Streamlining the development of prescription medicines: Peptides to biosimilars to GMOs

ARCS 2023

Dr Tony Gill

Principal Medical Adviser and Director Advanced and Biological Therapies Section

Prescription Medicines Authorisation Branch

Department of Health and Aged Care, TGA

Agenda

- Regulation of GMOs/ATMPs
- Application pathways
- Clinical Trials

Regulation of advanced therapies in Australia

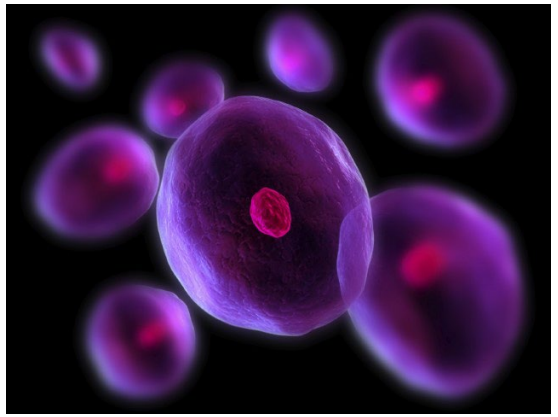
The TGA uses the following definition for advanced therapies:

a) Gene therapies
   i. Regulation of advanced therapies in Australia
   ii. the substance is used in or administered to human beings to regulate, repair, replace, add or delete a genetic sequence AND
   iii. the substance is involved in the therapeutic, prophylactic, or diagnostic effect of the product

b) Gene modified cell therapies

c) Cell and tissue therapies that:
   i. are not devices
   ii. have been classified as class 3 or 4 biologicals.

d) Either a or b in combination with a device



Advanced therapies in Australia

We don’t have a dedicated advanced therapies framework in Australia

Instead we regulate cell and gene therapies under our biologicals and prescription medicines framework

Advanced Therapies

Biologicals

Involve ex-vivo manipulation of human cells e.g CAR-T cells

Regulated under the biologicals framework

Gene therapies

Involve in-vivo manipulation of human cells

Regulated under the prescription medicines framework

- Different dossier requirements
- Different GMP requirements
- Different labelling requirements

Advanced therapies in Australia

Advanced Therapies

Class 1 biologicals

Class 2 biologicals

Class 3 biologicals

Class 4 biologicals

Regulated under the biologicals framework

- Comprises, contains or derived from human cells or human tissues
- Faecal microbiota transplant products
- A thing that comprises or contains live animal cells, tissues or organs

Regulated based on risk (Class 1 – 4)

Gene therapies

Regulated under the prescription medicines framework

- Does not come from human cells or tissues

Products that are regulated as biologicals include:

- tissue-based products (skin, bone, ocular, cardiovascular, amnion)
- cell-based products (genetically modified, in vitro cell expansion or depletion)
- immunotherapy products containing human cells
- combination products (for example, cell therapy and medical device)
- autologous human cells and tissue products (including stem cells)
- products that comprise or contain live animal cells, tissues or organs (for example, pancreatic islet cells isolated from pigs) **Note declared to be biologicals**
- faecal microbiota transplant (FMT) products (a thing that comprises, contains or is derived from human stool). **Note declared to be biologicals**

