as soon as it receives it.

The written information which will be passed on to the Transplant Centre by Anthony Nolan will include:

- the date of the international donor's medical
- the date of donation
- the date on which blood samples will be delivered to the Transplant Centre (if applicable)
- the expected date and time(s) of the delivery of the donated PBSC or bone marrow.

If the dates do not suit the Transplant Centre, Anthony Nolan will attempt to obtain new dates from the international registry until a mutually acceptable date is found.

8.5 International Donor Clearance

When Anthony Nolan receives the International Donor Clearance and results of virology screening from the international registry, Anthony Nolan will email these to the Transplant Centre, before the date on which patient conditioning begins. Any International Donor Clearance and results of virology screening received from a non-NMDP donor will be reviewed by an Anthony Nolan Medical Officer before being forwarded to the Transplant Centre.

8.6 Donors on Reserve, Postponements and Cancellations of Donations

The various international registries have different reservation policies. The Transplant Centre should ask Anthony Nolan for this information if it is required.

Anthony Nolan will immediately notify the Transplant Centre, both by telephone and in writing, of all postponements and cancellations of the scheduled donation.

The Transplant Centre must immediately notify Anthony Nolan of any postponement or cancellation by completing the Notification of Change (Cancellation or Postponement)

DOC2258 form.

The form must be emailed to Anthony Nolan. The cancellation or postponement request cannot be processed until this form is received by Anthony Nolan.

If these cancellations or postponements require urgent action by Anthony Nolan and occur outside office hours, the Transplant Centre must call the Anthony Nolan emergency telephone number: +44 7710 599 161.

9 SUBSEQUENT WORK-UP REQUESTS FOR DONORS

9.1 Requesting a Subsequent Work-Up from a Donor

If a Transplant Centre requires a further donation for a patient from a donor who has already donated PBSC or bone marrow to such patient, the Transplant Centre must complete and send Anthony Nolan, as applicable, the Formal Request for Subsequent Blood Stem Cell or Lymphocyte Collection – Previous Transplant History DOC1119 form or the Related Donors - Formal Request for Subsequent Blood Stem Cell or Lymphocyte Collection DOC4132 form by email or fax.

The Formal Request for Subsequent Blood Stem Cell or Lymphocyte Collection – Previous Transplant History DOC1119 form should be completed for all donors irrespective of whether they are on the Anthony Nolan Register, NHSBT register, WBMDR register, DKMS UK register or an international donor register.

9.2 Subsequent Work-Up from an Anthony Nolan Donor, or a Related Donor living inthe UK, or an NHSBT Donor if the original donation was within six months of subsequent date of request

On receipt of the Formal Request for Subsequent Blood Stem Cell or Lymphocyte Collection Previous Transplant History DOC1119 form or the Related Donors - Formal Request for Subsequent Blood Stem Cell or Lymphocyte Collection DOC4132 form, Anthony Nolan's Donor Consultant, or their deputy, will review the request. Anthony Nolan will aim to provide a decision within 72 hours of receipt of the request.

Anthony Nolan may request further information from the Transplant Centre. Subsequent donation requests may be referred by Anthony Nolan's Donor Consultant to Anthony Nolan's medical affairs group in the case of controversial indications. If the request for the subsequent donation is not approved, Anthony Nolan will provide the Transplant Centre with a brief summary of the reason(s) for the refusal.

9.3 Subsequent Work-Up from a DKMS UK Donor, WBMDR Donor, an International Donor, a Related Donor living outside the UK, or an NHSBT Donor if the original donation was outside of six months of the subsequent date of request

If the donor from whom the subsequent donation is required is a DKMS UK donor, WBMDR donor, an International donor, or an NHSBT donor and the original donation was outside of six months of the subsequent date of request, Anthony Nolan will forward the Formal Request for Subsequent Blood Stem Cell or Lymphocyte Collection – Previous Transplant History DOC1119 form to the relevant registry. If the request is for a related donor living outside the UK, the Related Donors - Formal Request for Subsequent Blood Stem Cell or Lymphocyte Collection DOC4132 form will be sent to the relevant International Establishment. If the subsequent donation is for a DKMS UK donor, WBMDR

donor, international donor or a related donor living outside the UK Anthony Nolan will also forward External Registry Virology Checklist (DLC) DOC5173 form for the relevant registry or International Establishment to complete.

If the donor from whom the subsequent donation is required is an NMDP donor and lymphocytes are requested, the Transplant Centre will send Anthony Nolan the NMDP form F00235 NMDP Prescription for MNC, Apheresis along with the Formal Request for Subsequent Blood Stem Cell or Lymphocyte Collection – Previous Transplant History DOC1119 form.

9.4 Frequency of Subsequent Work-Ups from an Anthony Nolan Donor

Any requests for further donations of haematopoietic stem cells or lymphocytes will be considered on a case-by-case basis by Anthony Nolan's Donor Consultant or their designee.

An Anthony Nolan donor may donate haematopoietic stem cells (which may be donated by PBSC or bone marrow) on a maximum of four occasions, to not more than two different patients.

An Anthony Nolan donor may also donate lymphocytes on a maximum of four occasions.

An Anthony Nolan donor who has undergone a PBSC or bone marrow donation, and despite repeated contact attempts is not participating in the post donation follow-up procedures required by Anthony Nolan, will not be considered for any further PBSC, bone marrow or lymphocyte donations.

An Anthony Nolan donor will not be approached to provide PBSC on a second occasion if the donor did not mobilise adequate haematopoietic progenitor cells at the time of the primary donation.

An Anthony Nolan donor will not be approached for a subsequent donation until the donor has reported full recovery from the previous donation.

9.5 Timings of Second Donations from an Anthony Nolan Donor

After the donation of PBSC, bone marrow or lymphocytes, an Anthony Nolan donor will not be available for other searches for a period of 24 months after donation, unless the patient to whom they have donated has died. NHSBT, WBMDR and DKMS UK have their own separate requirements regarding subsequent donations which Anthony Nolan can obtain upon request.

Anthony Nolan requires a period of four weeks to elapse between any primary donation and a subsequent donation by an Anthony Nolan donor for the same patient. This may be reviewed on a case-by-case basis.

9.6 Frequency and Timings of Subsequent Donations from International Donors

The rules regarding the frequency and timing of subsequent donations from an international donor vary between international registries. These rules can be requested from Anthony Nolan when required.

10 TRANSPORTATION OF PBSC AND BONE MARROW

10.1 Transport Arrangements to be made by Anthony Nolan

For Transplant Centres, Anthony Nolan will arrange the transportation of PBSC, bone marrow or lymphocytes from the UK Collection Centre or international collection centre to the Transplant Centre. Any specific requirements relating to shipment, including as to whether bone marrow should be transported at room temperature or cooled, will be required ahead of time.

Anthony Nolan will transport the PBSC, bone marrow or lymphocytes using an Anthony Nolan volunteer courier, or a third-party commercial stem cell courier. Anthony Nolan will do the following:

- Make all the transport and accommodation arrangements for Anthony Nolan's courier.
- Inform the Transplant Centre of the name of the courier and their expected arrival time (including back-up flight information where appropriate).
- Endeavour to ensure that the fastest and safest route of transportation is followed.
- Provide the necessary transportation equipment and documentation.
- For each shipment, send a completed collection report which contains the details of the donation including the number of CD34+/kg collected. The report will either be sent with the Cell Product, and/ or be emailed/faxed separately.
- Inform the Transplant Centre of any changes to the estimated delivery time.
- Notify the airport authorities, where necessary.

10.2 Paperwork on Receipt of Cell Product

The courier will request the receiving representative at the Transplant Centre to provide identifying paperwork to confirm that the Transplant Centre is expecting a delivery, and to sign the transit report. The courier will return this transit report to Anthony Nolan.

10.3 Cancellation or Postponement

The Transplant Centre must immediately notify Anthony Nolan of any postponement or cancellation of a transplant by completing the Postponement/Cancellation DOC2258 form and emailing it to the Donor Provision team. If a cancellation or postponement requires urgent action by Anthony Nolan and occurs outside office hours, the Transplant Centre must call the Anthony Nolan emergency number: +44 7710 599 161. The Transplant Centre shall be liable for any courier costs incurred as a result of this postponement or cancellation.

11 PROVISION OF CORD BLOOD UNIT(S) FROM THE ANTHONY NOLAN CORD BLOOD BANK

11.1 Provision of Cord Blood Unit(s)

The Anthony Nolan Cord Blood Bank provides Cord Blood Unit(s) to Transplant Centres.

Transplant Centres can also request optional free services from Anthony Nolan's Cord Support Programme – please see section 20 for further details.

11.2 Request for Cord Blood Unit Report(s)

To request a Cord Blood Unit Report(s) from the Anthony Nolan Cord Blood Bank, a Transplant Centre should email the Transplant Centre's designated Anthony Nolan email.

11.3 Request for Reservation of Cord Blood Unit(s)

If, after reviewing the Cord Blood Unit Report(s), the Transplant Centre decides to reserve such Cord Blood Unit(s), the Transplant Centre shall send Anthony Nolan a request to reserve the Cord Blood Unit(s) by fax or email using the form DOC1126 Formal Request for Cord Blood Unit(s) from TC.

11.4 Quality Assurance Tests

On receipt of a Cord Blood Unit(s) Reservation Request, the Anthony Nolan Cord Blood Bank will initiate the following quality assurance tests in accordance with the Human Tissue Authority regulations:

- Releasing tests, which include a thaw from an attached segment and several QC tests such as viability, TNC and CD34+ count and CFUs.
- Verification typing from an attached segment.
- Maternal HLA typing.
- Confirmatory gender.
- Confirmatory ABO.

These tests usually take 10 business days.

11.5 Shipment before Quality Assurance Tests Completed

If the Transplant Centre needs the Cord Blood Unit(s) before full testing has been completed, the Transplant Centre must send the form DOC1126 Formal Request for Cord Blood Unit(s) from TC by fax or email.

When completing this form, it is essential that the Transplant Centre includes the proposed date of the transplant. Anthony Nolan will not ship the Cord Blood Unit(s) until it is notified of this date.

11.6 Confirmation of Acceptance of Cord Blood Unit(s)

When a date for shipment of a Cord Blood Unit(s) has been confirmed and agreed, Anthony Nolan strongly recommends that the patient does not begin their conditioning regime until the Cord Blood Unit(s) has been received by the Transplant Centre. A

Transplant Centre may also consider identifying UK banked back-up units. Anthony Nolan will require the Transplant Centre complete and return to Anthony Nolan the Confirmation of Acceptability of Cord Blood Unit DOC1128 form before the Cord Blood Unit can be shipped.

11.7 Transportation of Cord Blood Unit(s) from the Anthony Nolan Cord Blood Bank tothe Transplant Centre

Anthony Nolan will arrange the transportation of Cord Blood Unit(s) from the Anthony Nolan Cord Blood Bank to a Transplant Centre using an external courier company with which Anthony Nolan has contracted.

11.8 Address to which the Cord Blood Unit(s) will be delivered

Anthony Nolan will book the courier for the transportation of the Cord Blood Unit(s) to the address stipulated by the Transplant Centre on the Formal Request for Cord Blood Unit(s) DOC1126 form.

11.9 Return of the Cryoshipper

Anthony Nolan will be responsible for making all the arrangements with a courier company to ensure the return of the cryoshipper to the Anthony Nolan Cord Blood Bank.

11.10 Arrangements

Anthony Nolan will notify the Transplant Centre of the courier details and shall liaise with the courier in order to arrange a delivery date and time. Anthony Nolan will notify the Transplant Centre of the tracking details. The Transplant Centre must ensure that there is a person waiting at the Transplant Centre's designated address to receive the Cord Blood Unit(s) at the stipulated time with appropriate documentation to confirm receipt of the correct Cord Blood Unit.

11.11 Receipt of Cryoshipper

On receipt of the cryoshipper, the Transplant Centre must check the integrity of the Cord Blood Unit(s), including the seals, the data logger, and cryoshipper and complete the Reception Form DOC1567. The Reception Form DOC1567 must be returned to Anthony Nolan by email to CTCrelease@anthonynolan.org

The Transplant Centre must notify Anthony Nolan immediately of any irregularity in the cryoshipper by emailing QualityTeam@anthonynolan.org. Where possible the supply of photographic evidence of the irregularity should be included with the report.

11.12 Thawing of Cord Blood Unit(s)

When thawing the Cord Blood Unit(s) the Transplant Centre must check the seals very carefully and thaw the Cord Blood Unit(s) precisely in accordance with the instructions given by the Anthony Nolan Cord Blood Bank. The Transplant Centre must thaw the Cord Blood Unit(s) in a sterile zip lock-type bag provided by Anthony Nolan and sent with the Cord Blood Unit(s).

11.13 Forms to be sent on Receipt of Cord Blood Unit(s)

Anthony Nolan will send the Transplant Centre relevant forms that must be completed and returned to Anthony Nolan once the Cord Blood Unit(s) has been received and/or infused.

11.14 Storage of Cord Blood Unit(s)

The Transplant Centre must have the ability to store the Cord Blood Unit(s) on delivery and prior to transplant. The Cord Blood Unit(s) must be cryopreserved at -150 ºC or below.

11.15 Outcome of Transplantation

Anthony Nolan requires details of the outcome of the transplant and will liaise with the Transplant Centre to follow up post-transplant. The Transplant Centre will be asked to complete a Confirmation of Receipt and Infusion DOC1139 form to confirm this information.

11.16 Transplant Centre issues about the quality of the Cord Blood Unit(s)

If the Transplant Centre has concerns regarding:

- the quality of the Cord Blood Unit(s) during shipment (e.g. if there has been a suspected significant warming event during shipment)
- the appearance of the Cord Blood Unit(s) (e.g. any unusual discolouration, bag integrity issues, visible air pockets, improper labelling etc.)
- the results of tests indicating poor viability/yield

then such concerns must be immediately reported to Anthony Nolan in accordance with section 15 of this User Guide.

11.17 Eurocord

Anthony Nolan has an agreement with the Eurocord Registry ("Eurocord") under which Eurocord handles follow up on behalf of Anthony Nolan. The Transplant Centre agrees that Anthony Nolan may pass the Transplant Centre's contact details to Eurocord, whereupon Eurocord will liaise with the Transplant Centre directly.

11.18 Cancellation of Reserved Cord Blood Unit(s)

If a Transplant Centre cancels a request for an Anthony Nolan Cord Blood Unit(s) after the initial Quality Assurance Tests have been completed, Anthony Nolan will not charge for such tests.

11.19 Procedures for Transplant Centres to which Anthony Nolan provides a Histocompatibility Laboratory Clinical Service

Prior to the conditioning regimen of any Cord Blood Unit(s) recipient, the Transplant Centre shall carry out verification typing of at least HLA-A, -B, and -DRB1 at a minimum level of low resolution upon receipt of the shipped Cord Blood Unit(s) (in addition to any verification typing already performed). In accordance with our European Federation for Immunogenetics (EFI) accreditation, typing must be performed on a segment of the tubing integrally attached to the unit, if available. Otherwise, a satellite vial shipped with the Cord Blood Unit(s) may be used.

If no segment is available, this step can be performed after transplantation and must be initiated as soon as possible after thawing the Cord Blood Unit(s). In these instances, it will be highlighted in the typing report returned to the Transplant Centre that the typing was performed on the post infusion sample provided.

As soon as possible after shipment of the Cord Blood Unit(s), a segment or vial must be sent by the receiving Transplant Centre to the Anthony Nolan laboratories for verification typing as set out in the Anthony Nolan Laboratories' User Guide.

The Anthony Nolan Laboratories' User Guide can be found on the Anthony Nolan website. https://www.anthonynolan.org/clinicians-and-researchers/services-transplant-centres/full-list-forms

11.20 Cancellation or Postponement

If a patient's transplant is postponed or cancelled, this may necessitate amendment or cancellation of a courier booking. The Transplant Centre which is purchasing the Cord Blood Unit(s) shall be liable to pay for the Cord Blood Unit(s) if it/they have been dispatched and shall also be liable for any courier costs incurred as a result of this postponement or cancellation.

12 FACILITATING THE PROVISION OF CORD BLOOD UNIT(S) FROM THE NHS CORD BLOOD BANK OR AN INTERNATIONAL CORD BLOOD BANK

12.1 Facilitating Search of the NHS Cord Blood Bank and WMDA Search & Match

If a Transplant Centre requests a Cord Blood Unit(s) search, and Anthony Nolan cannot find a suitable cord in the Anthony Nolan Cord Blood Bank, Anthony Nolan will facilitate a search of the NHS Cord Blood Bank and shall perform a worldwide search on WMDA Search & Match. This procedure is described in more detail in section 3 of this User Guide.

