STEM CELL & IMMUNOTHERAPY SERVICES

USER GUIDE

Contents

1. Purpose and scope of document

This guide outlines the stem cell services provided by NHS Blood & Transplant (NHSBT) and will be of use to consultants and other medical, nursing, and scientific staff in transplant units and other healthcare environments requiring our services. It contains information about the organisation of services, contact details for key members of staff and other information to enable healthcare staff to access services on behalf of their patients.

2. About CMT

The Cellular and Molecular Therapies (CMT) function within NHSBT (Figure 1) is responsible for the provision of cell therapies for transplantation and for the development and manufacture of novel advanced cell and gene therapies. CMT consists of the following three main areas:

I. Stem Cell and Immunotherapies (SCI) – provides cell therapy services
II. Advanced Therapies Units (ATU) – manufacture advanced cell therapies
III. Clinical Biotechnology Centre (CBC) – manufacture GMP-grade plasmids and viral vectors

This user guide focuses on the services provided by SCI, but more information on other services offered by CMT can be obtained via Home - Cellular and Molecular Therapies - NHS Blood and Transplant

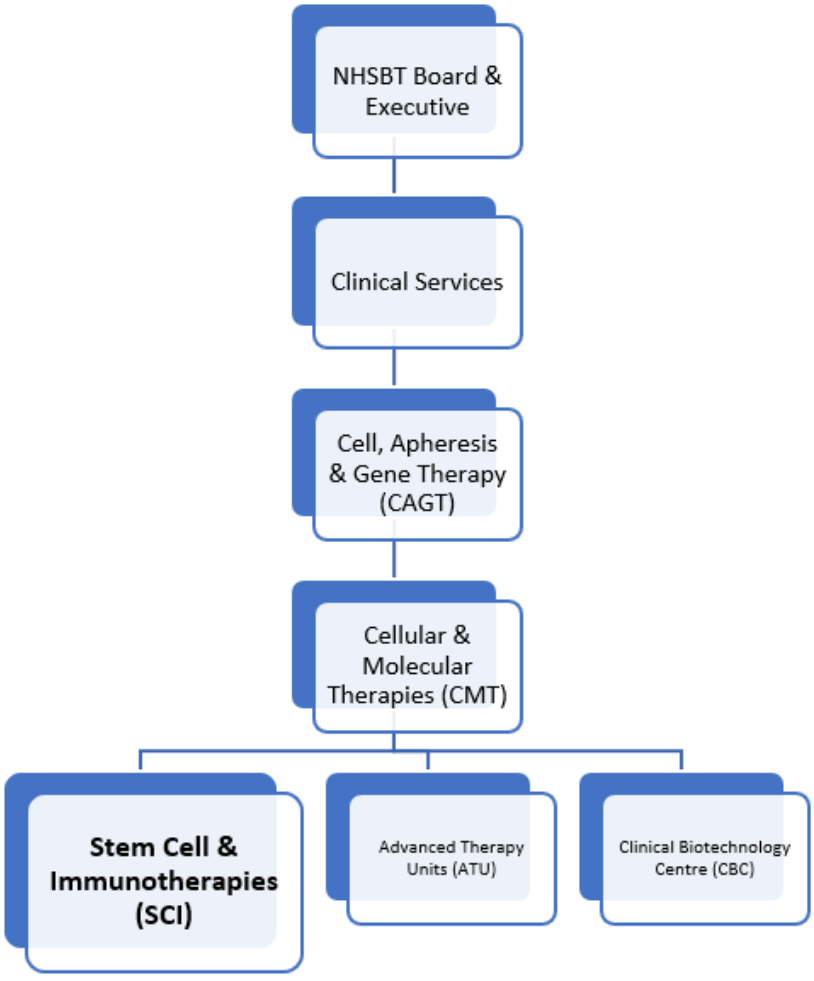

Figure 1 *Positioning of CMT function and SCI services within the NHSBT organisational structure.*

3. About Stem Cell and Immunotherapies (SCI)

Stem Cell and Immunotherapy services are provided by five SCI laboratories based within NHSBT facilities at Barnsley, Birmingham, Bristol (Filton), Oxford and Southampton.

The activities of SCI laboratories include the processing, storage, distribution and export of cellular therapy products for autologous and allogeneic transplantation. Sources of cells include haematopoietic progenitor cells (HPC) harvested via Apheresis (HPC(A)), from bone marrow (HPC(M)) and from cord blood (HPC(C), as well as T Cells (TC) and peripheral blood mononuclear cells (PBMC).

SCI laboratories also receive, hold and issue licenced CAR-T products and clinical trial products manufactured by authorised organisations ensuring appropriate regulatory requirements, for the treatment of a named patient. SCI Services are often accompanied by Therapeutic Apheresis Services (TAS) but TAS also provide services independently of SCI to some Trusts. TAS therefore have a separate Service Portfolio which can be provided on request.

4. Licensing and accreditation

It is a legal requirement that laboratories or organisations carrying out activities of procurement, testing, processing, storage, distribution and import/export of adult or post-natal human cells or tissues for human use are licensed for these activities by the competent authority, the Human Tissue Authority (HTA) in compliance with UK legislation. Other systems of accreditation such as FACT-JACIE are voluntary although JACIE is mandatory for paediatric processes and for handling licenced CAR-T products.

4.1. Human Tissue Authority (HTA) License

Each SCI laboratory is licensed by the HTA in accordance with the Human Tissue (Quality & Safety for Human Application) Regulations 2007 and their storage for research and other scheduled purposes defined in the Human Tissues Act 2004 (Table 1).

NHSBT Site	License No.	HTA Licensed activities performed by SCI laboratories				
		Processing	Storage	Storage of relevant material	Distribution	Export
Barnsley	22681	Y	Y	Y	Y	Y
Birmingham	11041	Y	Y	Y	Y	Y
Bristol - Filton	22518	Y	Y	Y	Y	Y
Oxford	11042	Y	Y	Y	Y	Y
Liverpool*	11018		Y	Y	Y	Y
Southampton	11053	Y	Y	Y	Y	Y

Table 1. HTA licenses held by NHSBT SCI laboratories

**The laboratory in Speke, Liverpool ceased processing stem cell donations in October 2022 but still stores stem cell donations for distribution and issue via the Barnsley SCI laboratory.*

Note that activities performed under each HTA license are according to tissue type and SCI laboratories do not hold licenses for all tissue types. Users should contact their respective laboratory to confirm the tissue types and activities they are licensed for if they require any changes to current arrangements.

4.2. JACIE Accreditation

SCI laboratories are accredited by the Joint Accreditation Committee ISCT-Europe & EBMT (JACIE), in accordance with FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product

Collection, Processing and Administration, with inspections for reaccreditation occurring every four years.

4.3. Wholesale Distribution Authorisation (WDA) License

NHSBT holds an MHRA licence for WDA which covers the receipt, storage and distribution of Advanced Therapeutic Medicinal Products for CAR-T Cell therapy.

5. SCI Contact Details

General enquires regarding services provided by SCI or CMT should be directed to cmt@nhsbt.nhs.uk. All other enquires should be sent to the local SCI laboratory, head of laboratory or CMT management using the contact details listed in **Tables 2 & 3,** depending on the nature of the enquiry.