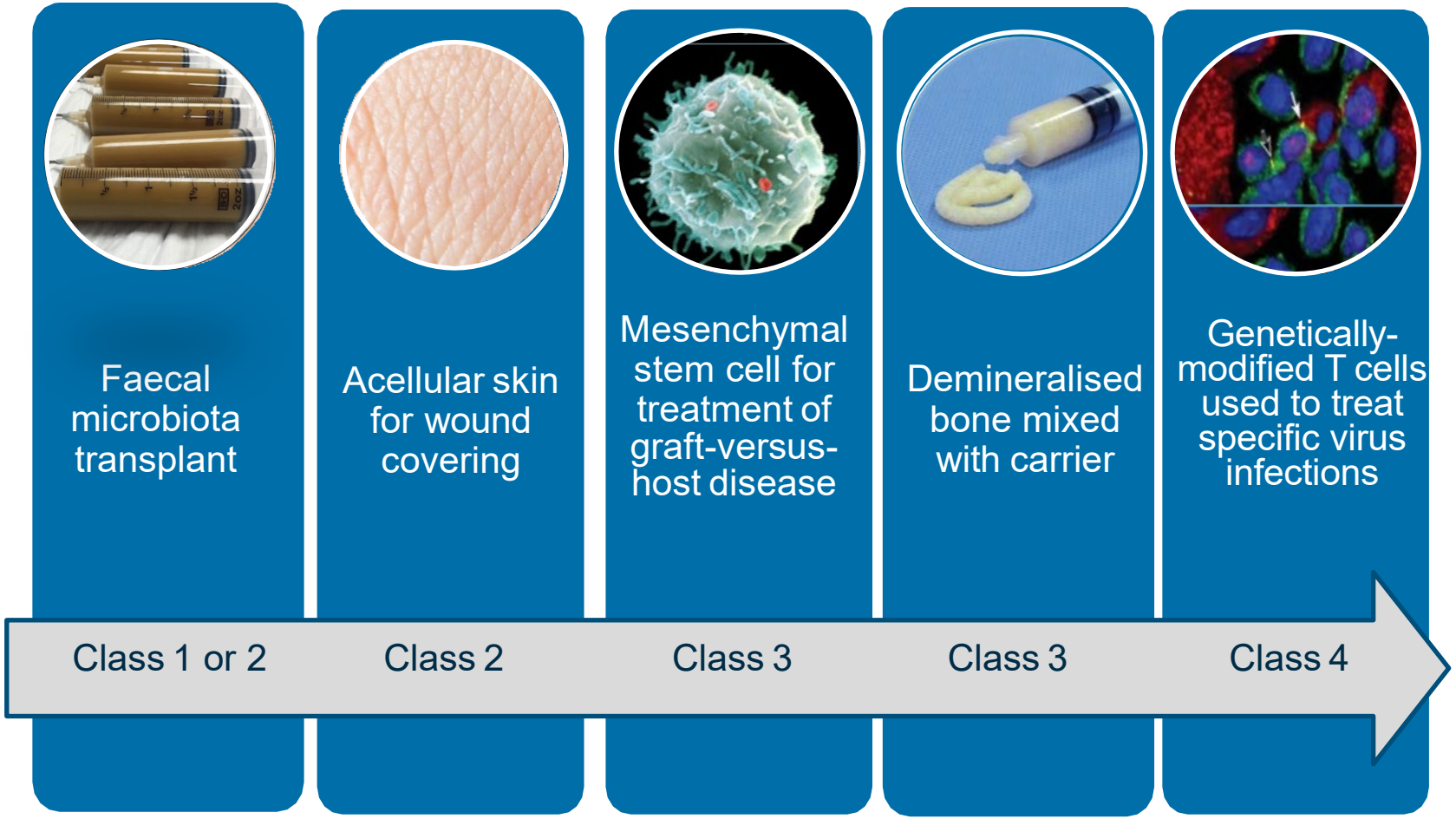
NOTE

Differs from other regulators as does not include biological medicines (e.g. recombinant products, monoclonal antibodies) which under TG legislation are medicines

https://www.tga.gov.au/products/biologicals-blood-and-tissues-and-advanced-therapies/biologicals

Biologicals are grouped into classes

Examples:



Class 3 biologicals

Definition

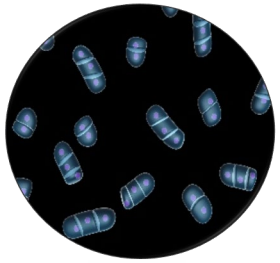
- for homologous use but have been prepared using more than minimal manipulation

  OR

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

Currently approved Class 3: chondrocytes

Examples of cell therapies: mesenchymal stem cells, T cells



Class 4 biologicals

- Definition (Schedule 16)
  - Animal cells, tissues and organs
  - Cells that have been modified to *artificially introduce a function* or functions of the cells or tissues; and
  - the artificially introduced function or functions were not intrinsic to the cells
  - *pluripotent stem cells*;
  - biologicals derived from *pluripotent stem cells*

Currently approved Class 4: CAR-T therapies

Examples of cell therapies: iPSCs, xenogeneic cell therapy, gene-modified cell therapies

Application pathways available

Application Pathways	Medicine	Biological
Orphan	Y	N
Provisional	Y	N
Priority	Y	Y
Orphan & Provisional	Y	N
Orphan & Priority	Y	N
Orphan & Provisional & Priority	N	N
Provisional & Priority	N	N
COR-A	Y	N
COR-B	Y	N
Export	Y	Y - commencement of legislation to allow for Export-only biologicals will be in place from June 23

Clinical Trials Pathways

Clinical Trial Pathway	Medicine	Biological
CTA	If requested by HREC	Class 4 biologicals mandatory unless: • it has received clinical trial approval for an equivalent indication from a national regulatory agency with comparable regulatory requirements; or • It has a history of previous usage that is supported by clinical evidence received by the TGA e.g. new indication
CTN	Y	Y for • Class 4 biological if allowed by above • Class 4 biological following CTA approval • Class 3 and below biological

HREC determining factors re CTA or CTN

If a HREC feels that it requires additional expertise to review a CTN, it may seek advice from external authorities or it may seek to collaborate with another HREC that has the required expertise.

A HREC may determine that it does not have access to the appropriate scientific and technical expertise to review the proposed trial under the CTN scheme and recommend review under the CTA scheme.

CTA requirements

Relates to safe use of investigational product

Consider:

- Trial product
- Quality e.g. viral safety, microbiological, endotoxin, container/packaging
- Pre-clinical
- Clinical especially trial protocol

Recommend pre-submission meeting

Guidelines used:

- Draft Guideline on quality, non-clinical and clinical requirements for investigational advanced therapy medicinal products in clinical trials https://www.ema.europa.eu/documents/scientific-guideline/draft-guideline-quality-non-clinical-clinical-requirements-investigational-advanced-therapy_en.pdf
- Guideline on the requirements for quality documentation concerning biological investigational medicinal products in clinical trials - https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-requirements-quality-documentation-concerning-biological-investigational-medicinal_en-0.pdf

There is a TGA presentation on clinical trials tomorrow

GMO applications and/or trials

Reminder that may require OGTR licences – contact OGTR

Website references

TGA website	www.tga.gov.au
Cells that have been modified to *artificially introduce a function*	https://www.tga.gov.au/resources/resource/guidance/classification-biologicals#approach-s16-class4-function
Draft Guideline on quality, non-clinical and clinical requirements for investigational advanced therapy medicinal products in clinical trials	https://www.ema.europa.eu/documents/scientific-guideline/draft-guideline-quality-non-clinical-clinical-requirements-investigational-advanced-therapy_en.pdf
Guideline on the requirements for quality documentation concerning biological investigational medicinal products in clinical trials	https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-requirements-quality-documentation-concerning-biological-investigational-medicinal_en-0.pdf
Biologicals	https://www.tga.gov.au/products/biologicals-blood-and-tissues-and-advanced-therapies/biologicals

Therapeutic Goods Administration (TGA)

Exhibition booth **No.1**

Want to chat with me further? Come visit us.

Questions?

www.tga.gov.au

Australian Government

Department of Health and Aged Care

Therapeutic Goods Administration