Regulatory Aspects of Autologous, non-expanded cell therapy

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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

- 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 intraoperative 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 – Biologica ls Framework

Biologica ls Regulatory Framework

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

Biologica ls
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 of 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**
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
“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)
Directive 2004/23/EC implemented in UK national law on 5\textsuperscript{th} 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
§ 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)
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.
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
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