5.1. Main laboratory

SCI laboratory	Contact email address*	Primary Telephone No.
Barnsley	sci.barnsleyreports@nhsbt.nhs.uk	0122 6868041
Birmingham	scibirm@nhsbt.nhs.uk	0121 2784171
Bristol - Filton	nhsbt.bmtbristol@nhs.net	0117 9125703
Oxford	sci.oxford@nhsbt.nhs.uk	0186 5387944
Southampton	nhsbt.scisouthampton@nhs.net	0238 0301324

Table 2. SCI laboratories contact details.
**Note that laboratory email addresses may be updated later in 2026, but hospitals will be notified separately if this occurs and the user guide updated accordingly.*

5.2. Head of laboratory & CMT management

Centre	Role	Email	Telephone No.
Barnsley	Head of BMT Clinical Services	mbithe.mutunga@nhsbt.nhs.uk	0747 114 7892
Birmingham	Head of Cell Therapies - Birmingham	Graham.caine@nhsbt.nhs.uk	0738 501 0504
Bristol - Filton	Head of Cell Therapies - Filton	Allison.blair@nhsbt.nhs.uk	0771 815 5264
Oxford	Head of Cell Therapies - Oxford	Gurman.kaur@nhsbt.nhs.uk	0738 597 2255
Southampton	Head of Cell Therapies - Southampton	Rachael.wyre@nhsbt.nhs.uk	0739 213 9972
National	National Operations Manager - CMT	Sue.davey@nhsbt.nhs.uk	0747 114 8197
National	Assistant Director for CMT	Jon.smythe@nhsbt.nhs.uk	0776 428 0838

Table 3. SCI Heads of Laboratory and CMT Management contact details

6. SCI laboratory working hours

NHSBT are committed to providing a service to enable stem cell collections to be received, manipulated, cryopreserved and/or issued at prearranged times outside normal working hours, which varies between laboratories, based on clinical demand (**Table 4**).

SCI laboratory	Normal working hours	Out of hours
Barnsley	Mon-Fri 07:30 – 19:30	19:30-07:30 Mon-Fri All day Sat-Sun & bank holidays
Birmingham	Mon-Fri 07:00 – 19:00	19:00-07:00 Mon-Fri All day Sat-Sun & bank holidays
Bristol - Filton	Mon-Fri 09:00 – 17:00	17:00-09:00 Mon-Fri All day Sat-Sun & bank holidays
Oxford	Mon-Fri 08:00 – 17:30	17:30-08:00 Mon-Fri All day Sat-Sun & bank holidays
Southampton	Mon-Fri 09:00 – 17:00	17:00-09:00 Mon-Fri All day Sat-Sun & bank holidays

Table 4. Working hours for each SCI laboratory.

6.1. Out of hours provision

Each SCI laboratory provides an on-call service operated by an experienced scientist 24 hours a day, 365 days a year, although the start and finish time differs between sites (**Table 4**) based on the working hours required for the routine work.

The on-call service will ensure an immediate response to any cryostorage alarms to preserve the integrity of frozen cellular products. Other out of hours work is limited to time critical activities that cannot wait until the following working day such as the issue of cells for infusion. More complex emergency activity requiring more than 1 member of staff may be possible by prior arrangement, but this will be dependent on volunteers as it is not feasible for SCI to have multiple staff on call at all times for only occasional more complex work.

Out of hours contact details are listed in **Table 5**, with NHSBT hospital services departments providing the initial point of contact at some sites, depending on local arrangements, who will be able to contact the on-call SCI scientist.

SCI Laboratory	Out of hours primary contact number(s)
Barnsley	Hospital services 01226 868061
Birmingham	07823 351714 (primary) – Lab on-call phone 0121 278 4037 (secondary) – Hospital Services
Bristol - Filton	On call phone 07711 447660
Oxford	On call phone 07764 280663
Southampton	On call phone 07764 280016

Table 5. Out of hours contact telephone numbers.

7. Business continuity strategy

Whilst the preferred position is for each SCI laboratory to be self-sufficient, there are occasions when SCI services can be reprovisioned between sites. This is typically because the primary SCI laboratory does not provide the service requested by their local hospital.

Reprovisioning may also be necessary during times of operational difficulty, in accordance with the CMT Business Continuity Plan. In such circumstances, the reprovisioning of stem cell services is coordinated centrally via the CMT National Operations Manager or designate.

Once reprovisioning has been agreed, all communication with the requesting hospital MUST be via the primary SCI laboratory to avoid any confusion, copying in the processing laboratory where relevant. This includes provision of reports generated by the processing laboratory which will be emailed to the primary SCI laboratory for onward distribution to the requesting hospital.

8. Summary of Services Provided by SCI Laboratories

All SCI laboratories can provide the following services, which are described in more detail throughout this user guide.

- Co-ordination with TAS or other collection centres to arrange collection and processing times suitable for patient treatment within laboratory working hours.
- Co-ordination with collection units and hospitals to evaluate samples and products from donors to ensure adequate CD34+ and/or CD3+ cell doses from cell collections.
- Use of flow cytometric assays to assess the viability, cell dose and purity of target cell populations and the efficiency of processing operations.
- Preparation of therapeutic T cells e.g. in measured CD3+ doses
    - excess peripheral blood stem cells (PBSC)
    - mononuclear cells (MNC) collection
- Cryopreservation and long-term storage of stem cells and related therapeutic cells.
- Co-ordination with NHSBT Testing and Microbiological Services Laboratories for microbiological testing to assure the suitability of donors and the safety of products.
- Organisation of safe transit of Cellular Therapy Products in a timely manner between processing facilities and hospitals in line with national and international guidelines.
- Receipt, storage and issue of cells from external organisations.

In addition, selected SCI laboratories offer more specialist cell processing and testing which are listed below. **Table 6** provides a summary of which laboratories support which services.

- Preparation and delivery of collection kits for directed cord blood (DCB).
- Cryopreservation and storage of DCB.
- Processing of bone marrow by validated methodology to:
    - reduce product volume e.g. prior to cryopreservation
    - deplete red blood cells e.g. to reduce the risk of ABO incompatible infusions
    - concentrate mononuclear cells, purge lymphocytes and purify stem cells
- Selection of CD34+ cells from stem cell apheresis collections.
- Depletion of TCRαβ plus CD19 depletion from stem cell apheresis collections.
- Washing and/or diluting of cryopreserved products after thawing.

- Perform colony forming unit (CFU) assay to demonstrate progenitor cell viability and process suitability.

If a hospital requires a service not provided by their affiliated laboratory, it is possible to arrange the transfer of products to an SCI laboratory that does, with appropriate notice.

Activity	Barnsley	Birmingham	Filton	Oxford	Southampton
Prepare and deliver DCB collection kits		Y		Y	
Cryopreservation and storage of DCB		Y		Y	
Adult Bone Marrow processing	Y		Y		
Low volume Bone Marrow processing	Y	Y	Y		
CD34+ cell selection	Y	Y	Y		
TCRαβ plus CD19 cell depletion	Y	Y			
Thaw wash of cord blood products		Y	Y		
CFU assay	Y	Y		Y	Y
Campath addition to product					Y

Table 6. SCI laboratories providing specialist services.

