Australian Government
Department of Health
Therapeutic Goods Administration

Exempt autologous human cells and tissues

Australian Regulatory Guidelines for Biologicals (ARGB)

Version 1.0, July 2018

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 exempt from some aspects of TGA regulation. It also explains what regulation **does apply** to exempt autologous HCT products.

If your autologous HCT is not excluded and not exempt from TGA regulation, go to Autologous HCT product guidance for information on regulation.

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 exemption

In order to qualify for regulatory exemption autologous HCT products must meet all of the following criteria:

- Ü 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
- Ü manufactured and used by the practitioner with primary responsibility for clinical care OR by a person or persons under the professional supervision of that practitioner
- Ü for a single indication in a single clinical procedure
- Ü HCT are minimally manipulated and for homologous use

Where one or more criteria are not met, full regulation by TGA will apply.

These criteria are in Schedules 5 and 7 of the Therapeutic Goods Regulations.

If your autologous HCT product does not meet all of these criteria, go to Autologous HCT product guidance.

How exempt autologous HCT products are regulated

Exempt autologous HCT products must still comply with some regulatory requirements, such as:

- Ü compliance with all standards applicable to blood components or biologicals
- Ü the need to report adverse events to the TGA
- Ü no advertising to consumers
- Ü being responsible for conducting a recall, if necessary

You are required to hold:

- information on compliance with applicable standards
- evidence that demonstrates safety and efficacy of the product.

Under most circumstances, we will not review such information. However, when a safety issue arises we may request it for review.

Criminal penalties may apply if the:

- quality, safety or efficacy of the product is found to be unacceptable
- advertising requirements are breached
- product does not comply with applicable standards
- sponsor does not respond to TGA questions about the product.

Not applicable to exempt products

An autologous HCT product that meets all of the exemption criteria would be exempt only from:

- Ü requirements for accessing 'unapproved' product (e.g. clinical trial notifications, special access schemes):
  - however, if you choose to investigate the safety or efficacy of the product as part of a clinical trial, a human research ethics committee (HREC) should approve the trial
- Ü inclusion on the ARTG
- Ü holding evidence that the manufacturing facility satisfies good manufacturing practice (GMP) requirements. The exemption from GMP requirements also applies to any contracted testing facilities used e.g. for sterility testing.

Differences between exempt biologicals and exempt medicines

Exempt autologous HCT products may be regulated as medicines or as biologicals. To understand the regulations that will apply to your product you will need to determine if it is a blood component or a biological. To determine this go to Autologous human cells and tissues products regulation.

Examples of likely exempt products

Below are examples of autologous HCT products that are likely to be regulated with exemptions, if their use satisfies all of the outlined criteria.

Bone graft for dental procedures (biological)

A dental practitioner may take a section of bone from another area of the body, and graft it onto the jaw bone (or other orofacial region) of the same patient in a single procedure, following major dental extraction (or maxillofacial surgery). This procedure would meet the conditions because:

- the processing of the bone is considered minimal manipulation
- the use is considered to be homologous
- this procedure would usually not occur in a hospital.

Platelet-rich plasma (blood component)

Platelet-rich plasma (PrP) is likely to be considered a blood component, being prepared only by centrifugation, filtration and freezing.

PrP is prepared from blood collected by a single uninterrupted venepuncture. The plasma is generally separated from the red blood cells by centrifugation, with the platelets present in the plasma. The next steps vary between protocols but are intended to discard both the red blood cells and the acellular plasma layers and to collect only the platelet rich plasma layer. Commercial kits are now available to assist in the preparation of PrP. Importantly, the preparation of PrP only separates and concentrates the cells without manipulating them.

An example of PrP that would meet the exemptions would be where a medical practitioner collects some blood from a patient outside of a hospital and manufactures the PrP using minimal manipulation. The intended use of the PrP must also be homologous.

The following points should be noted for the manufacture and use of PrP:

- The intended clinical use of PrP under these exemptions should still be justified based on proven evidence of safety and efficacy.
- The exemptions only apply when the PrP is manufactured and administered by or under the supervision of a registered medical practitioner for a patient under their care. **This exclusion does not apply to other health practitioners.**
- Where equipment (such as a commercial kit) is used in the manufacture of PrP or conditioned serum it may also be subject to regulation as a medical device.

Cosmetic use of injected PrP is likely to be fully regulated by TGA where therapeutic claims are made or inferred. Generally, injectable products fall under the Australian legal definition for therapeutic use (for example, as they are likely to be taken to be influencing, inhibiting or modifying a physiological process, even if it is only for 'aesthetic' purposes).

Explanation of key terms

For a single indication in a single procedure

Exempt autologous HCT products must be manufactured for a single indication and in a single procedure on that patient.

Single indication

The therapeutic application must be limited to a single indication. Sometimes the therapeutic purpose of the cell or tissue therapy is clear from the context of the admission or the description of a surgical treatment.

For example:

- Use of a saphenous vein to replace an occluded coronary artery during coronary artery bypass grafting.
- Use of an autologous skin graft to cover a burn.
- Use of small volumes of autologous bone to fill bony defects in dental practice.

However, clinical users of autologous HCT products may conclude that some HCTs have therapeutic value in more than one indication. The primary indication for the autologous HCT product in any procedure or treatment **should be clearly documented**.

Single procedure

Where a HCT is removed from a patient and transplanted back into the patient during a single clinical procedure the risks to the patient are the same as those typically associated with surgical procedures. These operations will normally be exempt from regulation by the TGA.

In contrast, any treatment that involves more than a single procedure, especially where storage of the HCT is required, can significantly increase the risks to safety associated with traceability, sterility and quality of the product. Treatments involving storage of the HCT **do not** fall within the scope of the exemption provisions.

Minimal manipulation and homologous use

An exempt autologous HCT product must be:

- manufactured using minimal manipulation
- intended for homologous use

Clinical care of a registered medical or dental practitioner

For an autologous HCT product to be 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 exemptions to apply a registered medical or dental practitioner must have the prime responsibility for, and assure, 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 exemptions 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 the Australian Health Practitioner Regulation Agency (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 exempted autologous HCT products

Medical and dental 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 exempted autologous HCT product:

- 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 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 autologous HCT products to be exempt 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

For the exemptions 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.

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 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.

Version history

Version	Description of change	Authors	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

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