

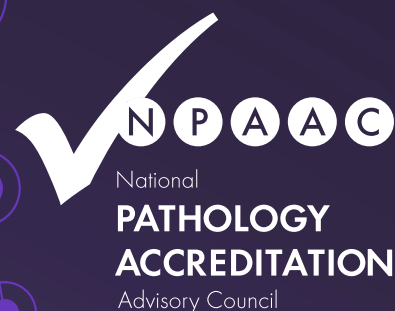


Australian Government
Department of Health

NPAAC TIER 4 DOCUMENT

REQUIREMENTS FOR PROCEDURES RELATED TO THE COLLECTION, PROCESSING, STORAGE AND ISSUE OF HUMAN HAEMOPOIETIC PROGENITOR CELLS

(Sixth Edition 2021)



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Australian Government Department of Health

Contents

Scope	vii
Abbreviations	vii
Definitions	viii
Introduction	1
1. Quality management	3
Quality system.....	3
2. Donor evaluation and selection	6
Donor selection	6
Donor testing	7
Additional requirements for allogeneic donors	8
Donor consent	8
3. Product collection	9
Collection facility.....	9
Personnel	9
Procedures	9
4. Product processing	11
Processing facility	11
Personnel	11
Procedures	11
5. Product testing	13
Routine processing	13
6. Labelling	14
Procedures	14
Collection label	15
Minimum label (partial label)	15
Final product issue label.....	16
Outer transport container label.....	17
Biohazard label.....	17
7. Product storage	18
Product storage areas.....	18
Storage duration	18
Temperature	18
Product safety	18
Monitoring of storage temperature.....	19
Alarm systems.....	19
Inventory control	20

8.	Cellular product issue and distribution	21
	Processing, tracking and issue criteria	21
	Distribution records.....	21
	Accompanying documentation at distribution	22
	Issue of non-conforming products	22
	Return of products from issue	22
	Product recall.....	22
9.	Transport and disposal.....	23
	Transport	23
	Receipt	24
	Transport of cryopreserved products	24
	Transport records	24
	Disposal.....	25
10.	Adverse events	26
11.	Health and safety.....	27
	Appendices.....	29
	Appendix A Infusion (Informative).....	31
	Appendix B Clinical transplantation facility (Informative).....	33
	Appendix C Clinical research (Informative)	41
	References	43
	Additional reading	44
	Further information.....	45

The National Pathology Accreditation Advisory Council (NPAAC) was established in 1979 to consider and make recommendations to the Australian, state and territory governments on matters related to the accreditation of pathology laboratories and the introduction and maintenance of uniform standards of practice in pathology laboratories throughout Australia. A function of NPAAC is to formulate Standards and initiate and promote education programs about pathology tests.

Publications produced by NPAAC are issued as accreditation material to provide guidance to laboratories and accrediting agencies about minimum Standards considered acceptable for good laboratory practice.

Failure to meet these minimum Standards may pose a risk to public health and patient safety.

Scope

The *Requirements for Procedures Related to the Collection, Processing, Storage and Issue of Human Haemopoietic Progenitor Cells (Sixth Edition 2021)* is a Tier 4 NPAAC document and must be read in conjunction with the Tier 2 NPAAC document *Requirements for Medical Pathology Services*. The latter is the overarching document broadly outlining standards for good medical pathology practice where the primary consideration is patient welfare, and where the needs and expectations of patients, Laboratory staff and referrers (both for pathology requests and inter-laboratory referrals) are safely and satisfactorily met in a timely manner.

Whilst there must be adherence to all the Requirements in the Tier 2 document, reference to specific Standards in that document are provided for assistance under the headings in this document.

The Standards and Commentaries in this document apply to Laboratories and other facilities involved in donor selection, collection, processing, storage and issue or disposal of directed minimally manipulated:

- haemopoietic progenitor cells (HPC)
- cord blood; and
- donor lymphocytes which are used for haemopoietic reconstitution; and
- donor lymphocytes which are issued for subsequent manufacture of a TGA approved product or under an approved clinical trial.

Activities related to other cellular therapies, including, but not limited to, HPC sourced from autologous or unrelated cord blood, are outside of the Scope of these Requirements. Similarly, collection of HPC sourced from, or on behalf of, overseas international Donor Registries are not captured by these Requirements.

Requirements for other clinical activities of transplantation facilities are outside the parameters of this document; however, guidelines for infusion of HPCs, structure and operation of the clinical transplantation facility (including medical and allied staff, training, therapy administration and related policy and procedures), and clinical research are included in *Appendices A, B and C*.

Abbreviations

ABMDR	Australian Bone Marrow Donor Registry
ABO	human erythrocyte A, B, O antigens
APHIA	Asia-Pacific Histocompatibility and Immunogenetics Association (formerly known as ASEATTA)
AS	Australian Standard
ASHI	American Society of Histocompatibility and Immunogenetics
CMV	cytomegalovirus
FACT	Foundation for the Accreditation of Cellular Therapy
HLA	human leukocyte antigen
HPC	haemopoietic progenitor cell
HPC(A)	haemopoietic progenitor cells–apheresis (other acceptable term: HPC,A)
HPC(CB)	haemopoietic progenitor cells-cord blood (other acceptable term: HPC,CB)
HPC(M)	haemopoietic progenitor cells–marrow (other acceptable term: HPC,M)
ISBT	International Society of Blood Transfusion
ISO	International Organization for Standardization
NATA	National Association of Testing Authorities, Australia
NPAAC	National Pathology Accreditation Advisory Council
RCPA	Royal College of Pathologists of Australasia
Rh	human erythrocyte rhesus antigens
TGA	Therapeutic Goods Administration
WMDA	World Marrow Donor Association

Definitions

Term	Definition
Adverse event	means any unintended and unfavourable sign, symptom, abnormality or condition associated temporally with an intervention which may or may not have a causal relationship with that intervention.
Adverse reaction	means an unfavourable and unintended response to the collection or infusion of any product for which there is a reasonable possibility that the product caused the response. Any adverse reaction is an adverse event.
Allogeneic	means cells obtained from a human donor who is genetically different from the intended human recipient. Compare with 'syngeneic', where the donor and recipient are genetically identical (e.g. monozygous identical twins).
Aseptic techniques	means practices designed to minimise contamination of products, reagents, Specimens or processing equipment with microorganisms and to prevent infection of patients and donors.
Audit	means a documented, independent inspection and review of one or more activities of a facility.
Autologous	means cells obtained from a donor who is also the intended recipient.
Biological product deviation	means a deviation from, or non-conformance with, applicable regulations, standards or established specifications for a biological product.
Clinical transplantation facility	means an integrated health care team housed in a dedicated and adequate space with a Director, common staff training programs, protocols and quality assessment systems.
Collection	means any procedure for harvesting haemopoietic progenitor cells regardless of technique or source.
Collection facility	means a facility that collects HPCs and/or lymphocytes as defined under 'product'.
Competency	means the ability to perform a specific task satisfactorily in conformance with the requirements of the quality system and according to direction.
Contamination	means the presence or introduction of microbial agents to products.

Term	Definition
Critical control points	means those points in the manufacture of HPCs to which controls or assessment are applied to assure continuing consistency of production to meet final product specifications.
Cross-contamination	means the contamination of one product with another product.
Demonstrable medical need	means a situation in which a comparable product is not available and the recipient is likely to die or suffer serious morbidity without the product, which may then be subject to exceptional release.
Designee	means a person delegated by the relevant Director to perform one or more duties or tasks. The Director is responsible for ensuring the designee is competent to perform the relevant activities.
Deviation	means the action of departing from an established course or accepted standard.
Director	<p>means, for the purpose of these Requirements, that Director includes the following responsible persons(s):</p> <p>Collection Facility Director</p> <p>The clinical designated person with relevant apheresis technical knowledge that is responsible for the operation of the apheresis unit. This person must have at least one year of experience in cellular therapy collection procedures.</p> <p>Program Director</p> <p>The medical practitioner ultimately responsible for all aspects of the transplantation program, including full compliance with these Standards.</p> <p>This person must be an appropriately qualified consultant physician experienced in haematology and/or medical oncology with expertise in all facets of HPC therapy. This person must have at least one year of specific clinical training in HPC transplantation or two years' experience as a medical practitioner responsible for the clinical management of HPC transplant patients and donors in the in-patient and out-patient settings.</p> <p>Collection Facility Medical Director</p> <p>The medical practitioner ultimately responsible for the pre-collection evaluation of the donor, final approval of the prospective donor for a collection procedure, conduct of the collection procedure, and care of complications arising from the collection including full compliance with these requirements.</p>

Term	Definition
	<p>This person must be an appropriately qualified medical practitioner experienced in haematology and/or medical oncology with expertise in cell collection procedures.</p> <p>The Program Director may also serve as the Collection Facility Medical Director.</p> <p>Laboratory Director</p> <p>An appropriately trained, qualified experienced pathologist or scientist with not less than five years' full time relevant Laboratory experience, who is responsible for all scientific, technical and administrative procedures of the cell processing facility.</p>
Directed	means collected by a medical practitioner, registered under a law of a State or Territory or a person under the supervision of such a practitioner, for a designated recipient with a pre-existing condition.
Donor	means a person who provides the source cells for a product.
Engraftment	means the process by which infused haemopoietic cells grow, reproduce and ultimately form the mature elements of the recipients' haemopoietic system.
Exceptional release	means a process by which a product that is non-compliant with these requirements is issued.
Expansion	means growth of one or more populations of HPCs or other cell populations in an in vitro culture system.
Facility	means any premises where some or all activities covered by these requirements are performed.
Haemopoietic progenitor cells	means haemopoietic cells capable of bone marrow repopulation.
Haemopoietic progenitor cell (HPC) therapy	means administration of haemopoietic cellular products with the intent of providing effector functions in the treatment of disease or support of other therapy that requires haematopoietic reconstitution.
Issue	means removal of the product from quarantine or in-process status for distribution or destruction.
Labelling	means identification, including but not limited to attachment of the appropriate labels, which ensures traceability of the original HPC collection or any part thereof, throughout collection, processing, storage, issuing, transport and administration of the product.