9. Request/Clinical Referral Process

The following clinical referral form and associated guidance on how they should be completed can be obtained from Stem cell forms - Hospitals and Science - NHSBT. These include the following:

- **FRM5071** – Request to collect and process stem cell and immunotherapy products
- **INF1243** – Referral of patients for stem cell collection and processing at NHSBT

Requestors are responsible for liaising with NHSBT to arrange cell collections and informing NHSBT of expected dates, types and locations of collections, where these are not performed by NHSBT. A period of reasonable notice, a minimum of ten (10) working days, when possible, should be given. The requester should advise NHSBT before the start of conditioning therapy and complete the appropriate processing prescription form at least seven (7) days prior to the first cell collection giving the date and location of collection (where appropriate) and a precise description of requirements e.g. cell depletion, volume reduction, red cell depletion, cryopreservation, preparation of Therapeutic T cells etc.

In relation to the donation of bone marrow, peripheral blood or other cells and tissues collected as starting material or for transplantation, the requestor is responsible for HTA licensing requirements for procurement of donations carried out by the Purchaser or for ensuring HTA licensing requirements for

procurement and processing are in place with registries or clinics supplying procured bone marrow, peripheral blood or other cells and tissues collected as starting material or for transplantation on behalf of the Purchaser.

Requestors must also ensure that bone marrow, peripheral blood stem cells, or cells collected as starting material or donor lymphocytes are collected, labelled and identified and packaged in accordance with the Regulations. NHSBT will allocate a unique identifier and provide collection labels for the Purchaser to apply to the collected cells. All end user establishments should record the unique identifier in recipient patient records. Further identifiers must be included as a minimum:

- patient's full name
- hospital number
- NHS number
- date of birth
- proper name of product
- date and time of collection
- approximate volume
- volume and type of anti-coagulant
- identity of the collection facility
- recommended storage temperature
- expiry date and time

Prior to the collection of any cells from an individual, it is the responsibility of the referring consultant to clearly specify what processes are to be performed on the harvest. Processing requirements should be provided in writing to the appropriate SCI laboratory at least seven (7) days before the collection. If process requirements are dependent upon collection counts, this must be clearly explained on the referral. Requirements should be provided using the referral form (FRM5071) which must be signed or approved by the referring consultant. Failure to provide adequate notice may result in the necessary postponement of processing.

Requests for novel or non-validated processes must be formally discussed with the SCI laboratory head in the first instance and may be subject to a separate written agreement.

9.1. Changes to requirements

The referring consultant must discuss and notify in writing any changes with the Head or nominated deputy of the SCI laboratory. There may be occasions where last minute changes to processing requests cannot be accommodated but NHSBT will also utilise other sites where possible.

10. Consent for Testing, Storage and Discard

The requestor is responsible for obtaining and documenting appropriate consent for collection, testing, storage and discard from the donor, patient or guardian in accordance with the HTA Codes of Practice and the JPAC/SaBTO Tissue Donor selection guidelines. Allogeneic donations from non-Gillick competent children and donations from adults who lack the capacity to consent must only proceed once approved by an Assessor accredited by the HTA. Documentary evidence of compliance with the HTA Codes of Practice must be provided to NHSBT as may be requested from time to time.

The requestor is responsible for determining suitability and eligibility of allogeneic donors. Documented evidence of donor suitability and eligibility must be provided to the SCI laboratory prior to the start of the collection procedure, including the name of the responsible person and date of determination.

The following consent form and associated guidance for healthcare professionals, patients and their families can be found via Stem cell forms - Hospitals and Science - NHSBT

- **FRM1570** - **2B** Consent for the testing, storage and discard of cellular therapy products

- **INF285** - Guidance for healthcare professionals in consenting for the testing, storage and discard of cellular therapy products
- **INF1750** – Patient/family information leaflet for the consent, testing, storage and disposal of cellular therapy products for patients undergoing stem cell transplantation

11. Sending samples and cell collections to SCI

The requester is responsible for arranging transportation of samples and cell collections, in conjunction with NHSBT, to the SCI laboratory in accordance with a documented, validated method. The collection facility must notify the NHSBT SCI laboratory of the precise time of arrival.

Products must be sent as soon as possible following collection and arrive during normal working hours, wherever possible.

If the time from end of collection to receipt by the SCI laboratory exceeds one hour, the collection facility must ensure that the donation is stored at 2-8°C and/or transported in validated transport containers with pre-chilled cool packs.

12. Testing of Samples, Cell Collections and Components

The SCI Laboratories will only process and store cord blood, bone marrow, mobilised peripheral blood or other cellular product harvests in accordance with the minimum standards and specifications detailed in POL99 including the Human Tissue Authority (HTA) directions 001/2021 (and subsequent amendments) given under the Human Tissue Act 2004 implementing the Human Tissue (Quality and Safety for Human Application) Regulations 2007.

Note that testing activities performed under each HTA license are according to tissue type and NHSBT laboratories do not hold testing licenses for all tissue types. Users should contact their respective SCI laboratory to confirm the tissue types requiring testing are licensed if they require any changes to current arrangements.

12.1. Mandatory Testing

It is a regulatory requirement that any patient or donor of material processed in a stem cell laboratory should undergo testing for infectious disease markers (IDM) no more than thirty (30) days prior to collection and on the day of collection. Tests are mandated by the Human Tissue Authority and include HIV antibody/antigen and nucleic acid testing (NAT), Hepatitis B & C virus serology and NAT, Hepatitis E virus NAT, HTLV1+2 serology and syphilis testing. These tests are undertaken by NHSBT on provision of appropriately labelled blood in a tube. Alternatively, results from an appropriately HTA licensed and accredited laboratory can be sent to the SCI laboratory.

If NHSBT are required to perform IDM testing, the requestor must provide appropriate blood samples or results from a licenced laboratory as specified for microbiology testing and blood grouping a maximum of thirty (30) days and minimum of five working (5) days prior to collection of haematopoietic progenitor cells (HPC), or cells collected as starting material. Appropriate blood samples must also be taken and sent to NHSBT on the day of collection to enable additional testing to reduce any window period.

Additionally, if a patient/donor has visited/was born/resides in a geographical area which presents an increased risk of exposure to infections such as malaria, T. cruzi and West Nile Virus (WNV), then supplementary testing should be instructed by the clinician. Information regarding the geographical disease risks can be found on the JPAC website.

ABO and Rh blood grouping are required on 2 independent samples prior to allogeneic transplantation but can be performed at any point pre-transplant by the hospital or can be performed by NHSBT.

Recipient ABO Antibody screening should also be performed prior to allogenic transplantation in accordance with JACIE requirements. Whilst this screening is usually performed by the hospital, results should also be provided to the respective SCI laboratory for their records.

12.1.1. Samples required

Sample volumes must be adequate for automated testing equipment used by NHSBT. For each patient or donor please send the following blood samples, which must be sent along with the consent FRM1570 at least 1 week prior to the proposed cell collection:

- two 6ml EDTA tubes
- one 6ml Greiner PPT tube.
- If blood grouping is required, an extra 6ml EDTA tube is needed.
- If a test for malaria/chagas (T. cruzi)/WNV is required, an additional 6ml EDTA tube is needed.

12.1.2. Sample labelling

All samples must be labelled, with sufficient information to ensure accurate patient/donor identity. Sample labels must be hand-written or printed 'on demand' and attached to the sample tube next to the patient at the time of phlebotomy. The minimum labelling requirements are:

- surname/family name and first name[s] in full [correctly spelt]
- date of birth [not age or year of birth]
- NHS Number
- Hospital number (if NHS number is not available)
- the place of sample collection
- time and date sample taken
- Signature of person taking the sample

The sample tube must be signed by the person taking the sample, have the time recorded and dated to ensure that it is fresh enough to give accurate results within the parameters of the test(s) requested.

