Regulatory Pathways to Market

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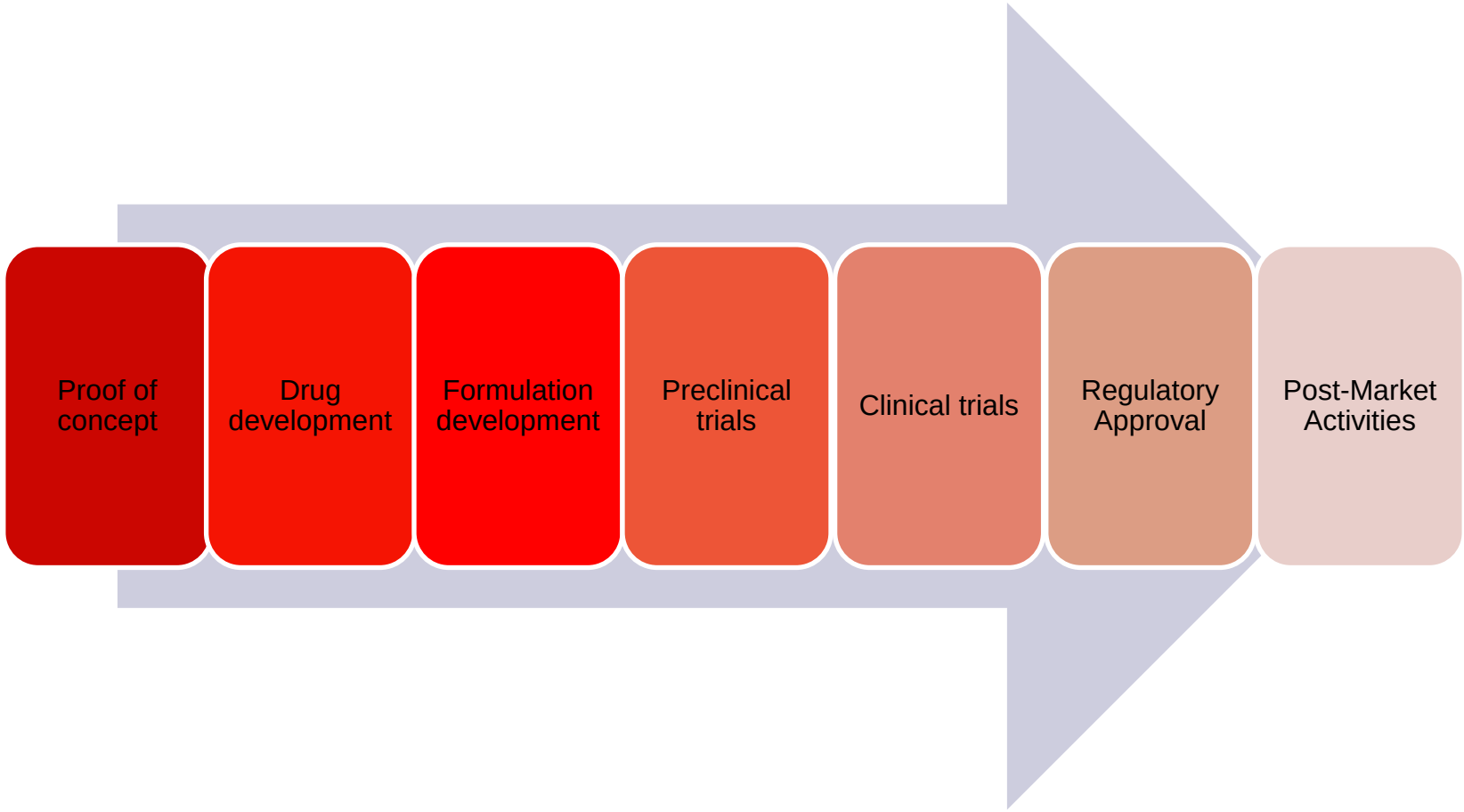
Agenda