12.2 Forms – Requests for Cord Blood Unit Report(s)

To request a Cord Blood Unit Report(s) from NHSBT or an international cord blood bank the Transplant Centre should email the request to the Transplant Centre's designated Anthony Nolan email address.

12.3 Request for Cord Blood Unit(s)

If, after reviewing the Cord Blood Unit Report(s), the Transplant Centre decides to request such Cord Blood Unit(s), the Transplant Centre shall complete and send Anthony Nolan, by fax or email, the Formal Request for Cord Blood Unit(s) DOC1126 form irrespective of the Cord Blood Bank from which the Cord Blood Unit(s) is requested. Each section of the form must be completed.

The Transplant Centre may also reserve Cord Blood Unit(s) by sending a fax or email to Anthony Nolan. No specialised form is required for reservations.

12.4 Quality Assurance Tests

On receipt of a Formal Request for Cord Blood Unit(s) DOC1126 form the relevant Cord Blood Bank will initiate its quality assurance and infectious disease marker tests.

These tests usually take approximately 10 business days.

Anthony Nolan will endeavour to make sure that all quality assurance and mandatory infectious disease marker tests are performed before Cord Blood Unit(s) are imported into the United Kingdom. Occasionally this is not possible. Anthony Nolan will inform and work with the international cord blood bank/registries and the Transplant Centre to meet all regulatory requirements in accordance with the guidance of the Human Tissue Authority.

12.5 Request for Shipment

The Transplant Centre may request shipment by completing the Formal Request for Cord Blood Unit(s) DOC1126 form.

When completing this form, it is essential that the Transplant Centre includes the date of which they plan to start patient conditioning and the scheduled transplant date. Many cord blood banks will not ship the Cord Blood Unit(s) until they receive notification of this date.

12.6 Confirmation of Acceptance of Cord Blood Unit(s)

Anthony Nolan will send all the relevant forms when a date for shipment of a Cord Blood Unit(s) has been confirmed and agreed. The Transplant Centre shall complete a Confirmation of Acceptance of Cord Blood Unit(s) DOC1128 form and return it by email or fax to Anthony Nolan.

The Cord Blood Unit(s) cannot be shipped until this form has been received by Anthony Nolan.

Anthony Nolan strongly advises that the Cord Blood Unit(s) is shipped and reaches the Transplant Centre before the patient begins their conditioning regime. The Transplant Centre may also consider identifying a domestically banked back-up Cord Blood Unit(s).

12.7 Transportation of Cord Blood Unit(s) from the NHSBT Cord Blood Bank or an International Cord Blood Bank to a Transplant Centre

Anthony Nolan will arrange the transportation of Cord Blood Unit(s) from the NHSBT Cord Blood Bank or an international cord blood bank to a Transplant Centre using a courier company which may be contracted by either Anthony Nolan, NHSBT or the international cord blood bank.

12.8 Address to which the Cord Blood Unit(s) will be delivered

Anthony Nolan will book the courier for the transportation of the Cord Blood Unit(s) to the address stipulated by the Transplant Centre on the Formal Request for Cord Blood Unit(s) DOC1126 form.

12.9 Return of the Cryoshipper

Anthony Nolan or the originating cord blood bank will be responsible for making all the arrangements with a courier company to ensure the return of the cryoshipper to the originating cord blood bank.

12.10 Arrangements

Anthony Nolan will notify the Transplant Centre of the courier details and shall liaise with the courier in order to arrange a delivery date and time. Anthony Nolan will notify the Transplant Centre of the tracking details. The Transplant Centre must ensure that there is a person waiting at the Transplant Centre's designated address to receive the Cord Blood Unit(s) at the stipulated time with appropriate documentation to confirm receipt of the correct Cord Blood Unit.

12.11 Storage of Cord Blood

The Transplant Centre must have the ability to store the Cord Blood Unit(s) on delivery and prior to transplant. The Cord Blood Unit(s) must be cryopreserved at -150 ºC or below.

12.12 Receipt of Cryoshipper

On receipt of the cryoshipper, the Transplant Centre must check the integrity of the Cord Blood Unit(s), including the seals and the data logger.

12.13 Thawing of Cord Blood Unit(s)

When thawing the Cord Blood Unit(s), the Transplant Centre must check the seals very carefully and thaw all Cord Blood Unit(s) precisely in accordance with the instructions given by the relevant cord blood bank. The Transplant Centre must thaw the Cord Blood Unit(s) in a sterile zip lock-type bag.

12.14 Outcome of Transplantation

Cord blood banks often require details about the thawed Cord Blood Unit and the outcome of the transplant. The Transplant Centre will be asked to complete a Confirmation of Receipt and Infusion DOC1139 form to confirm this information.

12.15 Transplant Centre concerns about the quality of the Cord Blood Unit(s)

If the Transplant Centre has concerns regarding:

- the quality of the Cord Blood Unit(s) during shipment (e.g. if there was a suspected significant warming event during shipment)
- the appearance of the Cord Blood Unit(s) (e.g. any unusual discolouration, bag integrity issues, visible air pockets, improper labelling etc.)
- the results of tests indicating poor viability/yield

then such concerns must be immediately reported to Anthony Nolan in accordance with the procedure on section 15 of this User Guide.

12.16 Procedures for Transplant Centres to which Anthony Nolan provides a Histocompatibility Laboratory Clinical Service- Cord Blood Unit (s) recipients

Prior to the conditioning regime of any Cord Blood Unit's recipient, the Transplant Centre shall carry out verification typing of at least HLA-A, -B, and -DRB1 at a minimum level of low resolution upon receipt of the shipped Cord Blood Unit(s).

This verification typing is in addition to any verification typing which has already been performed (usually by the Cord Blood Bank). Typing must be performed on a segment of the tubing integrally attached to the Cord Blood Unit(s), if available. Otherwise, a satellite vial shipped with the Cord Blood Unit(s) may be used. If no segment is available, this step can be performed after transplantation and must be initiated as soon as possible after thawing the Cord Blood Unit(s). As soon as possible after shipment of the Cord Blood Unit(s), a segment or vial must be sent by the receiving Transplant Centre to the Anthony Nolan laboratories for verification typing as set out in the Anthony Nolan Laboratories' User Guide.

If the cord blood bank is not performing verification typing, Anthony Nolan will arrange for DNA to be shipped to the Anthony Nolan laboratories for testing.

The Anthony Nolan Laboratories' User Guide can be found on the Anthony Nolan website. https://www.anthonynolan.org/clinicians-and-researchers/services-transplant-centres/full-list-forms

12.17 Cancellation or Postponement

If a patient's transplant is postponed or cancelled, this may necessitate amendment or cancellation of a courier booking. The Transplant Centre which is purchasing the Cord Blood Unit(s) shall be liable to pay for the Cord Blood Unit(s) if it/they have been dispatched and shall also be liable for any courier costs incurred as a result of this postponement or cancellation.

13 FACILITATING RELATED DONORS SERVICE FOR DONORS IN THE UNITED KINGDOM

13.1 Related Donor Sample Procurement

If a related donor is residing in the United Kingdom, Anthony Nolan can help facilitate the collection of samples from them for the purposes of testing to investigate if they are a suitable match for transplant.

If the Transplant Centre wishes to use this service, they must complete the Related Donor Sample Request for HLA Typing DOC3955 form and send it to the Transplant Centre's designated Anthony Nolan email address.

The Transplant Centre must have first contacted the related donor to confirm that they are willing to provide the samples before requesting this service from Anthony Nolan.

Providing the related donor is willing to donate, Anthony Nolan will arrange for the samples to be collected and shipped to the address indicated on the request form. Once the testing has been completed, the Transplant Centre must notify the related donor of the outcome. The Anthony Nolan Verification Typing Co-ordinator or Search Co-ordinator must also be told of this.

13.2 Related Donor Stem Cell Product Procurement

If a related donor is the best match for the patient, the Transplant Centre can request Anthony Nolan to help facilitate the cell product collection. The Transplant Centre must have first contacted the related donor to confirm that they are willing to donate before requesting this service.

The Transplant Centre must complete the Related Donors - Formal Request for Blood Stem Cell Collection DOC3983 form, a formal laboratory HLA typing report for both patient and related donor and, depending on which stem cell source is required (either PBSC or bone marrow) submit this to the work-ups' e-mail address: workups@anthonynolan.org. If verification typing has not been performed at this stage, the Related Donor Sample Request for HLA Typing DOC3955 form must also be submitted to facilitate the sample procurement.

Anthony Nolan will make all the necessary arrangements for collection of the stem cells from the related donor residing in the UK as per the applicable procedures set out on this User Guide.

13.3 Related Donor Clearance

The Anthony Nolan Donor Consultant has the final decision for medical sign off for any related donor residing in the UK. Any medical issues that the Anthony Nolan Donor Consultant considers may pose a potential risk to the patient will be discussed with the Transplant Centre.

13.4 Postponement and Cancellation of Transplant

The Transplant Centre must immediately notify Anthony Nolan of any postponement or cancellation of a transplant by completing the Postponement/Cancellation DOC2258 form. The Transplant Centre must also notify the related donor of such a change and confirm by email to Anthony Nolan this has been done. DOC2258 must be emailed to the Anthony Nolan Donor Provision team. Without it, the cancellation/postponement request cannot be processed. If a cancellation or postponement requires urgent action by Anthony Nolan and occurs outside office hours the Transplant Centre must call the Anthony Nolan emergency telephone number.

13.5 Procedure after Donation

Related donors residing in the UK will receive follow up for 10 years, as detailed in this User Guide. This includes the management of Serious Adverse Events, donors' physical and emotional recovery from donation and counselling post-donation if required. Anthony Nolan will not provide updates on the patient's progress for related donors or facilitate patient/donor correspondence, the related donor will be directed to the Transplant Centre if required.

13.6 Emergency Bone Marrow Donation from a Related Donor in the UK

If a Transplant Centre requires Anthony Nolan to facilitate an emergency bone marrow donation from a related donor in the UK, in the instance where a PBSC from the related donor performed at the Transplant Centre has been unsuccessful and the cell count of the PBSC collected from the related donor is less than 1x 10^6 CD34+ cells/kg patient weight after two days of apheresis, it should:

- confirm directly with the related donor their willingness to proceed with a bone marrow donation before approaching Anthony Nolan
- provide the full medical report, including virology results, to have been completed to JACIE standards within 30 days of the proposed emergency donation
- endeavour to give maximum possible notice to Anthony Nolan with a view to facilitating the donation as soon as possible. The Transplant Centre must contact the Director of Donor and Transplantation Services to inform them of the need for this request and in their absence the Head of Registry Services
- complete the Formal Request for Blood Stem Cell Collection Related Donors DOC3983 form and a formal laboratory HLA typing report for both patient and related donor and submit to the work-ups' e-mail address:
- workups@anthonynolan.org.

Anthony Nolan will then endeavour to facilitate the collection as quickly as possible following the notification of the need (within 24 hours where possible).

13.7 Related Donor Transport-only Requests

Upon request, Anthony Nolan can also provide a transportation service for haematopoietic stem cells (either fresh or cryopreserved) from a related donor where Anthony Nolan did not facilitate the collection. If agreed, Anthony Nolan will transport the product from the applicable UK collection centre to the Transplant Centre (a 'Transport-only Request'). Transport-only Requests are only available where the collection (and cryopreservation if applicable) is carried out at a UK hospital which is licensed by the HTA for the applicable licensed activities.

In order to fulfil a Transport-only Request, the Transplant Centre shall provide Anthony Nolan (via email to Anthony Nolan's nominated email address) with:

- such details of the product collection as may be requested by Anthony Nolan (including collection date(s)/time(s), HTA licence details of collecting hospital)
- confirmation of the full collection and delivery addresses
- a completed donor clearance form

Anthony Nolan's obligations in fulfilling a Transport-only Request are limited to the following:

- Anthony Nolan will arrange the transportation of the product using an Anthony Nolan volunteer courier, or a third-party commercial courier, to collect from and deliver to the addresses notified by the Transplant Centre to Anthony Nolan.
- Anthony Nolan will notify the Transplant Centre of the courier's expected collection and delivery times.

The Transplant Centre must ensure that there is a person waiting at the Transplant Centre's designated collection and delivery addresses to release and receive the product to and from the courier at the specified times.

If the product not infused within 48 hours of receipt, the Transplant Centre must ensure that it complies with all laws and regulations applicable to the storage (and cryopreservation where applicable) of the product (including ensuring its storage facility is appropriately licensed by, and complies at all times with, the requirements of the Human Tissue Authority).

The risk of loss or damage to the product shall only pass to Anthony Nolan when the courier physically collects the product and Anthony Nolan shall have no liability for any loss or damage to the product once the courier has physically delivered the product to the delivery address specified by the Transplant Centre.

The Transplant Centre expressly acknowledges and agrees that Anthony Nolan has no responsibility or liability to the Transplant Centre in connection with the procurement and/or processing of any product or the quality of any product transported under a Transport-only Request. Such products shall not be a considered 'cell products' under these procedures. The sole extent of Anthony Nolan's responsibilities in connection with any Transport-only Requests are the fulfilment of transportation arrangements as set out in this section.

The Transplant Centre shall report any Serious Adverse Events or Serious Adverse Reactions which relate to the transportation of the product to Anthony Nolan in accordance with section 15.1. The Transplant Centre is also responsible for notifying its own UK collection centre of any Serious Adverse Events or Serious Adverse Reactions which relate to the procurement and/or processing of the product and, where required, reporting such incidents to the HTA.

14 RELATED DONORS SERVICE FOR OVERSEAS DONORS

14.1 Related Donor Sample Procurement

If the related donor is residing in a country where Anthony Nolan has (or can put in place) an arrangement with a registry or hospital to arrange these requests, Anthony Nolan can help facilitate the collection of samples from a related donor for the purposes of testing to investigate if the related donor is a suitable match for transplant.

If the Transplant Centre wishes to use this service, they must complete the Related Donor Sample Request for HLA Typing DOC3955 form and send it to the Transplant Centre's designated Anthony Nolan email address.

The Transplant Centre must have first contacted the related donor to confirm that they are willing to provide the samples before requesting this service from Anthony Nolan.

Providing the related donor is willing to donate, Anthony Nolan will arrange for the samples to be collected and shipped to the address indicated on the request form. Once the testing has been completed, the Transplant Centre must notify the related donor of the outcome. The Anthony Nolan Verification Typing Co-ordinator or Search Co-ordinator must also be told of this.

14.2 Related Donor Stem Cell Product Procurement

If a related donor is the best match for the patient, the Transplant Centre can request Anthony Nolan to help facilitate the cell product collection provided the related donor is in a country where Anthony Nolan has (or can put in place) an arrangement with a registry or hospital to arrange these requests. The Transplant Centre must have first contacted the related donor to confirm that they are willing to donate before requesting this service.

The Transplant Centre must complete the Related Donors - Formal Request for Blood Stem Cell Collection DOC3983 form, a formal laboratory HLA typing report for both patient and related donor and, depending on which stem cell source is required (either PBSC or bone marrow) submit this to the work-ups' e-mail address: workups@anthonynolan.org. If verification typing has not been performed at this stage, the Related Donor Sample Request for HLA Typing DOC3955 form must also be submitted to facilitate the sample procurement.

For related donors residing overseas, Anthony Nolan will make all the necessary arrangements for collection of the stem cells as per the applicable procedures set out on this User Guide. Anthony Nolan can only arrange the import of cells where Anthony Nolan is coordinating the collection.

14.3 Postponement and Cancellation of Transplant

The Transplant Centre must immediately notify Anthony Nolan of any postponement or cancellation of a transplant by completing the Postponement/Cancellation DOC2258 form. The Transplant Centre must also notify the related donor of such a change and confirm by email to Anthony Nolan this has been done. DOC2258 must be emailed to the Anthony Nolan Donor Provision team. Without it, the cancellation/postponement request cannot be processed. If a cancellation or postponement requires urgent action by Anthony Nolan and occurs outside office hours, the Transplant Centre must call the Anthony Nolan emergency telephone number.

15 MANDATORY REGULATORY REQUIREMENTS

15.1 Serious Adverse Event/Reaction Reporting

Anthony Nolan's HTA licence obligation is to report all Serious Adverse Events (SAE) and Serious Adverse Reactions (SAR) to the HTA within 24 hours of being notified.

Therefore, Transplant Centres must report all Serious Adverse Events and Serious Adverse Reactions and any other event which has affected the cell product prior to infusion at the Transplant Centre and/or the patient outcome to Anthony Nolan within 24 hours of occurrence by emailing qualityTeam@anthonynolan.org

The report provided must include all the information required by the HTA for the reporting of Serious Adverse Events and Serious Adverse Reactions, as specified on the HTA website:
https://www.hta.gov.uk/policies/human-application-adverse-event-and-reaction-saears-reporting

The information should include:

- date of the adverse event / adverse reaction
- location of the adverse event /adverse reaction
- relevant material affected
- part of process the event was linked to
- suspected cause of event / reaction
- description of event
- action taken to date

The Anthony Nolan Quality team will follow up with the Transplant Centre while preparing the follow up report to the HTA.