Term	Definition
Lymphocytes	means donor cells collected for the purpose of therapeutic infusion after allogeneic transplant.
Manufacture	means, but is not limited to, any or all steps including the recovery, processing, packaging, labelling, storage or distribution of any human cellular or tissue-based product, and the screening and testing of a cell or tissue donor ¹ . Refer also to Therapeutic Goods Act 1989.
Minimal manipulation	means processing that does not alter the biological characteristics of cells that are relevant to their clinical utility.
Mobilisation	means administration of drugs or haemopoietic growth factors to a donor to increase the number of HPCs in the blood circulation.
NAT	means Nucleic Acid Amplification Technique.
Outcome analysis	means process by which the result of a procedure is formally assessed.
Partial label	means minimum essential elements that must appear on all product containers.
Policies	means a documented program of principles and actions that sets out the goals of the organisation and provides guidance for achieving them. Policies will also provide the means for delegating authority.
Potency	means the therapeutic activity of a product as indicated by appropriate laboratory tests or adequately developed and controlled clinical data.
Procedure	means a detailed and specific description of the sequence of actions required to accomplish a task.
Procedures manual	means a compilation of detailed written instructions required to perform procedures in a facility.
Process development	means the delineation of a series of procedures performed sequentially to achieve the required result(s).
Processing	means some or all aspects of handling, labelling, cryopreservation, storage and issue of products See Minimal Manipulation.
Processing facility	means premises where product processing is performed. These may be part of the same institution as the clinical facility or may be situated elsewhere.

Term	Definition
Product	<p>means, for the purposes of these Requirements, ‘product’ is defined as one of:</p> <p>Haemopoietic progenitor cells, apheresis (HPC(A)) — HPCs collected from the peripheral blood of a donor using an apheresis technique, usually after administration of recombinant haemopoietic growth factor and/or chemotherapy.</p> <p>Haemopoietic progenitor cells, marrow (HPC(M)) — HPCs aspirated from the iliac crests, sternum or other bones of a donor.</p> <p>Haemopoietic progenitor cells, cord blood (HPC(CB)) - whole blood, including HPC, collected from placental and umbilical cord blood vessels after the umbilical cord has been clamped.</p> <p>T cells, apheresis — donor lymphocyte products collected by apheresis.</p> <p>T cells, whole blood — donor lymphocyte products collected as whole blood.</p> <p>T cells, marrow – donor lymphocyte products collected by bone marrow aspiration.</p>
Product attributes	<p>means processing applied to a product.</p> <p><i>Refer to the current listing in ISBT 128 standard.</i></p>
Proficiency test (External Quality Assessment)	<p>means a program in which multiple samples are periodically sent to Laboratories for analysis and/or identification, in which each Laboratory’s results are compared with those of other Laboratories in the group and/or with an assigned value, and reported to the participating Laboratory and others.</p> <p>Such a program may also compare an individual’s results with their peer group.</p>
Quality	means conformance of a product or process with pre-established specifications or standards.
Quality assurance	means part of quality management focussed on providing confidence that quality requirements will be fulfilled.
Quality control	means operational techniques and activities that are used to fulfil requirements of quality.
Quality improvement	means actions taken to review and improve the quality of a product and/or process.

Term	Definition
Quality manager	means a designated individual approved by the relevant Facility Director to establish procedures to review, modify, approve and implement all procedures intended to maintain quality and efficiency in the operation of the facility, and to monitor compliance with these requirements.
Quality system	means those management activities involved in the direction and control of the organisation with regard to quality.
Quality system assessment	means actions planned and performed to evaluate all systems and elements that may influence the quality of the product or service.
Quarantine	means the storage or identification of a product in a physically separate, clearly identified area in order to prevent improper issue or any cross-contamination of the product.
Requirements for Medical Pathology Services (RMPS)	<p>means the overarching document broadly outlining standards for good medical pathology practice where the primary consideration is patient welfare, and where the needs and expectations of patients, Laboratory staff and referrers (both for pathology requests and inter-Laboratory referrals) are safely and satisfactorily met in a timely manner.</p> <p>The standard headings are set out below –</p> <p>Standard 1 – Ethical Practice</p> <p>Standard 2 – Governance</p> <p>Standard 3 – Quality Management</p> <p>Standard 4 – Personnel</p> <p>Standard 5 – Facilities and Equipment</p> <p style="padding-left: 40px;">A – Premises</p> <p style="padding-left: 40px;">B – Equipment</p> <p>Standard 6 – Request-Test-Report Cycle</p> <p style="padding-left: 40px;">A – Pre-Analytical</p> <p style="padding-left: 40px;">B – Analytical</p> <p style="padding-left: 40px;">C – Post-Analytical</p> <p>Standard 7 – Quality Assurance</p>
Safety	means relative freedom from harmful effects to persons affected, directly or indirectly, by a product.
Storage facility	means the accommodation of products for subsequent processing and/or distribution.
Time of collection	means the local time of the end of the product collection procedure.

Term	Definition
Tracking	means to follow the history of a process, product or service by review of all documents from start to finish.
Validation	means the confirmation by examination and the provision of objective evidence that the particular requirements for a specific process, endpoints or intended use are fulfilled.

Introduction

The *Requirements for Procedures Related to the Collection, Processing, Storage and Issue of Human Haemopoietic Progenitor Cells* is a Tier 4 NPAAC document which may be used by bodies evaluating the competence of haemopoietic progenitor cell (HPC) transplant facilities seeking accreditation. It describes the minimum requirements for competence and quality to be met by facilities, including collection (apheresis procedures), and individuals preparing cells for infusion, and for providing assured safety and quality of the product.

It is the intention of this document that any HPC product within its Scope must be collected, processed, tested and stored in a facility accredited to these Requirements, or a facility which has undergone a satisfactory NATA/RCPA Advisory Visit and is seeking NATA/RCPA accreditation. Any manufacturing and use of products may still be subject to regulatory oversight by the Therapeutic Goods Administration (TGA). If clinical trials are required, then the usual ethics approval from the relevant institution must be obtained in addition to a clinical trial notification or exemption approval from the TGA.

These Requirements are written as broad principles and do not set out the details of all procedures and practices that a facility or individual should implement in HPC-related activities. Each facility and individual should analyse their respective, discrete practices and procedures to determine whether additional standards should apply.

These Standards have been developed with reference to current and proposed Australian regulations and other standards from the International Organization for Standardization (ISO) including:

AS ISO 15189 *Medical laboratories – Requirements for quality and competence*

This document should be read within the national pathology accreditation framework including the current versions of the following NPAAC documents:

Tier 2 Document

- *Requirements for Medical Pathology Services*

All Tier 3 Documents

In addition to these Standards, Laboratories must comply with all relevant state and territory legislation (including any reporting requirements).

In each section of this document, points deemed important for practice are identified as either ‘Standards’ or ‘Commentaries’.

- A Standard is the minimum requirement for a procedure, method, staffing resource or facility that is required before a Laboratory can attain accreditation – Standards are printed in bold type and prefaced with an ‘S’ (e.g. **S2.2**).
The use of the word ‘**must**’ in each Standard within this document indicates a mandatory requirement for pathology practice.

- A Commentary is provided to give clarification to the Standards as well as to provide examples and guidance on interpretation. Commentaries are prefaced with a ‘C’ (e.g. C1.2) and are placed where they add the most value.

Commentaries may be normative or informative depending on both the content and the context of whether they are associated with a Standard or not. Note that when comments are expanding on a Standard or referring to other legislation, they assume the same status and importance as the Standards to which they are attached. Where a Commentary contains the word ‘**must**’ then that commentary is considered to be **normative**.

Please note that any Appendices attached to this document are **informative** and should be considered to be an integral part of this document.

All NPAAC documents can be accessed at: <http://www.health.gov.au/npaac>.

