



**Australian Government**

**Department of Health**

Therapeutic Goods Administration

# Classification of biologicals

## Australian Regulatory Guidelines for Biologicals (ARGB)

Version 2.1, November 2020

**TGA** Health Safety  
Regulation

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All biologicals must be classified **before** they can be included on the Australian Register of Therapeutic Goods (ARTG).

If you are **developing a biological product**, you need to consider the classification of your product to understand the level of supporting data required to support your application for inclusion on the ARTG.

This guidance will help you understand **how** to classify your biological.

Before classifying your biological, check that your product:

- ✓ meets our definition of a biological
- ✓ is regulated as a biological
- ✗ is not **excluded** from regulation
- ✗ is not **exempt** from certain regulatory requirements

If you are unsure whether your biological is required to be included on the ARTG, refer to our guidance:

- [What is regulated as a biological](#)

## Risk basis for classification

We have classified biologicals according to the level of risk to patients associated with their use. This will be influenced by the level of processing applied to the biological and the intended use of the product, but also the level of external governance and clinical oversight.

- Class 1 biologicals are low risk and have an appropriate level of external governance and clinical oversight.
- Class 2 biologicals are low risk.
- Class 3 biologicals are medium risk.
- Class 4 biologicals are high risk.

# Approach to classification of biologicals

Classification of biologicals is based on either of the following:

- mention in Schedule 16 (Class 1 and 4 biologicals)

OR

- [Method of preparation and intended use](#) (Class 2 and 3 biologicals)

Additional criteria are used to determine exemptions.

## Classification by mention in Schedule 16

All Class 1 and Class 4 biologicals **must** be mentioned in Schedule 16 of the [Therapeutic Goods Regulations 1990](#).

Class 2 and Class 3 biologicals **may** also be mentioned in Schedule 16 to clarify any ambiguity associated with classification based on [method of preparation and intended use](#).



Individual products must be included on the ARTG even if a product or its category is mentioned in Schedule 16 of the [Therapeutic Goods Regulations 1990](#).

## Applying for mention in Schedule 16

If you believe your biological should be specified as a particular class of biological, please [contact us](#).

## Class 1 biologicals

The intent of this low-risk classification is that a Class 1 biological product would:

- be a low risk to public health
- have an appropriate means of oversight such as
  - accreditation
  - a high level of practitioner oversight

To supply a Class 1 biologicals your product:

- ✓ must comply with all applicable standards
- ✓ must be mentioned in Schedule 16
- ✓ must be included on the ARTG, following a declaration of compliance
- ✗ does not require manufacturers to hold a GMP manufacturing license or certificate
- ✗ does not require pre-market assessment of supporting data



At the time of publication of this guidance, only faecal microbiota transplant products (subject to certain conditions) are defined as Class 1 biologicals.

## Class 4 biologicals

Class 4 biologicals are high risk products that are currently defined in Schedule 16 as:

- a. biologicals that comprise or contain:
  - i. live animal cells; or
  - ii. live animal tissues; or
  - iii. live animal organs;
- b. biologicals to which both of the following paragraphs apply:
  - i. the biologicals comprise, contain or are derived from human cells or human tissues that have been modified to [artificially introduce a function](#) or functions of the cells or tissues;
  - ii. the artificially introduced function or functions were not intrinsic to the cells or tissues when they were collected from the donor;
- c. *pluripotent stem cells*;
- d. biologicals derived from *pluripotent stem cells*



[Live animal organs, cells or tissue](#) are Class 4 biologicals and are always [fully regulated](#).

These are specified as biologicals through the [Therapeutic Goods \(Things that are Biologicals\) Specification](#), and defined as Class 4 biologicals through reference in Schedule 16.

### ‘Artificially’ introduce a function

The artificial altering of the function or functions of the human cells & tissues (HCT) is intended to capture only modifications that are **not intrinsic** to the HCT *in vivo*.

