Regulation of autologous cells and tissues

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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

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

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

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

Regulation of autologous cells and tissues
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

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

Further questions
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