While this document is for use in the accreditation process, comments from users would be appreciated and can be directed to:

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1. Quality management

(Refer to Standard 2, Standard 3, Standard 4 and Standard 5 in *Requirements for Medical Pathology Services*)

The quality system relating to HPC infusion can be found at *Appendix A*, which complements this section.

Quality system

- S1.1 HPC collection and processing facilities must establish and maintain a quality system. For the purpose of these Requirements:**
- (a) use of the term ‘laboratory’ within AS ISO 15189 *Medical laboratories — Requirements for quality and competence*, must also be taken to include HPC collection and processing facilities.
 - (b) use of the term ‘examination’ within AS ISO 15189 *Medical laboratories — Requirements for quality and competence*, must also be taken to include all aspects of HPC collection, processing and issue.
- S1.2 The relevant Director must be responsible for the quality system as it pertains to the scope and content of these Requirements.**
- S1.3 A register of staff signatures and initials must be maintained. Entries must be updated at regular written intervals and the previous records archived.**
- S1.4 The quality system must include a process for recording, review and communication of HPC efficacy, as appropriate, following administration.**
- C1.4(i) The quality system **must** include a process for documentation and review of time to engraftment following product administration.
- C1.4(ii) This review should be communicated across all aspects of the service.
- S1.5 The quality system must include a mechanism for regular review of records relating to donor selection, cellular product collection, processing, storage, issue and transportation.**
- S1.6 The quality system must include documented evidence:**
- (a) of a process for product tracking from the donor to the recipient or final distribution and from the recipient to donor
 - (b) to permit tracing of facility parameters that may affect product viability, integrity, contamination and cross-contamination during collection, processing, storage or release
 - (c) of validation and implementation of changes to a process.

- S1.7** The quality system must include a process for validation, checking and tracing supplies, reagents, equipment, procedures and facilities. The process must include the following:
- (a)** supplies and reagents used in the collection, processing, testing, cryopreservation, storage and administration of products must be stored in a secure, sanitary and orderly manner at the appropriate temperature with records of the temperatures maintained
 - (b)** all supplies and reagents coming into contact with products during collection, processing, storage and administration must be sterile and must be of appropriate quality for the intended use
 - (c)** reagents that are not of the appropriate grade must undergo validation and checking for the intended use
 - (d)** expired reagents, supplies and obsolete labels must not be used
 - (e)** equipment and reagents used to collect, or process products must be used in a manner that prevents product mix-ups, contamination and cross-contamination and that does not compromise cellular product function and integrity
 - (f)** there must be a system to document the identity and availability of critical reagents and supplies to ensure that there are adequate stocks for the procedures to be performed
 - (g)** there must be a system to identify and track all critical reagents and supplies used for each product, and a system to trace the products for which each supply or reagent was used.
- S1.8** The quality system must include a process for controlling and monitoring the collection and manufacture of products to ensure products meet predetermined release specifications, including:
- (a)** the relevant Director must prescribe tests and procedures for measuring and assaying products to ensure their safety, viability and integrity and to record that products meet predetermined release specifications. Results of all such tests and procedures must become part of the permanent record of the product processed
 - (b)** tests required by these standards must be performed in a NATA/RCPA accredited or TGA-licensed or equivalent accredited laboratory
 - (c)** products that do not meet release or donor eligibility requirements may be distributed only if there is recorded demonstrable medical need for the product. Records must include, at a minimum, the approval of the recipient's treating physician and the Program Director as well as consent of donor and recipient.
- S1.9** Collection and processing facilities must show plainly the extent of their responsibility.
- S1.10** Each clinical, collection and processing facility must maintain a listing of the names, addresses and responsibilities of other facilities that perform manufacturing and testing steps on a product to be used in the former facility.

- S1.11 There must be a system to allow each facility access to information that tracks all manufacturing steps performed by other participating facilities.**
- S1.12 Each facility must provide to the facility of final destination a copy of all records relating to the collection and processing procedures performed, in so far as they concern the safety, purity and potency of the product involved.**

2. Donor evaluation and selection

(Refer to Standard 1 and Standard 6A in *Requirements for Medical Pathology Services*)

These standards apply to all aspects of allogeneic and autologous donor selection, safety and treatment in a clinical transplant or collection facility where donors are involved in the donation of HPCs or lymphocytes for themselves or for another recipient. For the purposes of this document, syngeneic donors will be included in Requirements for allogeneic donors.

Donor selection

S2.1 Donor evaluation procedures must be in place to protect the safety of the donor, cellular product and recipient. The results of donor evaluation and selection test results must be recorded. The procedures must include the following:

- (a) there must be written criteria for donor selection, evaluation and management**
- (b) there must be documented procedures for testing, screening, determining donor eligibility and for ensuring compliance with any additional national or state requirements including, for unrelated donors, those of the Australian Bone Marrow Donor Registry**
- (c) before implementing these procedures, they must be approved by the relevant Director or designee**
- (d) if a non-conforming donor is used, there must be demonstrable medical need and records of the rationale for the selection by the transplant medical practitioner must be maintained.**

C2.1 The donor should have an opportunity to ask questions and has the right to refuse to donate.

S2.2 Allogeneic donors must be counselled regarding alternative collection methods

C2.2 The collection procedure should be explained in terms that the donor can understand and should include information about any significant risks and/or benefits of the procedure, tests performed to protect the health of the donor and the recipient, and the rights of the donor to review the results of such tests.

Donor testing

S2.3 All donors must be tested for evidence of clinically relevant infection by any of the following communicable disease agents within 30 days before collection:

- (a) human immunodeficiency virus, type 1**
- (b) human immunodeficiency virus, type 2**
- (c) hepatitis B virus**
- (d) hepatitis C virus**
- (e) human T lymphotropic virus I/II**
- (f) *Treponema pallidum* (syphilis)**
- (g) cytomegalovirus (CMV) antibodies (allogeneic only).**

C2.3(i) NAT and serological testing **must** be performed for (a), (c) and (d).

C2.3(ii) If indicated, tests should also be done for Epstein–Barr virus, hepatitis A virus, varicella zoster virus, herpes simplex virus, toxoplasmosis.

C2.3(iii) Additional tests should be carried out for donors of paediatric recipients where clinically relevant, including tests for measles, tetanus and diphtheria.

S2.4 Donors must be tested for ABO group and Rh (D) type at least seven days before the first collection. If there are previous records, there must be a comparison of ABO group and Rh (D) type with the latest available record. Any discrepancies must be resolved and recorded before issue of the product.

S2.5 Obstetric history must be recorded and a pregnancy assessment must be performed for female donors of childbearing potential within seven days before initiation of a recipient's conditioning regimen or commencement of mobilisation therapy.

S2.6 Donor eligibility and suitability must be communicated to the collection and cell processing facilities in writing.

S2.7 Laboratory testing of all donors must be performed by a NATA/RCPA-accredited or Therapeutic Goods Administration (TGA)-licensed or equivalent accredited Laboratory.

Additional requirements for allogeneic donors

- S2.8 Allogeneic donors must be tested for human leukocyte antigen (HLA)-A, -B and -DR type by a laboratory that is accredited or licensed to perform such testing.**
- S2.9 Allogeneic donors must be assessed for infectious disease risk using a current blood donation statement.**
- C2.9 The use of the blood donation statement is to screen for infectious disease risk that is not captured by the testing for specific communicable diseases. It enables the physician to make an assessment of the overall risk to the recipient (and by extension, the suitability of the donor), and what, if any additional testing is required to protect the safety of the recipient.
- S2.10 Allogeneic donor suitability must be evaluated by a health care professional who is not the primary transplant physician overseeing care of the recipient.**
- S2.11 If a non-conforming donor is used, consent of both the donor and the recipient must be obtained.**

Donor consent

- S2.12 Informed consent from the donor must be obtained and recorded by the transplant medical practitioner or other health care provider familiar with the collection procedure.**
- S2.13 Allogeneic donors must give written informed consent and authorisation to permit release of their health information to the transplant physician and recipient as appropriate. This consent must be viewed by the collection facility staff before the collection procedure.**
- S2.14 If the donor is not legally able to consent, informed consent must be obtained from the donor's parents or legal guardian in accordance with applicable laws, and must be recorded.**

3. Product collection

(Refer to Standard 3, Standard 4, Standard 5 and Standard 6A in *Requirements for Medical Pathology Services*)

The collection of HPC–Marrow is outside the scope of this section.

S3.1 The collection facility staff must perform product collections for at least one year before being eligible for accreditation.

C3.1(i) A satisfactory NATA/RCPA Advisory Visit **must** be undertaken prior to procedures commencing in any new collection facility.

C3.1(ii) A minimum of 10 HPC-A procedures **must** be performed by the new collection facility prior to a NATA/RCPA accreditation assessment.

C3.1(iii) New collection facilities **must** achieve NATA/RCPA accreditation within 18 months of the Advisory Visit.

