Australian Government
Department of Health
Therapeutic Goods Administration

Excluded autologous human cells and tissues

Australian Regulatory Guidelines for Biologicals (ARGB)

Version 1.2, September 2019

TGA Health Safety Regulation

Contents

This guidance is for sponsors of autologous human cells and tissues (HCT) products. It will help you work out if your product is excluded from TGA regulation.

The level of regulation for autologous HCT products is based on the level of risk to the public associated with the manufacturing processes and intended use of the product. If your product is not excluded from TGA regulation, go to Autologous HCT products guidance for information on levels of regulation.

The TGA considers that there are circumstances in which there is sufficient regulation by other bodies to mitigate possible risks that may arise as a result of manufacturing and use of autologous HCT products.

Medical devices or equipment used for manufacture of autologous HCT products may be regulated under the medical devices framework, where it is to be used for treatment, diagnosis or modification of a patient's anatomy or physiological process. In such cases, manufacturers of the equipment must have sufficient evidence, including clinical evidence, to substantiate their claims about safety and performance of the autologous HCT products. This information would need to be provided to the TGA if requested.

Criteria for exclusion

We will not regulate autologous HCT products if they meet **all of the following criteria**:

1. collected from a patient who is under the clinical care of a medical or dental practitioner registered under a law of a State or an internal Territory
2. manufactured by that medical or dental practitioner, or by a person or persons under the professional supervision of that medical or dental practitioner in a hospital (except storage and testing), for that patient who must be a patient of that hospital
3. not advertised directly to consumers

Where one or more criteria are not met, including advertising to consumers, regulation by TGA will apply.

These criteria are in the Therapeutic Goods (Excluded Goods) Determination 2018.

If your HCT product is not excluded from TGA regulation, go to Autologous HCT products guidance.

The conditions for exclusion **do not include any restrictions** on:

- the level of manufacturing (including storage and processing beyond minimal manipulation)
- the intended use

How excluded autologous HCTs products are regulated

Exclusion from TGA regulation is not exclusion from all regulation. There is regulation by other bodies that is sufficient to mitigate possible risks that may arise as a result of manufacturing and using autologous HCT products that are excluded from TGA regulation.

Relevant regulatory bodies include:

- Australian Health Practitioner Regulation Agency (AHPRA)
- state, territory and national medical and dental boards or councils
- states and territory management and administration of public hospitals
- state and territory licensing of private hospitals
- the Australian Competition and Consumer Commission (ACCC)

Examples of likely excluded products

Below are examples of autologous HCT products that are likely to be excluded from TGA regulation. However, they need to meet all eligibility criteria, including being used, manufactured in a hospital and not being advertised directly to consumers.

Autologous blood to seal cerebrospinal fluid leaks

The brain and spinal cord are cushioned by a clear fluid called cerebrospinal fluid (CSF), encased in a protective membrane called the meninges. If the meninges are torn as a result of injury, surgery or sometimes spontaneously, the CSF may leak out and the patient is at risk of infection and other complications. Small tears in the meninges may be closed by applying fresh blood, which clots and seals the opening.

Autologous blood components

Some patients with rare blood types that are difficult to match may need to prepare for surgery by providing autologous donations a few weeks in advance of surgery. The blood is stored and reinfused when needed. Another approach to autologous blood replacement is the process of catching, filtering and reinfusing lost blood during surgery (cell salvage).

Bone grafts

Small sections of bone may be taken from healthy sites (usually the iliac crest of the hip bone) and transplanted into injured sites of the same patient to assist healing after elective orthopaedic surgery (for example knee reconstruction), and traumatic bone injuries. Osteochondral transfer (OATS, transfer of small sections of bone and attached cartilage) procedures may be used for repair of well-defined cartilage defects in joints like the knee.

Cosmetic or reconstructive procedures (skin, bone and fat transfers)

Bone grafts and mucous membranes may be used as autologous transplant materials for patients requiring dental and maxillofacial surgery (dental implants for crowns or bridges, gum recession, facial prostheses). Adipose tissue may be collected from one area (usually stomach, thighs or waist) using a procedure termed liposuction, and reinjected into another area to increase fat content in the receiving site. This is often used for breast reconstruction after breast cancer surgery, and other cosmetic and reconstructive surgery.

Craniotomy and parathyroidectomy

Under specific circumstances sections of tissue may be removed and temporarily stored, to facilitate treatment of traumatic injuries and other disorders. The removed sections of tissue may be stored for a number of days and then returned to the patient when appropriate.