15.2 Traceability: Compliance with certain requirements of HTA Directions 001/2021 (asmay be amended or superseded from time to time)

The Transplant Centre will comply with such procedures and supply such information, as Anthony Nolan may from time to time specify to ensure that the traceability requirements of the HTA's Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment (as may be amended or superseded from time to time) are met. In particular, the Transplant Centre will ensure that Anthony Nolan is in possession of all the information listed in numbered paragraph 157 from the HTA Guide which is as follows:

> "157. The minimum information to be provided to the tissue establishments by end users is:
>
> a. identification of the supplier tissue establishment
> b. identification of the clinician or end user/facility
> c. type of tissues and cells
> d. product identification
> e. identification of the recipient
> f. date of application or date of disposal
> g. the SEC (if applicable)."

The Transplant Centre confirms that it maintains traceability information as required by the HTA.

16 CRYOPRESERVATION OF HAEMATOPOIETIC STEMCELLS

16.1 Infusion and Cryopreservation

The Transplant Centre must not store or cryopreserve collected haematopoietic stem cells for more than 48 hours without the prior written agreement of the Anthony Nolan Donor Consultant or their deputy. If it has been agreed that the Transplant Centre can store collected haematopoietic stem cells for more than 48 hours, then this must be done by a storage facility with an appropriate HTA license.

The Transplant Centre must notify Anthony Nolan in writing when the cryopreserved cell product is either infused or discarded. Excess material post-transfusion may be cryopreserved for therapeutic purposes or discarded according to standard protocols without applying to Anthony Nolan for the donor's permission.

The Transplant Centre shall promptly complete and return a Cell Processing Report to Anthony Nolan in respect of each cell product received. This records (amongst other things) the amount of the cell product which is either cryopreserved or discarded.

16.2 Cryopreservation of Lymphocytes

(a) Unless otherwise notified by Anthony Nolan that approval from an International Establishment is required, the Transplant Centre may cryopreserve lymphocytes without the prior approval of Anthony Nolan provided that the first aliquot is infused within 14 days of the lymphocytes being donated, and this date of infusion is stated in the Cell Processing Report referred to in section 16.1 above. However, prior approval is still required for some International Establishments. Where required, Anthony Nolan will contact the International Establishment on the Transplants Centre's behalf upon request.

(b) If the Transplant Centre desires to cryopreserve the lymphocytes for longer than 14 days before administering the first dose, it must notify Anthony Nolan and must also notify Anthony Nolan in writing when the cryopreserved product is either infused or discarded.

The Transplant Centre must report any Serious Adverse Event and/or Serious Adverse Reaction affecting the Cell Product in accordance with the procedures in section 15.1 of this User Guide.

16.3 Cryopreservation of Haematopoietic Stem Cells on Behalf of the Transplant Centre

If the Transplant Centre is unable to cryopreserve the cell product at their establishment, the Transplant Centre can request that Anthony Nolan arranges this on their behalf. This can be requested at any point during the work-up process but at the point of request is preferred, or as early as possible. Once the request has been made, Anthony Nolan will confirm:

- following review of their cryopreservation processes to ensure they meet the UK requirements, if the Collection Centre or international registry arranging collection of the cell product is able to fulfil the request. If there is any shortfall/non-compliance identified, Anthony Nolan will notify the Transplant Centre
- if the Collection Centre or international registry arranging collection of the cell product is unable to fulfil the request, if the Anthony Nolan Cell Therapy Centre is able to fulfil the request (at present the Anthony Nolan Cell Therapy Centre is unable to cryopreserve bone marrow).

In all circumstances, the Transplant Centre will be asked to complete the Cryopreserved Adult Cells TC Questionnaire DOC4986 form and return this before the donor starts their G-CSF injections (for PBSC collections) or travels to attend their bone marrow or lymphocyte collection.

The establishment cryopreserving and storing the cell product shall do this in line with its standard processing procedures.

If cryopreservation is carried out by the Anthony Nolan Cell Therapy Centre, the Anthony Nolan Cell Therapy Centre can store a cryopreserved cell product for a maximum period of 12 months. At the one year anniversary of the initial storage, either arrangements will need to be made between the parties for the transport of the cryopreserved cell product to the Transplant Centre's storage facility of choice or, alternatively, an agreement for long term storage at the Anthony Nolan Cell Therapy Centre will need to be agreed between the parties in writing.

Prior to release, the establishment cryopreserving and storing the cell product shall complete the relevant tests for its release, such as viability tests and microbiology testing, in accordance with its standard processing procedures and will complete a Cryopreserved Cell Product Release DOC4987 form which will be forwarded to the Transplant Centre. This form details the cryopreservation process and provides information with regards to the viability of the cryopreserved cell product. The form requires confirmation of receipt from the Transplant Centre by signing and returning to Anthony Nolan.

The Transplant Centre will then advise of a suitable shipment date and confirm it is happy to proceed by completing the Confirmation of Cryopreserved Cell Product Acceptability DOC4988 form. The Transplant Centre must return a signed copy of the Confirmation of Cryopreserved Cell Product Acceptability DOC4988 form by email to Anthony Nolan

before the cryopreserved cell product can be released and transportation arrangements can be made.

If the Transplant Centre cancels the request for cryopreservation after the cell product has been cryopreserved, but before transportation of the cell product, Anthony Nolan may dispose of the cell product in accordance with Anthony Nolan's standard operating procedures.

16.4 Shipment of Cryopreserved Haematopoietic Stem Cells

Anthony Nolan will arrange the transportation of the cryopreserved cell product from the Anthony Nolan Cell Therapy Centre, UK Collection Centre or the international registry's collection centre, as applicable, to the Transplant Centre using an external courier company with which Anthony Nolan has contracted.

Anthony Nolan will book the courier for the transportation of the cryopreserved cell product to the address stipulated by the Transplant Centre on the initial work-up request form – Formal Request For Blood Stem Cell Collections DOC3842, or the Formal Request for subsequent Blood Stem Cell or Lymphocyte Collection DOC1119 form.

Anthony Nolan will notify the Transplant Centre of the courier details and shall liaise with the courier in order to arrange a delivery date and time. Anthony Nolan will notify the Transplant Centre of the tracking details. The Transplant Centre must ensure that there is a person waiting at the Transplant Centre's designated address to receive the cryopreserved cell product at the stipulated time.

On receipt of the cryoshipper, the Transplant Centre must check the integrity of the cryopreserved Cell Product, including the seals, the data logger and cryoshipper, and complete Reception Form DOC1567 provided by Anthony Nolan and return this completed form to Anthony Nolan by email. The Transplant Centre must notify Anthony Nolan immediately of any irregularity in the cryoshipper by emailing the Donor Provision Co-ordinator responsible for the patient's work-up. Where possible the supply of photographic evidence of the irregularity should be included with the report.

Anthony Nolan will be responsible for making all the arrangements with a courier company to ensure the return of the cryoshipper.
When thawing the cryopreserved cell product, the Transplant Centre must check the seals very carefully and thaw the cryopreserved cell product precisely in accordance with the instructions contained in the shipment packet accompanying the cell product (Recommended Thawing Procedures DOC1570).

For storage of the cryopreserved cell product, the Transplant Centre will need to follow the guidance on the Confirmation of Cryopreserved Cell Product Acceptability DOC4988 form.

The Transplant Centre must have the ability to store the cryopreserved cell product on delivery and prior to transplant. The cell product must be cryopreserved at -150 ºC or below.
If the cryopreserved cell product is not infused within 48 hours of receipt, the Transplant Centre must ensure that it complies with all laws and regulations applicable to the storage of the cryopreserved cell product (including ensuring its storage facility is appropriately licensed by, and complies at all times with, the requirements of the Human Tissue Authority).

16.5 Bespoke Arrangements

If Anthony Nolan and the Transplant Centre have entered into a separate agreement for cryopreservation and storage services to be carried out by the Anthony Nolan Cell Therapy Centre, the terms of such agreement shall apply in place of sections 16.3 and 16.4 above.

17 PROCEDURE AFTER DONATION FOR UNRELATED DONORS

17.1 Post Donation Follow-Up

Anthony Nolan donors are followed up for a period of 10 years post donation. Short term follow-up ensures that donors recover both physically and emotionally from donation, as well as manging any serious adverse events post-donation. Donors can access a specialist counsellor if needed. Long term follow-up monitors the donors' continuing availability for subsequent donations, and the development of long-term health conditions which may impact the patient's health or their ability to remain on the register. All other registries have their own follow-up procedures, according to local regulations and WMDA guidelines.

17.2 Possible Future Donation

Anthony Nolan will ask donors about their willingness to be approached for future donations. Anthony Nolan will notify the Transplant Centre in writing if the donor is not willing to consider any future donation, or if, for any reason, the donor has been removed from the relevant register.

17.3 Updates on Patient's Progress

Each donor is asked following donating if they would like an update on the patient's progress within the first year after donation. Anthony Nolan shall obtain information on UK patients from the BSBMTCT at around six months after donation.

17.4 Donor / Patient Contact

Anthony Nolan's Direct Contact policy states that the identities of both donor and patient must remain confidential for at least two years after the date of the latest transplant, or for at least one year following a DLI donation. During the two-year period, anonymous correspondence (i.e. no identifying information such as names or living/working locations) may be exchanged, and no gifts or photographs are allowed to be exchanged. The correspondence is screened by the Transplant Centre and Anthony Nolan. Anthony Nolan will take advice from the Transplant Centre on the appropriateness of any correspondence to the Transplant Centre's patient. Correspondence for non-Anthony Nolan donors will be sent to the relevant registry to be passed to the donor.

Two years after the transplant, it may be possible for Anthony Nolan to arrange direct contact between the donor and the patient, but only on the instigation of the patient and if the Transplant Centre has not raised any concerns, both parties will need to complete a signed consent form.

Anthony Nolan's policy on direct and indirect contact between the donor and the patient will be discussed directly with the donor as part of the donor's follow-up.

All registries have their own patient/donor contact and anonymity policies which may include life-long anonymity for patients and donors. For non-Anthony Nolan donors, Anthony Nolan will work with Transplant Centre on request to advise the Transplant Centre of the patient/donor contact rules of the applicable UK registry or international registry so that patients can be informed of these for their donor.

Messages or correspondence between patients and donors can take effect after the transplant has taken place. To ensure donor and patient confidentiality, any messages received prior to the transplant will be retained by Anthony Nolan and not forwarded on to the intended patient. If a patient would like to send their donor a message of thanks once the transplant has taken place, these can be handed to their transplant team to send on to Anthony Nolan who will then forward on to the donor directly for Anthony Nolan donors, or to the relevant registry to forward to non-Anthony Nolan donors. Alternatively, the patient can post or email their message directly to Anthony Nolan with a covering letter advising who it is from.

If the family of a deceased patient wishes to contact the donor, then any messages can be passed to the transplant team or sent directly to Anthony Nolan. Direct contact may be allowed on case-by-case basis in these circumstances and should be initially discussed with the Donor Follow-Up Manager.

Correspondence should be mailed to:

Donor Follow-Up Team
Anthony Nolan
2 Heathgate Place
75-87 Agincourt Road
London
NW3 2NU

or sent by email to donor@anthonynolan.org

If a Transplant Centre is aware that a patient wishes to blog or share their experience on social media, then the Transplant Centre should advise the patient to follow Anthony Nolan's guide which can be obtained from the Patient Services team, to ensure the donor remains anonymous. Patients must not post any information about the donor's location, age or gender, and make sure the information label on their stem cell bag is not visible if they post a photograph. In addition, patients must not try to contact the donor directly on social media or share any correspondence with the donor without express permission from Anthony Nolan.

In the case of any queries or possible breaches of confidentiality please contact the Donor Follow-Up Manager.

17.5 Audit of Transplant Centre

The Transplant Centre shall permit Anthony Nolan to carry out such audits as are required to comply with WMDA standards.

17.6 Retention of Records

The Transplant Centre must retain all records associated with the cell product for 30 years from date of clinical use or disposal of the cell product.

18 PATIENT SERVICES

18.1 Accessing Patient information that is Specific to Post Transplant Recovery and Late Effects

All Anthony Nolan patient information is available via the 'Patients and Families' section of the Anthony Nolan website at www.anthonynolan.org/patients-and-families.

- Booklets can be ordered or downloaded at anthonynolan.org/booklets
  - To order, scroll to the bottom of the page, complete the information form and submit.
  - To download, select the publication of choice.
  - To order publications over the telephone, call 0303 3030303.
  - To read Anthony Nolan's wide selection of patient blogs, go to blog.anthonynolan.org
  - To watch Anthony Nolan's patient experience videos, go to anthonynolan.org/patients-and-families/patient-insight-videos
  - To access Anthony Nolan podcasts, go to anthonynolan.org/podcast
  - To download My Transplant Tracker app, go to anthonynolan.org/mytransplanttracker
  - To join the online forum, go to anthonynolan.org/forum

18.2 Accessing the Peer Support Service

- For more information about the peer support service, go to anthonynolan.org/peer_support
- A questionnaire will be sent to the patient prior to being connected to a peer supporter.
- There are a limited number of spaces available for this service at one time. For any questions regarding peer support, email patientinfo@anthonynolan.org or call 0303 3030303.

18.3 Accessing the Vocational Rehabilitation Service

- For more information about support returning to work or to be referred, healthcare professionals and patients/families can email the Patient Services team at patientinfo@anthonynolan.org and a member of the team will be in touch, or call 0303 303 0303
- For more information about Working to Wellbeing, visit the website working2wellbeing.com/

18.4 Accessing the Telephone Emotional Support Service

- For more information about the emotional support service or to be referred, healthcare professionals and patients/families can go to anthonynolan.org/patients-and-families/get-support-us/telephone-emotional-support or email the Patient Services team at patientinfo@anthonynolan.org and a member of the team will be in touch. Alternatively, they can call 0303 303 0303.
- For more information about Working to Wellbeing visit the website working2wellbeing.com/

18.5 Applying for an Anthony Nolan Patient Grant

- Healthcare professionals or patients/families can download and complete a grant

form by going to anthonynolan.org/grant or by emailing patientinfo@anthonynolan.org
- The first half of the application form can be completed by a patient or family member and the back page must be completed by a healthcare professional (i.e. Clinical Nurse Specialist) in order to validate the application.
- The Grants Panel meets every two weeks to discuss grant applications.

18.6 Healthcare Professional Education Days

The Patient Services team run Transplant Healthcare Professional Education Days throughout the year. These are for adult and paediatric services and are Royal College of Nursing Accredited. For more information on dates and locations please email lead.nurse@anthonynolan.org

18.7 Patient and Family Share and Support Days

The Patient Services Team run Share and Support events throughout the year for patients and families going through transplant. These may be virtual or face to face. For more information on dates and locations, please email Clare.McCrudden@anthonynolan.org

18.8 Anthony Nolan Healthcare Professional Funding Programme

Anthony Nolan funds healthcare professionals who work in post-transplant services. Funding is for a period of three years. These roles include Clinical Nurse Specialists (CNS) and Clinical Psychologists. Notification of the opening of applications for a funded post will be emailed to all UK Transplant Centres via the British Society of Blood and Marrow Transplantation and Cellular Therapy (BSBMTCT) at the appropriate time. To express an interest and to find out more, healthcare professionals should email lead.nurse@anthonynolan.org

19 HISTOCOMPATIBILITY SERVICES

19.1 Specialised Histocompatibility Services

Anthony Nolan provides certain specialised histocompatibility services which are in addition to the standard histocompatibility services as part of the donor selection and matching procedures.

These specialised histocompatibility services are described in brief in this section and will be provided by Anthony Nolan if the Transplant Centre has requested these.

19.2 HLA Typing

(a) HLA typing, ABO and Rh D blood group testing and CMV screening on Patients under consideration for a haematopoietic stem cell transplant
(b) HLA typing, ABO and Rh D blood group testing and CMV screening for potential Related Donors for Patients awaiting a haematopoietic stem cell transplant
(c) HLA typing, ABO and Rh D blood group testing, CMV, HIV, Hepatitis B and C testing on blood samples from all requested unrelated Donors selected for Patients
(d) HLA typing to a minimum of intermediate level of resolution for HLA-A, -B, -C, DRB1, DRB3, DRB4, DRB5, DQB1 and DPB1

19.3 Additional Testing

Anthony Nolan shall perform additional testing, which may include typing to high resolution and typing of HLA-DPB1, on patients and probable matching donors as deemed necessary by Anthony Nolan and the Transplant Centre in accordance with The European Federation for Immunogenetics (EFI) Standards.