- Product development Lifecycle
- Regulation of Therapeutic Goods
- Case study 1 – Biotech company
- Case study 2 – Getting the wrong advice
- Conclusions/Question time

Product development lifecycle

Product Development Lifecycle



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Regulation of therapeutic goods

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Regulation of Therapeutic Goods

- Underpinned by the *Therapeutic Goods Act 1989* ("Act")
- Subordinate legislation
  - *Therapeutic Goods Regulations 1990*
  - *Therapeutic Goods (Medical Device) Regulations 2002*
  - Various Orders and Determinations

Regulation of Therapeutic Goods

- Therapeutic Goods Administration (TGA) is responsible for administering the Act
- Provide a national system of controls relating to quality, safety and efficacy and timely availability of therapeutic goods
- All therapeutic goods must be included in the Australian Register of Therapeutic Goods (ARTG) prior to supply, import, manufacture or export
  - > Unless exempt or excluded goods

Exemptions

- Exempt from listing and registration requirements
- 4 kinds of exemptions
  - Under the Regulations
    - Schedule 5 and 5A of the Regulations
  - In emergencies
    - Made by the Minister where there is a threat to public health
  - For special and experimental uses
    - Clinical trials
    - Personal importation
    - Special Access
    - Authorised Prescriber
  - Where substitutes are unavailable or in short supply

What is a therapeutic good?

- Defined in section 3 of the Act
- Therapeutic goods are goods that are:
  - for “therapeutic use”; or
  - for use as an ingredient/component in the manufacture of therapeutic goods

What is “therapeutic use”?

- Also defined in section 3 of the Act
- Therapeutic use is use in or in connection with:
  - Preventing, diagnosing, curing or alleviating a disease, ailment, defect or injury;
  - Influencing, inhibiting or modifying a physiological process;
  - Testing the susceptibility or person to a disease or ailment;
  - Influencing, controlling or preventing conception;
  - Testing for pregnancy; or
  - The replacement or modification of part of the anatomy in persons.

Types of Therapeutic Goods

- Medicines
  - Prescription medicines
  - OTC medicines
  - Complementary medicines
- Medical devices
  - Class I, IIa, IIb, III, Active implantable medical devices (AIMD)
  - In vitro diagnostic medical devices (IVDs)
- Biologicals
  - Class 1, 2, 3, 4

Definition of Medicine

- Section 3 of the Act:
  - *Therapeutic goods (other than biologicals) that are represented to achieve, or are likely to achieve, their principal intended action by pharmacological, chemical, immunological or metabolic means in or on the body of a human*.

Regulation of Prescription Medicines

- Must be registered in the ARTG
- Require pre-market risk evaluation by TGA
  - Must submit quality, safety and efficacy data to TGA
- TGA often obtains advice from the Advisory Committee for Prescription Medicines (ACPM) before making a final decision
- If not satisfied with the decision, may appeal internally under s 60 of the Act and then appeal to the Administrative Appeals Tribunal (AAT)

Definition of Medical Devices

Section 41BD of the Act

- Any instrument, apparatus, appliance, material or other article intended, by the person under whose name it is or is to be supplied, to be used for human beings for the purpose of one or more of the following:
  - (i) diagnosis, prevention, monitoring, treatment or alleviation of disease;
  - (ii) diagnosis, monitoring, treatment, alleviation of or compensation for an injury or disability;
  - (iii) investigation, replacement or modification of the anatomy or of a physiological process;
  - (iv) control of conception;
- and that does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but that may be assisted in its function by such means

Regulation of Medical Devices

- Different regulatory requirements depending on the classification of the medical device
  - > Class I, IIa, IIb, III, AIMD
- Conformity assessment required
  - > Establishes safety and performance
  - > Based on 14 essential principles
  - > Risk analysis
  - > Declaration of conformity

Regulation of Biologicals

- On 31 May 2011, the TGA implemented the Biologicals Regulatory Framework
- Distinguishes biologicals from medicines
- Three year transition period for goods currently registered in the ARTG
- New biologicals need to be registered in the ARTG

