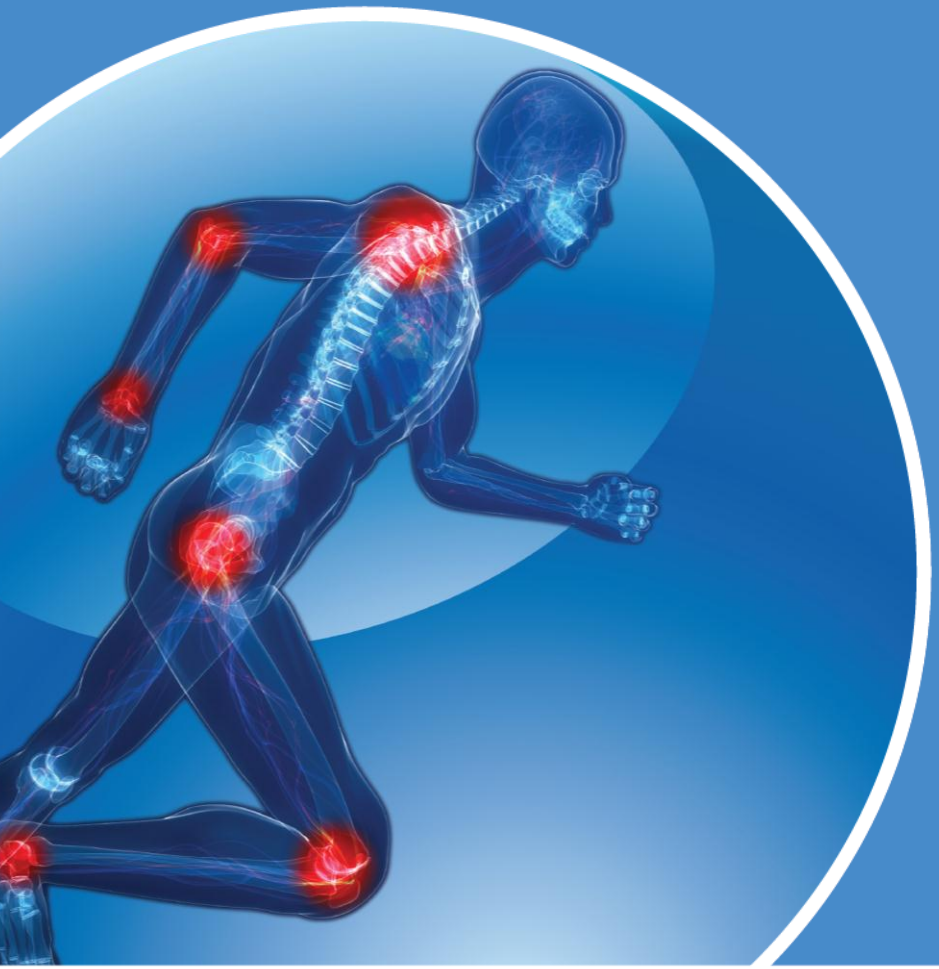

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Regulatory Aspects of Autologous, non-expanded cell therapy

ISCT Annual Meeting Auckland, April 2013
Richard Lilischkis, Ph.D

Company Overview

- Regenerative medicine company, Sydney
- Focus on regenerative cells from adipose tissue
- Develops and commercialises technologies for:
  - autologous, intra-operative, non-expanded adipose-derived cell therapy for humans; and
  - allogeneic, off-the-shelf adipose-derived cell therapy for animals
- Initial focus on musculoskeletal conditions (e.g. knee-OA)
- Committed to clinical data and on-going research

The HiQCell Procedure

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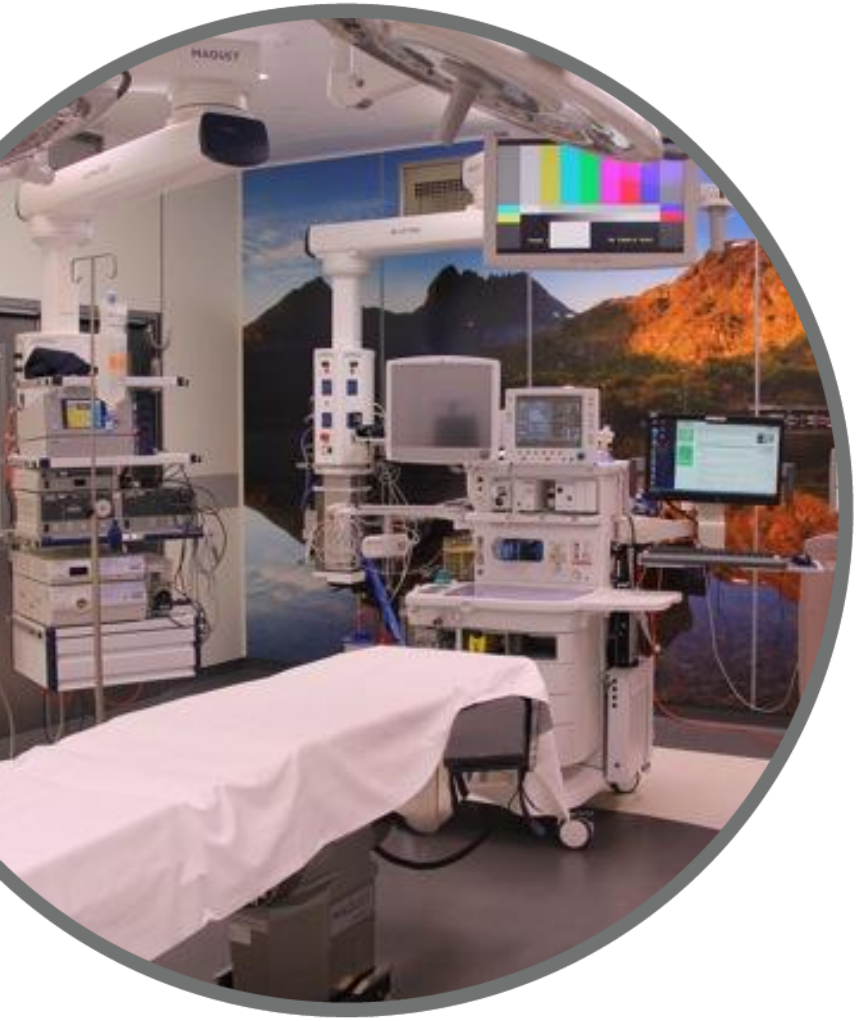