19.4 Written Report

Anthony Nolan shall prepare a written report of results which show the degree of matching between potential donors and patients and shall send this report by email to the person nominated by the Transplant Centre.

19.5 Storage of Samples

Anthony Nolan shall store samples of blood, DNA and serum derived from blood, according to the relevant guidelines.

20 CORD SUPPORT PROGRAMME

20.1 Cord Support Programme

The Cord Support Programme is a comprehensive suite of optional free services for Transplant Centres including training, additional information and advice, on shortlisting, quality evaluation and handling of Cord Blood Units. The Transplant Centre can customise their request and choose to receive any or all these services free of charge. These services include:

- a Cord Blood Unit shortlisting service. This is a full or an ad-hoc service for Transplant Centres requiring support in making the initial selection of the best possible Cord Blood Units. Cord Blood Unit search results will be accompanied by a table of the 5-10 best Cord Blood Units for the Patient based on BSBMTCT recommendations (2015)
- a Cord Blood Unit report checklist service. This is a full or an ad-hoc service for Transplant Centres requiring support in evaluating Cord Blood Unit reports. A comprehensive checklist to highlight any potential quality issues or missing information for Cord Blood Units based on FACT standards will be provided to accompany any requested Cord Blood Unit reports
- provision of briefs on Cord Blood Bank (CBB) operational specifics to accompany Cord Blood Unit reports. These information documents provide extensive information on the operational processes and protocols of different CBBs worldwide
- consultancy services. This is an ad-hoc Cord Blood Unit advice service for all Transplant Centres. A dedicated mailbox cordsupport@anthonynolan.org
- is available for all customer queries related to Cord Blood Units
- access to a Cord Blood Unit quality enquiries phone line (managed by CBB expert) for urgent queries
- a regular Cord Blood Unit service update for Transplant Centres with news on Cord Blood Unit related topics, references to new papers, feedback from related conferences and other useful information
- education sessions which are specifically targeted to Transplant Centres based on their needs with the choice of 'in-house' or roadshow type events. These can cover any aspect of Cord Blood Unit acquisition including selection, quality evaluation and provision

- on-site training sessions for Transplant Centres on thawing, infusion and troubleshooting with common Cord Blood Unit thawing problems and infusion issues including damaged Cord Blood Units

21 ANTHONY NOLAN'S ACCREDITATIONAND REGULATION

21.1 Companies House

Anthony Nolan is registered as a company limited by guarantee in England and Wales, registration number 2379280 with its registered office at:

Royal Free Hospital
Pond Street
London NW3 2QG

21.2 Charity Commission and Office of the Scottish Charity Regulator

Anthony Nolan is registered as a charity with the Charity Commission in England and Wales, registration number 803716 and with the Office of the Scottish Charity Regulator in Scotland, registration number SCO 38827.

21.3 Care Quality Commission (CQC)

Anthony Nolan is registered with the Care Quality Commission Provider ID: 1-240372502

21.4 WMDA

Anthony Nolan is accredited by the World Marrow Donor Association ("WMDA") in the following categories:

- General Organisation of Registry
- Donor Recruitment
- Donor Characterisation
- Information Technology
- Facilitation of search requests
- Second/subsequent donations
- Collection/processing/transport of stem cells
- Follow up of Patient/Donor
- Financial/legal liabilities

Anthony Nolan complies with WMDA International Standards for Unrelated Hematopoietic Cell Donor Registries which can be found on the WMDA website: https://wmda.info/professionals/quality-and-accreditation/wmda-standards/.
For clarity, these standards also apply to related donors.

21.5 HTA

Anthony Nolan holds the following HTA licences:

- Licence 22513 permits the Anthony Nolan Registry to carry out the procurement, distribution and/or import/export of tissues and/or cells intended for human application.
- Licence 22527 permits the Anthony Nolan Cord Blood Bank to carry out the procurement, processing, testing, distribution and storage of cells intended for human application.

21.6 National Ethical Approval

The Anthony Nolan Cord Blood Bank holds National Ethical Approval to act as a research tissue bank.

21.7 FACT- NetCord Accreditation

The Anthony Nolan Cord Blood Bank has FACT-NetCord Accreditation.

21.8 UKAS and the European Federation for Immunogenetics

The Anthony Nolan Histocompatibility Laboratories are accredited to ISO 15189:2012 - Medical Laboratories (ref 8630) by the United Kingdom Accreditation Service (UKAS); and by the European Federation for Immunogenetics (EFI) (ref 03-GB-005-995).

22 RESEARCH

22.1 Research Requests by a Transplant Centre

The Transplant Centre may request that donors are invited to consent to being involved in a research programme, project or study. An application must be submitted by the study sponsor or chief investigator of the Transplant Centre to involve Anthony Nolan donors in any and all research programmes, projects or studies to researchstudies@anthonynolan.org for attention of the AN Clinical Trials Supervisor. Such an application must consist of:

- the Donor Research Study Application DOC3323 form
- evidence of relevant institutional review board approval
- a statement detailing how any costs incurred by Anthony Nolan as a result of the donor participating in the study will be reimbursed, e.g. additional blood draws, donor travel expenses and loss of earnings
- the Research Protocol
- donor / participant information sheet and
- the donor's consent form.

Anthony Nolan will then consider the request in respect of an Anthony Nolan donor. All research studies involving Anthony Nolan donors will require the approval of the Anthony Nolan medical affairs committee.

In the case of an NHSBT donor, Anthony Nolan will forward all the study documents on to NHSBT for its review and consideration. Anthony Nolan will inform the requester of the decision with regards to participation of NHSBT's donors as soon as a decision has been made. Any issues raised by NHSBT regarding their donors' participation in the study must

be resolved directly with NHSBT by the requester.
Donors from NHSBT have their stem cell collection process managed by Anthony Nolan and can only be approached for their consent once NHSBT has approved the study.

In the case of a WBMDR or DKMS UK donor, the WBMDR or DKMS UK will need to be contacted separately by the study sponsor or chief investigator of the Transplant Centre regarding approval for its donor's participation.

Donors from International Registries are not managed by Anthony Nolan. Therefore, each international registry will need to be contacted separately by the study sponsor or chief investigator of the Transplant Centre regarding approval for their donors' participation. Anthony Nolan will forward such applications to international registries on behalf of the study sponsor or chief investigator of the Transplant Centre. Country specific regulations and consent processes may also need to be taken into consideration. Correspondence will then be directly between the study sponsor or chief investigator of the Transplant Centre and the international registry. Once approval from the international registry has been received by the study sponsor or chief investigator of the Transplant Centre, such approval must be forwarded by the study sponsor or chief investigator of the Transplant Centre to Anthony Nolan.

22.2 Use of Donor Cells for Generic Research

Anthony Nolan donors, and any donors from NHSBT who have their stem cell collection process managed by Anthony Nolan, are asked if they will agree to any surplus tissue/ DNA from their collection being used anonymously for future medical research projects. These donors are informed that any medical research project would have to be approved by a properly constituted research ethics committee and undertaken in accordance with appropriate ethical, legal and professional standards and that they will not benefit financially from any research undertaken and waive all rights to any registered patents. The Transplant Centre will be informed whether or not the donor agrees to this.

23 CHARGES AND FINANCE

23.1 Charges Payable by the Transplant Centre to Anthony Nolan

The Transplant Centre must pay Anthony Nolan the charges set out in the relevant fee schedule in force at the time of invoicing, together with VAT at the prevailing rate.

23.2 Cancellation and Postponement Charges

The charges referred to above, include, without limitation, the following:

Postponement Charge
A postponement charge may be charged each time a scheduled transplant date is changed to cover postponement of appointments and further administration.

Cancellation Charge
A collection charge may be charged to cover activities undertaken before a request is cancelled. If tests are underway at the time of cancellation, the Transplant Centre may be charged the normal rate provided the results are reported within a month by Anthony Nolan.

Cancellation Prior to Donor Medical
If a transplant is cancelled after Anthony Nolan has received a request for a donor work-up but before the donor medical examination has taken place, Anthony Nolan may only apply an administrative charge.

Cancellation after the Donor Medical
If a transplant is cancelled after the donor has undergone the medical examination, Anthony Nolan may charge the full cancellation charge.

Additional Charge for G-CSF
An additional charge will be made for G-CSF if the drug has already been prescribed and issued to a donor who would have undergone a haematopoietic stem cell collection.

Cancellation of Cryopreservation Services
If a request for cryopreservation is cancelled before the cryopreservation has been carried out, a cancellation charge may be charged to cover activities undertaken before the request was cancelled. If a request for cryopreservation is cancelled after the cryopreservation has been carried out, including if the transplant is cancelled, Anthony Nolan may charge the full amount for the services.

23.3 International Charges

International charges vary. See the relevant fee schedule.

24 COMPLAINTS

24.1 Complaints Procedure

Comments on the services provided by the Operations and Patient Services are welcome and help us to improve. Please send details in an email to the Quality Team: QualityTeam@anthonynolan.org

If you wish to make a formal complaint regarding the services provided by the Operations and Patient Services, or to report a Serious Adverse Event or Reaction (SAE/SAR), please send details in an email to the Quality Team: QualityTeam@anthonynolan.org

25 ANTHONY NOLAN DETAILS

Staff List
For full list of staff, please refer to the Anthony Nolan website, www.anthonynolan.org

Address for Notices
For the attention of the Chief Operating Officer
Anthony Nolan
2 Heathgate Place
75-87 Agincourt Road
London
NW3 2NU

Operations and Patient Services Emergency Telephone number	**07710 599 161**
Operations and Patient Services Administration Fax number	**020 7284 8226**

Anthony Nolan Donor Recruitment Team
Healthcare professionals wishing to raise an appeal for a patient should contact this team on 0207 284 1234 or by emailing info@anthonynolan.org

26 LIST OF FORMS

The following is a list of the forms referred to in this User Guide.

FORM	TITLE	DESCRIPTION
DOC1119	Formal Request for Subsequent HPC or Lymphocyte (DLC) Collection	The Transplant Centre will send this to Anthony Nolan when requesting a subsequent donation
DOC1126	Formal request for Cord Blood Unit from TC	
DOC1128	Confirmation of Acceptability of Cord Blood Unit	The Transplant Centre or International Establishment must complete this form before shipment of a cord blood unit
DOC1139	Confirmation of Receipt and Infusion of Cord Blood Unit	
DOC1567	Reception Form	
DOC1570	Recommended Thawing Procedures	
DOC1671	Verification Typing Request Form	The Transplant Centre or International Establishment must complete this to request a sample to be tested in the Transplant Centre or International Establishment's designated laboratory
DOC1672	Extended Typing Request Form	The Transplant Centre or International Establishment must complete this form if it requires Anthony Nolan to perform extended typing
DOC1685	Preliminary Search Request Form	If HLA typing of the patient is carried out at a laboratory other than the AN H&I Laboratories, the Transplant Centre must complete a search request form
DOC2258	Cancellation or Postponement form	Postponement or cancellation of donation form
DOC2857	HLA Histocompatibility Testing Request form	
DOC3092	External Registry Virology Checklist - HPC	

DOC3323	Donor Research Study Application form	For use to involve donors in all research programmes, projects or studies
DOC3842	Formal Request for Blood Stem Cell Collections including BM & PBSC Prescription forms	
DOC3983	Related Donors - Formal Request for Blood Stem Cell Collection	Transplant Centre or International Establishment to use this form if requesting a related donor for work-up
DOC3955	Related Donor Sample Request for HLA Typing	
DOC4132	Related Donors - Formal Request for Subsequent Donation	
DOC4256	Work-up schedule template - UK Donor	
DOC4986	Cryopreserved Adult Cells TC Questionnaire	
DOC4987	Cryopreserved Cell Product Release Form	
DOC4988	Confirmation of Cryopreserved Cell Product Acceptability	
DOC5173	External Registry Virology Checklist – DLC	
FOO 235	NMDP Prescription for MNC, Apheresis	

NOTE: The Anthony Nolan **Laboratories' User Guide** can be found on the Anthony Nolan website.

DEFINITIONS

In this User Guide the following terms have the meanings set below them.

Anthony Nolan and NHS Stem Cell Register
A database containing details of donors on all UK registers. This database consists of Anthony Nolan Donors, NHSBT donors, WBMDR donors and DKMS UK donors. This register is managed by Anthony Nolan.

Anthony Nolan and NHS Stem Cell Registry
A registry which holds the Anthony Nolan and NHS Stem Cell Register. This registry is managed by Anthony Nolan and is informally referred to as the 'aligned registry'.

Anthony Nolan Cord Blood Bank
The Anthony Nolan Cell Therapy Centre situated at Nottingham Trent University, Clifton Campus, Nottingham NG11 8NS, which holds a bank of Cord Blood Units managed by Anthony Nolan.

Anthony Nolan donor
A donor listed on the Anthony Nolan Register. Anthony Nolan donors are also listed on the Anthony Nolan and NHS Stem Cell Register.

Anthony Nolan laboratories
The Anthony Nolan Histocompatibility Laboratories situated at 77B Fleet Road, Hampstead, London NW3 2QG.

Anthony Nolan Register
A searchable register of both cord blood units and volunteers, recruited by Anthony Nolan, who are willing to donate haematopoietic stem cells or lymphocytes. This register is managed by Anthony Nolan.

BSBMTCT
British Society of Blood and Marrow Transplantation and Cellular Therapy.

Business day
A day other than a Saturday, Sunday or a public holiday in England and Wales.

Cell product
Haematopoietic stem cells or other lymphocytes and/or, where applicable, a Cord Blood Unit(s).

Collection Centre
A hospital at which the cell product is collected, which is appropriately accredited and/or licensed or otherwise acceptable to Anthony Nolan and which operates in accordance with the Human Tissue Authority's Code of Practice G 'Donation of Allogeneic Bone Marrow and Peripheral Blood Stem Cells for Transplantation'.

Cord Blood Bank
A bank of Cord Blood Units situated in the UK or abroad.

Cord Blood Unit(s)
A processed unit of umbilical cord blood.

Cord Support Programme
Optional services provided by Anthony Nolan, including short listing and quality evaluation of cord blood units.

DKMS UK donor
Donors on a database managed by DKMS UK, which is the working name of the UK charity DKMS Bone Marrow Donor Centre. DKMS UK Donors are also listed on the Anthony Nolan and NHS Stem Cell Register.

DLI
Donor lymphocyte infusion.

Donor
A volunteer or a relative of the patient who is over the age of 16 and who is a suitable HLA match willing to donate haematopoietic stem cells or lymphocytes. Unless the context otherwise requires, 'donor' shall include donors listed on the Anthony Nolan and NHS Stem Cell Register, and international donors.

EBMT
European Society for Blood and Marrow Transplantation.

EMDIS
European Marrow Donor Information System.

FACT
Foundation for the Accreditation of Cellular Therapy.

Fee schedule
The Schedule of Charges provided by Anthony Nolan to the relevant Transplant Centre or International Establishment, as such schedule may be amended from time to time.

GIAS
Graft Identification Advisory Service.

Gift of Life
The Gift of Life Bone Marrow Foundation which is a US donor programme.

G-C SF
Granulocyte colony stimulating factor.

HLA
Human leukocyte antigen molecules which have to be matched between donor and patient. These molecules exist in many similar but different forms.

HTA
The Human Tissue Authority.

International Cord Blood Bank
A bank of Cord Blood Unit(s) located outside the UK.

International Cord Blood Unit(s)
A Cord Blood Unit(s) which is held by an international cord blood bank.

International donor
A donor on a register held by an International Establishment.

International Establishment
- An international registry, or
- A hospital, situated outside the UK, which is seeking to perform transplantation of haematopoietic stem cells or lymphocytes for patients with various malignant and non-malignant conditions and is
  - accredited by EBMT or
  - listed as an International or US NMDP Transplant Centre, or which has provided Anthony Nolan with information regarding its clinical activity and has been approved by the Anthony Nolan medical director.

International registry
A registry situated outside the UK which holds a register of international donors.

ISCT
International Society for Cellular Therapy.

JACIE
Joint Accreditation Committee - ISCT & EBMT.

Laboratory
A laboratory which is (i) licensed under the HTA or is the subject of a Third-Party Agreement made pursuant to regulations under the Human Tissue Act 2004; or (ii) is otherwise acceptable to Anthony Nolan. ("Third Party Agreement" is defined in the regulations.)

Lymphocytes
A type of white blood cell. A subset called T cells is used in Donor Lymphocyte Infusion. Lymphocytes are vital components of the body's immune system - the defence against invading organisms.

MDT
Multi-disciplinary Team Meeting.

NHSBT
National Health Service Blood and Transplant.