Collection facility

S3.2 The collection of products must occur in a designated area. Product collection and storage must occur in separate areas.

C3.2(i) Collection equipment **must** not be used for non-patient related work.

C3.2(ii) There **must** be designated, physically separate areas for the storage of products during quarantine.

Personnel

S3.3 There must be a Collection Facility Medical Director.

C3.3 The Medical Director **must** appoint a quality liaison officer for the collection facility.

S3.4 There must be a Collection Facility Director.

S3.5 All staff performing collection procedures on paediatric patients must have specific training and experience for patients of this age. This training and experience must be recorded.

Procedures

S3.6 For every collection, the recipient's transplant medical practitioner must submit to the collection facility a written and signed request that includes approved identifiers for the recipient and donor, details of the procedure, target cell number and the expected date and time of the collection.

C3.6(i) A duplicate of this request **must** be forwarded to the processing facility.

- C3.6(ii) Information to accompany the medical practitioner's request **must** include a statement of donor suitability. For non-conforming donors, a statement to show the reason for the use of that donor, records of demonstrable medical need and donor, recipient and medical practitioner consent for use must be provided.
- S3.7 A donor blood test to determine HPC numbers must be performed during the 24 hours before HPC collection by apheresis.**
- S3.8 Immediately before each collection, a responsible person designated by the Medical Director must assess donor suitability and record the result in writing on the donor assessment record.**
- S3.9 Detailed worksheets must be completed concurrently with collection and must be available and maintained for all procedures.**
- C3.9(i) The identity of the individual responsible for each significant step of collection **must** be documented.
- S3.10 Collection procedures must be validated to ensure acceptable cell recovery and viability.**
- S3.11 Products must be packaged in transfer packs approved for blood or bone marrow products.**

4. Product processing

(Refer to Standard 4, Standard 5 and Standard 6 in *Requirements for Medical Pathology Services*)

Processing facility

S4.1 Processing facilities must only accept products from:

- (a) NATA/RCPA accredited collection centres; or
- (b) TGA licensed apheresis units; or
- (c) **new collection facilities that have undergone a satisfactory NATA/RCPA Advisory Visit.**

C4.1(i) Processing facilities may only accept product from a new collection facility for a period of 18 months from the date of the NATA/RCPA Advisory Visit unless the new collection facility gains NATA/RCPA accreditation.

C4.1(ii) HPCs sourced from overseas registries or products under clinical trial notification or clinical trials are exempt from S4.1.

S4.2 The processing of products must occur in a designated area.

C4.2(i) Laboratory equipment used for processing products **must** be segregated from equipment used for microbial cultures or non-patient-related work.

C4.2(ii) There **must** be designated, physically separate areas for the storage of products during quarantine.

Personnel

S4.3 There must be a suitably qualified, competent and experienced Laboratory Director.

Procedures

S4.4 The Laboratory must receive a written and signed request from the recipient's transplant medical practitioner before the collection, specifying the product type, the recipient and donor identifier, the type of processing that is to be performed and the anticipated date of processing.

C4.4 Information to accompany the medical practitioner's request **must** include a statement of donor eligibility and suitability. For non-conforming donors, a statement to show the reason for the use of that donor, records of demonstrable medical need, and donor, recipient and medical practitioner consent for use, **must** be provided.

S4.5 Cryopreservation procedures must be described in the processing facility's standard operating procedures manual and must include the following information:

- (a) **proper name of the product**

- (b) cryoprotectant solution and its final concentration
 - (c) maximum cell concentration that can be frozen
 - (d) cooling rate(s)
 - (e) endpoint temperature of cooling
 - (f) storage temperature
 - (g) Alternative validated procedure in case of equipment failure during the freezing process.
- S4.6 Processing procedures must be validated in the processing facility to indicate acceptable target cell viability and recovery. The validation must be fully recorded and retained in the facility records.**
- S4.7 Critical control points must be identified and associated assays performed on each product as defined in the standard operating procedures manual.**
- S4.8 Procedures for processing must use aseptic techniques and must be performed in a manner that minimises the risk of cross-contamination. They must be validated to result in acceptable viability and recovery.**
- S4.9 The objectives and acceptable endpoints for each procedure must be specified in the standard operating procedure manuals.**
- S4.10 The processing facility must monitor and record microbial cultures of the final products.**
- (a) The results of microbial cultures must be reviewed by the Laboratory Director or designee before issue.
 - (b) The recipient's medical practitioner and the donor's medical practitioner must be notified of any positive microbial cultures.
 - (c) Issue of product with positive microbial culture requires exceptional release.
 - (d) A root cause analysis must be performed for products with positive microbial cultures.
- S4.11 Detailed worksheets must be completed concurrently with processing and must be available and maintained for all procedures.**
- (a) The identity of the individual responsible for each significant step of processing must be recorded.
- S4.12 The Laboratory Director or designee must review the processing record for each product before issue.**
- (a) When clinically relevant processing endpoints are not met, the Laboratory Director and the recipient's medical practitioner must be notified in a timely manner.
 - (b) Notification and appropriate corrective actions, if taken, must be recorded.

5. Product testing

(Refer to Standard 6B in *Requirements for Medical Pathology Services*)

Routine processing

- S5.1** A nucleated cell count must be performed on each product after collection and after all subsequent processing.
- S5.2** A CD34+ cell count and/or clonal progenitor cell assay must be performed on the final product.
- S5.3** A target CD34+ or nucleated cell count must be monitored against transplant outcomes for each product.
- S5.4** For products undergoing cryopreservation, at least two test samples of the product (cryopreserved and stored under conditions that ensure a valid representation of the clinical product) must be available for testing, as and when required.
- S5.5** Before the issue of a cryopreserved product, the viability and enumeration of a relevant target cell population must be evaluated from a cryopreserved sample of the product using a relevant and validated test.
- C5.5 This testing should be completed prior to initiation of conditioning therapy.
- S5.6** The Laboratory must validate a time interval of storage after which testing must be repeated before issue.
- S5.7** Immediately prior to cryopreservation, a sample of the product must be tested for microbial growth.
- C5.7 The result **must** be made available to the recipient's medical practitioner.
- S5.8** Procedures must be in place for the identification and handling of test samples to ensure that they accurately relate (where applicable) to the product, the donor and the recipient.
- S5.9** Tests not performed by the cell collection or processing facility must be performed in a NATA/RCPA-accredited or TGA-licensed or equivalent accredited Laboratory.

6. Labelling

(Refer to Standard 6A in *Requirements for Medical Pathology Services*)

Information on the International Society of Blood Transfusion (ISBT) **128 Standard**² for the identification, labelling, and information transfer of human blood, cell, tissue, and organ products across international borders and disparate health care systems can be found on the International Council for Commonality in Blood Banking Automation (ICCBBA) website*. Refer to *ISBT 128 Standard Terminology for Blood, Cellular Therapy, and Tissue Product Descriptions* for proper product names, abbreviations and manipulations*.

Procedures

- S6.1 Each product must be assigned a unique identifier by which it is possible to associate the product with its donor, the donor's medical record, and to all records describing the handling, processing (if applicable), and final issue of the product. If a single product is stored in multiple containers, there must be a system for identifying each container.**
- S6.2 The labelling must be clear and legible:**
- (a) The ink must be permanent and able to withstand fading and disfigurement during processing, transport and storage**
 - (b) Labels must be affixed or securely attached to the container using appropriate materials. Labels must be validated as suitable for the storage conditions.**
- S6.3 The labelling procedures must include the following quality management elements:**
- (a) labels and labelling systems must be reviewed or validated to ensure accuracy regarding identity, content and conformity to templates approved by the facility Medical Director or designee**
 - (b) production, storage and distribution of labels must be controlled to prevent unauthorised access to and issuance of labels**
 - (c) stocks of unused labels representing different products must be stored in a controlled manner to prevent errors**
 - (d) there must be a procedure for discarding labels in the standard operating procedure manual**
 - (e) a system for container label version control must be used**
 - (f) a system of checks in labelling procedures must be used to prevent errors in transcribing information to all container labels. Container label information shall be verified by at least two staff members and all data fields must be completed**

* See [International Council for Commonality in Blood Banking Automation](#)

- (g) products that are repackaged into new containers must be labelled with new labels before they are detached from the original container. Records that track products, including relabelled and repackaged products, must be maintained
- (h) supplementary identifiers must not obscure the original product identifier and sufficient area of the container must be uncovered to permit inspection of the contents
- (i) labelling requirements of applicable government regulations, if any, must be observed
- (j) to maintain confidentiality, products shipped by registries must not be labelled with the donor name or collection facility but there must be sufficient written information to allow tracking to the original donor and collection facility.

Collection label

S6.4 On completion of the collection procedure, the primary container or associated documentation must be labelled before being disconnected from the donor, with the following information:

- (a) proper name of product or accepted abbreviations, as defined in the ISBT 128 Standard²
- (b) at least two identifiers attributable to the donor
- (c) date and time of collection
- (d) approximate volume
- (e) name and volume or concentration of anticoagulant and other additives
- (f) name or initials of collector
- (g) unique numeric or alphanumeric identifier
- (h) identity and address of collection facility
- (i) recommended storage temperature
- (j) biohazard label (if applicable, see S6.9)
- (k) recipient name and identifier or the statement 'FOR AUTOLOGOUS USE ONLY'.