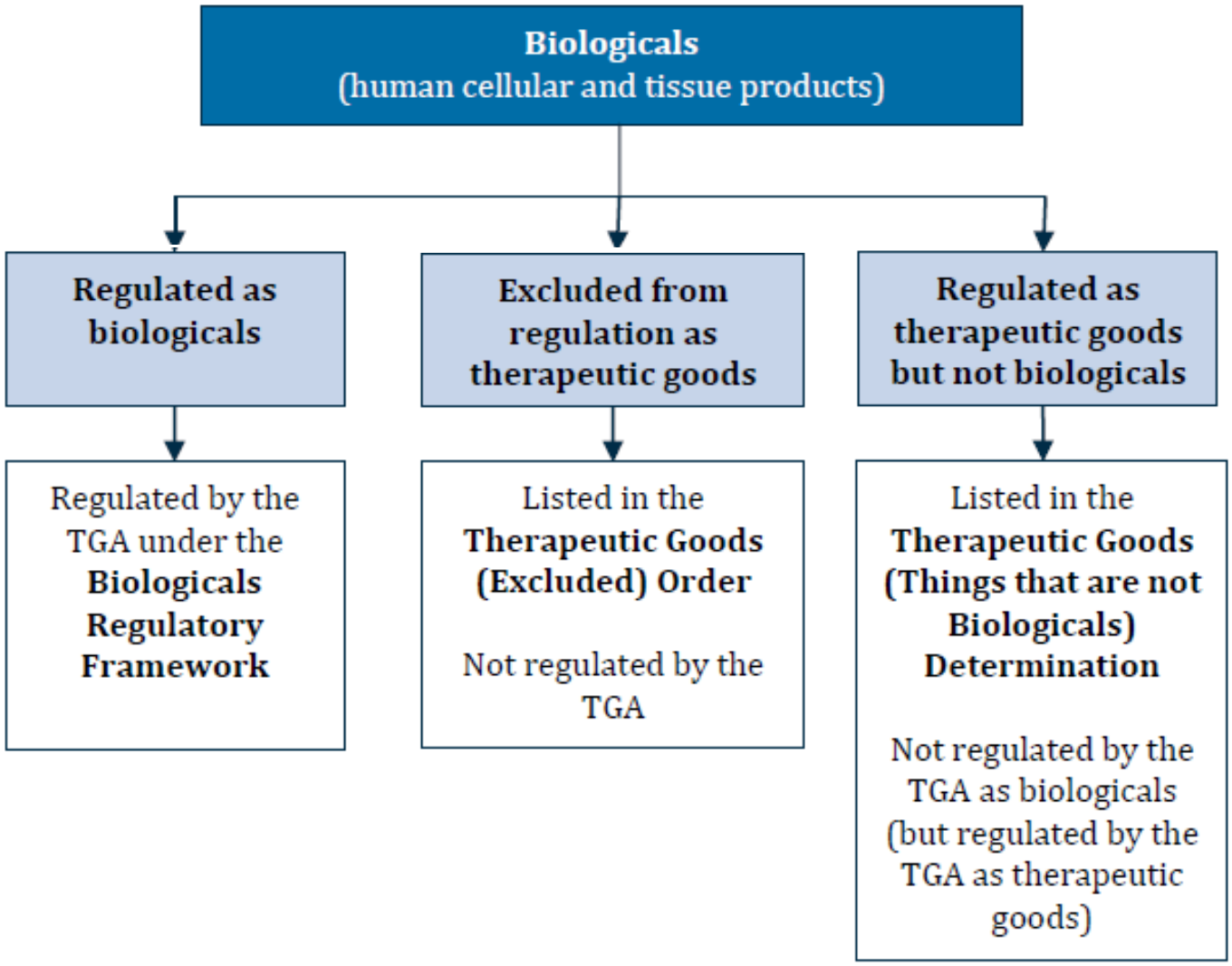
Definition of Biologicals

- Section 32A of the Act
  - Biological is a "thing" made from, or that contains, human cells or human tissues, and that is used to:
    - treat or prevention disease, ailment, defect or injury; or
    - diagnose a condition; or
    - influence, inhibit or modify a physiological process; or
    - test the susceptibility of persons to a disease or ailment; or
    - replace or modify a person's body parts.

