Australian Government
Department of Health
Therapeutic Goods Administration

Intended use: Interpretation of homologous use

Australian Regulatory Guidelines for Biologicals (ARGB)

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TGA Health Safety Regulation

Contents

This guide is for sponsors, manufacturers, health practitioners and consumers to explain how the intended use of a biological product influences:

- its classification as a Class 2 or 3 biological
- whether autologous HCT products are exempt from specific requirements

Homologous use

Homologous use of the goods is use of the goods to repair, reconstruct, replace or supplement the cells or tissues of a person (the recipient), if the goods will perform the same basic function or functions in the recipient as the original cells or tissues performed in the person from whom they were collected (donor).

The distinction between homologous and non-homologous use also applies to autologous use of HCT products, where the donor and recipient are the same person.

When we determine whether the use of the HCT product is homologous, we carefully consider the intended use, including the manufacturer's and/or sponsor's labelling material and associated supporting documents.

The determination of homologous use may be complex in some circumstances where the donor HCT is not identical to the cells or tissue that will be repaired, reconstructed, replaced or supplemented in the recipient, but it performs the same basic functions. Generally, in this situation it would be considered to be homologous use if the manufacturer provides sufficient evidence to support the claim. Where treatment involves an unproven clinical use it is likely to be considered to be a non-homologous use.

Defining basic functions of human cells and tissues

When defining the basic function or functions of HCT product we mean:

- those that are well understood (scientifically) to apply to the donor tissue

AND

- where functionality can be assumed in the recipient, in the absence of a need to perform testing

It is not necessary for all functions of the HCT product to be maintained and performed in the recipient, only those claimed in the intended use.

The HCT may perform the same basic function or functions even when it is not used in the same anatomic location where it existed in the donor.

Examples of homologous and non-homologous uses

Below are examples of our interpretation of homologous use. Some of the examples are taken from the FDA guidance which aligns with our interpretation, while other examples demonstrate how our interpretation differs from the FDA's.

Adipose tissue and cell extracts

Adipose tissue may be collected and then re-injected with minimal manipulation, or may be subjected to processing to extract the cellular portion from the tissue. Generally the HCT product extracted from adipose includes various cellular fractions (of varying purity), and are collectively referred to as Stromal Vascular Fraction (SVF).

Where the adipose tissue is the HCT to be provided to the recipient the **basic functions** include:

- providing cushioning and support for other tissues, including the skin and internal organs
- storing energy in the form of lipids
- insulating the body

In contrast, where the HCT provided to the recipient is a SVF, the determination of homologous use would make reference to the basic functions of the cells located in the adipose, rather than those of the tissue collectively. This may be complicated by the need to understand the cells and mechanisms responsible for the desired mode of action. The following represents our interpretation of homologous use of adipose tissue and cell extracts from this tissue:

1. Adipose tissue is used for transplantation into the subcutaneous areas of breast for reconstruction or augmentation procedures. This is **homologous use** because providing cushioning and support is a **basic function** of adipose tissue.
2. Stromal Vascular Fraction (SVF) isolated from adipose tissue is used to treat musculoskeletal conditions, such as arthritis or tendonitis by regenerating or promoting the regeneration of articular cartilage or tendon. This is considered to be **non-homologous use** because regenerating or promoting the regeneration of cartilage or tendon is **not a basic function** of the cells isolated from adipose tissue.

Amniotic membrane

Some **basic functions** of amniotic membrane include:

- serving as a selective barrier for the movement of nutrients between the external and in utero environment
- protecting the fetus from the surrounding maternal environment
- serving as a covering to enclose the fetus and retain fluid in utero

Some **potential functions** of amniotic membrane may include:

- reducing scarring, angiogenesis, and inflammation

The FDA considers that the use of the amniotic membrane for '**potential functions'** to be **non-homologous** because they are **not** basic functions when associated with the fetus.

In contrast, if the '**potential functions'** can be demonstrated experimentally by a manufacturer to also be active in the donor, we will consider the use of the amniotic membrane to be **homologous**.

The following examples represent our perspective on homologous use of amnion:

3. An amniotic membrane product is applied to the surface of the eye to cover or offer protection from the surrounding environment in ocular repair and reconstruction procedures. This is **homologous use** because serving as a covering and offering protection from the surrounding environment are **basic functions** of amniotic membrane.

4. Amniotic membrane is used to support bone regeneration following surgery to repair or replace bone defects. This is **non-homologous use** because bone regeneration is **not a basic function** of amniotic membrane.

5. An amniotic membrane product is to be used for wound healing and/or to reduce scarring and inflammation. The barrier function of the membrane is considered **homologous use**. However, based on current evidence, the other functions are considered to be **non-homologous use**, unless these additional functions can be demonstrated by a manufacturer to also be active in the donor.

HPC examples

Sources of haematopoietic progenitor cells (HPCs) include cord blood, peripheral blood, and bone marrow. The basic functions of HPCs include forming and replenishing the lymphohaematopoietic system.

6. HPCs from mobilised peripheral blood are intended for transplantation into an individual with a disorder affecting the hematopoietic system that is inherited, acquired, or the result of myeloablative treatment. This is **homologous use** because the peripheral blood product performs the same basic function of reconstituting the haematopoietic system in the recipient.

7. HPCs from bone marrow are intended for infusion into an artery with a balloon catheter for the purpose of limiting ventricular remodelling following acute myocardial infarction. This is **not homologous use** because limiting ventricular remodelling is not a basic function of bone marrow.

8. HPCs from cord blood are intended for intravenous infusion to treat cerebral palsy purportedly through the repair of damaged tissue in the brain through paracrine signalling or differentiation into neuronal cells. This is **not homologous use** because there is currently insufficient evidence to support that repair of neurologic tissue through paracrine signalling or differentiation into neuronal cells is a basic function of these cells in the donor.

Platelet-rich plasma (PrP): example of blood component

9. The mechanism of platelet–rich plasma action in the treatment of musculoskeletal disorders remains to be determined and evaluation of platelet–rich plasma in clinical trials is in its infancy. The basic functions that would apply to platelet-rich plasma are based on the understanding of the normal healing process of musculoskeletal tissue. The repair response of musculoskeletal tissues starts with the formation of a blood clot and degranulation of platelets. This degranulation of platelets releases a range of growth factors and cytokines into the local environment that trigger a cascade of events that lead to healing of the wound. Where it can be demonstrated or justified that the intended use of PrP can augment or stimulate healing by turning on the same repair response it could be considered to be a **homologous use**.

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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