C6.4 Clause (k) is not applicable where there is a requirement for anonymity of donor and/or recipient.

Minimum label (partial label)

S6.5 If the container can only bear a partial label, the label must show, as a minimum, the unique product identifier, the proper name of the product and appropriate modifiers, as well as the name and identifier of the intended recipient, if known.

- S6.6** At the time of issue for transfer to another facility or for infusion, containers bearing a partial label must be accompanied by a document containing the full information outlined in S6.7, or must have the full information on an attached tag.

Final product issue label

- S6.7** The label or document accompanying the product must contain the following information at the time of distribution or issue:

- (a)** unique product identifier
- (b)** proper name of the product, including any attributes, as defined in the ISBT 128 Standard
- (c)** date and (for non-cryopreserved products) time of collection
- (d)** approximate volume
- (e)** name and volume of anticoagulant or other additives (if applicable)
- (f)** identity and address of processing facility or donor registry
- (g)** recipient name and identifiers
- (h)** ABO group and Rh (D) type donor (if applicable)
- (i)** expiration time and date (if applicable)
- (j)** identity and address of collection facility or donor registry (if applicable)
- (k)** biohazard label (if applicable, see S6.9)
- (l)** donor identifiers and name (if applicable)
- (m)** statements (as applicable): ‘DO NOT IRRADIATE’ ‘FOR AUTOLOGOUS USE ONLY’, ‘FOR USE BY INTENDED RECIPIENT ONLY’, or ‘FOR NONCLINICAL USE ONLY’
- (n)** red blood cell compatibility testing results (if applicable)
- (o)** recommended storage temperature
- (p)** statement indicating that leukoreduction filters should not be used
- (q)** date of distribution.

Outer transport container label

Additional details regarding the transport and packing of pathology Specimens are included in the Tier 3 NPAAC publication *Requirements for the Packaging and Transport of Pathology Specimens and Associated Materials*.

S6.8 This label must contain the following information:

- (a) container handling instructions
- (b) date of distribution and time (if appropriate)
- (c) name, street address and phone number of contact person at receiving institution
- (e) recommended storage temperature
- (f) statements 'Human cells for administration' or equivalent and "Handle with care"
- (g) statement 'DO NOT IRRADIATE' and/or 'DO NOT X-RAY'
- (h) name, street address and telephone number of the contact person at the sending facility.

Biohazard label

S6.9 A biohazard label must be affixed to the product if the results of mandatory testing indicate the risk of communicable disease transmission other than CMV.

7. Product storage

(Refer to Standard 5 and Standard 7 in *Requirements for Medical Pathology Services*)

HPC products are stored using various procedures and temperatures depending on the required duration of storage. Institutional policies and procedures will dictate specific storage requirements.

Product storage areas

S7.1 There must be physically separate areas designated for the storage of products during quarantine, before issue and for non-conforming products.

C7.1 Oxygen monitors **must** be installed in all areas where liquid nitrogen storage tanks are located.

S7.2 All products must be contained in a controlled environment and stored under appropriate conditions.

S7.3 Product storage devices must be secure and accessible only to authorised personnel.

Storage duration

S7.4 Facilities storing products must establish policies for the duration and conditions of storage and indications for their disposal.

C7.4 Patients, donors and associated facilities should be informed about these policies before product collection.

S7.5 Facilities processing, storing and/or releasing products for issue must assign an expiration date for both fresh products and for products thawed after cryopreservation.

Temperature

S7.6 Products stored in a liquid state must be maintained within specified temperature range to maintain viability and function, to inhibit infectious agents and for a period of time not to exceed that specified in the standard operating procedures.

S7.7 Cryopreserved products must be stored within a temperature range appropriate for the products and the cryoprotectant solution used and as defined in the standard operating procedures.

Product safety

S7.8 Materials that may adversely affect products must not be stored in the same refrigerators or freezers as the cellular products.

- S7.9 For products immersed in liquid nitrogen, procedures to minimise the risk of cross-contamination of products must be used.**
- S7.10 Facilities storing products must quarantine the product as defined by government regulations until completion of the donor eligibility determination.**
- C7.10 All products with positive infectious disease test results for relevant communicable disease agents and/or microbial cultures **must** be quarantined.
- S7.11 Quarantined products must be easily and reliably identifiable. They must be stored in a manner that minimises risk of cross-contamination and inappropriate issue.**

Monitoring of storage temperature

- S7.12 Refrigerators and freezers for product storage must have a system to monitor the temperature continuously and record the temperature at least every four hours.**
- C7.12 If products are always fully immersed in liquid nitrogen, continuous temperature monitoring is not required.
- S7.13 There must be a mechanism to ensure that levels of liquid nitrogen in liquid nitrogen freezers are maintained constantly to ensure that products remain within the specified temperature range.**
- C7.13 An automatic fill mechanism is recommended.

Alarm systems

- S7.14 Storage devices for products or reagents for product processing must have alarm systems that are active continuously.**
- C7.14 Alarm systems **must** be checked periodically for function.
- S7.15 Alarm systems must have audible signals or other effective notification procedures.**
- S7.16 If trained personnel are not always present in the immediate area of the storage device, there must be a system to alert responsible personnel of alarm conditions 24 hours a day.**
- S7.17 Alarms must be set to activate at a temperature or level of liquid nitrogen that will allow time to salvage products.**
- S7.18 Written instructions to be followed if the storage device fails, must be displayed in the immediate area containing the storage device and at each remote alarm location and include the following:**
- (a) a procedure for notifying processing personnel

- (b) procedures to ensure that products are maintained at safe temperatures and the process for documentation of any corrective actions in order to maintain integrity of the products.

S7.19 Additional storage devices of appropriate temperature must be available for product storage if the primary storage device fails. Off-site storage devices must conform to these requirements.

Inventory control

S7.20 An inventory control system to identify the location of each product and associated sample aliquots must be in use.

S7.21 The inventory control system records must include:

- (a) recipient name (if known) or unique identifier
- (b) product name or Specimen type
- (c) date of collection
- (d) storage device identifier
- (e) location within the storage device of product and associated sample aliquots.

8. Cellular product issue and distribution

(Refer to Standard 6 in *Requirements for Medical Pathology Services*)

Processing, tracking and issue criteria

- S8.1 A request for the HPC product must be signed by the treating medical practitioner, transmitted to the processing facility and retained.
- S8.2 Appropriate arrangements must be made before issue of the cellular products to minimise the time between issue and infusion.
- S8.3 The processing and tracking records for each cellular product must be reviewed before product issue by the Laboratory Director or designee, for compliance with these requirements, with standard operating procedures and applicable regulations.
- S8.4 Tracking records must demonstrate traceability between the donor and the recipient.
- S8.5 Before issue from the processing facility, each cellular product must meet predetermined issue criteria, including donor eligibility.
- S8.6 When the cellular product is non-conforming, the Program Director or designee must give specific authorisation for exceptional release.
 - C8.6 Records of such authorisation, including the agreement between the Program Director, the recipient's medical practitioner, and the recipient to consent to use any non-conforming products **must** be retained.
- S8.7 Prior to commencement of conditioning, and again before issue, each cryopreserved product must be visually inspected to confirm appropriate labelling and integrity of the product container.

Distribution records

- S8.8 The product processing records must contain evidence of product distribution, including the distribution date, name and unique identifier of the intended recipient, the proper product name and identifier, records of donor eligibility determination, and identification of the facility that supplied the product.
- S8.9 The distribution record must include the identity of the responsible individual in receipt of the product.

Accompanying documentation at distribution

- S8.10** A product infusion form must accompany each product issued. This form must include all the information required on the final product issue label.

Issue of non-conforming products

- S8.11** If products are to be issued *before* completion of the donor eligibility determination or upon exceptional release, additional documentation (which must be provided at or immediately after issue) must include:
- (a) a list of any screening or testing that has not been completed
 - (b) written notification and approval from the Program Director and the recipient's medical practitioner of the incomplete screening or testing
 - (c) records that donor eligibility determination was completed during or after the use of the product
 - (d) authorisation for product release by the Medical Director or designee.

Return of products from issue

- S8.12** Products accepted for return must meet the following conditions:
- (a) the integrity of the primary container must not have been compromised subsequent to issue by the processing facility
 - (b) evidence must be provided that the product has been maintained at all times within the specified temperature range.
- S8.13** If the conditions in Standard S8.12 (a) and S8.12 (b) have not been met, the Laboratory Director or designee must give specific authorisation to accept such products for return to inventory.
- S8.14** The Laboratory Director or designee must consult with the recipient's medical practitioner regarding reissue or disposal of the returned product. This must be documented.
- S8.15** Documentation of the events requiring return, the results of inspection upon return, and all subsequent action taken to ensure product safety and viability must be retained in the Laboratory record.

