Australian Government
Department of Health
Therapeutic Goods Administration

Regulation of autologous cells and tissues

Dr Glenn Smith
Director, Biological Science Section
Scientific Evaluation Branch
Medicines Regulation Division, TGA
ARCS Scientific Congress Canberra 2016

10-11 August 2016

TGA Health Safety Regulation

Therapeutic Goods Administration (TGA)

- A division of the Australian Government Department of Health
- Regulates the safety, quality and efficacy of therapeutic goods in Australia
- Regulates medicines, devices, biologicals and blood
- Operates under cost recovery arrangements

Exemptions under the biologicals framework

- Non-viable **tissues of animal origin** e.g. porcine heart valves
- **Fresh viable human organs** for direct donor-to-host transplantation
- Fresh viable human **haematopoietic progenitor cells for direct donor-to-host transplantation** (e.g. bone marrow cells, cord blood)
- **Reproductive tissue** (e.g. sperm, eggs, embryos) that have not been processed in any way apart from freezing
- Autologous tissue and cells
  - collected from a patient **under the care of a medical practitioner**, and
  - manufactured for therapeutic treatment of a **single indication**, and
  - in a **single course of treatment** of that patient **by the same medical practitioner**, or by a person under their supervision
- **Other Autologous uses** are not exempt in Australia

What's in & what's out

Not regulated by the TGA

- Assisted reproductive technologies (in vitro fertilisation)
- Fresh viable organs
- Fresh haematopoietic progenitor cells (bone marrow transplants)
- Cells and tissues made by a medical practitioner for a single patient under the care of that medical practitioner

Regulated as biologicals

- Human stem cells
- Tissue-based products (skin, bone, ocular, cardiovascular)
- Cell-based products (genetically modified, in vitro cell expansion/depletion)
- Combined cell and tissue products (collagen matrices for localised cell delivery)

Regulated, but not as biologicals

- Biological prescription medicines (vaccines, plasma derivatives)
- Animal tissue products (xenotransplantation)
- Labile blood and blood components
- Haematopoietic progenitor cells (non-fresh transplants)

Why have an Excluded Goods Order?

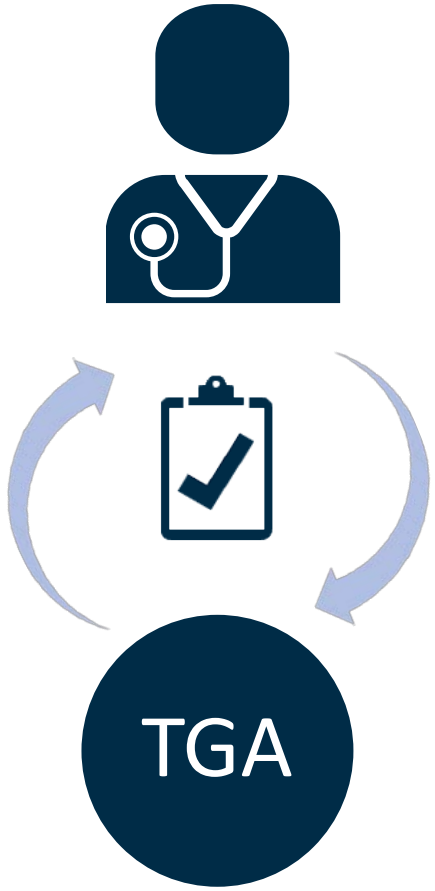
- Some products have been declared not to be therapeutic goods and thus not regulated by TGA as a result of:

- **Government policy** and to reflect Australian Health Ministers Advisory Council decisions
  - e.g. assisted reproductive therapy, fresh haematopoietic progenitor cells and organs for direct transplantation

- **Alternative regulatory pathways apply**
  - Self-regulation for assisted reproductive therapy
  - NPAAC guidelines and NATA accreditation for haematopoietic stem cell programs
  - Organ and Tissue Authority requirements for organ transplantation
  - **Medical practice**