HPCs for reconstitution of blood after treatment of cancer (i.e. bone marrow transplants)

Patients with a range of blood cancers often undergo powerful chemical therapies to destroy the cancerous cells. HPCs are collected before the treatment and stored while the patient undergoes treatment. After the treatment the patient is re-infused with the cells to help the blood re-establish. Australian hospitals providing HPC transplants are currently subject to National Pathology Accreditation Advisory Council (NPAAC) or National Association of Testing Authorities (NATA) accreditation.

Pancreatic islet cells

Some patients with chronic or recurrent inflammation of the pancreas may need the pancreas surgically removed. The insulin-producing islet cells are isolated from the removed pancreas and transplanted into the liver to prevent diabetes. This procedure is considered minimal manipulation as the dissociation of the pancreas maintains the function of the islets. If a patient already has diabetes, islet cell transplantation decreases the risk of the diabetes becoming worse.

Skin grafts (including keratinocyte sprays)

Where healthy skin is removed from one area of the body (leg, arm, buttocks) and transplanted to an injured area (used in burns) of the same patient. In addition, some hospital burns centres are taking keratinocytes (skin cells) and culturing them before applying the cells to the injured area as part of mesh grafts or sprays. This processing is considered greater than minimal manipulation and the intended use may also involve storage of the cells and multiple treatments over the course of the treatment, but is still likely to meet the exclusion criteria.

Vascular conduits

Blood vessels (usually veins) are used to replace injured or blocked arteries in a different area. Vascular conduits are commonly used in coronary artery bypass grafting for heart disease and in the treatment of peripheral vascular disease (poor blood flow to the lower limbs). Autologous blood vessels may also be transplanted to facilitate heart transplants.

Explanation of key terms

Hospital manufacture and use

Excluded autologous HCT products must be:

- manufactured **in a hospital** (except storage and testing)
- for a patient of the hospital of manufacture

Regulation in a hospital setting

Public and private hospitals in Australia are subject to regulation under various state, territory and national provisions. Accreditation of hospitals is a requirement for funding by governments and other funding organisations. A national accreditation scheme for health service organisations and the National Safety and Quality Health Service (NSQHS) Standards have been endorsed by the Australian Health Ministers.

The credentialing processes applied by hospitals should enable hospitals to decide whether the risks that may arise as a result of manufacturing and using excluded autologous HCT products are acceptable and controlled, and also to ensure that medical and dental practitioners do not work outside of their scope of practice.

Commonwealth hospital declaration

The Australian Government Department of Health regularly updates a list of Commonwealth declared hospitals.

- Inclusion of public hospitals requires State or Territory Department of Health confirmation of a public hospital and evidence of accreditation.
- Inclusion of private hospitals requires a copy of a state or territory hospital licence and evidence of accreditation.

NSQHS Standards considered applicable to biologicals and blood components

While the following National Safety and Quality Health Service (NSQHS) Standards do not specifically apply to autologous HCT, we believe that the principles applied to achieve the required standards are relevant and applicable to the safe use of autologous HCT products in accredited hospitals:

- NSQHS Standard 3: *Preventing and controlling healthcare associated infections* includes criteria for governance and systems of infection prevention, control and surveillance, and for cleaning, disinfection and sterilisation.
- NSQHS Standard 4: *Medication safety* includes criteria for governance and systems for medication safety and medication management processes that outline mechanisms for 'safe prescribing, dispensing, administering, storing, manufacturing, compounding and monitoring…' of medicines.
- NSQHS Standard 7: *Blood and blood products* is directly applicable to autologous human cells and tissues that are blood or blood components. However, the principles that underlie safe and appropriate prescribing in this standard are applicable to all autologous HCT products. The criteria for Standard 7 apply to governance systems and systems to 'receive, store, transport and monitor wastage of blood and blood products safely and efficiently'.

Institutional credentialing of health practitioners

Health practitioners who work in hospitals are subject to mandatory institutional credentialing processes, to ensure the quality and safety of patient care. Credentialing:

- includes review of qualifications, professional standing and professional registration and indemnity
- requires the practitioner to undertake to work within his or her professional scope of practice

The Australian Commission on Safety and Quality in Health Care has published Credentialing health practitioners and defining their scope of clinical practice, a guide for managers and practitioners. There is also the *Standard for credentialing and defining the scope of clinical practice: a national standard for credentialing and defining the scope of clinical practice of medical practitioners, for use in public and private hospitals*.

Clinical care of a registered medical or dental practitioner

For an autologous HCT product to be excluded or exempted from TGA regulation, the HCT must be collected from a patient who is under the **clinical care** of a **medical or dental practitioner registered** under a law of a State or an internal Territory.