12.1.3. *Actions in the event of a positive IDM result*

The SCI laboratory will inform the requestor of any sample which tests as potentially IDM positive within 24 hours of being informed by the NHSBT testing department, where practical. Confirmatory IDM testing will then be undertaken by NHSBT's Microbiology Services Laboratory, with results forwarded accordingly. The requestor is responsible for subsequent counselling and referral of patients/donors where microbiological test results are positive.

The SCI laboratory should be informed by the requestor if the patient/donor is known to be positive for an IDM. A positive microbiology test result does not preclude collection, processing and storage but known positive products will only be processed by prior agreement and if timing permits the NHSBT Stem Cell and Immunotherapy laboratory to not be undertaking any other process at the same time.

12.2. Evaluation of HPC mobilisation, cell dose and cell quality

The tests and procedures for measuring, assaying and monitoring the properties of cell products is essential to evaluate their safety and efficacy prior to clinical use.

12.2.1. Pre-collection assessment

If the requestor requires the SCI laboratory to perform an assessment of HPC mobilisation prior to apheresis e.g. CD34+ cells in the case of HPC collection, an EDTA blood sample with associated documentation must be sent to the SCI laboratory as soon as possible.

The requesting apheresis unit will be informed by telephone when the results are ready and the associated report emailed to them.

12.2.2. Harvest evaluation

All products are evaluated by NHSBT for CD34+ and/or CD3+ cell content, according to sample type, as soon as they reach the SCI laboratory. This typically takes 75 minutes from product receipt.

CD34 positive cell counts and viability assays by flow cytometry are performed on all HPC cell collections on receipt, and after more than minimal processing, e.g. cell selection. CD3 positive cell counts and viability assays by flow cytometry are performed on TC/PBMC collections on receipt and after more than minimal processing.

Preliminary written reports of cell counts, volumes, viability, CD34+ numbers, CD3+ numbers, depletion efficiency and other markers where appropriate are prepared on the day of process and sent and received by email to an agreed member of the transplant team and/or collection staff. Cell counts may also be provided by telephone where requested in addition to a written report.

If processing and or cryopreservation are completed outside normal working hours, the relevant counts will be telephoned to the Referring Consultant or agreed representative as soon as results are available. A report will then be sent and received by email within the hour to confirm the telephone message.

The requestor is responsible for ensuring trained personnel are available at all times to receive CD34, CD3 and other cell counts as necessary to facilitate stem cell collection, processing, and storage options and the management of growth factor administration, where required, to patient or donor.

If the reported CD34+ dose is below 0.2 x 10^6/kg, the dose is considered substandard. In these circumstances, the patient's consultant may decide it is not required and the product discarded with their agreement.

12.3. Bacterial contamination

Product specifications require that all products have been tested and found negative for bacterial and fungal contamination after processing, using either the finished product or an equivalent processing residue. Sources of contamination can include:

a) Contamination present or introduced at the point of collection, either originating from the patient, or from the equipment used during the donation.
b) Contamination at the point of processing/sampling/inoculation of culture bottles
c) Contamination at the point of microbiological analysis

Due to the low risk of contamination during the collection process, products collected by apheresis are only tested for bacterial contamination post processing, whereas bone marrow is tested pre and post processing, summarised in **Table 7**. Cord blood is not tested pre-processing due to the limited volume collected to maximise the number of cells available for clinical use.

Anaerobic and aerobic culture bottles inoculated with the relevant samples are sent for culture, examination and interpretation to either the NHSBT Microbiology Services Laboratory (MSL), based in Colindale, or to a local hospital microbiology laboratory. Following isolate identification, positive samples may need to be referred to an external laboratory for antibiotic sensitivity testing. Responsibilities for all non-NHSBT laboratories used are defined by third party agreements.

Due to incubation times of up to 10 days and the potential for onward referral for additional testing if contamination is identified, results of bacterial testing may not be available before the products are issued for patient infusion.

Product	Sample at
Bone Marrow- Unmanipulated -fresh issue	Receipt
Bone Marrow- Volume reduction then fresh issue	Receipt AND after Volume reduction
Bone Marrow- Volume reduction then cryopreservation	Receipt AND at cryopreservation
Allo PBSC- Fresh issue	Fresh issue
Allo MNC- Fresh Issue	Fresh issue
Allo PBSC- to be cryopreserved	Cryopreservation
Allo MNC- to be cryopreserved	Cryopreservation
Auto PBSC	Cryopreservation
Auto PBMC	Cryopreservation
Cord Blood	Cryopreservation

Table 7. Testing protocol for the bacteriology contamination of cell products

Any evidence of contamination will be reported via telephone and/or email to the respective clinical team as soon as possible. Positive results will also be reported to the HTA, logged as a quality incident and investigated to root cause.

Cryopreserved products with outstanding bacterial testing results or collections positive for bacterial or fungal contamination will be issued as non-conforming products under concession after discussion with the patient's consultant.

12.4. Colony Forming Unit (CFU) analysis

The CFU assay quantifies the growth potential of HPCs contained within a bone marrow, peripheral blood stem cell or cord blood collection by stimulation of committed progenitor cells to form colonies in a semi-solid tissue culture medium. Visualisation and enumeration of colonies is performed following incubation for 14-16 days and results are sent to the requesting clinician via email.

When a request is received for the issue of cells stored for more than five years, a CFU assay is routinely performed on a stored cryovial taken from the respective product at the time of cryopreservation. Viability checks and CFU assays are also indicated for investigations of delayed engraftment, for other circumstances that may indicate potential loss of product viability and future engraftment potential. Regular performance of this procedure also supports the NHSBT's stability program for viability of cell therapy products stored for many years.

The required specification for a CFU dose for transplant is ≥1 x 10^5/kg. Failure to meet this requirement may require issue of any product under concession.

13. Cell processing

If processing of a cell collection is required prior to cryopreservation or infusion, it is necessary to agree a suitable date for processing in advance with the respective laboratory. Adequate notice is essential to ensure the availability of specialist equipment and to allow sufficient time to order any specialist reagents required that are not routinely held in stock due to a short shelf life.

Some specialist processes can be performed in the SCI laboratory, such as bone marrow volume reduction, because they are closed processes which do not expose the cell product to the external environment. Other procedures, such as cell selection and depletion require processing in a clean room to ensure product sterility. Any procedure performed in a cleanroom takes additional time due to lengthy operator gowning procedures and environmental monitoring required. Less frequently requested procedures are not provided by all laboratories.

13.1. Volume reduction & red cell depletion of bone marrow

Some of the SCI laboratories have specialist equipment capable of volume reduction and red cell depletion of cell collections. The equipment employed for each process is determined by the type of cells harvested, the volume of the collection and its red cell content.

The majority of adult bone marrow harvests can be volume reduced using the Terumo Optia to a volume of less than 150ml, suitable for transplant or cryopreservation. Processing is expected to achieve a CD34+ cell recovery of ≥50% and if required, RBC depletion to a volume <20ml.

Paediatric and smaller adult bone marrow donations require processing with a Sepax device, which reduces the volume to 25% of the initial packed cell volume, obtaining ≥50% CD34+ cell recovery.

Note that volume reduction of BM will always be required if the product requires cryopreservation.