Medical practice and therapeutic product regulation intersect

- Different regulatory frameworks oversee **medical practice** (Medical Board of Australia/ AHPRA) and **therapeutic products** (TGA), but the boundaries can overlap
- Concerns may also arise under the **Australian Consumer Law** where consumers are misled or deceived into believing that certain treatments are safe or effective when that is not the case
- Some autologous cell products are **excluded from TGA regulation under the Therapeutic Goods (Excluded Goods) Order 1 of 2011 under certain conditions**



Excluded Goods Order No.1 of 2011

Goods that are not treated by the TGA as coming within the regulatory framework created by the *Therapeutic Goods Act 1989* (the Act) and Regulations:

o. fresh viable organs, or parts of human organs, for direct donor-to-host transplantation and used in accordance with applicable laws and standards

p. fresh viable human haematopoietic progenitor cells for direct donor-to-host transplantation for the purpose of haematopoietic reconstitution

r. reproductive tissue for use in assisted reproductive therapy

Excluded Goods Order No.1 of 2011

q. human tissue and cells that are:

i. collected from a patient who is under the clinical care and treatment of a medical practitioner registered under a law of a State or an internal Territory

and

i. manufactured by that medical practitioner, or by a person or persons under the professional supervision of that medical practitioner, for therapeutic application in the treatment of a single indication and in a single course of treatment of that patient by the same medical practitioner, or by a person or persons under the professional supervision of the same medical practitioner

Excluded Goods Order

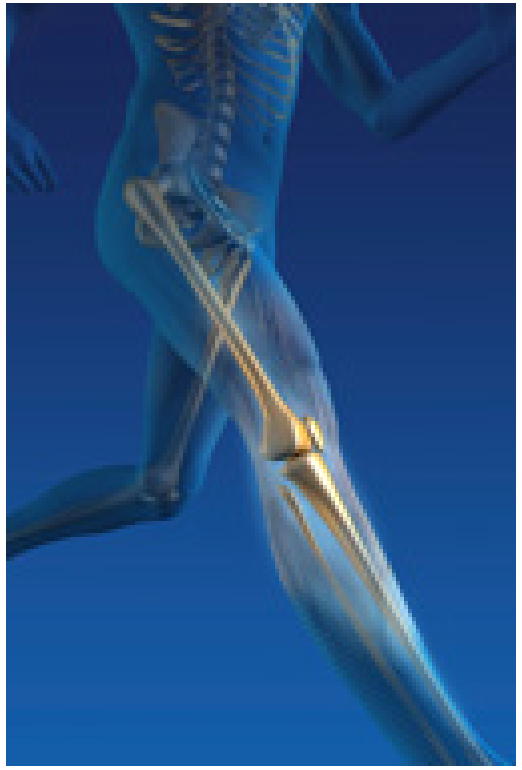
Key considerations

- Autologous cells and tissues only
- Patient under the care of the same registered medical practitioner
- Collection, ‘manufacture’ and application of cells or tissues under professional supervision of that medical practitioner
- Single course of treatment and indication
- Responsibility

Clinical procedures/treatments potentially within the current Item 4(q) exclusion

Autologous

- Skin grafts
- Skull flaps
- Vascular conduits
- Pancreatic islet cells
- Bone grafts
- HPCs for reconstitution of blood after treatment for cancer
- Blood components
- Cosmetic/reconstructive procedures (bone, skin and fat transfers)
- Autologous stem cells



Excluded Goods Order

Other considerations

- Standards relating to professional performance and advertising - regulated by the Australian Health Practitioner Regulation Agency
- Professional obligations of medical practitioners to maintain satisfactory standards of practice
- Whether the treatment being undertaken is necessary and safe and if efficacy is supported by credible clinical evidence
- Provision of adequate information to patients to enable them to give informed consent to treatment
- Regulation of advertising including under the provisions of the *Competition and Consumer Act 2010*
- Equipment and materials that are used for the manufacture of the product that may still be therapeutic goods subject to regulation by the TGA