NHS Cord Blood Bank
A bank of Cord Blood Units managed by the NHS. Searches of this NHS Cord Blood Bank on behalf of UK patients are handled by Anthony Nolan. Searches requested by international registries on behalf of overseas patients are managed by NHSBT.

NHSBT Database
A searchable register of volunteers who are willing to donate haematopoietic stem cells or lymphocytes. Searches of this NHSBT Database on behalf of UK patients are managed by Anthony Nolan. Searches on behalf of overseas patients are managed by NHSBT.

NHSBT donor
A donor listed on the NHSBT Database.
NHSBT donors are also listed on the Anthony Nolan and NHS Stem Cell Register.

Non-Anthony Nolan donor
A donor that is not an Anthony Nolan donor.

NMDP
The National Marrow Donor Program, which is a US donor programme.

Patient
The person intended to receive the donation of the cell product.

PBSC
Peripheral blood stem cells.

Promise
A UK database of the patients who have undergone a haematopoietic stem cell transplant.

Related donor
A biological relative of the patient who is a suitable HLA match for a stem cell donation who may reside in the United Kingdom and who is over the age of 16 years, or who may reside in the United States of America or any other country outside the United Kingdom, provided Anthony Nolan has (or can put in place) an arrangement with a registry or hospital in the applicable country to facilitate such requests, and who is over the age of 16 years.

Serious Adverse Event
Any untoward occurrence which may be associated with the procurement, testing, processing, storage or distribution of tissue or cells intended for human application and which, in relation to a donor of tissue or cells intended for human application, or a recipient of tissue or cells:

(a) might lead to the transmission of a communicable disease, to death or life-threatening, disabling or incapacitating conditions, or

(b) might result in, or prolong, hospitalisation or morbidity.

Serious Adverse Reaction
An unintended response, including a communicable disease, in a donor of tissue or cells intended for human application or a recipient of tissue or cells, which may be associated with the procurement or human application of tissue or cells and which is fatal, life-threatening, disabling, incapacitating or which results in, or prolongs, hospitalisation or morbidity.

Service Level Agreement
An agreement between two parties both of which are licensed by the Human Tissue Authority.

Transplant Centre
A hospital in the UK which carries out transplantation of haematopoietic stem cells or lymphocytes for patients with various malignant and non-malignant conditions. The hospital must have been approved by the Anthony Nolan medical director.

WBMDR
Welsh Bone Marrow Donor Registry which is a searchable register of volunteers who are willing to donate haematopoietic stem cells or lymphocytes. It is managed by the Welsh Blood Service.

WBMDR donor
A donor listed on the Welsh Bone Marrow Donor Registry. Welsh Bone Marrow donors are also listed on The Anthony Nolan and NHS Stem Cell Register.

Welsh Blood Service
The division of Velindre NHS Trust which has legal responsibility for the Welsh Bone Marrow Donor Registry.

WMDA
World Marrow Donor Association.

WMDA Search and Match Service
The searchable online global database for adult unrelated donors and cord blood units.

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London NW3 2NU

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0303 303 0303
@anthonynolan
anthonynolan

Anthony Nolan is a registered charity no 803716/SC038827 and registered as a limited company no 2379280 in England and Wales. Registered address: Royal Free Hospital, Pond Street, London NW3 2QG.

FRSB FundRaising Standards Board

WMDA Accredited

OPERATIONS AND PATIENT SERVICES

USER GUIDE

PART 2
INTERNATIONAL

ANTHONY NOLAN

saving the lives of people with blood cancer

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DEFINITIONS

1 INTRODUCTION

1.1 Introduction

Anthony Nolan is a charity which saves the lives of people with blood cancer and other blood disorders who need a blood stem cell transplant.

More information about the work and history of Anthony Nolan can be found on the website http://www.anthonynolan.org

The services provided by Anthony Nolan are set out in more detail in this User Guide.

Anthony Nolan complies with the WMDA International Standards for Unrelated Hematopoietic Stem Cell Donor Registries which can be found on the WMDA website (https://wmda.info/). For clarity these also apply to donations by related donors.

1.2 User Guide

This Operations and Patient Services User Guide sets out the procedures to be followed by International Establishments using Anthony Nolan's services.

This User Guide and the signed service level agreement together form the contract between Anthony Nolan and the International Establishment.

This document may be amended by Anthony Nolan from time to time to take account of changes in medical practice, applicable laws or regulations or operational or administrative procedures. Except as set out below, the International Establishments shall be bound to comply with such change(s) from the date of notification provided by Anthony Nolan.

Anthony Nolan will give the International Establishments twenty (20) Business Days' notice by email of any proposed material change to this User Guide and if the International Establishment does not object within such notice period, such change(s) shall be deemed to be agreed by the parties.

1.3 Services Provided by Anthony Nolan

Anthony Nolan:

- recruits potential Donors of haematopoietic progenitor cells to the Anthony Nolan Register
- manages the Anthony Nolan Register
- facilitates the procurement and distribution of haematopoietic cells and Lymphocytes
- maintains a bank of Cord Blood Units and a cord blood inventory
- liaises with Transplant Centres, International Establishments and Cord Blood Banks
- provides laboratory testing and histocompatibility services
- undertakes research
- provides cryopreservation services of adult stem cell materials
- provides Related Donor sample procurement and procurement and distribution of haematopoietic progenitor cells and Lymphocytes from Related Donors.

1.4 Anthony Nolan's Operations and Patient Services Division

The Operations and Patient Services Division of Anthony Nolan is made up of several sections, including Donor Services and Transplantation Services. Donor & Transplantation Services co-ordinates the collection and delivery of blood samples and oversees the provision of haematopoietic progenitor cells and lymphocytes.

1.5 Search and Selection

Search and Selection Co-ordinators within the Anthony Nolan Search team run computerised searches of UK and International Donor Registries and Cord Blood Banks to identify suitable unrelated donors and/or Cord Blood Units for a patient.

1.6 Verification and Extended HLA Typing

The Anthony Nolan Search and Selection Co-ordinators and Donor Liaison team arrange for the collection and shipment of blood or saliva samples for the verification and/or extended HLA typing of Anthony Nolan Donors and Cord Blood Units.

Typing is carried out either at the Anthony Nolan Laboratories or at the laboratory nominated by the International Establishment.

1.7 Donor Provision and Donor Follow-Up Teams

The Anthony Nolan Donor Provision Team is responsible for the work-up of Anthony Nolan Donors and Cord Blood Units. Working alongside the Anthony Nolan medical team, the physical and emotional well-being of Anthony Nolan Donors is managed prior to and during donation by the Donor Provision team and post donation by the Anthony Nolan Donor Follow Up team.

2 THE SEARCH PROCESS

2.1 Patients for Whom a Search Is Requested

Each patient for whom a search is requested must be recommended by a physician for a stem cell transplant and must satisfy Anthony Nolan's requirements regarding diagnosis, age and any other factors which Anthony Nolan may, in its discretion, consider relevant.

When considering the diagnosis of a patient, Anthony Nolan will use the recommendations set out in the latest BSBMTCT indications table.

http://bsbmtct.org/indications-table/

If the indication for which the International Establishment is requesting a donor is not a standard indication, Anthony Nolan may request further clinical information from the International Establishment.

The International Establishment's physicians may exercise their discretion about whether a patient is of a suitable age for a stem cell transplant, provided that such physicians follow the relevant national and international standards and ethically approved protocols.

The International Establishment must refer any unusual request to Anthony Nolan and must provide a brief clinical history of the patient with a copy of any supporting information, e.g. relevant publications or consensus expert opinions.

The International Establishment may specify whether it requires PBSC or bone marrow derived stem cells, or a Cord Blood Unit(s).

2.2 Procedure for an International Establishment to Request a Search for a Donor and/or Cord Blood Unit(s)

An International Establishment may request a search using the European Marrow Donor Information System (EMDIS). If EMDIS is not used, users may email or fax a search request form – DOC1685 – to Anthony Nolan or send a similar form which contains the information set out in section 2.3 below and as set out in the WMDA standards.

2.3 Information to be Contained in an EMDIS or Email/Fax Search Request from an International Establishment

All the following information must be contained in an EMDIS or email/fax search request from an International Establishment:

- Patient's name.
- Patient's gender.
- Patient's date of birth.
- Patient's ethnicity (if available).
- Diagnosis and current status of patient.
- HLA typing of patient (minimum HLA-A, - B and -DRB1).
- Registry reference.
- Invoice address.

If a Cord Blood Unit(s) search is required, the request must also state the patient's weight.

2.4 Checking of Data on Search Requests

Anthony Nolan will check all search requests to ensure that appropriate and adequate data is given before the search is initiated. If any information is illegible or missing, Anthony Nolan will ask the International Establishment to resubmit the request including this information.

2.5 Search of the Anthony Nolan Register and the Anthony Nolan Cord Blood Bank atthe Request of an International Establishment

At the request of an International Establishment, Anthony Nolan will search only the Anthony Nolan Register for a match for an overseas patient. Anthony Nolan will not search the Anthony Nolan and NHS Stem Cell Registry for details of NHSBT donors, WBMDR donors or DKMS UK donors. The reason for this is that NHSBT, WBMDR and DKMS UK each retains control over its own international sales.

Anthony Nolan will also perform a Cord Blood Unit(s) search of the Anthony Nolan Cord Blood Bank if the International Establishment specifically requests this. Anthony Nolan will not search the NHS Cord Blood Bank.

Search results requested via EMDIS will be returned to the International Establishment via EMDIS to be viewed in their own system.

For non-EMDIS users, Anthony Nolan will send the International Establishment a search report, consisting of the Anthony Nolan Donor listings and details of Cord Blood Unit(s) from the Anthony Nolan Cord Blood Bank, within approximately two business days of receipt of the search request.

2.6 Repeating Searches

At the request of an International Establishment, Anthony Nolan shall re-run a search for the same patient after an interval of three months, or a shorter period, which may, in exceptional circumstances, be agreed by Anthony Nolan. If the International Establishment requires further repeat searches (in addition to the initial repeat search referred to above), International Establishment must submit a new repeat search request.

2.7 Cancellation of Search

To cancel a search, the International Establishment shall email Anthony Nolan with details of, and the reason for, the cancellation.

2.8 All Communications between Anthony Nolan and the International Establishment

In compliance with HTA and WMDA requirements and standards, and to ensure traceability and accuracy of information, all communications relating to the services provided by Anthony Nolan concerning the patients, donors and Cord Blood Units must only be channelled through Anthony Nolan.

For changes in staffing, the International Establishment must notify Anthony Nolan immediately of the departure of any senior member of staff, including, but not limited to, the Transplant Director, whose absence may adversely affect the running of the programme, and advise of their replacement, whether interim or permanent.

2.9 Communication

Communications regarding search reports shall be by encrypted mail message or other secure means.

3 MATCHING OF PATIENTS AND DONORS

3.1 Matching Programme - Anthony Nolan Laboratories

The matching programme developed by Anthony Nolan includes the HLA–A, -B, -C, -DRB1 and -DQB1 molecular typing data in the sorting algorithm. Where ambiguities exist, resulting in intermediate resolution results, the allele codes developed by the National Marrow Donor Program, USA are utilised to enter data onto the computer (http://bioinformatics.nmdp.org/).

If Anthony Nolan deems this appropriate, Anthony Nolan will extend searches to look for donors with a single mismatch at the HLA-A, -B, -C, -DRB1 or –DQB1 locus.

The standard format for listing donors is younger before older, within the resolution of the donor HLA typing.

Additional information used for matching donors includes ABO and RhD blood group, cytomegalovirus (CMV) status, ethnic group and weight. Most of these factors may be applied as optional filters to reduce a long list of matching donors, e.g. a list of CMV negative matching donors only may be requested.

The status of the donor will be clearly indicated on the UK search report. This will highlight any matched donors who are temporarily unavailable, in test for another patient, reserved for another patient or whom have already previously donated.

The higher the HLA typing resolution provided on the patient, the more informative a donor listing will be.

3.2 Advice and Responsibility

Anthony Nolan can provide advice on matching donors and patients. The final decision, however, on donor suitability is always the responsibility of the International Establishment.

4 VERIFICATION TYPING

4.1 Potential Donor Matches – Verification Typing

On identifying potential donor matches to the patient, further verification testing by a laboratory is necessary to ensure that the donor's initial HLA-typing results and level of matching with the patient are correct and still fulfil the medical requirements for donation.

The International Establishment can submit a verification typing request by EMDIS, or the International Establishment can request verification typing by sending the **Verification Typing Sample Request form DOC1671** by email to **VTTeam@anthonynolan.org**

If an Anthony Nolan donor is selected, and a fresh blood sample is needed, Anthony Nolan will discuss donation procedures, health, and availability with the Anthony Nolan donor.

Anthony Nolan will inform the International Establishment if Anthony Nolan has been unable to contact the donor and shall request new instructions before proceeding further and as set out in section 4.3 - Procedure if Anthony Nolan Donor Unavailable.

Once arrangements have been made, Anthony Nolan will notify the International Establishment of when to expect the blood sample from the donor, together with details of donor availability, medical issues which could affect the donation, and the donor's preference of method of donating the stem cells, if known.

4.2 Potential Donor Matches – Extended Typing

If the International Establishment requests extended typing of an Anthony Nolan donor, the International Establishment may submit an extended typing request by EMDIS, or the International Establishment can request extended typing by sending the **Extended Typing Request Form DOC1672** by email to **VTTeam@anthonynolan.org**

Extended typing may be performed on a stored DNA sample, if such sample is available.

If the extended typing of an Anthony Nolan donor is to be performed on stored material, Anthony Nolan will contact the donor to discuss the proposed typing, donation procedures, health, and availability. Anthony Nolan will inform the International Establishment if Anthony Nolan has been unable to contact the donor and shall request new instructions before proceeding further and as set out in section 4.3 - Procedure if Anthony Nolan Donor Unavailable.

4.3 Procedure if Anthony Nolan Donor Unavailable

If an Anthony Nolan Donor does not respond within seven (7) calendar days, Anthony Nolan will contact the International Establishment to establish whether to continue with the request. The International Establishment will be required to confirm its decision by email.

The request will expire should an Anthony Nolan donor still not have contacted Anthony Nolan within 28 days from the original request. Anthony Nolan will contact the International Establishment to establish whether to continue with the request.

- If the International Establishment wishes to continue, email confirmation will be accepted.

- If the International Establishment wishes to cancel, email confirmation will be required to confirm formal cancellation of the request.

4.4 Cancellation of Typing or Blood Sample Procurement

An International Establishment may cancel requests for further typing, or for blood sample procurement or blood sample shipment, at any time.

Anthony Nolan requires at least two business days' notice to allow time for the donor to be contacted and the procurement of the blood sample from the donor to be cancelled.

If notice of cancellation is received by Anthony Nolan when the typing, sample procurement or sample shipment has begun, the International Establishment shall still be required to pay the full charge for such typing or sample.

4.5 Virology Screening for Donors

If an Anthony Nolan donor who has been selected for verification typing has not been tested for virology within the last three months, Anthony Nolan will perform virology screening (Hep B, Hep C, HIV, CMV and blood grouping) on newly obtained (fresh) blood samples.

4.6 Typing Results

For typing performed in Anthony Nolan laboratories**,** Anthony Nolan will send the typing results by EMDIS (if applicable) or email the tissue typing report to the International Establishment approximately seven business days after Anthony Nolan receives the blood sample.

For verification typing performed in the International Establishment's designated laboratories, the International Establishment must send the donor typing results to Anthony Nolan as soon as possible, by EMDIS or email, indicating whether the donor should be released or reserved.

4.7 Release of Donors

If the International Establishment does not instruct Anthony Nolan to reserve a donor, Anthony Nolan will hold the donor for 60 days after the date on which the verification typing samples were shipped and then release the donor.

4.8 Concurrent Verification Typing Sample and Work-up Request for an Anthony NolanDonor

International Establishments can request concurrent verification typing/work-ups for urgent patient cases where there is insufficient time to perform the verification typing of the donor separately to work-up. Anthony Nolan will process concurrent verification typing/work-ups for Anthony Nolan donors who have not yet been typed in the laboratory associated with the patient's transplant centre. In such cases, the International Establishment must provide high resolution verification typing results of the donor to Anthony Nolan prior to the patient starting conditioning, or before the donor begins G-SCF, whichever happens first, along with a written statement confirming that they have reviewed the verification typing results of the donor and wish to proceed with the work-up.

4.9 Reporting of Discrepancies in HLA Typing Results

The International Establishment must report all discrepancies in HLA typing results to Anthony Nolan as soon as possible.

5 FACILITATING A WORK-UP OF PBSC OR BONE MARROW FROM AN ANTHONY NOLAN DONOR

5.1 Requesting a work-up of an Anthony Nolan Donor for a PBSC or Bone Marrow Collection

An International Establishment which requires PBSC or bone marrow from a donor on the Anthony Nolan Register must send Anthony Nolan a Formal Request for Blood Stem Cell Collection (First Transplants Only) DOC3842 form, and a formal laboratory HLA typing report for both patient and donor, or their local version of this form.