Product recall

- S8.16** If an unexpected non-conformity of the product is identified after issue and before infusion, the product must be recalled and the treating clinician and relevant Directors notified.

9. Transport and disposal

(Refer to Standard 6A and Standard 6C in *Requirements for Medical Pathology Services*)

Further information on the transport and courier requirements of cellular products can be found in the ABMDR Guidelines³ and NPAAC's *Requirements for the Packaging and Transport of Pathology Specimens and Associated Material*.

Transport

- S9.1 Procedures must be established, maintained and recorded for transportation, shipping and receipt of products.**
- S9.2 In order to protect the integrity and safety of the products during transit, and the health and safety of individuals in the immediate area, procedures for transport of non-frozen and/or cryopreserved products must be established and maintained.**
- S9.3 All products must be transported with requisite accompanying records, including determination of allogeneic donor suitability and eligibility.**
- S9.4 The primary product container for non-frozen products must be placed in a secondary container and sealed to prevent leakage.**
- S9.5 Products that require a temperature-controlled environment and that are transported over an extended period of time must be transported in a container validated to maintain the appropriate temperature range.**
- S9.6 All products that leave the collection or processing facility must be transported in an outer transport container. Extended transport time of cryopreserved or non-frozen products that require a temperature-controlled environment must be in an approved transport container.**
- S9.7 The outer transport container must conform to the applicable regulations regarding the mode of transport.**
- S9.8 The outer transport container must be made of material adequate to withstand leakage of contents, shocks, pressure changes and other conditions incident to ordinary handling in transportation.**
- S9.9 During transport, the product temperature must be maintained at the storage temperature specified by the receiving facility.**
- S9.10 The outer transport container must be labelled as outlined in S6.8 and in accordance with applicable regulations regarding the cryogenic material used and the transportation of biological materials.**
- S9.11 Appropriate transport arrangements must be made and communicated between sending and receiving facilities.**

S9.12 If the intended recipient has received high-dose myeloablative therapy, the product must be transported by a qualified courier.

C9.12(a) The products should not be passed through X-ray irradiation devices designed to detect metal objects.

C9.12(b) If inspection is necessary, the contents of the container should be inspected manually.

S9.13 There must be plans for alternative transport in the event of delay.

Receipt

S9.14 Procedures must be established and maintained for acceptance, rejection and quarantine of products.

S9.15 The receipt of each product must include inspection to verify the integrity of the product container, the appearance of the product, appropriate labelling, and to evaluate for evidence of microbial contamination.

S9.16 There shall be procedures to verify that the product was appropriately transported or shipped. The receiving facility must document the temperature on arrival.

C9.16 For cryopreserved products, the transit temperature range **must** be recorded.

S9.17 There must be procedures to maintain products in quarantine until they have been determined to meet criteria for release from quarantine.

Transport of cryopreserved products

S9.18 The transport container must be of appropriate design and construction for transportation of the cryogenic material used.

S9.19 Cryopreserved products with an indicated storage temperature below –80°C must be shipped in a liquid nitrogen ‘dry shipper’ that contains adequate absorbed liquid nitrogen to maintain temperature for at least 48 hours beyond the expected time of arrival at the receiving facility.

C9.19 Unabsorbed liquid nitrogen **must** not be used.

Transport records

S9.20 Transport records must include the identity of the courier and all delays or problems occurring during transportation of the product.

S9.21 Transport records must permit tracing of the product from one facility to another.

S9.22 Transport records must identify the date and time the product is shipped and received.

S9.23 Transport records must identify the sending facility, the receiving facility and the personnel responsible for sending and receiving the product.

Disposal

S9.24 There must be a documented policy for disposal of products that must comply with relevant legislation including any applicable *Human Tissue Act* or *Regulations*.

C9.24 Before collection, there should be a written agreement between the donor or donor's legal representative, patient or designated recipient and the storage facility defining length of storage and the circumstances for disposal or transfer of products.

- (i) If there is no pre-existing recorded agreement describing conditions for product storage and/or discard, the storage facility should communicate with the designated recipient's medical practitioner about the continuing need for storage of the products and make a recorded effort to notify the donor or designated recipient about product transfer or disposal.
- (ii) Disposal of products obtained through donor registries should adhere to conditions mutually agreed upon by the storing facility and the donor registry.

S9.25 The records for all discarded products must indicate the product discarded, date of discard and method of disposal. Retention of such records must comply with the requirements for medical record retention of the relevant jurisdiction or legislation.

S9.26 The Program Director, in consultation with the recipient and the recipient's medical practitioner, must give written approval of product discard and method of disposal.

S9.27 Where surplus unused samples are used for research, this must be in accordance with the National Health and Medical Research Council (NHMRC) *National Statement on Ethical Conduct in Human Research* ⁴ unless this is in contravention of specific legislation, including the applicable *Human Tissue Act*, which would then apply.

10. Adverse events

(Refer to Standard 6C and Standard 7 in *Requirements for Medical Pathology Services*)

These Requirements apply to any incidents, adverse event or reaction that occurs during the collection, processing, storage, issue or transport or any other related activity associated with performing these procedures.

Adverse events include, but are not limited to, suspected disease transmission, significant accidental loss of cells, equipment failure that may affect the final cellular product integrity or any other unintended event associated with infusion of the HPC product.

- S10.1 Adverse reactions or events must be recorded and reported in a manner that complies with institutional requirements and applicable laws.**
- S10.2 Adverse events or reactions must be documented and reviewed by the relevant medical practitioner and the Facility Program Director and any other relevant personnel.**
- S10.3 The donor and/or the recipient must be notified about the event and any possible consequences. How the consequences will be addressed must also be documented.**

11. Health and safety

(Refer to Standard 3, Standard 4 and Standard 5 in *Requirements for Medical Pathology Services*)

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Appendices

Appendix A Infusion (Informative)

Appendix B Clinical transplantation facility (Informative)

Appendix C Clinical research (Informative)

Appendices: A, B, C have been derived from the material contained in FACT 3rd Edition 2007¹.

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Appendix A Infusion (Informative)

1. To minimise time between issue and infusion, appropriate arrangements should be made between the processing and clinical facilities.
2. Each product issued for infusion should be inspected visually by two trained personnel immediately before infusion, in order to confirm appropriate labelling and integrity of the product container.
3. The product infusion form as described in S8.10 should be completed by the clinical staff at the time of infusion and will be placed in the recipient's medical record.
4. There should be documentation in the patient medical records of the facility identifier and a copy of the product infusion form.
5. The intended recipient and the product identifiers should be properly verified by two trained personnel, before the product is administered, according to facility standard operating procedures.
6. Products should be infused as soon as possible after processing or thawing, preferably through a central venous catheter.
7. Aseptic technique should be used.
8. Products must not be administered through a filter designed to remove leukocytes.
9. Products containing visible lumps may be infused through a blood administration filter of equal to or greater than 170 µm–260 µm pore size.
10. The Program Director and/or Laboratory Director or designee should give specific authorisation for use when the container integrity is compromised.
11. A procedure to manage the splitting or bursting of a product container should be established. Such occurrences should be reported immediately to the Laboratory Director who should discuss the matter with the recipient's medical practitioner. An aliquot of the product should be sent for a microbial contamination test.
12. Medical and scientific staff responsible for infusion of products should be trained in corrective action procedures if the product container integrity is compromised during transport or during the infusion procedure.
13. Periodic observation of the patient should be performed before and after the infusion procedure to detect adverse reactions.

14. For each type of product, the processing Laboratory should maintain a current document containing recommendations on the following, as appropriate, and the document should be available to the clinical staff caring for the recipient:
- (a) the use of products
 - (b) indications and contraindications
 - (c) side effects and hazards
 - (d) infusion procedure
 - (e) instructions for handling in order to minimise the risk of contamination or cross-contamination. All appropriate warnings must be provided outlining how to prevent the spread of communicable diseases.

Appendix B Clinical transplantation facility (Informative)

1. General

- 1.1 The clinical transplantation facility should consist of an integrated medical team housed in a geographically contiguous or proximate space, with a single Program Director and common staff training procedures and quality management systems. Clinical transplantation facilities that include non-contiguous institutions in the same metropolitan area should demonstrate common protocols, staff training procedures, quality management systems, review of clinical results and evidence of regular interaction. Several clinical sites, particularly those with different Directors, or those that are outside a single metropolitan area, and combine for the purposes of meeting criteria to qualify as a clinical transplantation facility, do not fulfil the intent of these requirements.
- 1.2 Persons delegated by the Program Director and who have responsibility for procedures, administrative procedures, performing tests and reporting of results, should be listed for the purpose of limiting access to patient information.
- 1.3 The clinical transplantation facility may have more than one clinical site in different hospitals if the other criteria in 1.1 are met.
 - 1.31 A general guide for units undertaking centres undertaking allogeneic transplantation is that a minimum of 10 new allogeneic patients should be transplanted per year. Centres undertaking allogeneic transplantation will usually perform autologous transplantation as well while centres may perform autologous transplantation only and those should undertake a minimum of five transplants per year. Syngeneic transplants should only be undertaken by centres performing allogeneic transplants.
 - 1.3.2 For a combined clinical transplantation facility caring for paediatric and adult patients on the same site, facilities should perform a minimum of five transplants for each patient population.