13.2. Cell selection & depletion of HPC(A)

Cell selection and depletion techniques are only performed on HPC collected via apheresis. Each process requires specialist equipment that uses very expensive monoclonal antibodies with a short shelf life, so are usually ordered only when required for specific patients. Therefore, at least 2 weeks' notice is required to ensure the process can be scheduled and all reagents are ordered in time, so they are available in the laboratory *before* the day of cell harvest.

It is recommended that the cells are less than 24 hours old prior to selection or depletion, so collections travelling from abroad may not yield as high recoveries. A high CD34+ cell dose is required for these processes and may require one or two vials of the commercial beads/antibodies, depending on the number of cells to be processed (**Table 8**).

Parameter	**CD34+ Selection**		**Cell depletion**	
Max. target cell count	0.6x10^9 CD34+	1.2x10^9 CD34+	24×10^9 TCRα/β+ 5×10^9 CD19+	45×10^9 TCRα/β+ 10×10^9 CD19+
Max. total cell count	60x10^9 WBC	120x10^9 WBC	40x10^9 WBC	80x10^9 WBC
Application	Normal scale	Large scale	Normal scale	Large scale
No. of vials of beads/antibodies	1	2	1	2

Table 8. Key parameters for cell selection and depletion procedures

Cell selections and depletions are technically complex and protracted procedures, taking up to 14 hours and require a team of experienced SCI scientists working within a cleanroom environment. Therefore, laboratories offering this service are limited to a maximum of one cell selection or depletion process per week.

Note that it is not possible to create DLI doses from negative fractions generated during selection or depletion procedures.

13.3. *CD34+ cell selection*

Three of the five SCI laboratories have a CliniMACS Prodigy automated cell processing instrument which has been validated for the selection and enrichment of CD34+ cells from HPC apheresis collections.

Following selection, HPC(A) collections should expect to achieve a CD34+ cell recovery of ≥50% and a CD34+ cell purity of ≥80%. This process also results in a ≥4 log depletion of CD3+ cells.

13.3.1. Cell depletion

The CliniMACS Prodigy instruments have been validated for the automated depletion of TCRα/β+ and CD19+ cells from HPC apheresis collections at two SCI laboratories.

This process can expect to achieve a ≥ 3.5 log depletion of TCRα/β+ content, and CD19+ cells depletion by ≥ 2 logs, with ≥50% CD34+ cell recovery.

13.4. Thaw washing

Thaw washing can be performed to remove DMSO cryoprotectant and red cell debris from cryopreserved products prior to patient infusion. This would typically be required for patients with a low body weight receiving a cord blood transplant and/or those sensitive to DMSO.

The cells are thawed by the SCI laboratory and then washed using specialist equipment within a cleanroom environment, with the aim of achieving ≥ 50% CD34 cell recovery. This process takes 3-4 hours. Once thawed and washed, the cells are issued immediately and must be infused within 4 hours of processing.

14. Cryopreservation

To ensure that cells remain suitable for clinical use, any product that will not be infused into a patient within 72 hours from collection will be cryopreserved. It may be appropriate to cryopreserve the entire collection to store for transplantation later e.g. for autologous transplantation, or to freeze excess cells from an allogeneic harvest and store for future use if required.

Products may be stored overnight in a temperature-controlled environment prior to cryopreservation. However, SCI laboratories are required to dilute local apheresis collections for holding at 2-8°C overnight, if the cell concentration is more than 200 x 10^9/L.

Processing of cells should commence within 24 hours of the end of collection procedure, although this will not always be feasible for allogeneic harvests, particularly if they are collected outside the UK.

To maintain the integrity and viability of cells during cryopreservation and ongoing storage, a solution of cryoprotectant is prepared using DMSO diluted with either plasma collected during apheresis or using Human Albumin Solution (HAS). Alternative diluents may be used subject to further validation. When this cryoprotectant is added to the cells, it results in a final DMSO concentration of approximately 10%.

Following addition of the cryoprotectant, the cells are transferred into multiple cryostorage bags, ensuring each bag contains equal volume / cell dose, unless otherwise specified by the clinician. The filled cryostorage bags are then double wrapped, vacuum packed and frozen using a controlled rate freezer prior to storage at less than -150°C. Separate samples of all cryopreserved cell therapy products are also frozen in cryovials at the same time for long term viability assays and any follow up investigations required, such as delayed engraftment.

All bags and cryovials are then transferred to the vapour phase of liquid nitrogen for storage.

15. Preparation of T-Cell doses / DLI

Specific T cell doses, also described as donor lymphocyte infusions (DLI) are commonly used in patient treatment for Allogeneic Stem Cell Transplantation. T cell doses can be prepared from a variety of donations; specifically collected cells for T-cell manufacture, whole blood, MNC Apheresis or HPC-A donations.

The product used for T-cell preparation is evaluated for CD3 count prior to DLI preparation. The doses prepared should be taken from the Consultants referral or following review of collection doses and a discussion with the consultant. Note that the maximum number of T cell doses that can be prepared from each collection is 18 bags.

16. Product storage & Discard

Each SCI laboratory has Cryogenic storage facilities which house cryogenic storage vessels connected to an automatic supply of liquid nitrogen and access to similar off-site storage. All products are stored in the vapour phase of liquid nitrogen. Cryostorage vessels are continually temperature monitored with an alarm system in place 24/7 which alerts the SCI team to risk of temperature excursions so that mitigating action can be taken, including out of hours. Contingency tanks are available at each site should there be a fault with a working vessel.

SCI have a significant number of cryostorage vessels stored off-site at a commercial HTA licensed facility due to limited onsite storage capacity. As well as additional storge space, the off-site facility provides NHSBT with emergency contingency storage for business continuity purposes.

16.1. Storage/ Inventory management.

Costs associated with storage using liquid nitrogen are significant due to the specialist facilities required and therefore there is a need to regularly review requirements for ongoing storage of cellular products..

To facilitate this review, SCI laboratories provide hospitals with details of each patient's HPC and TC products in storage. Consultants responsible for the care of transplant patients are required to indicate, at least annually, which components are no longer required for clinical use since:

- the patient may have died; or
- it may be agreed that the patient is well and long-term survival is expected; or
- the component may no longer be indicated due to the patient's disease status; or
- the component may no longer be considered acceptable or safe for clinical use.

16.2. Discard process

Consultants responsible for the care of transplant patients are required to inform NHSBT, at least annually, of any cellular product no longer required for clinical use. Applications to discard products should be made by the hospital transplant clinician by completing '***FRM1960*** *Request for authorisation to discard HPC or other cellular therapy product*', available via Stem cell forms - Hospitals and Science - NHSBT).

All requests for discard must be reviewed and approved by the Head of SCI / Processing facility director. If the respective patient is still alive, evidence of patient consent is required and requests for discard must also be reviewed and approved by the processing facility Medical Director. Once approved, the discard of each product is managed by an HCPC registered scientist.

16.3. Transfer of cryopreserved cellular therapy products to a private facility

Where a product is recommended for discard the hospital must offer the patient (if still alive) the opportunity for their donation to be transferred to another storage facility at the patient's or hospital's expense in line with BSBMTCT and JACIE recommendations. The hospital must notify the respective SCI laboratory via email that a transfer request has been made, providing patient details and unique product codes for the bags to be transferred. The SCI laboratory will then provide a form for the hospital to complete. The patient will need to independently contact an external private cryostorage company and confirm availability. Note that SCI laboratories are not permitted to recommend external companies to hospitals or patients, but they will liaise and make the necessary arrangements, following contact from the external cryostorage company.