The International Establishment must complete each section of the form. Any gaps may delay processing the request.

When completing the Formal Request for Blood Stem Cell Collection (First Transplants Only) DOC3842, the International Establishment should insert '1' next to the preferred stem cell source, and '2' if the other stem cell source will also definitely be accepted. The International Establishment should insert '0' if the other source is not an option (i.e. the International Establishment will prefer to use another donor if the selected donor will not donate via option 1, the preferred stem cell source).

Unless otherwise instructed by the International Establishment on the relevant prescription form:

- PBSC collections will be diluted with autologous plasma to get an approximate final concentration of less than 200x106ml TNC (Total Nucleated Cell)
- Bone marrow will be diluted with ACD (acid-citrate-dextrose) at a dilution of 1:7 vol ACD/vol BM (bone marrow).

If the International Establishment requires different dilutions, the International Establishment must specify this on the relevant prescription form.

Anthony Nolan will test for the following infectious disease markers as part of the donor's medical: anti-HIV1, anti-HIV2, p24 antigen, anti-HTLV 1 and 2, HIV-RNA, anti-HBc, HBsAg, HBV-DNA, anti-HCV, HCV-RNA, HEV RNA, anti-CMV IgG and IgM, anti-toxoplasmosis IgG and IgM, Treponema Palladium serology, VZV IgG, EBV (anti-VCA IgG and IgM).

If any additional tests are required at the point of work-up, the International Establishment will need to contact their co-ordinator requesting additional pre-collection blood samples from the donor.

5.2 Confirmation and Checking of Work-Up Request

Anthony Nolan will confirm receipt of each work-up request by email to the International Establishment within one business day.

Anthony Nolan will check all work-up requests for an Anthony Nolan donor to ensure that the appropriate (HLA matched) donor has been selected for the patient. This will be done by verifying initial donor eligibility based on HLA requirements, age, previous medical and social history, and information provided by the donor. Anthony Nolan will also check that the patient's criteria (age, diagnosis, disease status) and transplant protocol comply with Anthony Nolan's standards.

Anthony Nolan will notify the International Establishment, by email, of the name of the Donor Provision Coordinator responsible for the patient's work-up request.

5.3 Anthony Nolan's Contact with the Donor

Anthony Nolan will notify the donor by telephone immediately.

Anthony Nolan shall check with the selected donor that they are still willing to proceed and are available on the dates requested by the International Establishment.

5.4 Procedure if Donor is Unavailable

If the donor does not respond to the various forms of communication within a period of 48 hours, Anthony Nolan will inform the International Establishment of the potential delay.

If the donor is not available on the requested dates, this information, with alternative dates proposed by the donor, will immediately be relayed to the International Establishment.

5.5 Preferred Method of Donation

Anthony Nolan will make the donor fully aware of the options regarding the two methods of haematopoietic progenitor cell (HPC) donation, PBSC and bone marrow. Anthony Nolan will tell the donor the International Establishment's preferred method of donation, but Anthony Nolan will not at any point put pressure on the donor to select the preferred method.

If the donor's chosen method of donation is not the International Establishment's preferred option, Anthony Nolan will notify the International Establishment accordingly to find out whether this is an acceptable option for the International Establishment, and whether or not it is still willing to proceed with the donor. If confirmed by the International Establishment, Anthony Nolan will then proceed with making the arrangements for donation. If the donor's chosen method of donation is not an option for the International Establishment, Anthony Nolan will not persuade or pressure the donor into changing their mind.

5.6 Booking the Medical, Counselling, Consenting and Collection Procedure at the Collection Centre

When the dates for the donation and transplantation have been agreed by the donor and the International Establishment, Anthony Nolan will book a full medical for the donor at one of Anthony Nolan's contracted Collection Centres to ensure that the donor is medically fit to donate.

Anthony Nolan will arrange all the logistics of the medical examination and the donation, including all necessary travel arrangements and the reimbursement of any out-of-pocket expenses, including subsistence, for an accompanying relative or friend. Anthony Nolan will arrange the following appointments, and will notify the International Establishment of

the confirmed dates for:

- the donor's medical examination, consenting and counselling for the donation procedure (if pre-collection samples are required by the International Establishment, Anthony Nolan will endeavour that this examination does not take place on a Friday, but this cannot be guaranteed)
- the estimated date on which the results of the donor's clearance will be received
- if the method of donation is PBSC, the dates of the G-CSF injections
- the date(s) of the donation
- the date and time for expected delivery of the donated PBSC or bone marrow.
- The International Establishment must complete and return the Confirmation of Work-Up Schedule DOC4256 form.

5.7 No Donor/Patient Contact (Unrelated Donors)

Unrelated donors will never donate in the same hospital as the hospital in which the patient is being treated. Unrelated donors will never be attended by a physician who is involved in the care of the patient.

5.8 Donor Clearance

When the donor's full medical report has been received, an Anthony Nolan Medical Officer will confirm that the donor is suitable and able to proceed with donation and complete the Donor Clearance form. The International Establishment shall sign and return this form to Anthony Nolan to confirm that the International Establishment accepts the donor, the dates, and the proposed collection regime. Any medical issues discovered during the donor medical that do not impact upon the donor's fitness to donate (donor suitability) but which may have implications for the patient (donor eligibility) will be communicated via the Donor Clearance form so that the International Establishment can confirm it is happy to proceed with the donor.

5.9 Procedure if a Donor Fails Medical

If any tests or examination results are not within the accepted range, such results will be reviewed immediately by Anthony Nolan. If any condition is uncovered which prevents the donor from donating, Anthony Nolan will immediately notify the International Establishment that the donor will not donate. Anthony Nolan will not give the International Establishment any details of the reasons why the donor has failed their medical.

On occasion, the Anthony Nolan Medical Officer may decide that further medical investigations are required before a final decision on the donor's suitability to donate can be made by Anthony Nolan.

The Anthony Nolan Donor Provision Coordinator will inform the International Establishment in writing that the donor requires further testing before a decision regarding the donor's suitability to donate can be given.

Details of the further testing will not be given to the International Establishment, but the expected date on which the results will be available will be given for the proposed transplant date to be changed if necessary and/or other appropriate actions to be taken.

The International Establishment will be notified of any donor results that could be clinically important to the patient's care.

5.10 Procedure if the Cell Count Collected from the Donor is Low

If the cell count of the PBSC collected from the donor is less than 1x 10^6 CD34+ cells/kg patient weight after two days of apheresis, Anthony Nolan will discuss the situation with the International Establishment.

Provided that the CD34+ cell dose per kg patient weight exceeds 1x10^6, arrangements for further haematopoietic progenitor cell (HPC) collection will not be made unless the patient fails to engraft and unless there are concerns about loss of viability, e.g. the cells are being cryopreserved or there are valid clinical concerns about engraftment from the International Establishment.

5.11 Postponements and Cancellations of Donations

Anthony Nolan will immediately notify the International Establishment by email of all postponements and cancellations of the scheduled donation. If out of hours the International Establishment will be informed by telephone. The International Establishment must provide a 24-hour telephone number for this purpose.

In rescheduling a donation, if the last virology testing was performed on a donor sample taken more than 30 days prior to the donation date, Anthony Nolan will ensure that repeat virology testing is performed.

If the transplant has been postponed by more than 60 days, Anthony Nolan will arrange for the haematology and biochemistry tests to be repeated. These tests will be carried out at Anthony Nolan's designated Collection Centre.

If the transplant has been delayed by more than six months, Anthony Nolan will arrange a repeat full medical examination of the donor.

The International Establishment must immediately notify Anthony Nolan of any postponement or cancellation by completing the Notification of Change (Cancellation or Postponement) DOC 2258 form.

The form must be emailed to Anthony Nolan. The cancellation or postponement request cannot be processed until this form is received by Anthony Nolan.

If these cancellations or postponements require urgent action by Anthony Nolan and occur outside office hours, the International Establishment must call the Anthony Nolan emergency telephone number: +44 7710 599 161.

6 SUBSEQUENT WORK-UP REQUESTS FOR DONORS

6.1 Requesting a Subsequent Work-Up from a Donor

If an International Establishment requires a further donation for a patient from a donor who has already donated PBSC or bone marrow to such patient, the International Establishment must complete and send Anthony Nolan, as applicable, the Formal Request for Subsequent Blood Stem Cell or Lymphocyte Collection – Previous Transplant History DOC1119 form for the Related Donors – Formal Request for Subsequent Blood Stem Cell or Lymphocyte Collection DOC4132 form by email.

6.2 Subsequent Work-Up from an Anthony Nolan Donor or a Related Donor living inthe UK

On receipt of the Formal Request for Subsequent Blood Stem Cell or Lymphocyte Collection – Previous Transplant History DOC1119 form or the Related Donors – Formal Request for Subsequent Blood Stem Cell or Lymphocyte Collection DOC4132 form, Anthony Nolan's Donor Consultant, or their deputy, will review the request. Anthony Nolan will aim to provide a decision within 72 hours of receipt of the request.

Anthony Nolan may request further information from the International Establishment. Subsequent donation requests may be referred by Anthony Nolan's Donor Consultant to Anthony Nolan's medical affairs group in the case of controversial indications. If the request for the subsequent donation is not approved, Anthony Nolan will provide the International Establishment with a brief summary of the reason(s) for the refusal.

6.3 Frequency of Subsequent Work-Up from an Anthony Nolan Donor

Any requests for further donations of haematopoietic stem cells or lymphocytes will be considered on a case-by-case basis by Anthony Nolan's Donor Consultant or their designee.

An Anthony Nolan donor may donate haematopoietic stem cells (which may be donated by PBSC or bone marrow) on a maximum of four occasions, to not more than two different patients.

An Anthony Nolan donor may also donate lymphocytes on a maximum of four occasions.

An Anthony Nolan donor who has undergone a PBSC or bone marrow donation, and despite repeated contact attempts is not participating in the post donation follow-up procedures required by Anthony Nolan, will not be considered for any further PBSC, bone marrow or lymphocyte donations.

An Anthony Nolan donor will not be approached to provide PBSC on a second occasion if the donor did not mobilise adequate haematopoietic progenitor cells at the time of the primary donation.

An Anthony Nolan donor will not be approached for a subsequent donation until the donor has reported full recovery from the previous donation.

6.4 Timings of Second Donations from an Anthony Nolan Donor

After the donation of PBSC, bone marrow or lymphocytes, an Anthony Nolan donor will

not be available for other searches for a period of 24 months after donation, unless the patient to whom they have donated has died.

Anthony Nolan requires a period of four weeks to elapse between any primary donation and a subsequent donation by an Anthony Nolan donor for the same Patient. This may be reviewed on a case-by-case basis.

7 TRANSPORTATION OF PBSC AND BONE MARROW

7.1 Provision of Couriers by International Establishments

International Establishments usually arrange for the transportation of PBSC, bone marrow or lymphocytes from the UK Collection Centre to the appropriate overseas hospital, using the International Establishment's own volunteer or commercial courier.

If the International Establishment requires, a courier can be arranged by Anthony Nolan for an additional fee.

7.2 Cancellation or Postponement

The International Establishment must immediately notify Anthony Nolan of any postponement or cancellation of a transplant by completing the Postponement/ Cancellation DOC2258 form and emailing it to the Donor Provision team. If a cancellation or postponement requires urgent action by Anthony Nolan and occurs outside office hours, the International Establishment must call the Anthony Nolan emergency number: +44 7710 599 161. The International Establishment shall be liable for any courier costs incurred as a result of this postponement or cancellation.

8 PROVISION OF CORD BLOOD UNIT(S) FROM THE ANTHONY NOLAN CORD BLOOD BANK

8.1 Provision of Cord Blood Unit(s)

The Anthony Nolan Cord Blood Bank provides Cord Blood Unit(s) to International Establishments.

8.2 Request for Cord Blood Unit Report(s)

To request a Cord Blood Unit Report(s) from the Anthony Nolan Cord Blood Bank, the International Establishment should email searchteam@anthonynolan.org

8.3 Request for Reservation of Cord Blood Unit(s)

If, after reviewing the Cord Blood Unit Report (s), the International Establishment decides to reserve such Cord Blood Unit(s), the International Establishment shall send Anthony Nolan a request to reserve the Cord Blood Unit(s) by email.

8.4 Quality Assurance Tests

On receipt of a Cord Blood Unit(s) Reservation Request, the Anthony Nolan Cord Blood Bank will initiate the following quality assurance tests in accordance with the Human Tissue Authority (HTA) regulations:

- Releasing tests, which include a thaw from an attached segment and several QC tests such as viability, TNC and CD34+ count and CFUs.
- Verification typing from an attached segment.
- Maternal HLA typing.
- Confirmatory gender.
- Confirmatory ABO.

These tests usually take 10 business days.

8.5 Shipment before Quality Assurance Tests Completed

If the International Establishment needs the Cord Blood Unit(s) before full testing has been completed, the International Establishment must send a Formal Request for Cord Blood Unit(s) DOC1126 form by email.

When completing this form, it is essential that the International Establishment includes the proposed date of the transplant. Anthony Nolan will not ship the Cord Blood Unit(s) until it is notified of this date.

8.6 Confirmation of Acceptance of Cord Blood Unit(s)

When a date for shipment of a Cord Blood Unit(s) has been confirmed and agreed, Anthony Nolan strongly recommends that the patient does not begin their conditioning regime until the Cord Blood Unit(s) has been received by the International Establishment. An International Establishment may also consider identifying domestically banked back-up units. Anthony Nolan will require the International Establishment to complete and return to Anthony Nolan the Confirmation of Acceptability of Cord Blood Unit DOC1128 form before the Cord Blood Unit can be shipped.

8.7 Transportation of Cord Blood Unit(s)

The Cord Blood Unit(s) shall be transported in accordance with the procedure in section 8.16 of this User Guide.

8.8 Receipt of Cryoshipper

On receipt of the cryoshipper, the International Establishment must check the integrity of the Cord Blood Unit(s), including the seals, the data logger, and cryoshipper and complete the Reception Form DOC1567. The Reception Form DOC1567 must be returned to Anthony Nolan by email to CTCrelease@anthonynolan.org

The International Establishment must notify Anthony Nolan immediately of any irregularity in the cryoshipper by emailing QualityTeam@anthonynolan.org. Where possible the supply of photographic evidence of the irregularity should be included with the report.

8.9 Thawing of Cord Blood Unit(s)

When thawing the Cord Blood Unit(s) the International Establishment must check the

seals very carefully and thaw the Cord Blood Unit(s) precisely in accordance with the instructions given by the Anthony Nolan Cord Blood Bank. The International Establishment must thaw the Cord Blood Unit(s) in a sterile zip lock type bag provided by Anthony Nolan and sent with the Cord Blood Unit(s).

8.10 Forms to be sent on Receipt of Cord Blood Unit(s)

Anthony Nolan will send the International Establishment relevant forms that must be completed and returned to Anthony Nolan once the Cord Blood Unit(s) has been received and/or infused.

8.11Storage of Cord Blood Unit(s)

The International Establishment must have the ability to store the Cord Blood Unit(s) on delivery and prior to transplant. The Cord Blood Unit(s) must be cryopreserved at -150 ºC or below.

8.12 Outcome of Transplantation

Anthony Nolan requires details of the outcome of the transplant and will liaise with the International Establishment to follow up post-transplant. The International Establishment will be asked to complete a Confirmation of Receipt and Infusion DOC1139 form to confirm this information.

8.13 International Establishment Concerns about the Quality of the Cord Blood Unit(s)

If the International Establishment has concerns regarding:

- the quality of the Cord Blood Unit(s) during shipment (e.g. if there has been a suspected significant warming event during shipment)
- the appearance of the Cord Blood Unit(s) (e.g. any unusual discolouration, bag integrity issues, visible air pockets, improper labelling etc.)
- the results of tests indicating poor viability/yield

then such concerns must be immediately reported to Anthony Nolan in accordance with section 10 of this User Guide.

8.14 Eurocord

Anthony Nolan has an agreement with the Eurocord Registry ("Eurocord") under which Eurocord handles follow up on behalf of Anthony Nolan. The International Establishment agrees that Anthony Nolan may pass the International Establishment's contact details to Eurocord, where upon Eurocord will liaise with the International Establishment directly.

8.15 Cancellation of Reserved Cord Blood Unit(s)

If the International Establishment cancels a request for an Anthony Nolan Cord Blood Unit(s) after the initial quality assurance tests have been completed, Anthony Nolan will not charge for such tests.

8.16 Transportation of Cord Blood Unit(s) under Anthony Nolan's HTA Licence

Cord Blood Unit(s) shall be exported from the Anthony Nolan Cord Blood Bank under Anthony Nolan's HTA licence.