2. Clinical transplantation facility

- 2.1 There should be a designated inpatient unit that minimises airborne microbial contamination.
- 2.2 There should be suitable and confidential space for donor examination and evaluation.
- 2.3 There should be a designated area for out-patient care that reasonably protects the patient from transmission of infectious agents and can provide, as necessary, appropriate patient isolation, administration of intravenous fluids, medications and/or blood products.
- 2.4 There should be provisions for prompt evaluation and treatment by a transplant medical practitioner available each day on a 24-hour basis.

- 2.5 All donors should have a post-collection procedure medical assessment.
- 2.6 There should be an adequate number of nurses experienced in the care of transplant patients.
- 2.7 There should be a pharmacy providing 24-hour availability of medications needed for the care of transplant patients.
- 2.8 There should be ready access to renal replacement therapy.
- 2.9 An appropriately qualified anaesthetist should be available for procedures associated with cell collection that requires general or regional anaesthesia should be performed by an appropriately qualified anaesthetist.
- 2.10 Central venous catheters, where applicable, should be placed by a medical practitioner qualified to perform the procedure.
 - 2.10.1 Adequacy of line placement should be verified by a radiologist or medical practitioner qualified to perform the procedure.
- 2.11 Administration of mobilisation agents should be under the supervision of a medical practitioner experienced in the administration and management of complications in people receiving these agents.
- 2.12 There should be a transfusion service providing 24-hour availability of CMV-appropriate and irradiated blood products needed for the care of transplant patients.
- 2.13 There should be immediate access to on-site intensive care facilities or equivalent coverage for critically ill patients.
- 2.14 There should be a collection and processing facility that meets these requirements with respect to their interaction with the clinical transplantation facility.
- 2.15 Clinical transplantation facilities performing allogeneic haemopoietic cell transplants should also use HLA-testing Laboratories accredited by ASEATTA or ASHI, or an equivalent Laboratory, and have the capability of carrying out high-resolution HLA-typing.

3. Staff and training

3.1 Facility Director

- 3.1.1 A dedicated transplant team, including a Program Director and at least one other medical practitioner trained and/or experienced in HPC therapy is essential.
- 3.1.2 Transplantation facilities performing paediatric transplants should have a transplant team trained in the management of paediatric patients.

- 3.1.3 For transplantation facilities performing paediatric transplantation, there should be at least one medical practitioner who is qualified in paediatric haematology/oncology.
- 3.1.4 The clinical transplantation facility should have access to appropriately qualified haematology and/or medical oncology medical practitioners who are trained and competent in bone marrow harvesting and cellular product collection by apheresis in facilities that meet NPAAC requirements.
- 3.1.5 The Facility Director should have at least one year of specific clinical training in HPC transplantation as defined in 3.3, or two years' experience as a medical practitioner responsible for the clinical management of HPC transplant patients in in-patient and out-patient settings. The Program Director should have written confirmation of his/her training or experience from the Director of the facility or institution in which that training or experience was obtained.
- 3.1.6 The Program Director should participate regularly in educational activities related to the field of HPC transplantation.
- 3.1.7 The Program Director is responsible for administrative and clinical procedures, including compliance with these standards. The Program Director should have oversight of all elements of the design of the clinical transplantation facility, including quality management, the selection and care of patients and donors, cell collection and processing.
- 3.1.8 The Program Director should have oversight of the medical care provided by the clinical transplantation facility, including medical care provided by the medical practitioners on the transplant team. The Program Director is responsible for verifying the knowledge and skills of the medical practitioners of the transplant team. Management of the clinical transplantation facility may be delegated to a Medical Director who fulfils the requirements.

3.2 Other medical staff and nurse practitioners

- 3.2.1 Other medical practitioners working in the clinical transplantation facility should be appropriately qualified to practise medicine in the jurisdiction of the clinical facility.
- 3.2.2 Other medical practitioners working in the clinical transplantation facility should have specific clinical training in HPC transplant medicine as defined in 3.3, and should participate regularly in educational activities related to the field of HPC transplantation.
- 3.2.3 Appropriately credentialed nurse practitioners may perform the roles of medical practitioners within their approved scope of practice.

3.3 Training for medical and nurse practitioner staff

- 3.3.1 Clinical skills
 - 3.3.1.1 Adequate specific clinical training in HPC transplant medicine should be defined as a minimum of one year's experience in the

management of transplant patients in both the in-patient and out-patient settings.

- 3.3.1.2 Clinical transplantation facilities transplanting paediatric patients should have medical practitioners experienced in treating paediatric patients, as defined in 3.1.3.

3.3.2 Cognitive skills

- 3.3.2.1 Specific training and competency in each of the following areas is required for medical practitioners in HPC transplantation facilities:

- (a) indications for haemopoietic progenitor cell transplantation
- (b) selection of appropriate patients and preparative high-dose therapy regimens
- (c) pre-transplant patient evaluation, including assessment of appropriate patient eligibility and haemopoietic progenitor cell adequacy with respect to collection
- (d) administration of high-dose therapy
- (e) administration of growth factors for HPC mobilisation and for post-transplant haemopoietic cell reconstitution
- (f) management of neutropenic fever
- (g) diagnosis and management of infectious and non-infectious pulmonary complications of transplantation
- (h) diagnosis and management of fungal disease
- (i) diagnosis and management of veno-occlusive disease (sinusoidal obstructive syndrome) of the liver
- (j) management of thrombocytopenia and bleeding
- (k) management of haemorrhagic cystitis
- (l) management of nausea and vomiting
- (m) management of pain
- (n) management of terminal care patients
- (o) documentation and reporting for patients on investigational protocols
- (p) diagnosis and management of HPC graft failure.

- 3.3.2.2 Specific clinical training and competency in each of the following additional areas is required for medical practitioners in clinical transplantation facilities for allogeneic HPC transplantation:

- (a) identification and selection of HPC source, including use of donor registries

- (b) methodology and implications of HLA typing
- (c) management of patients receiving ABO-incompatible haemopoietic progenitor cellular products
- (d) diagnosis and management of CMV infection and disease
- (e) diagnosis and management of other viral infections in immunocompromised hosts
- (f) diagnosis and management of acute and chronic graft versus host disease
- (g) diagnosis and management of post-transplant immunodeficiency's
- (h) evaluation of Chimerism.

3.3.3 Procedural skills

- 3.3.3.1 The HPC transplant medical practitioner should be proficient in HPC product infusion procedures.
- 3.3.3.2 The HPC transplant medical practitioner should be knowledgeable in the following procedures:
 - (a) HPC processing
 - (b) HPC cryopreservation
 - (c) bone marrow harvest procedures
 - (d) apheresis procedures.

3.4 Consulting medical staff

- 3.4.1 The transplantation facility should have access to appropriately qualified consulting medical practitioners from key disciplines who are capable of assisting in the management of patients requiring medical care, including but not limited to surgery, pulmonary medicine, intensive care, gastroenterology, nephrology, infectious disease, cardiology, pathology, psychiatry and, if radiation therapy is administered, radiation oncology, with experience in large-field (e.g. total body or total lymphoid) irradiation treatment protocols.
- 3.4.2 Transplantation facilities treating paediatric patients should have consultants, as defined in 3.4.1, qualified to manage paediatric patients.

3.5 Nursing staff

- 3.5.1 Clinical transplantation facilities should have nurses and nurse supervisors formally trained and experienced in managing patients receiving haemopoietic progenitor cell transplants.
- 3.5.2 Clinical transplantation facilities treating paediatric patients should have nurses formally trained and experienced in managing paediatric patients.

- 3.5.3 Training should include haematology or oncology patient care; administration of high-dose chemotherapy and radiation therapy, growth factors and immunosuppressive medications; management of infectious complications associated with compromised host defence mechanisms; administration of blood products; and an appropriate degree of intensive medical or paediatric nursing care.
- 3.5.4 There should be written policies for all relevant nursing procedures, including, but not limited to, infection prevention and control, administration of the preparative regimen, infusion of HPCs, use of immunosuppressive agents, growth factor administration, oral care, central venous catheter care, blood product infusion and transplant nurse competency evaluation processes.

