Australian Government
Department of Health
Therapeutic Goods Administration

Regulation of cell and gene therapies in Australia

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Cell & Gene Therapy Products (CGTP): Manufacturing, Quality and Regulatory Considerations

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TGA Health Safety Regulation

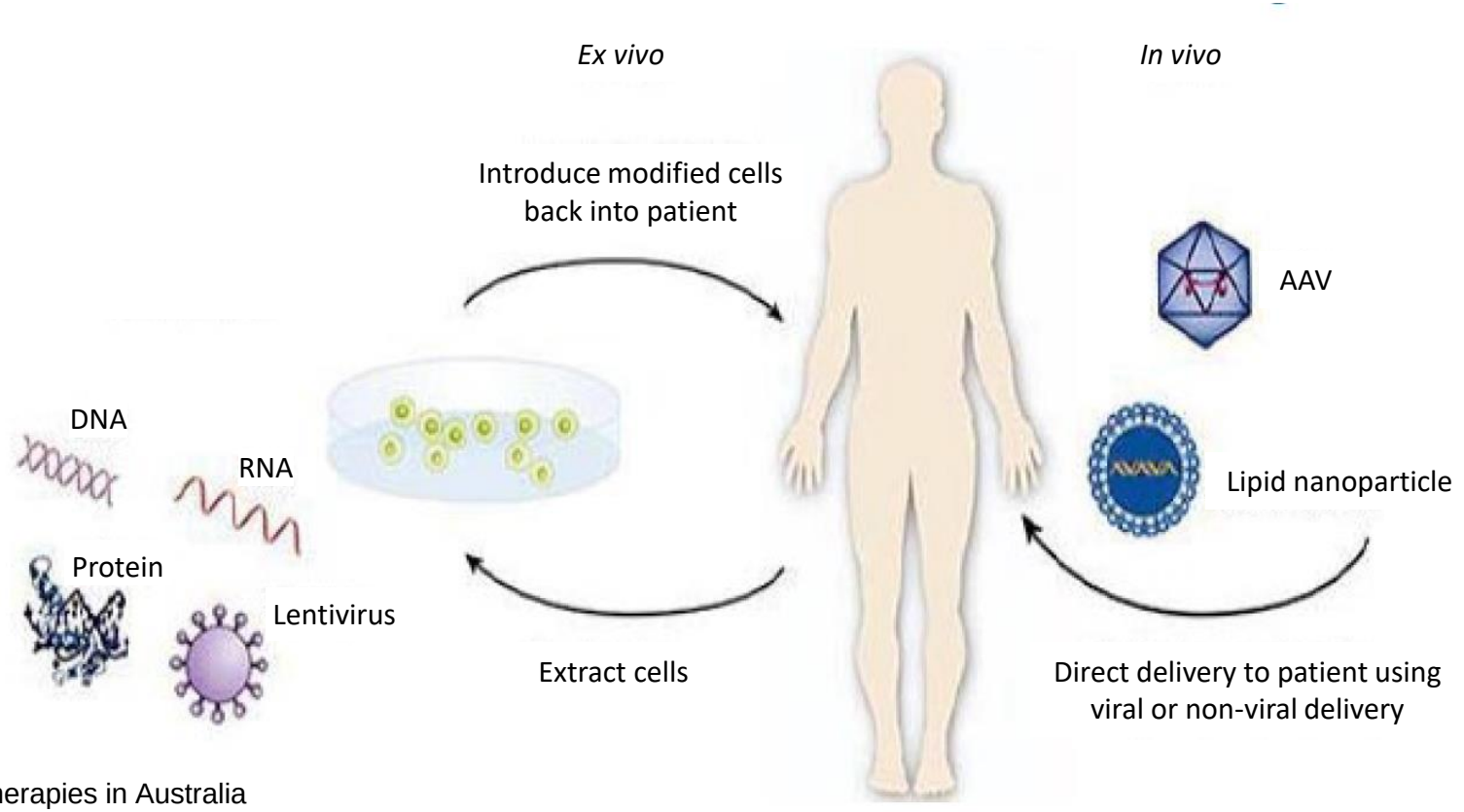
Role of the TGA

- Australian Commonwealth Government
- Department of Health
- The TGA regulates:
  - medicines
  - medical devices
  - vaccines, blood products
  - biologicals

Regulation of gene versus cell therapies

- Gene and cell therapies are regulated under different legislation in Australia
- Biological medicines versus biologicals