- Pre-op workup
- Fat harvest by mini liposuction
- Cell separation (65 min)
- Injection of cell suspension in recovery / treatment room
- Autologous, non-expanded and intra-operative
- Local anaesthetic, half day procedure
- Regeneus provides in-clinic cell processing services to medical specialist who is responsible for the cell therapy

Treatments so far

- Veterinary (AdiCell™)
  - Commenced early 2008
  - > 400 dogs and horses treated with autologous, unexpanded intra operative adipose derived cell therapy
  - Development of allogeneic off-the-shelf adipose-derived cell therapy product (CryoShot™) in response to market demand

- Human (HiQCell™)
  - Commenced 2011
  - > 250 patients with >400 joints treated

- Clinical Research
  - Ethics approved registry
  - RCT pilot study in knee OA

Australia – Biologicals Framework

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Biologicals Regulatory Framework

Products made from or containing human cells or human tissues (or otherwise specified)

Biologicals

Australia – Biologicals Framework

Biologicals excluded from regulation as Therapeutic Goods:

Human tissue and cells that are

- collected from a patient who is under the **clinical care and treatment** of a **medical practitioner registered** under a law od a state or an internal Territory; and
- manufactured by **that medical practitioner**, or 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 that **same medical practitioner**

Australia – Biologicals Framework

Medical Practitioner Exemption: Key Elements

1. Single patient, autologous
2. Single, registered practitioner
3. Manufacturing under professional supervision
4. Single indication
5. Single course of treatment
6. Patient information and consent

European Union

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European Union Tissue and Cells Directives (EUTCD)

Directive 2004/23/EC
on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells

"This directive shall not apply to:
(a) tissues and cells used as an autologous graft within the same surgical procedure
(b) blood and blood components as defined by Directive 2002/98/EC
(c) organs or parts of organs if it is their function to be used for the same purpose as the entire organ in the human body"

Directive 2004/23/EC, Article 2(2)

United Kingdom

Directive 2004/23/EC implemented in UK national law on 5th July 2007
"Human Tissue (Quality and Safety for Human Application) Regulations 2007

- "autologous graft" means tissue or cells removed from and applied in the person within the same surgical procedure
- "human application", in relation to tissue or cells, means use on or in a human recipient, including use in extracorporeal applications **but not including use for autologous graft**

Human Tissue Authority (HTA) is the competent authority

Germany

Transposition of EUTCD into German law: Gewebegesetz (Tissue Law)

§ 4a
Ausnahmen vom Anwendungsbereich
Dieses Gesetz findet keine Anwendung auf
…
3. Gewebe, die innerhalb eines Behandlungsvorgangs einer Person entnommen werden, um auf diese **ohne Änderung ihrer stofflichen Beschaffenheit** rückübertragen zu werden.

§ 4a
Exemptions to the area of application
This law does not apply to
…
3. Tissues which are removed from a person to reinsert them **without changing their material composition** into the same person in one and the same medical procedure"
(unofficial translation)

Singapore

Three Acts covering the use of medical products are administered by:

i) The Ministry of Health: **(1) the Private Hospitals and Medical Clinics Act** (Chapter 248; PHMC) - *provides for the control, licensing and inspection of private hospitals, medical clinics, clinical laboratories and healthcare establishments, and for purposes connected therewith*

i) The Health Science Authority: **(2) the Medicines Act** (Chapter 175; MA) and **(3) the Health Product Act** (Chapter 122D; HPA) – administered to ensure provision of quality, safety and efficacy

Conclusions:

- The "one surgical" procedure applies to treatments like HiQCell in Singapore as it does in Australia. In Singapore it is defined in Section 7 of the Medicines Act (Chapter 176)
- For any provision of such a procedure to administered by a third party, Sections 5 and 6 of the Medicines Act (Chapter 176) would apply and a Product License and perhaps a Manufacturing License would be required.

Summary (1)

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Medical Practitioner Exemption

- Enable surgeons to prepare autologous cells in the theatre environment
- Need facility in theatre or laboratory close by (same hospital)
- MP must be on top of and in charge of all aspects of the procedure
- Need for quality system:
  - High standard facilities
  - Risk analysis and mitigation
  - Standard Operation Procedures
  - Adverse Reaction and Event Monitoring
  - Continuous Improvement
  - Documentation and Reporting

Summary (2)

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Central Facility to serve multiple Medical Practitioners

- Procure and/or process tissue in centralised facilities

- Overseen by central or local authority
- Need for procurement license
- Need for manufacturing license