Examples of 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

Regulation of Biologicals



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Examples of Excluded / Not Biologicals

- Excluded biologicals
  - > Human tissue and cells for autologous use
  - > Fresh haematopoietic progenitor cells
  - > Reproductive tissue that is unmanipulated
- “Things” that are not biologicals
  - > Blood and blood components
    - – Regulated as medicines
  - > Biological prescription medicines
    - – Vaccines, recombinant products

Case studies

Case Study 1 – Biotech company

- Biotech company developed stem cell therapy
- Contacted a number of law firms seeking legal and regulatory advice
  - > Particularly clinical trial advice
- The treatment consisted of:
  - > Extraction of peripheral blood
  - > Isolation of mononuclear cells
  - > Conversion to cord-like stem cells
  - > Reinfusion into the same patient (autologous use)

Regulatory/Legal Questions

- Was the “treatment” a therapeutic good?
- If so, what type of therapeutic good?
  - > Medicine?
  - > Biological?
  - > Exempt Good?
- What regulatory requirements did the company need to meet?
  - > What was the best regulatory strategy?

Regulatory Classification

- The treatment was a therapeutic good
- The treatment was a biological
- Did it require regulation as a biological?
- Was it in the *Therapeutic Goods (Things that are not Biologicals) Determination"*?
- Was it in the *Therapeutic Goods (Excluded Goods) Order*?

Excluded Goods Order - Clause 4(q)

- Clause 4(q) of the *Therapeutic Goods (Excluded Goods) Order* (the Order)
  - Not therapeutic goods if human tissue and cells are:
    - Collected and manufactured under a medical practitioner's supervision
    - Single indication
    - Single course of treatment

Application of Clause 4q

- Advised the client to adapt the protocol relating to the treatment to “fit” clause 4q
- Benefits of classifying as an excluded good
  - > No regulatory oversight by the TGA
  - > HUGE ramifications in terms of development cost and commercialisation
  - > Offered client a fast track to market

The Autologous Stem Cell Treatment Protocol

- All carried out in under the medical practitioner's strict direction and supervision

- Use of stem cells derived from peripheral blood
  - Peripheral blood collected from a patient
  - Mononuclear cells separated from the leukocytes
  - De-differentiate the mononuclear cells into cord-like stem cells
- Stem cells injected back into the same patient by the medical practitioner
  - Single course of treatment
  - Single indication

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Consultation with TGA

- Proposed treatment was mapped out for TGA
- TGA confirmed in writing that the treatment as customised by us fell within Clause 4(q)
  - > No regulatory oversight by the TGA
  - > Oversight under consumer protection laws
  - > Liability rests with the medical practitioner
- No issues following surprise inspection by TGA

Consequences of Operating under Clause 4(q)

- No regulatory requirements to establish quality, safety and efficacy
- Subject to consumer protection laws
- Risks shifts to the medical practitioner
  - > Practitioner must ensure treatment is administered safely and in the best interests of the patient (duty of care)
- Proper informed consent from patients
- Appropriate insurance and indemnities

The client that kept on giving

- Regulatory hurdles along the way
  - > Reagent 1
  - > Reagent 2
  - > Blood bag used to administer treatment to patient

Reagent 1 – was it a therapeutic good?

- Reagent 1 was used to separate mononuclear cells from blood collected
- Supplier refused to supply until reagent was approved by the TGA
- BUT TGA approves <u>therapeutic goods</u>
- Therapeutic goods are goods that are:
  - for therapeutic use; or
  - for use as an ingredient/component in the manufacture of therapeutic goods

Reagent 1 – was it for therapeutic use?