Biological



Biological medicine

Regulation of gene versus cell therapies

- Biological medicine
  - a medicine (other than an antibiotic) that is:
    - a vaccine, a peptide, a protein or polysaccharide-based; and
    - human, animal or other organism derived, or produced through recombinant technology/biotechnology;
    - certain human blood products
  - *e.g. vector based gene therapies, monoclonal antibodies*

- Regulated as a prescription medicine
  - Submission of dossier using ICH Common Technical Dossier Format module 3 (quality/CMC)
  - Application of Pharmacopoeia (Ph Eur) standards, ICH, EMA guidelines
    and Australian-specific legislation including Therapeutic Goods Orders (TGOs)

Regulation of gene versus cell therapies

- Biological
  - Something that comprises, contains or is derived from human cells or human tissues
  - *e.g. cellular therapies, CAR-T cells*

- Governed using the regulatory framework for biologicals 2011
  - Biologicals separated into classes based on risk from low risk class 1 to high risk class 4
  - Dossier submitted based on ICH CTD or TGA biologicals dossier
    - Application of ICH and EMA guidance
    - Use of Australian Therapeutic Goods Orders

Regulation of gene versus cell therapies

- TGA dossier
  - 1 INTRODUCTION
  - 2 SCOPE
  - 3 RISK MANAGEMENT
  - 4 QUALITY AND MANUFACTURING ASPECTS
  - 4.1 Biological starting materials
  - 4.2 Manufacturing process
  - 4.3 Characterisation
  - 4.4 Control of final product
  - 4.5 Storage and stability
  - 4.6 Product development
  - 4.7 Labelling and release documentation
  - 4.8 Transportation
  - 5 INTENDED USE – Class 2 only
  - 5 NON-CLINICAL DEVELOPMENT - Class 3 & 4 only
  - 6 CLINICAL DEVELOPMENT - Class 3 & 4 only

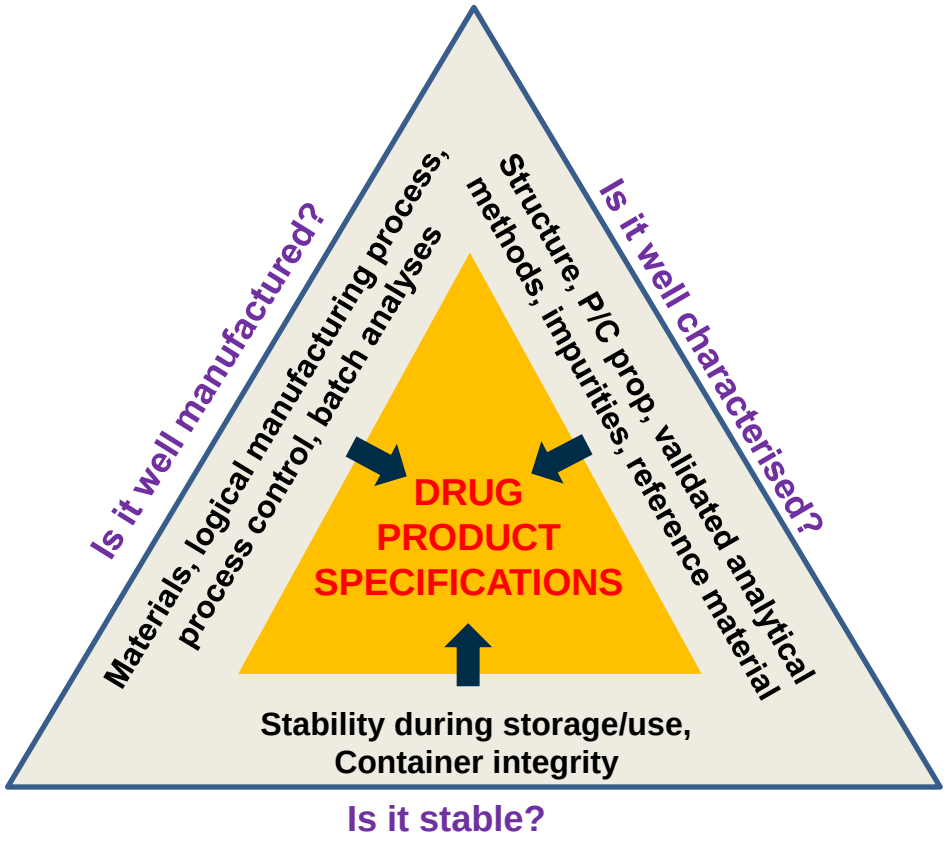
Pathways for submission

- Standard pathway for medicines and biological allows 255 days from acceptance of evaluation to decision