16.4. Use of products for non-clinical issue

If a patient has provided appropriate consent via FRM1570, their cellular products may be used for research, service development or for education and training purposes rather than be discarded, following receipt of a completed FRM1960 from the respective clinician.

CMT manage any requests for products via the NHSBT's Non-Clinical Issue process. Information is available online for potential requestors of products for Non-Clinical Issue (NCI) via Non clinical issue - Hospitals and Science - NHSBT (blood.co.uk), including the application form.

17. Product labelling

All labelling of cellular therapy products complies to the ISBT standard. At completion of processing, the product label or package insert will contain the following information:

- Unique numeric or alphanumeric identifier
- Proper name of the product
- Product attributes (previously called modifiers and manipulations)
- Recipient name and/or identifier
- Identity and address of collection facility or donor registry
- Date, time collection ends, and (if applicable) time zone
- Approximate volume
- Name and quantity of anticoagulant and other additives
- Donor identifier and (if applicable) name
- Recommended storage temperature range
- Biohazard and/or Warning labels (as applicable)
- As applicable:
    - Statement 'NOT EVALUATED FOR INFECTIOUS SUBSTANCES'.
    - Statement 'WARNING: Advise Patient of Communicable Disease Risks'
    - Statement 'WARNING: Reactive Test Results for (name of disease agent or disease)'
- Identity and address of processing and distribution facility(ies)
- Statement 'Do Not Irradiate'
- Expiration Date (if applicable)
- Expiration Time (if applicable)
- ABO and Rh of donor (if applicable)
- Statement "FOR AUTOLOGOUS USE ONLY" (if applicable)

When the product is to be distributed for administration, in addition to above it must be labelled with the following information:

- RBC compatibility determination (if applicable)
- Statement indicating that leukoreduction filters shall not be used
- Date of distribution

Partial labels may be used under the JACIE guidelines, if there is a lack of space on the label. Full labelling details are provided in the FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing and Administration.

17.1. Provision of labels

SCI laboratories create labels for distribution to NHSBT TAS units and SCI affiliated collection facilities. Note that SCI can only provide labels for harvests collected by apheresis, from bone marrow and/or cord blood.

18. Reporting

SCI laboratories produce reports associated with each transplant request to ensure the clinical team are kept informed at each stage of the process, detailed below.

18.1. Pre-collection cell count report

This report shows the concentration of CD34+ cells in the peripheral blood of a potential HPC(A) donor and is produced immediately upon completion of testing. The apheresis coordinator will be called to inform them that results are being emailed so they can make urgent decisions regarding scheduling of apheresis procedures.

18.2. Interim report of donation

This report shows the cell doses collected for the respective patient and is produced immediately upon completion of testing, usually within 75 minutes from receiving the products.

Written reports of cell counts, volumes, viability, CD34+ and/or CD3+ numbers, where appropriate are sent and received by secure email to an agreed member of the transplant team and/or collection staff. Cell counts may also be provided by telephone, where requested in addition to a written report.

If receipt of the product is completed outside normal working hours, the relevant counts will be telephoned to the referring consultant or agreed representative as soon as results are available. A report will then be sent and received by secure email within the hour to confirm the telephone message.

18.3. Preliminary report

These reports can be prepared and issued upon request and contain processing and cryopreservation information, which will be detailed in the final report, excluding as yet incomplete test data.

Reports will be sent via secure email.

18.4. Final report of donation and processing

The final report confirms and expands on the preliminary report and is completed on receipt of the following data:

- Bacteriology testing results
- Further mandatory marker testing results (if applicable)
- CFU analysis on the product or a representative sample (if applicable)
- Stem cell viability analysis, post cryopreservation (if applicable)

The report will summarise all of the collections and processing completed in response to the original request and will only be issued following data review and authorisation by the Head of SCI laboratory/laboratory director or designated deputy.

Final reports should be issued typically within twenty-one (21) days from product receipt and include:

- A table of all donations associated with the request, including cell counts and doses described for preliminary report plus blood group and bacteriology.
- Processing outcomes, detailing final fresh issue products of all donations, products of all donations remaining in clinical storage and any cryopreserved issued products of all donations
- Laboratory comments
- Clinical advice/comment (where applicable)

18.5. Summary of products issued report

This report accompanies the cells for infusion, either fresh or cryopreserved. It is created when issuing cells and sent in paper form with the transplant. It includes space for the nurses to add details of thawing times, lot numbers and serial numbers of equipment used. These should be returned via secure e-mail after the infusion has taken place, along with the adverse incident report (see section 21)

19. Product Specifications & Clinical Concessions

SCI laboratories will only process and store cord blood, bone marrow, mobilised peripheral blood or other cellular product harvests in accordance with the minimum standards and specifications required by the licencing and accreditation bodies detailed in section 4.

However, SCI recognises the unique nature of the products it handles and will allow HPC donations or products which fail to meet the defined minimum criteria to be processed and released for clinical use providing the consultant responsible for the care of the patient or an SCI Consultant agrees that the clinical benefits of receiving the transplant outweigh any risks to the patient of not receiving the transplant.

Systems for product release involve quality checks against a series of product specifications prior to product issue for patient infusion. **Any products failing to meet specification will be discussed with the transplant physician.**

Where a product, or a series of products, does not meet the requested cell dose, they may be issued under a clinical concession e.g. when the CD34+ cell dose is low or viability poor.

In addition to these generic requirements, there are several product-specific specifications which, depending on the product in question, detail requirements in respect of:

- anticoagulant
- cell viability
- WBC concentration
- platelet concentration
- MNC (%)
- age prior to processing
- storage temperature prior to processing
- Product volume
- red cell depletion
- CD34 cell recovery and purity
- CD3 and/or CD19 depletion
- TCRαβ (alpha beta) depletion
- cryopreservation temperature profile
- storage temperature
- cryoprotectant concentration

Full product specifications are available on request from SCI Heads of laboratory.

20. Product issue

SCI expects hospitals to handle and infuse the processed HPC and TC provided in accordance with these same standards in the interest of patient care and safety. This forms part of the SCI approach to managing clinical risks. Therefore, SCI laboratories will provide instruction and guidance to hospital users to inform their policies, practice and procedures.

The SCI laboratory head/director or designated deputy must authorise the release of all cell collections and components for issue and/or storage. The SCI laboratory head or deputy, with assistance from the SCI consultant where appropriate, must liaise with the transplant clinician responsible for the care of the patient to determine and record the suitability for clinical application of products which do not meet the required specification.

Reinfusion dates and times for all Products must be agreed in advance and prior to conditioning of the patient with the SCI Head of laboratory or nominated deputy and confirmed in writing using the appropriate form supplied by NHSBT. This will enable the SCI laboratory to check the location of the products prior to the start of conditioning.

The transplant centre shall arrange with the SCI laboratory to transport the cells in validated transport containers to the transplant centre, either using either NHSBT staff and transport or appropriately registered couriers. Where genetically modified organisms are transported, couriers must comply with the agreement concerning the carriage of dangerous goods by road (ADR) special provision 637.

20.1. Requesting product(s) for issue

The transplant centre must provide appropriate completed SCI request forms and paperwork to request the issue of the cellular products. The ABO blood group of patient and donor (as applicable), dose, volume and/or number of bags, date/time and location for delivery must be specified. The Products, cell doses and any further processing required must be clearly identified on the request form, including the unique identifier of the product.