3.6 Allied staff

- 3.6.1 The clinical transplantation facility should have one or more designated staff to assist in the provision of appropriate pre-transplant patient evaluation, treatment and post-transplant follow-up and care.
- 3.6.2 The clinical transplantation facility should have pharmacy staff knowledgeable in the use and monitoring of pharmaceuticals used by the clinical transplantation facility.
- 3.6.3 Dietetic staff should be capable of providing dietary consultation regarding the nutritional needs of the transplant recipient, including enteral and parenteral support, and appropriate dietary advice to avoid food-borne illness.
- 3.6.4 Social services staff should be fully experienced and qualified in dealing with donors, recipients, and their relatives as well as related staff involved in the apheresis, processing and infusion processes.
- 3.6.5 Physical therapy staff should be adequately trained and experienced in dealing with both donors and recipients of products. They should also be cognisant of the full process involved in the collection and administration of products.
- 3.6.6 Data management staff should be aware of the importance of confidentiality and attention to detail. Approved organisational client and product identification protocols are required to be followed at all times.

4. Therapy administration

- 4.1 There should be a written policy to ensure that the preparative therapy regimen is administered safely.
 - 4.1.1 The treatment orders should include patient height and weight, specific dates, daily doses (if appropriate) and route of each agent. Pre-printed orders should be used for protocols and standardised regimens.
 - 4.1.2 The pharmacist preparing the chemotherapy should confirm the doses against the protocol or standardised regimen listed on the orders.

- 4.1.3 Before administration of chemotherapy, two people qualified to administer chemotherapy should confirm the drug and dose against the orders and the protocol, and the identity of the patient to receive the chemotherapy.
- 4.1.4 There should be a written request for radiotherapy, including details of diagnosis, any prior radiotherapy that the patient has received, and any other factors that may increase the toxicity of radiotherapy.
- 4.1.5 There should be a written consultation from a radiation therapist before initiation of therapy. The consultation should include radiotherapy planning.
- 4.1.6 Before administration of each dose of radiotherapy treatment, the dose should be verified and recorded as per radiation therapy standards.
- 4.1.7 A final report of the radiotherapy details administered should be filed in the patient's records.

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Appendix C Clinical research (Informative)

1. Clinical transplantation facilities should have a formal review of investigational treatment protocols and patient consent forms, if so required by applicable regulations.
2. Facilities using applicable investigational treatment protocols should have in place a pharmacy equipped for research activities. This pharmacy should have a mechanism for tracking, inventory and secured storage for investigational drugs.
3. Records for all research protocols performed by the clinical facility (including all audits, documentation of ethics committee and/or local institutional review board or equivalent approval, correspondence with regulatory agencies, and any adverse outcomes) should be maintained in accordance with institutional policies and applicable laws and regulations.
4. For clinical research, informed consent should be obtained from each research subject or his/her legally authorised representative, in language he or she can understand and under circumstances that minimise the possibility of coercion or undue influence. The research subject should be given the opportunity to ask questions and to have them answered to his/her satisfaction, and to withdraw from the research without prejudice. Informed consent for a research subject should contain at least the following elements and comply with applicable laws and regulations:
 - 4.1 A plain-language statement describing the research purposes, a description of the procedures to be followed, expected duration of the subject's participation, the identification of experimental procedures, a description of the reasonably expected risks, discomforts, benefits to the subject or others, and alternative procedures.
5. A statement of the extent to which confidentiality will be maintained should be included.
6. There should be a mechanism in place to ensure, as appropriate, the financial disclosure of any issues that may represent a conflict of interest in clinical research.

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References

These requirements have been developed with reference to current Australian and other international requirements, including:

1. Foundation for the Accreditation of Cellular Therapy and the Joint Accreditation Committee (FACT and JACIE) — International Society for Cellular Therapy (ISCT) and the European Group for Blood & Marrow Transplantation (EBMT), *International Standards for Cellular Therapy Product Collection, Processing and Administration, Eighth Edition*, JACIE Secretariat, Barcelona, Spain, 2012.
2. International Society of Blood Transfusion (ISBT), *ISBT 128 Standards: Standard Terminology for Blood, Cellular Therapy, and Tissue Product Descriptions Version 5.2*, ICCBBA, San Bernardino, United States of America, 2014, viewed 6 August 2014, < [International Council for Commonality in Blood Banking Automation](#) >.
3. Australian Bone Marrow Donor Registry, *Guidelines for Couriers of HPC*, AMBDR, Alexandria, Australia, 2014, viewed 6 August 2014, < [ABMDR website](#) >.
4. National Health and Medical Research Council, *National Statement on Ethical Conduct in Human Research*, NHMRC, Canberra, 2007, viewed 29 September 2021, <<https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018>>.

Additional reading

Foundation for the Accreditation of Cellular Therapy and the Joint Accreditation Committee (FACT and JACIE) — International Society for Cellular Therapy (ISCT) and the European Group for Blood & Marrow Transplantation (EBMT), *Cellular Therapy Accreditation Manual, Version 5.3*, JACIE Secretariat, Barcelona, Spain, 2012, viewed 6 August 2014, <<http://www.factwebsite.org/>>

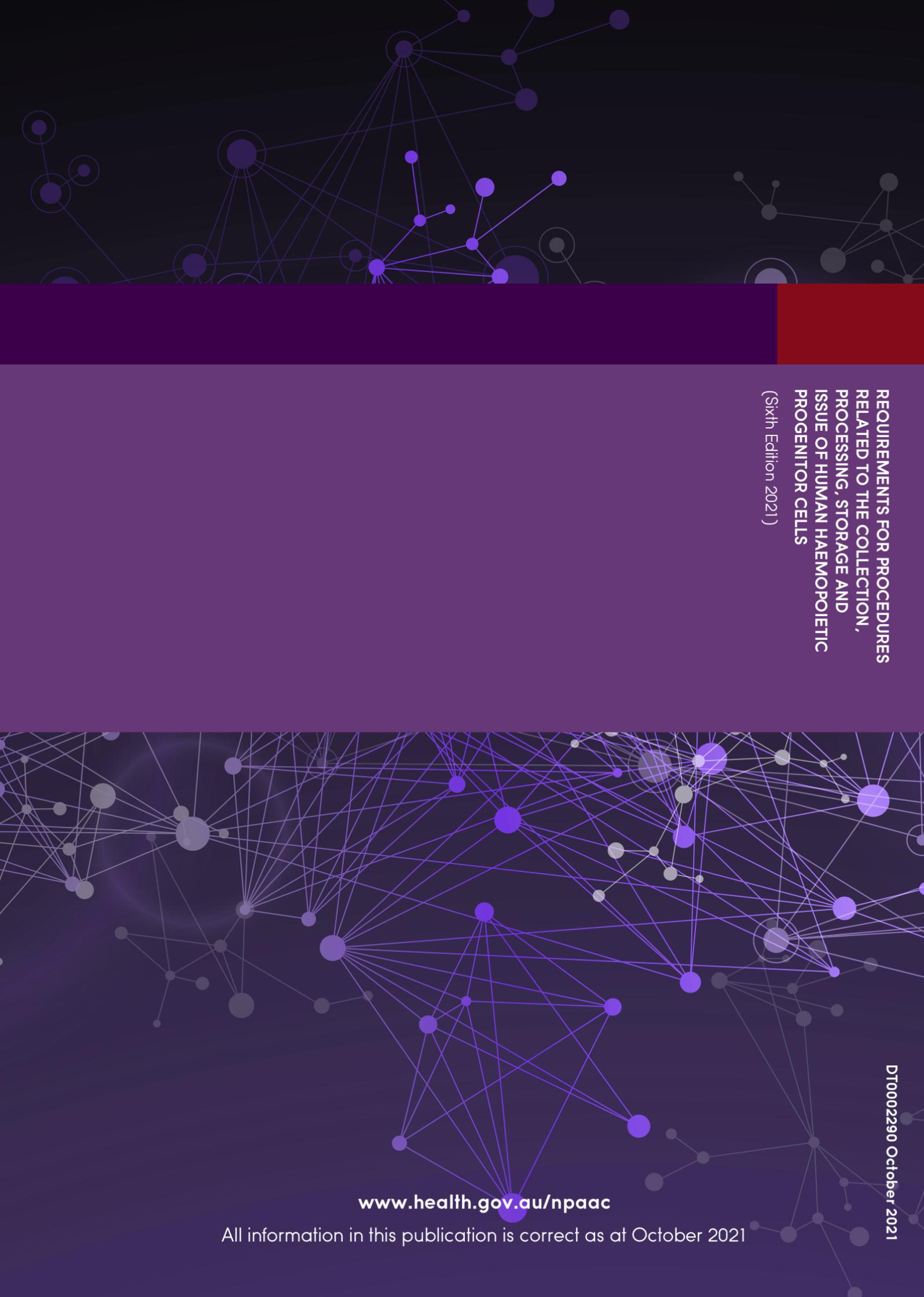
Therapeutic Goods Administration, *Australian Code of Good Manufacturing Practice for human blood and blood components, human tissues and human cellular therapy products*, TGA, Woden, Australia, 2013, viewed 29 September 2021, <<https://www.tga.gov.au/publication/australian-code-good-manufacturing-practice-human-blood-and-blood-components-human-tissues-and-human-cellular-therapy-products>>

Further information

Other NPAAC documents are available from:

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