Concerns with the current regulatory model

- **Lack of evidence to support the efficacy** of autologous stem cells
- Large sums of money being charged for **unproven treatments**
- **Safety of some stem cell products** – either direct safety impacts or safety issues incidental to the therapy
- **Lack of mechanisms** for reporting of adverse effects of the products
- **Inappropriate advertising** of the products

Stem cell 'tourists' flock to Australia

- The Australian
- 2:00AM August 5, 2016

Stem cell clinics exploiting regulatory loop holes to sell questionable treatments: experts
ABC Online

Untested stem cell treatments proliferate in Australia, study finds
The Guardian

Unproven stem cell treatments multiply amid loophole
5 August 2016 *Medical Observer*

Understanding of risks of cell therapies is limited

- Can **risk of infectious disease transmission** ever be **eliminated**?
  - Cells and tissues often cannot be sterilised fully
  - Donor screening – difficult to obtain complete history for deceased donors
  - Subjective nature of exclusion decisions
  - Evolving knowledge e.g. prions and degenerative neurological diseases
- Many biologicals **cannot be stopped** once in a recipient's body
- **Limited adverse event reporting** because only some stem cell therapies are in formal clinical trials and adverse events can also be masked by poor prognosis of critically ill patients
- **Unforseen reactions** have been reported
  - e.g. heart attack, severe thrombosis, encephalomyelitis, bone tissue

What are some other regulators doing?

FDA

- New guidances are more prescriptive about what defines ‘homologous use’ and ‘minimal manipulation’
- ‘Right to try’ movements also have momentum

Europe

- Only about five ‘advanced therapy medicinal products’ have been approved by EMA
- ‘Hospital exemption system’ for some cell and tissue products rather than private clinics performing treatments

Japan

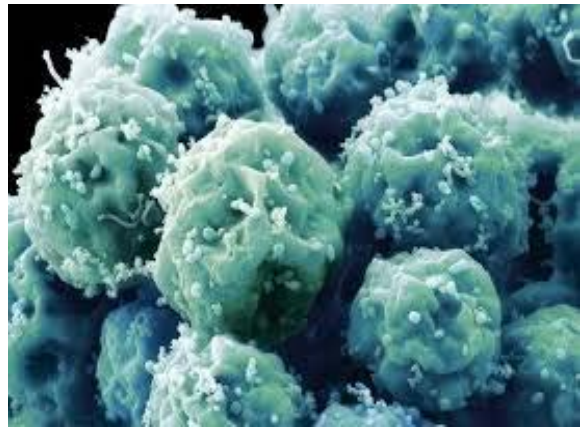
- ‘Provisional licensing’ system for cell therapies (SAKIGAKE initiative)
- Where initial safety and manufacturing results positive; limited term commercial licensing to establish product efficacy and confirm safety

Is current Australian regulation of autologous stem cell appropriate ?

- Interpretation of '**minimally manipulated'** and **'homologous use'** is relevant
- **USFDA takes a narrow view** of 'minimally manipulation' and 'homologous use' for fat stem cells in Dec 2014 draft industry guidance documents
- In Australia, a **public consultation** (Jan-Mar 2015) was held to seek input on **five potential options for regulation** of these cells as therapeutic goods
- 80 submissions received

Next steps

- Cell and tissue regulation is a **new and evolving area** internationally
- **Response to the autologous stem cell consultation** will help inform what, if any, change is required to therapeutic goods regulation
- A second public consultation paper will be released in the near future, with a number of regulatory options developed as a result of the first consultation in 2015
- Further input from stakeholders is welcomed



More information

Therapeutic Goods (Excluded Goods) Order No. 1 of 2011

- https://www.tga.gov.au/therapeutic-goods-excluded-goods-order-no-1-2011

Excluded Goods Order No. 1 of 2011: Guideline for items 4(o) – 4(r)

- https://www.tga.gov.au/excluded-goods-order-no-1-2011-guideline-items-4o-4p-4q-and-4r

Further questions

- bloodandtissues@tga.gov.au

Australian Government

Department of Health

Therapeutic Goods Administration