20.2. Issue of fresh products

Non-cryopreserved Products will be delivered to a nominated representative of the Transplant Centre by either a member of the SCI laboratory, NHSBT transport or by an approved courier as soon as processing and quality checks have been completed, unless temperature-controlled storage is required.

Each primary storage pack will be overwrapped in a sealed single-use bag and transported in a validated and approved container along with associated paperwork. On arrival at the transplant centre, a member of the nursing or medical staff will be required to sign the transit form to accept delivery.

Any discrepancies between products delivered and those expected or incorrect details on pack labels or accompanying paperwork should be noted at this time.

The product must only be handled and prepared for infusion by trained NHSBT or hospital staff and handling instructions (INF288) which accompanies each delivery is read by the recipient's clinical team prior to infusion.

The infusion of the product should be commenced within a timeframe that ensures safe infusion of the product within 4 hours of its removal from the transit container. All fresh issue cells must be infused into the recipient within 72 hours of the donation end time.

20.3. Issue of cryopreserved products

The transplant centre should provide at least one (1) week notice for cryopreserved products to be issued, wherever possible. This is to ensure products can be returned to site (if stored remotely) and enable the necessary quality checks to be performed to ensure the product(s) are suitable for clinical use. Patients should not start conditioning therapy until the laboratory has confirmed the cells are available and suitable for issue. It is acknowledged that this may not always be possible in unexpected clinical circumstances and in these cases the hospital must inform the SCI laboratory prior to conditioning therapy being given.

The number of cryopreserved bags issued for infusion is determined by the cell count not by the original product collection volumes and will need to be considered when calculating the total DMSO and red cell volume per patient.

If the total volume of red cells in cryoproducts is > 0.25mL/Kg patient weight, there is an increased risk of an adverse reaction post infusion. The volume of DMSO should be limited to <1ml/Kg patient weight per day to reduce the risk of adverse reactions post infusion. If either of these issues are identified, the transplant centre will be informed prior to issuing the transplant and the clinician asked to authorise concessionary issue.

It is essential that the product information and handling instructions (INF284) that accompanies each delivery of cryopreserved products is read by the recipient's clinical team prior to thawing and infusion of any cryopreserved products.

Cryopreserved cells, once thawed, must be infused within 15 minutes of the completion of the thawing process, except for thawed and washed cells, which should be infused within 4 hours of processing.

21. Transplant outcome

Information provided by hospitals on any adverse incident or event that occurs following infusion of products issued by SCI laboratories, alongside transplant engraftment data, is vital for the continued quality assurance of services SCI provides and is required by the HTA and EBMT/JACIE.

21.1. Reporting adverse events

Hospitals must evaluate and report to the SCI laboratory all serious adverse reactions as soon as possible and at least within 24 hours and patient/donor reactions to stem cell collection or transplantation in accordance with the Regulations. Any adverse events and adverse reactions associated with the administration of a cellular product issued by SCI should be reported immediately on the adverse incident report form (FRM1567) supplied with the product and emailed to the SCI department.

Any potential major, critical or serious adverse reactions or events should also be reported immediately via the Head of SCI laboratory to the NHSBT's Medical Director, NHSBT's Assistant Director for the Cellular and Molecular Therapies Function and NHSBT's Designated Individual, who will review and advise on these. The NHSBT Designated Individual is required by law to report any serious adverse reactions or events to the HTA within twenty-four (24) hours of the discovery of the reported occurrence.

Guidance for the classification of adverse events is contained within INF1857, which can be found on the NHSBT stem cells forms website Stem cell forms - Hospitals and Science - NHSBT under 'Submission of outcome data'.

21.2. Reporting engraftment – 2G forms

The SCI laboratory is obliged to maintain a record of clinical outcome data for all transplants involving products processed and/or tested in the laboratory. This is an essential aspect of assuring the quality of the services provided and is an HTA requirement.

Patient specific clinical outcome forms are sent to the referring consultant or an agreed representative after every transplant procedure. The referring consultant should return these forms with engraftment and other outcome data in a timely manner, at or around 30 days post infusion of HPC(A) and HPC(M) and on or around 42 days following HPC(C) transplants. Blank patient outcome forms are available on the NHSBT website- Stem cell forms - Hospitals and Science - NHSBT

22. Directed Cord Blood Collection

SCI laboratories in Oxford and Birmingham support the collection, cryopreservation and storage for directed or family cord blood donation.

Referrals must be made (or supported) by a transplant consultant using form 2C (FRM1571) which can be obtained via Stem cell forms - Hospitals and Science - NHSBT, along with associated information and guidance for healthcare professionals (HCP) on the collection of cord blood for directed transplantation (INF286). Initialisation of request for directed cord blood collection should commence a minimum of 8 weeks prior to estimated date of delivery.

All referrals must be checked for suitability by NHSBT SCI using the UK Paediatric BMT Group HSCT indications. The NHSBT SCI Medical Adviser will give medical clarification where the justification for collecting is unclear or if the mother has been reported to be virology positive.

The minimum criteria for sending a collection kit are 2C (FRM1571) & 2D (FRM1571) completed with no referral/consent issues & agreement received from obstetrician/midwives to collect.

- **FRM1572** – 2D Consent and eligibility for directed cord blood collection, testing, cryopreservation and storage
- **INF286** – 2L Information and guidance for healthcare professionals on collection of cord blood for directed transplantation
- **INF1153** – 2R – Information for mothers on directed cord blood collection, testing, cryopreservation and storage

DCB collection cannot proceed without these completed referral & consent forms. NHSBT does not support DCB collection for home births. Directed cord blood is collected by trained phlebotomists via a third party, who are contracted by NHSBT under a third-party agreement and acting under the HTA license of the SCI laboratory that will cryopreserve the donation. Collections are made in accordance with UK Paediatric BMT Group HSCT Indications, 15 October 2022 (Paeds-BMT-indications-2022.pdf via bsbmtct.org).

23. Storage and issue of commissioned cell therapy products

NHSBT can receive, hold and issue NICE approved, licensed cell therapies, such as CAR-T products, that are manufactured by authorised organisations ensuring appropriate regulatory requirements, for the treatment of a named patient.

The hospital must have secured all necessary approvals and fully executed all supporting agreements (including but not limited to, agreements with suppliers, manufacturers and sponsors as applicable), prior to requesting any associated services from NHSBT. The hospital must hold a certificate for IEC awarded by JACIE for handling immune effector cells. It is the hospitals responsibility to ensure that NHSBT are made fully aware in writing of specifications and requirements, even where services have been requested for a similar licensed cell therapy previously and allow sufficient time for the onboarding of new products.

Where Services are requested for a NICE approved licensed cell therapy product, the relevant SCI forms detailed in **Section 9** must be completed in full by the hospital and any requested information entered into an IT interface, if required. The licensed cell therapy products for which the services is being requested must be clearly stated at the time of referral. Delivery details, infusion dates and times for cryopreserved products must be agreed with the SCI Head of laboratory or nominated deputy.

24. Support for Clinical Trials

SCI laboratories routinely provide services to hospitals in support studies or clinical trials authorised by the MHRA (Medicines and Healthcare products Regulatory Agency) in which the hospital is the sponsor

or a participating site or is in any way collaborating with the trial. The number of licensed and unlicensed ATMPs available is increasing, and all programmes need to follow product/sponsor-specific processes and documentation.