8.17 Transportation of Cord Blood Unit(s) from the Anthony Nolan Cord Blood Bank to International Establishments

Anthony Nolan will arrange the transportation of Cord Blood Unit(s) from the Anthony Nolan Cord Blood Bank to the International Establishment. Anthony Nolan will use its own contracted external courier company.

8.18 Address to which the Cord Blood Unit(s) will be Delivered

Anthony Nolan will book the courier for the transportation of the Cord Blood Unit(s) to the address stipulated by the International Establishment on the Formal Request for Cord Blood Unit(s) DOC1126 form.

8.19 Return of the Cryoshipper

Anthony Nolan will be responsible for making all the arrangements with a courier company to ensure the return of the cryoshipper to the originating Anthony Nolan Cord Blood Bank.

8.20 Arrangements

Anthony Nolan will notify the International Establishment of the courier details and shall liaise with the courier in order to arrange a delivery date and time.

Anthony Nolan will notify the International Establishment of the tracking details.

The International Establishment must ensure that there is a person waiting at the International Establishment's designated address to receive the Cord Blood Unit(s) at the stipulated time with appropriate documentation to confirm receipt of the correct Cord Blood Unit.

8.21 Cancellation or Postponement

If a patient's transplant is postponed or cancelled, this may necessitate amendment or cancellation of a courier booking. The International Establishment which is purchasing the Cord Blood Unit(s) shall be liable to pay for the Cord Blood Unit(s) if it/they have been dispatched and shall also be liable for any courier costs incurred as a result of this postponement or cancellation.

9 RELATED DONOR SERVICE

9.1 Related Donor Sample Procurement

If a related donor is residing in the United Kingdom, Anthony Nolan can help facilitate the collection of samples from them for the purposes of testing to investigate if they are a suitable match for transplant.

If the International Establishment wishes to use this service, they must complete the Related Donor Sample Request for HLA Typing DOC3955 form. The International Establishment should send the form by email to VTTeam@anthonynolan.org

The International Establishment must have first contacted the related donor to confirm that they are willing to provide the samples before requesting this service from Anthony Nolan.

Providing the related donor is willing to donate, Anthony Nolan will arrange for the samples to be collected and shipped to the address indicated on the request form. Once the testing has been completed, the International Establishment must notify the related donor of the outcome. The Anthony Nolan Verification Typing Coordinator or Search Coordinator must also be told of this.

9.2 Related Donor Stem Cell Product Procurement

If a related donor is the best match for the patient, the International Establishment can request Anthony Nolan to help facilitate the cell product collection provided the related donor is residing in the United Kingdom. The International Establishment must have first contacted the related donor to confirm that they are willing to donate before requesting this service.

The International Establishment must complete the Related Donors – Formal Request for Blood Stem Cell Collection DOC3983 form, a formal Laboratory HLA typing report for both patient and related donor and submit this to the work-up team's e-mail address: Workups@anthonynolan.org

Anthony Nolan will make all the necessary arrangements for collection of the stem cells from the related donor residing in the UK as per the applicable procedures set out in section 5 of this User Guide.

9.3 Related Donor Clearance

The Anthony Nolan Donor Consultant has the final decision for medical sign off for any related donor residing in the UK. Any medical issues that the Anthony Nolan Donor Consultant considers may pose a potential risk to the patient will be discussed with the International Establishment.

9.4 Postponement and Cancellation of Transplant

The International Establishment must immediately notify Anthony Nolan of any postponement or cancellation of a transplant by completing the Postponement/ Cancellation DOC2258 form. The International Establishment must also notify the related donor of such a change and confirm by email to Anthony Nolan this has been done. DOC2258 must be emailed to the Anthony Nolan Donor Provision team. Without it, the cancellation/postponement request cannot be processed. If a cancellation or postponement requires urgent action by Anthony Nolan and occurs outside office hours the International Establishment must call the Anthony Nolan emergency telephone number.

9.5 Procedure after Donation

Donors will receive follow-up care for 10 years, as detailed in this User Guide. This includes the management of Serious Adverse Events (SAE), a donor's physical and emotional recovery from donation, and counselling post-donation if required. Anthony Nolan will not provide updates on the patient's progress for related donors or facilitate patient and donor correspondence. The related donor will be directed to the International Establishment if required.

9.6 Subsequent Donations from Related Donors

An International Establishment may request a subsequent PBSC, bone marrow or lymphocyte donation from a related donor as set out in section 6 of this User Guide.

10 MANDATORY REGULATORY REQUIREMENTS

10.1 Serious Adverse Event/Reaction Reporting

Anthony Nolan's HTA licence obligation is to report all Serious Adverse Events (SAE) and Serious Adverse Reactions (SAR) to the HTA within 24 hours of being notified.

Therefore, International Establishments must report all Serious Adverse Events and Serious Adverse Reactions, and any other event which has affected the cell product prior to infusion at the International Establishment and/or the patient outcome, to Anthony Nolan within 24 hours of occurrence by emailing QualityTeam@anthonynolan.org

The report provided must include all the information required by the HTA for the reporting of Serious Adverse Events and Serious Adverse Reactions, as specified on the HTA website: https://www.hta.gov.uk/policies/human-application-adverse-event-and-reaction-saears-reporting.

The information should include:

- date of the adverse event / adverse reaction
- location of the adverse event /adverse reaction
- relevant material affected
- part of process the event was linked to
- suspected cause of event / reaction
- description of event
- action taken to date.

The Anthony Nolan Quality team will follow up with the International Establishment while preparing the follow up report to the HTA.

10.2 Traceability: Compliance with Certain Requirements of HTA Directions 001/2021(as may be amended or superseded from time to time)

The International Establishment will comply with such procedures and supply such information, as Anthony Nolan may from time to time specify to ensure that the traceability requirements of the HTA's Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment (as may be amended or superseded from time to time) are met. In particular, the International Establishment will ensure that Anthony Nolan is in possession of all the information listed in numbered paragraph 157 from the HTA Guide which is as follows:

> "157. The minimum information to be provided to the tissue establishments by end users is:
>
> a. identification of the supplier tissue establishment;
> b. identification of the clinician or end user/facility;
> c. type of tissues and cells;
> d. product identification;
> e. identification of the recipient;

f. date of application or date of disposal;
g. the SEC (if applicable)."

The International Establishment confirms that it maintains traceability information as required by the HTA.

11 CRYOPRESERVATION

11.1 Infusion and Cryopreservation

The International Establishment must not store or cryopreserve collected haematopoietic stem cells for more than 48 hours without the prior written agreement of the Anthony Nolan Donor Consultant or their deputy. The International Establishment must notify Anthony Nolan in writing when the cryopreserved cell product is either infused or discarded. Excess material post-transfusion may be cryopreserved for therapeutic purposes or discarded according to standard protocols without applying to Anthony Nolan for the donor's permission.

The International Establishment shall promptly complete and return a Cell Processing Report to Anthony Nolan in respect of each Cell Product received. This records (amongst other things) the amount of the cell product which is either cryopreserved or discarded.

11.2 Cryopreservation of Lymphocytes

(a) The International Establishment may cryopreserve lymphocytes without the prior approval of Anthony Nolan provided that the first aliquot is infused within 14 days of the lymphocytes being donated, and this date of infusion is stated in the Cell Processing Report referred to in section 11.1 above.

(b) If the International Establishment desires to cryopreserve the lymphocytes for longer than 14 days before administering the first dose, it must notify Anthony Nolan and must also notify Anthony Nolan in writing when the cryopreserved product is either infused or discarded.

The International Establishment must report any Serious Adverse Event and/or Serious Adverse Reaction affecting the cell product in accordance with section 10.1 of this User Guide.

11.3 Cryopreservation of Haematopoietic Stem Cells on Behalf of the International Establishment

If the International Establishment is unable to cryopreserve the cell product at their establishment, the International Establishment can request that Anthony Nolan arranges this on their behalf. This can be requested at any point during the work-up process but at the point of request is preferred, or as early as possible. Once the request has been made, Anthony Nolan will confirm:

- if the Collection Centre is able to fulfil the request
- if the Collection Centre is unable to fulfil the request, if the Anthony Nolan Cell Therapy Centre is able to fulfil the request (at present the Anthony Nolan Cell Therapy Centre is unable to cryopreserve bone marrow).

In all circumstances, the International Establishment will be asked to complete the

Cryopreserved Adult Cells TC Questionnaire DOC4986 form, and return this before the donor starts their G-CSF injections (for PBSC collections) or travels to attend their bone marrow or lymphocyte collection.

The establishment cryopreserving and storing the cell product shall do this in line with its standard processing procedures.

If cryopreservation is carried out by the Anthony Nolan Cell Therapy Centre, the Anthony Nolan Cell Therapy Centre can store a cryopreserved Cell Product for a maximum period of 12 months. At the one year anniversary of the initial storage, either arrangements will need to be made between the parties for the transport of the cryopreserved cell product to the International Establishment's storage facility of choice or, alternatively, an agreement for long term storage at the Anthony Nolan Cell Therapy Centre will need to be agreed between the parties in writing.

Prior to release, the establishment cryopreserving and storing the cell product shall complete the relevant tests for its release, such as viability tests and microbiology testing, in accordance with its standard processing procedures and will complete a Cryopreserved Cell Product Release DOC4987 form which will be forwarded to the International Establishment. This form details the cryopreservation process and provides information with regards to the viability of the cryopreserved cell product. The form requires confirmation of receipt from the International Establishment by signing and returning to Anthony Nolan.

The International Establishment will then advise of a suitable shipment date and confirm it is happy to proceed by completing a Confirmation of Cryopreserved Cell Product Acceptability DOC4988 form. The International Establishment must return a signed copy of the Confirmation of Cryopreserved Cell Product Acceptability DOC4988 form by email to Anthony Nolan before the cryopreserved cell product can be released and transportation arrangements can be made.

The International Establishment is responsible for verifying that the cryopreservation of the cell product and its export to the International Establishment's country comply with any of its own local legal and regulatory requirements relating to the processing, cryopreservation, storage and transport of cells. Anthony Nolan has no responsibility for, and excludes all liability to, the International Establishment if the cryopreservation and export of the cell product does not comply with such local requirements.

If the International Establishment cancels the request for cryopreservation after the cell product has been cryopreserved, but before transportation of the cell product, Anthony Nolan may dispose of the cell product in accordance with Anthony Nolan's standard operating procedures.

11.4 Shipment of Cryopreserved Haematopoietic Stem Cells

Anthony Nolan will arrange the transportation of the cryopreserved cell product from the Anthony Nolan Cell Therapy Centre or UK Collection Centre to the International Establishment using an external courier company with which Anthony Nolan has contracted.

Anthony Nolan will book the courier for the transportation of the cryopreserved cell product to the address stipulated by the International Establishment on the initial work-up request form – Formal Request For Blood Stem Cell Collections DOC3842 or Formal

Request for subsequent Blood Stem Cell or Lymphocyte Collection DOC1119.

Anthony Nolan will notify the International Establishment of the courier details and shall liaise with the courier in order to arrange a delivery date and time. Anthony Nolan will notify the International Establishment of the tracking details. The International Establishment must ensure that there is a person waiting at the International Establishment's designated address to receive the cryopreserved cell product at the stipulated time.

On receipt of the cryoshipper, the International Establishment must check the integrity of the cryopreserved cell product, including the seals, the data logger and cryoshipper, and complete the Reception Form DOC1567 provided by Anthony Nolan and return this completed form to Anthony Nolan by email. The International Establishment must notify Anthony Nolan immediately of any irregularity in the cryoshipper by emailing the Donor Provision Coordinator responsible for the patient's work-up. Where possible the supply of photographic evidence of the irregularity should be included with the report.

Anthony Nolan will be responsible for making all the arrangements with a courier company to ensure the return of the cryoshipper.

When thawing the cryopreserved cell product, the International Establishment must check the seals very carefully and thaw the cryopreserved cell product precisely in accordance with the instructions contained in the shipment packet accompanying the cell product – Recommended Thawing Procedures DOC1570.

For storage of the cryopreserved cell product, the International Establishment will need to follow the guidance on the Confirmation of Cryopreserved Cell Product Acceptability DOC4988 form.

The International Establishment must have the ability to store the cryopreserved cell product on delivery and prior to transplant. The cell product must be cryopreserved at -150 ºC or below.
If the cryopreserved cell product is not infused within 48 hours of receipt, the International Establishment must ensure that, where applicable, the International Establishment and its transplant centre comply with all laws and regulations applicable to the storage of the cryopreserved cell product (including ensuring its storage facility is appropriately licensed by, and complies at all times with, the requirements of any regulatory authority).

11.5 Bespoke Arrangements

If Anthony Nolan and the International Establishment have entered into a separate agreement for cryopreservation and storage services to be carried out by the Anthony Nolan Cell Therapy Centre, the terms of such agreement shall apply in place of sections 11.3 and 11.4 above.

Anthony Nolan is also able to cryopreserve cells on behalf of an International Establishment even if Anthony Nolan is not involved in the work-up process. The International Establishment will need to enter into an agreement with Anthony Nolan for the provision of such services. To request further information about such services, please contact donorprovision@anthonynolan.org

12 PROCEDURE AFTER DONATION FOR UNRELATED DONORS

12.1 Post Donation Follow-Up

Donors are followed up for a period of 10 years post donation. Short term follow-up ensures that donors recover both physically and emotionally from donation, as well as manging any serious adverse events post donation. Donors can access a specialist counsellor if needed. Long term follow-up monitors the donors' continuing availability for subsequent donations, and the development of long-term health conditions which may impact the patient's health or their ability to remain on the register.

12.2 Possible Future Donation

Anthony Nolan will ask donors about their willingness to be approached for future donations. Anthony Nolan will notify the International Establishment in writing if the donor is not willing to consider any future donation, or if for any reason the donor has been removed from the relevant register.

12.3 Updates on Patient's Progress

Each donor is asked following donating if they would like an update on the patient's progress within the first year after donation. Anthony Nolan shall obtain information on International Patients by contacting the International Establishment at around six months after donation, either by email or fax.

12.4 Donor/Patient Contact

Anthony Nolan's policy on direct and indirect contact between the donor and the patient will be discussed directly with the donor during the course of the donor's follow-up after donation. Anthony Nolan will inform all donors, and the International Establishment will inform all patients that sometimes contact is not possible for a variety of reasons. International Registries may have policies of life-long anonymity for patients and donors.

Messages or correspondence between patients and donors can take effect after the transplant has taken place. To ensure donor and patient confidentiality, any messages received prior to the transplant will be retained by Anthony Nolan and not forwarded on to the intended patient.

In accordance with Anthony Nolan's policy, the identities of both donor and patient must remain confidential for at least two years after the date of the latest transplant, or for at least one year following a DLI donation. During the two-year period, anonymous correspondence (i.e. no identifying information such as names or living/working locations) may be exchanged. The correspondence is screened by the International Establishment and Anthony Nolan. Anthony Nolan will take advice from the International Establishment on the appropriateness of any correspondence to the International Establishment's patient.

If a patient would like to send their donor a message of thanks once the transplant has taken place (no gifts or photographs are accepted), these can be handed to their transplant team to send on to Anthony Nolan via the International Establishment who will then forward on to the donor.

If the family of a deceased patient wishes to contact the donor, then any messages can be

passed to the International Establishment to be sent to Anthony Nolan. Direct contact may be allowed on case by case basis in these circumstances and should be initially discussed with the Donor Follow-Up Manager.

Correspondence should be mailed to:

Donor Follow-Up Team
Anthony Nolan
2 Heathgate Place
75-87 Agincourt Road
London
NW3 2NU

Or emailed to donor@anthonynolan.org

Two years after the transplant, it may be possible for Anthony Nolan to arrange direct contact between the donor and the patient, but only on the instigation of the patient and if the International Establishment has not raised any concerns. Both parties will need to complete a signed consent form.

If an International Establishment is aware that a patient wishes to blog or share their experience on social media, then the International Establishment should advise the patient to follow Anthony Nolan's guide which can be obtained from the Patient Services team, to ensure the donor remains anonymous. Patients must not post any information about the donor's location, age or gender, and make sure the information label on their stem cell bag is not visible if he/she posts a photograph. In addition, patients must not try to contact the donor directly on social media or share any correspondence with the donor without express permission from Anthony Nolan.

In the case of any queries or possible breaches of confidentiality please contact the Donor Follow-Up Manager.

12.5 Retention of Records

The International Establishment must retain all records associated with the cell product for 30 years from date of clinical use or disposal of the cell product.

13 HISTOCOMPATIBILITY SERVICES

13.1 Specialised Histocompatibility Services

Anthony Nolan provides certain specialised histocompatibility services which are in addition to the standard histocompatibility services as part of the donor selection and matching procedures.