- Therapeutic use is use in or in connection with:
  - > preventing, diagnosing, curing or alleviating a disease, ailment, defect or injury; or
  - > influencing, inhibiting or modifying a physiological process

Reagent 1

- Reagent 1 was used *solely* to separate mononuclear cells from blood collected
- NOT for a therapeutic purpose
- If NOT for a therapeutic use, then it is NOT a therapeutic good
  - > No regulatory requirement for approval by the TGA for use for a non-therapeutic purpose.
- Written confirmation obtained from the TGA

Reagent 2

- Reagent 2 was used only to prevent blood cells sticking to inner walls of the blood bag
  - > “Washed out” completely before administration of treatment
- Reagent was for a non-therapeutic purpose
- Not a therapeutic good and therefore no requirement for TGA approval

Blood Bags

- One blood bag used to convert blood to stem cells and to administer stem cells to patient
- The blood bag was a “medical device” insofar as administration of treatment to patient
  - > An instrument or apparatus
  - > Intended to be supplied to administer a treatment
  - > Does not achieve its principal intended action by pharmacological, immunological or metabolic means
- *Prima facie* approval of blood bag as a medical device required prior to administration of treatment

Blood Bags Used to Administer Treatment

- Definition of ‘supply’
  - “*Supply by way of administration to, or application in the treatment of, a person*”
- Unapproved bags were necessary for processing stem cells
  - Not for administering stem cell treatment
  - NOT medical devices when used for this purpose
- Processed cells transferred to TGA-approved bag for administration to patients

Case study 2 – Getting the wrong advice

- Related to the regulation of adipose tissue
- Must start with regulatory classification
  - > Is it a therapeutic good?
  - > Is it a medicine?
  - > Is it a biological?
  - > Is it an exempt good?
  - > Is it an excluded good?

Regulation of adipose tissue

- It is a therapeutic good
  - Treatment of inflammatory diseases and joint and tendon diseases arising from injury/old age
  - Ultimate use is “therapeutic use”
- Not a medicine if it is a biological
- It is a biological
  - *“Derived from human tissues”*
  - *“…for use in the treatment or prevention of a disease…or injury…”*

Regulation of adipose tissue

- Biologicals ordinarily require registration in the ARTG
  - > Unless excluded goods; or
  - > Unless exempt goods

Adipose Tissue as an Excluded Good

- Possible excluded good pursuant to clause 4q of the Excluded Goods Order
  - > Adipose tissue collected by a medical practitioner
  - > Manufactured by that medical practitioner
  - > Single course of treatment for a single indication
  - > Must be supervised by the same medical practitioner
  - > Autologous use

Is Adipose Tissue an Exempt Good?

- Provides an exemption from the requirements for registration
- Possible exemption under:
  - > Item 6 of Schedule 5 of the Regulation

Item 6 of Schedule 5 of the Regulations

- *"Medicines that are dispensed or extemporaneously compounded for a particular person for therapeutic application to that person"*
- Do you think that adipose tissue falls within that exemption?

Item 6 of Schedule 5 of the Regulations

- What is a medicine?
  - *"….therapeutic goods (**other than biologicals**) that are represented to achieve their principal action by pharmacological, immunological or metabolic means…."*
- Is adipose tissue a medicine?
- NO!! It's a BIOLOGICAL
- Item 6 of Schedule 5 of the Regulations does NOT apply

Consequences of the wrong advice

- Company was advised that adipose tissue was an exempt good
- Proceeded on the basis that there was no requirement for registration in the ARTG
- No focus on generating regulatory data to support registration
- Significant legal, regulatory and commercial ramifications for unlawful manufacture and supply

Workable solution for the company

- Structure administration of treatment in accordance with clause 4q of excluded goods order
- If operation under clause 4q is not feasible, mechanism for use under Special Access Scheme until registered.

Conclusion

- Navigating through the regulatory regime has become increasingly complex
- Regulatory pathway to market is not easy, but may not be as onerous as you might think
- Getting the best and right advice is crucial
- A relationship with the TGA is crucial
- Requires legal, regulatory, scientific and commercial expertise

Any Questions?

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