Clinical care and treatment

For the exclusion to apply a registered medical or dental practitioner must have and assure the prime responsibility for the clinical care of their patient throughout the course of treatment in which the autologous HCT product is used. This provision **does not** apply to other health practitioners.

Registered medical and dental practitioners

Medical and dental practitioners are the health care providers that most frequently prescribe or administer therapeutic goods including medicines, medical devices and biologicals. The TGA accepts that clinical and dental practice is sufficiently regulated such that, if the conditions outlined in the exclusion are satisfied, additional regulation by the TGA of some autologous HCT products may impose unnecessary burden.

The conduct of these practitioners (including advertising) is regulated by AHPRA and the relevant state, territory and national boards and councils. To maintain registration in their respective specialities, medical and dental practitioners are required to participate in appropriate continuing professional development, to work within their scope of practice and to maintain recency of practice. Guidance for professional practice is contained in Code of conduct for registered health practitioners and Good medical practice: A code of conduct for doctors in Australia.

The Australian Health Practitioner Regulation Agency (AHPRA) also has the power to prosecute for particular advertising offences which may infringe the Health Practitioner Regulation National Law Act (in force in each state and territory).

Responsibilities of using excluded or exempt autologous HCT products

Health practitioners have professional obligations to maintain satisfactory standards of practice that are appropriate to their profession. A registered medical or dental practitioner that is using excluded or exempt autologous HCT products:

- must have prime responsibility for the clinical care of his/her patient throughout the course of treatment in which the autologous HCT products are used
- should be mindful of adherence to professional standards when using products that have not been evaluated for safety and efficacy by the TGA, including consideration of whether the treatment being undertaken is necessary and safe and whether its efficacy is supported by credible clinical evidence
- should ensure that prior to treatment of any patient with a product that has not been approved for use in Australia, that patient receives appropriate and adequate information about the material risks and benefits of that product to allow informed consent.

Professional supervision

For an autologous HCT product to be excluded from TGA regulation, the manufacture and use of the autologous HCT products:

- must be by the medical or dental practitioner with primary responsibility for clinical care

OR

- by a person or persons under the **professional supervision** of that practitioner

Manufacture does not have to be by the practitioner themselves

For the exclusion to apply, the autologous HCT product is to be manufactured by that medical or dental practitioner or by a person or persons under the professional supervision of that medical or dental practitioner. The fact that the products being used for a patient are not directly manufactured by the treating medical or dental practitioner does not mean that the exclusion does not apply.

What is professional supervision?

Professional supervision in this context requires that the medical or dental practitioner with primary responsibility for the clinical care of a patient is party to all manufacturing steps that are performed in a formal governance arrangement with the person or persons undertaking the manufacturing. This would include input into the protocols and quality systems used in the manufacturing process. This enables use of goods that are not directly manufactured by the treating medical or dental practitioner.

An example of professional supervision

Pancreatic tissue might be collected from a patient by a medical practitioner (surgeon) in collaboration with an endocrinologist, for processing of the islet cells in a laboratory. Subsequent to processing, the islet cells are infused into that same patient as an autologous transplant.

The collection, processing and infusion must remain under the professional supervision, as described above, of the endocrinologist caring for the patient.

Specialised testing on a representative sample of the product by a third-party facility, for example sterility testing, would still be considered to fit within the professional supervision of the medical or dental practitioner.

All steps in manufacture must occur in the hospital, except storage and testing

To qualify for the exclusion, generally all steps of manufacturing must occur within the hospital, including pathology testing. However, a minor amendment was made to the exclusion criteria to allow third party storage and testing to occur outside of the hospital.

This change was introduced to reflect that in some instances, HCT products, which are collected from donors in hospitals by registered medical or dental practitioners and manufactured by that practitioner in the hospital for use in the same patient from whom those products were collected, may be stored or tested at other premises. We emphasise that the contract for such services must be between a person under contract **with the hospital** (rather than the individual practitioner). This is consistent with current practice whereby a hospital may need to contract out storage or testing to a third party if it is not able to store such products on its own premises, or if specialised testing is not performed by the hospital's in-house pathology provider.

Advertising to consumers is prohibited

Excluded autologous HCT products cannot be advertised to consumers.

Version history

Version	Description of change	Author	Effective date
V1.0	Original publication incorporating new legislative changes and information previously published on the TGA website.	Biological Science Section Regulatory Guidance Team	July 2018
V1.1	Revision incorporating clarification to exclusion criteria as per Therapeutic Goods Amendment (Excluded Goods) Determination 2019	Biological Science Section Regulatory Guidance Team	June 2019
V1.1	Update of links	Biological Science Section	September 2019

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Reference/Publication #