These specialised histocompatibility services are described in brief in this section and will be provided by Anthony Nolan if the International Establishment has requested these.

13.2 HLA Typing

(a) HLA typing, ABO and Rh D blood group testing and CMV screening on patients under consideration for a haematopoietic stem cell transplant.

(b) HLA typing, ABO and Rh D blood group testing and CMV screening for potential related donors for patients awaiting a haematopoietic stem cell transplant.

(c) HLA typing, ABO and Rh D blood group testing, CMV, HIV, Hepatitis B and C testing on blood samples from all requested unrelated donors selected for patients.

(d) HLA typing to a minimum of intermediate level of resolution for HLA-A, -B, -C, -DRB1, DRB3, -DRB4, -DRB5, DQB1 and –DPB1.

13.3 Additional Testing

Anthony Nolan shall perform additional testing, which may include typing to high resolution and typing of HLA-DPB1, on patients and probable matching donors as deemed necessary by Anthony Nolan and the International Establishment in accordance with The European Federation for Immunogenetics (EFI) Standards.

13.4 Written Report

Anthony Nolan shall prepare a written report of results which show the degree of matching between potential donors and patients and shall send this report, by email, to the person nominated by the International Establishment.

13.5 Storage of Samples

Anthony Nolan shall store samples of blood, DNA and serum derived from blood according to the relevant guidelines.

14 ANTHONY NOLAN'S ACCREDITATION AND REGULATION

14.1 Companies House

Anthony Nolan is registered as a company limited by guarantee in England and Wales, registration number 2379280 with its registered office at:

Royal Free Hospital
Pond Street
London
NW3 2QG

14.2 Charity Commission and Office of the Scottish Charity Regulator

Anthony Nolan is registered as a charity with the Charity Commission in England and Wales, registration number 803716 and with the Office of the Scottish Charity Regulator in Scotland, registration number SCO 38827.

14.3 Care Quality Commission (CQC)

Anthony Nolan is registered with the Care Quality Commission Provider ID: 1-240372502.

14.4 WMDA

Anthony Nolan is accredited by the World Marrow Donor Association (WMDA) in the following categories:

- General Organisation of Registry
- Donor Recruitment
- Donor Characterisation
- Information Technology
- Facilitation of search requests
- Second/subsequent donations
- Collection/processing/transport of stem cells
- Follow up of Patient/Donor
- Financial/legal liabilities

Anthony Nolan complies with WMDA International Standards for Unrelated Hematopoietic Cell Donor Registries which can be found on the WMDA website: https://wmda.info/professionals/quality-and-accreditation/wmda-standards/.
For clarity, these standards also apply to related donors.

14.5 HTA

Anthony Nolan holds the following Human Tissue Authority (HTA) licences:

- Licence 22513 permits the Anthony Nolan Register to carry out the procurement, distribution and/or import/export of tissues and/or cells intended for human application.
- Licence 22527 permits the Anthony Nolan Cord Blood Bank to carry out the procurement, processing, testing, distribution and storage of cells intended for human application.

14.6 National Ethical Approval

The Anthony Nolan Cord Blood Bank holds National Ethical Approval to act as a research tissue bank.

14.7 FACT- NetCord Accreditation

The Anthony Nolan Cord Blood Bank has FACT-NetCord Accreditation.

14.8 UKAS and the European Federation for Immunogenetics

The Anthony Nolan Histocompatibility Laboratories are accredited to ISO 15189:2012 - Medical Laboratories (ref 8630) by the United Kingdom Accreditation Service (UKAS) and by the European Federation for Immunogenetics (EFI) (ref 03-GB-005-995).

15 RESEARCH

15.1 Research

The International Establishment may request that donors are invited to consent to being involved in a research programme, project, or study. An application must be submitted by the study sponsor or chief investigator of the International Establishment to involve Anthony Nolan donors in any and all research programmes, projects, or studies to researchstudies@anthonynolan.org for attention of the AN Clinical Trials Supervisor. Such an application must consist of:

- a Donor Research Study Application DOC3323 form
- evidence of relevant institutional review board approval
- a statement detailing how any costs incurred by Anthony Nolan as a result of the donor participating in the study will be reimbursed, e.g. additional blood draws, donor travel expenses and loss of earnings
- the research protocol
- the donor / participant information sheet
- the donor's consent form.

Anthony Nolan will then consider the request in respect of an Anthony Nolan donor. All research studies involving Anthony Nolan donors will require the approval of the Anthony Nolan medical affairs committee.

15.2 Use of Donor Cells for Generic Research

Anthony Nolan donors are asked if they will agree to any surplus tissue/DNA from their collection being used anonymously for future medical research projects. These donors are informed that any medical research project would have to be approved by a properly constituted research ethics committee and undertaken in accordance with appropriate ethical, legal and professional standards, and that they will not benefit financially from any research undertaken and waive all rights to any registered patents. The International Establishment will be informed whether or not the donor agrees to this.

16 CHARGES AND FINANCE

16.1 Charges Payable by the International Establishment to Anthony Nolan

Each International Establishment must pay Anthony Nolan the charges set out in the relevant fee schedule in force at the time of invoicing, together with VAT at the prevailing rate.

16.2 Cancellation and Postponement Charges

The charges referred to above include, without limitation, the following:

Postponement Charge
A postponement charge may be charged each time a scheduled transplant date is changed to cover postponement of appointments and further administration.

Cancellation Charge
A collection charge may be charged to cover activities undertaken before a request is cancelled. If tests are underway at the time of cancellation, the International Establishment may be charged the normal rate provided the results are reported within a month by Anthony Nolan.

Cancellation Prior to Donor Medical
If a transplant is cancelled after Anthony Nolan has received a request for a donor work-up but before the donor medical examination has taken place, Anthony Nolan may only apply an administrative charge.

Cancellation after the Donor Medical
If a transplant is cancelled after the donor has undergone the medical examination, Anthony Nolan may charge the full cancellation charge.

Additional Charge for G-CSF
An additional charge will be made for G-CSF if the drug has already been prescribed and issued to a donor who would have undergone a haematopoietic stem cell collection.

Cancellation of Cryopreservation Services
If a request for cryopreservation is cancelled before the cryopreservation has been carried out, a cancellation charge may be charged to cover activities undertaken before the request was cancelled. If a request for cryopreservation is cancelled after the cryopreservation has been carried out, including if the transplant is cancelled, Anthony Nolan may charge the full amount for the services.

17 COMPLAINTS

17.1 Complaints Procedure

Comments on the services provided by the Operations and Patient Services are welcome and help us to improve. Please send details in an email to the Quality Team: QualityTeam@anthonynolan.org

If you wish to make a formal complaint regarding the services provided by the Operations and Patient Services, or to report a Serious Adverse Event or Reaction (SAE/SAR), please send details in an email to the Quality Team: QualityTeam@anthonynolan.org

18 ANTHONY NOLAN DETAILS

Staff List
For full list of staff, please refer to the Anthony Nolan website, www.anthonynolan.org

Address for Notices
For the attention of the Chief Operating Officer
Anthony Nolan
2 Heathgate Place
75-87 Agincourt Road
London
NW3 2NU

Operations and Patient Services Emergency Telephone number	**07710 599 161**
Operations and Patient Services Administration Fax number	**020 7284 8226**

Anthony Nolan Donor Recruitment Team
Healthcare professionals wishing to raise an appeal for a patient, should contact this team on 0207 284 1234 or email info@anthonynolan.org

19 LIST OF FORMS

The following is a list of the forms referred to in this User Guide.

FORM	TITLE	DESCRIPTION
DOC 1119	Formal Request for Subsequent HPC or Lymphocyte (DLC) Collection	The Transplant Centre will send this to Anthony Nolan when requesting a subsequent donation.
DOC 1126	Formal request for Cord Blood Unit from TC	The International Establishment must complete this form before shipment of a cord blood unit.
DOC1128	Confirmation of Acceptability of Cord Blood Unit	
DOC1139	Confirmation of Receipt and Infusion of Cord Blood Unit	
DOC1567	Reception Form	
DOC1570	Recommended Thawing Procedures	
DOC1671	Verification Typing Request Form	The International Establishment must complete this to request a sample to be tested in the International Establishment's designated laboratory.
DOC1672	Extended Typing Request Form	The International Establishment complete if it requires Anthony Nolan to perform extended typing
DOC1685	Preliminary Search Request Form	If HLA typing of the patient is carried out at a laboratory other than the Anthony Nolan laboratories, the Transplant Centre must complete a search request form
DOC3323	Donor Research Study Application Form	For use to involve donors in any and all research programmes, projects or studies

DOC3842	Formal Request for Blood Stem Cell Collections including BM & PBSC Prescription Forms	
DOC3955	Related Donor Sample Request for HLA Typing	
DOC3983	Related Donors - Formal Request for Blood Stem Cell Collection	International Establishment to use if requesting a related donor for work-up
DOC4132	Related Donors - Formal Request for Subsequent Donation	International Establishment to use if requesting a related donor for subsequent donation
DOC4256	Work-up schedule template - UK Donor	
DOC4986	Cryopreserved Adult Cells TC Questionnaire	
DOC4987	Cryopreserved Cell Product Release Form	
DOC4988	Confirmation of Cryopreserved Cell Product Acceptability	
NOTE: The Anthony Nolan Laboratories' User Guide can be found on the Anthony Nolan website.		

DEFINITIONS

In this User Guide the following terms have the meanings set below them.

Anthony Nolan and NHS Stem Cell Register
A database containing details of donors on all UK registers. This database consists of Anthony Nolan donors, NHSBT donors, WBMDR donors and DKMS (UK) donors. This register is managed by Anthony Nolan.

Anthony Nolan and NHS Stem Cell Registry
A registry which holds the Anthony Nolan and NHS Stem Cell Register. This registry is managed by Anthony Nolan and is informally referred to as the 'aligned registry'.

Anthony Nolan Cord Blood Bank
The Anthony Nolan Cell Therapy Centre situated at Nottingham Trent University, Clifton Campus, Nottingham NG11 8NS, which holds a bank of Cord Blood Units managed by Anthony Nolan.

Anthony Nolan donor
A donor listed on the Anthony Nolan Register. Anthony Nolan donors are also listed on the Anthony Nolan and NHS Stem Cell Register.

Anthony Nolan laboratories
The Anthony Nolan Histocompatibility Laboratories situated at 77B Fleet Road, Hampstead, London NW3 2QG.

Anthony Nolan Register
A searchable register of both cord blood units and volunteers, recruited by Anthony Nolan, who are willing to donate haematopoietic stem cells or lymphocytes. This register is managed by Anthony Nolan.

BSBMTCT
British Society of Blood and Marrow Transplantation and Cellular Therapy.

Business day
A day other than a Saturday, Sunday or a public holiday in England and Wales.

Cell product
Haematopoietic stem cells or other Lymphocytes and/or, where applicable, a Cord Blood Unit(s).

Collection Centre
A hospital at which the cell product is collected, which is appropriately accredited and/or licensed or otherwise acceptable to Anthony Nolan and which operates in accordance with the Human Tissue Authority's Code of Practice G "Donation of Allogeneic Bone Marrow and Peripheral Blood Stem Cells for Transplantation".

Cord Blood Bank
A bank of Cord Blood Units situated in the UK or abroad.

Cord Blood Unit(s)
A processed unit of umbilical cord blood.

Cord Support Programme
Optional services provided by Anthony Nolan, including shortlisting and quality evaluation of cord blood units.

DKMS UK donor
Donors on a database managed by DKMS UK, which is the working name of the UK charity DKMS Bone Marrow Donor Centre. DKMS UK donors are also listed on the Anthony Nolan and NHS Stem Cell Register.

DLI
Donor lymphocyte infusion.

Donor
A volunteer or a relative of the patient who is over the age of 16 and who is a suitable HLA match willing to donate haematopoietic stem cells or lymphocytes. Unless the context otherwise requires, 'donor' shall include donors listed on the Anthony Nolan and NHS Stem Cell Register, and international donors.

EBMT
European Society for Blood and Marrow Transplantation.

EMDIS
European Marrow Donor Information System.

FACT
Foundation for the Accreditation of Cellular Therapy.

Fee schedule
The schedule of charges provided by Anthony Nolan to the relevant International Establishment, as such schedule may be amended from time to time.

GIAS
Graft Identification Advisory Service.

Gift of Life
The Gift of Life Bone Marrow Foundation which is a US donor programme.

G-C SF
Granulocyte colony stimulating factor.

HLA
Human leukocyte antigen molecules which have to be matched between donor and patient. These molecules exist in many similar but different forms.

HTA
The Human Tissue Authority.

International cord blood bank
A bank of Cord Blood Unit(s) located outside the UK.

International Cord Blood Unit(s)
A Cord Blood Unit(s) which is held by an International Cord Blood Bank.

International donor
A donor on a register held by an International Establishment.

International Establishment
- An international registry, or
- A hospital, situated outside the UK, which is seeking to perform transplantation of haematopoietic stem cells or lymphocytes for patients with various malignant and non-malignant conditions and is
  - accredited by EBMT, or
  - listed as an International or US NMDP Transplant Centre, or which has provided Anthony Nolan with information regarding its clinical activity and has been approved by the Anthony Nolan medical director.

International registry
A registry situated outside the UK which holds a register of international donors.

ISCT
International Society for Cellular Therapy.

JACIE
Joint Accreditation Committee - ISCT & EBMT.

Laboratory
A laboratory which is (i) licensed under the HTA or is the subject of a Third-Party Agreement made pursuant to regulations under the Human Tissue Act 2004; or (ii) is otherwise acceptable to Anthony Nolan. ("Third Party Agreement" is defined in the regulations.)

Lymphocytes
A type of white blood cell. A subset called T cells is used in donor lymphocyte infusion. Lymphocytes are vital components of the body's immune system - the defence against invading organisms.

MDT
Multi-disciplinary Team Meeting.

NHSBT
National Health Service Blood and Transplant.

NHS Cord Blood Bank
A bank of Cord Blood Units managed by the NHS. Searches of this NHS Cord Blood Bank on behalf of UK patients are handled by Anthony Nolan. Searches requested by international registries on behalf of overseas patients are managed by NHSBT.

NHSBT Database
A searchable register of volunteers who are willing to donate haematopoietic stem cells or lymphocytes. Searches of this NHSBT Database on behalf of UK patients are managed by Anthony Nolan. Searches on behalf of overseas patients are managed by NHSBT.

NHSBT donor
A donor listed on the NHSBT Database. NHSBT donors are also listed on the Anthony Nolan and NHS Stem Cell Register.

NMDP
The National Marrow Donor Program, which is a US donor programme.

Patient
The person intended to receive the donation of the cell product.

PBSC
Peripheral blood stem cells.

Promise
A UK database of the patients who have undergone a haematopoietic stem cell transplant.

Related donor
A biological relative of the patient who is a suitable HLA match for a stem cell donation who may reside in the United Kingdom and who is over the age of 16 years, or who may reside in the United States of America or any other country outside the United Kingdom provided Anthony Nolan has (or can put in place) an arrangement with a registry or hospital in the applicable country to facilitate such requests, and who is over the age of 16 years.

Serious Adverse Event
Any untoward occurrence which may be associated with the procurement, testing, processing, storage or distribution of tissue or cells intended for human application and which, in relation to a donor of tissue or cells intended for human application, or a recipient of tissue or cells:

(a) might lead to the transmission of a communicable disease, to death or life-threatening, disabling or incapacitating conditions, or

(b) might result in, or prolong, hospitalisation or morbidity.

Serious Adverse Reaction
An unintended response, including a communicable disease, in a donor of tissue or cells intended for human application or a recipient of tissue or cells, which may be associated with the procurement or human application of tissue or cells and which is fatal, life-threatening, disabling, incapacitating or which results in, or prolongs, hospitalisation or morbidity.

Service Level Agreement
An agreement between two parties both of which are licensed by the Human Tissue Authority.

Transplant Centre
A hospital in the UK which carries out transplantation of haematopoietic stem cells or lymphocytes for patients with various malignant and non-malignant conditions. The hospital must have been approved by the Anthony Nolan medical director.

WBMDR
Welsh Bone Marrow Donor Registry which is a searchable register of volunteers who are willing to donate haematopoietic stem cells or lymphocytes. It is managed by the Welsh Blood Service.

WBMDR Donor
A donor listed on the Welsh Bone Marrow Donor Registry. Welsh Bone Marrow donors are also listed on The Anthony Nolan and NHS Stem Cell Register.

Welsh Blood Service
The division of Velindre NHS Trust which has legal responsibility for the Welsh Bone Marrow Donor Registry.

WMDA
World Marrow Donor Association.

WMDA Search and Match Service
The searchable online global database for adult unrelated donors and cord blood units.

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