The following examples **are Class 4** biologicals because the **intrinsic function** of the donor biological **has been changed**:

- ✓ genetic modification of cells (e.g. CAR T cells, iPSCs)
- ✓ induction of pluripotency in cells (iPSCs)

The following examples **are not Class 4** biologicals because the **intrinsic function** of the donor biological **has not been changed**:

- ✗ compounds and growth factors that are used to expand, maintain or induce differentiation of cells in culture, but their influence is only on the intrinsic functions, ability and plasticity of the HCTs
- ✗ the uptake by cells using normal endocytic processes of exogenous non-pharmaceutical proteins or peptides (e.g. tumour antigen-pulsed dendritic cells)

## Pluripotent cells, and biologicals derived from pluripotent cells

By definition, pluripotent cells are able to give rise to cells found in all tissues of the embryo, except for germ cells, so the use of these cells raises significant safety concerns. The *in vitro* differentiation of these cells may address some safety concerns, but raises others over the ability to control the quality and safety of the defined population. These pluripotent cells and the products derived from them are therefore defined as being Class 4 biologicals.

Other biologicals that contain or are derived from stem cells may still have multipotent potential, but the safety concerns are not as great as for pluripotent cells. These other stem cell derived products will generally be treated as Class 3 biologicals.



All clinical trials using a Class 4 biologicals **must** get approval through the clinical trial ([CTA Scheme](#)), unless:

- you have supporting evidence from a previous clinical trial
- you have obtained approval for an equivalent indication from a national regulatory body with comparable regulatory requirements

## Classification by method of preparation and intended use

If your biological is not mentioned in Schedule 16, then it is likely to be classified as a Class 2 or Class 3 biological. The classification will be determined by:

- [method of preparation](#)

AND

- [intended use](#)

### Definition of Class 2 biologicals

Class 2 biologicals are restricted to those that:

- have been subjected to **only minimal manipulation**

AND

- are only for **homologous** use

### Definition of Class 3 biologicals

Class 3 biologicals cover those that are either:

- for **homologous** use but have been prepared using **more than minimal manipulation**

OR

- for **non-homologous** use, regardless of whether they have been prepared using **minimal manipulation** or **more than minimal manipulation**

## Distinguishing between Class 2 and Class 3 biologicals

The classification of class 2 and 3 biologicals is summarised in the matrix below.

### Classification matrix for class 2 and 3 biologicals

	Intended use: <b>Homologous</b>	Intended use: <b>Non-homologous</b>
Method of preparation: <b>Minimal manipulation</b>	Class 2 (LOW risk)	Class 3 (MEDIUM risk)
Method of preparation: <b>More than minimal manipulation</b>	Class 3 (MEDIUM risk)	Class 3 (MEDIUM risk)



Check that the level of processing and intended use does not result in your product being classified as a [Class 4 biological](#).

### Method of preparation

Method of preparation for biologicals refers to how the biological has been **processed** and if it has been **modified**. This is determined by whether the biological has been processed using:

- only the actions of *minimal manipulation*

OR

- more than *minimal manipulation*

For the definition of **minimal manipulation** and guidance on how it is applied to the classification of biologicals see: [Method of preparation: Interpretation of minimal manipulation of biologicals](#).

### Intended use

The intended use of a biological refers to how it can function in the recipient. A key consideration is how closely the intended use matches the original biological function. This is determined by whether the biological will be for:

- homologous use

OR

- non-homologous use

There are increased safety and efficacy concerns with the use of the HCT when the intended use is non-homologous, because there is less information on which to predict the behaviour of the product.

For the definition of **intended use** and guidance on how it is applied to the classification of biologicals see: [Intended use: Interpretation of homologous use](#).

## Advice on classifying your biological

If you have any questions regarding the classification of your biological and would like to discuss this with us, you need to:

- complete the [Request for TGA advice on biologicals form](#)
- submit the [Request for TGA advice on biologicals form](#) to us

Only after we have received the details of your biological, on the request for advice form, are we able to assist you in determining the most appropriate classification level for your product.

## Version history

<b>Version</b>	<b>Description of change</b>	<b>Authors</b>	<b>Effective date</b>
V1.0	Original publication, using material from the previous ARGB and incorporating recent legislative changes.	Biological Science Section Regulatory guidance Team	July 2018
V2.0	Minor updates to reflect introduction of FMT products as Class 1 biologicals	Biological Science Section	January 2020
V2.1	Minor updates to reflect CTA name change	Biological Science Section	November 2020

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