It is the hospitals responsibility to ensure that NHSBT are made fully aware in writing of specifications and requirements and allow sufficient time for the onboarding of new clinical trials.

24.1. Onboarding process of clinical trials

The onboarding process is managed centrally across CAGT, with SCI laboratories working in close collaboration with NHSBT Therapeutic Apheresis Services (TAS), for trials where NHSBT supports the collection of starting material. Therefore, any request for support of a clinical trial should be made to the CAGT clinical trials email account CAGTClinicalTrials@nhsbt.nhs.uk.

SCI engages with hospitals and trial sponsors through the clinical trial onboarding process, ensuring completion of actions to confirm operational readiness for the first patient, including documentation and training required. The clinical trial sponsor will have a contract with the hospital to participate, with SCI laboratories then completing the required clinical trial activities under the existing service level agreements with the hospital. The sponsor will have a contract with the courier for movement to/from the manufacturing facility. NHSBT will invoice the hospital for the work, the hospital will then invoice the sponsor.

An important distinction from 'traditional' cell therapy products is that ATMPs are medicinal products and are subject to MHRA governance rather than the HTA. During the onboarding process all aspects of the ATMP process will be discussed with the sponsor and relevant stakeholders including the NHSBT Biological Safety Officer and agreed to ensure staff and patient safety.

24.2. Services provided in support of clinical trials

SCI laboratories can receive, hold and issue ATMPs, Specials, IMPs or cell therapy products manufactured by authorised organisations ensuring appropriate regulatory requirements, for the treatment of a named patient.

24.2.1. Collection

The sponsor will organise collection of the ATMP starting material with the SCI laboratory, and then manufacture the ATMP as required, often overseas.

Collection of the starting material for ATMPs may occur at NHSBT TAS units or separate collection hospitals. Where applicable, labels for the starting product can be provided by the SCI laboratory, using the standard ICCBBA ISBT compliant format. Once collected, the cells may either be delivered straight to the manufacturer, or to a SCI lab for cryopreservation. If the starting material is delivered straight to the manufacturer, a sample may be taken for enumeration at the SCI laboratory.

24.2.2. Cryopreservation

Where cryopreservation is required prior to manufacture, laboratories will follow the routine cryopreservation procedures but there may be deviations required which are listed in specific trial documentation, which may include alternative freezing profiles. Sponsors may have their own databases in which to enter information concerning the collection and cryopreservation process, with training provided by the sponsor.

The sponsor will organise collection of the cryopreserved ATMP starting material with the SCI laboratory, and then manufacture the ATMP as required, often overseas.

24.2.3. Receipt and storage of manufactured product from the sponsor

The sponsor will arrange delivery of the manufactured product to the Stem Cell laboratory via courier who unpack the cells, check and transfer to a vapour phase cryostorage. The product segregated in a vapour phase cryostorage vessel with continuous temperature monitoring until re-infusion.

24.2.4. Issue of the ATMP to the hospital

Request to issue the ATMP will follow routine SCI procedures and delivered to the respective hospital using NHSBT transport. In addition to the routine process, additional information may be requested by the Hospital/Pharmacists such Liquid Nitrogen Tank temperature logs for the duration of the ATMP storage. Any deviations in process will be noted as Quality Incidents, recorded in the Quality Management System, and the Hospital Pharmacist will be notified.

24.2.5. Recall and Disposal of ATMPs

In the situation where an ATMP needs to be recalled or returned, the sponsor specific documentation will be followed. As SCI are not the manufacturer of the ATMP, there would be no occasion where SCI would need to initiate a recall or return.

In the situation where the ATMP is no longer required, permission to dispose of ATMPs must be granted by the Sponsor and recorded. Once permission is granted, the product will be disposed of via SCI processes. During the onboarding of new ATMPs the appropriate disposal method should be discussed with the sponsor and NHSBTs Biological Safety Officer to ensure disposal is carried out in a controlled and safe manner.

25. Customer Service

SCI laboratories are committed to providing a high quality and responsive service to hospitals and welcome feedback from service users which can be provided directly to their associated laboratory and/or CMT management using details in Section 5 and/or via the following channels:

25.1. SCI User Group Meetings

NHSBT will convene at least annually, a meeting of a Steering Group comprising the Assistant Director of Cellular and Molecular services, NHSBT or designee, the head of the local SCI laboratory, an NHSBT consultant, an apheresis representative and NHSBT quality manager plus a representative from each user hospital of the NHS Trust.

25.2. Customer satisfaction

Approximately every two years, NHSBT circulates a customer satisfaction survey to evaluate hospital satisfaction with SCI laboratory performance under the NHSBT service level agreement for stem cell services. It is important that hospitals engage with the survey to help SCI improve the services provided.

25.3. Compliments and complaints

NHSBT is committed to continuously improving the quality and range of services provided and welcomes any comments or suggestions from the service users. There is always the risk of failures in any service delivery and it is essential that these be reported to ensure the causes can be fully investigated to, reduce the risk of recurrence, help improve the service and ensure compliance with clinical governance policies (specific forms have been made available to every service user for this and can be found on the NHSBT “Hospital & Science” website at: Complaints and compliments - Hospitals and Science - NHSBT

Please do not hesitate to discuss complaints with either the relevant Head of Laboratory or national CMT Management using contact details in Section 5.2. We always strive to provide a satisfactory response to any complaint.

Definitions

ATMP	Advanced Therapeutic Medicinal Products
ATU	Advanced Therapies Unit
BM	Bone Marrow
BMT	Bone Marrow Transplant
BSBMTCT	British Society of Blood and Marrow Transplantation and Cellular Therapy
CAR-T	Chimeric Antigen Receptor T
CBC	Clinical Biotechnology Centre
CFU	Colony Forming Unit
CMT	Cellular and Molecular Therapies
DCB	Directed Cord Blood
DMSO	Dimethyl Sulphoxide
FACT	Foundation for the Accreditation of Cellular Therapy
HAS	Human Albumin Solution
HPC	Haematopoietic Progenitor Cells
HPC(A)	Haematopoietic Progenitor Cells harvested via Apheresis
HPC(M)	Haematopoietic Progenitor Cells harvested from bone marrow
HPC(C)	Haematopoietic Progenitor Cells harvested from cord blood
HTA	Human Tissue Authority
ICCBBA	International Council for Commonality in Blood Banking Automation
IMP	Investigational Medicinal Product
ISBT	International Society for Blood Transfusion
JACIE	Joint Accreditation Committee ISCT-Europe & EBMT
JPAC	Joint UK Blood Transfusion & Tissue Transplantation Services Professional Advisory Committee
MHRA	Medicines and Healthcare products Regulatory Authority
MNC	Mononuclear Cells
MSL	Microbiology Services Laboratory (NHSBT)
NAT	Nucleic Acid Testing
NCI	Non-Clinical Issue

NHSBT	National Health Service Blood and Transplant
NICE	National Institute for Health and Care Excellence
PBMC	Peripheral Blood Mononuclear Cells
PBSC	Peripheral Blood Stem Cells
RBC	Red Blood Cell
SaBTO	Advisory Committee on the Safety of Blood, Tissues and Organs
SCI	Stem Cell and Immunotherapies
TAS	Therapeutic Apheresis Services (NHSBT)
TC	T cells
WBC	White Blood Cells
WDA	Wholesale Distribution Authorisation
WNV	West Nile Virus