- For medicines where there is a high unmet clinical need other pathways are available
  - Provisional
    - Registered on basis of preliminary clinical data where benefit outweighs risk
    - Requires further submission of clinical data for full registration

  - Priority
    - Target timeframe of 150 days

Quality review of active ingredient



- For a typical biological medicine we would expect evidence of:
  - Consistent manufacture
  - Thorough characterisation
  - Stability studies performed

Regulation of gene versus cell therapies

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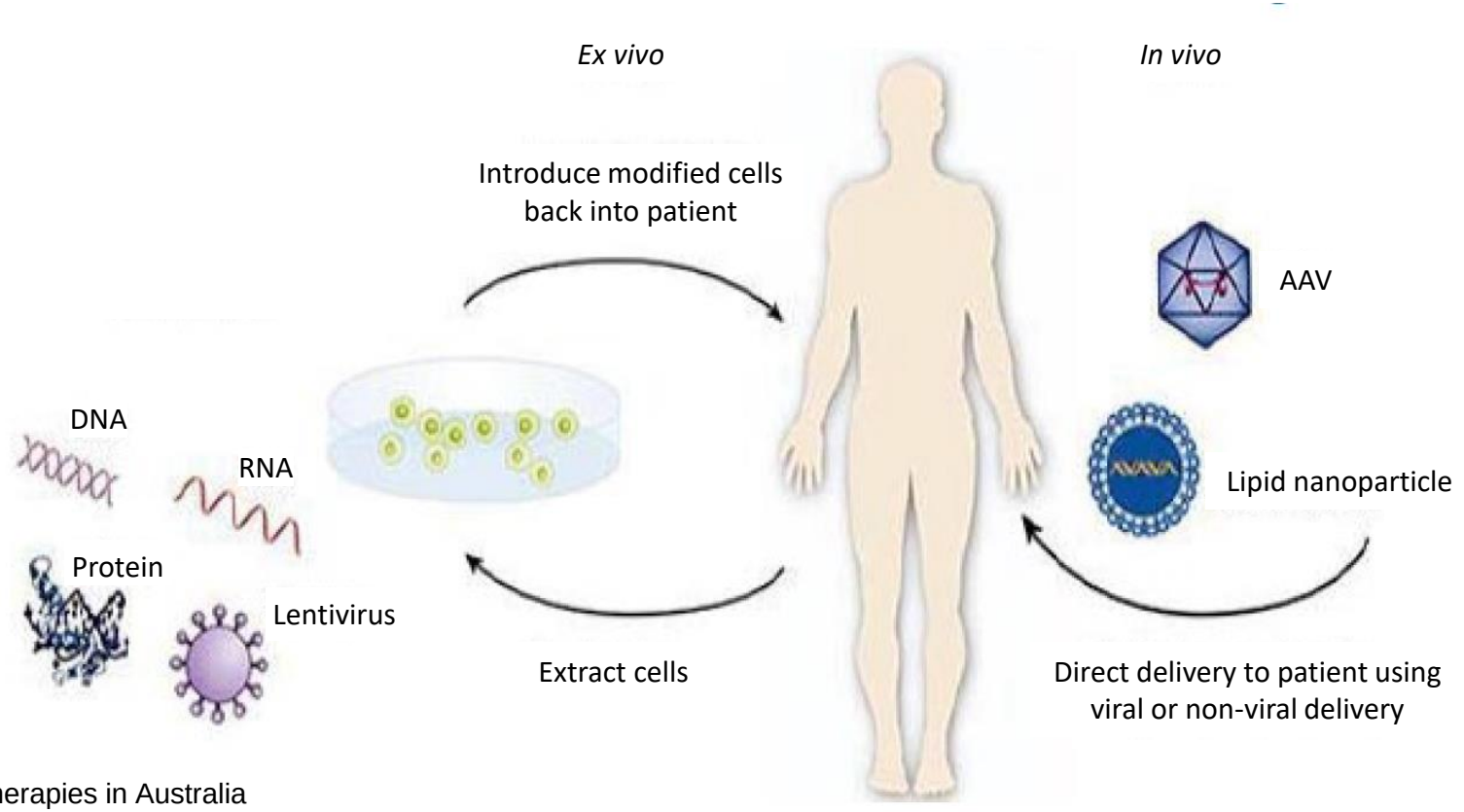
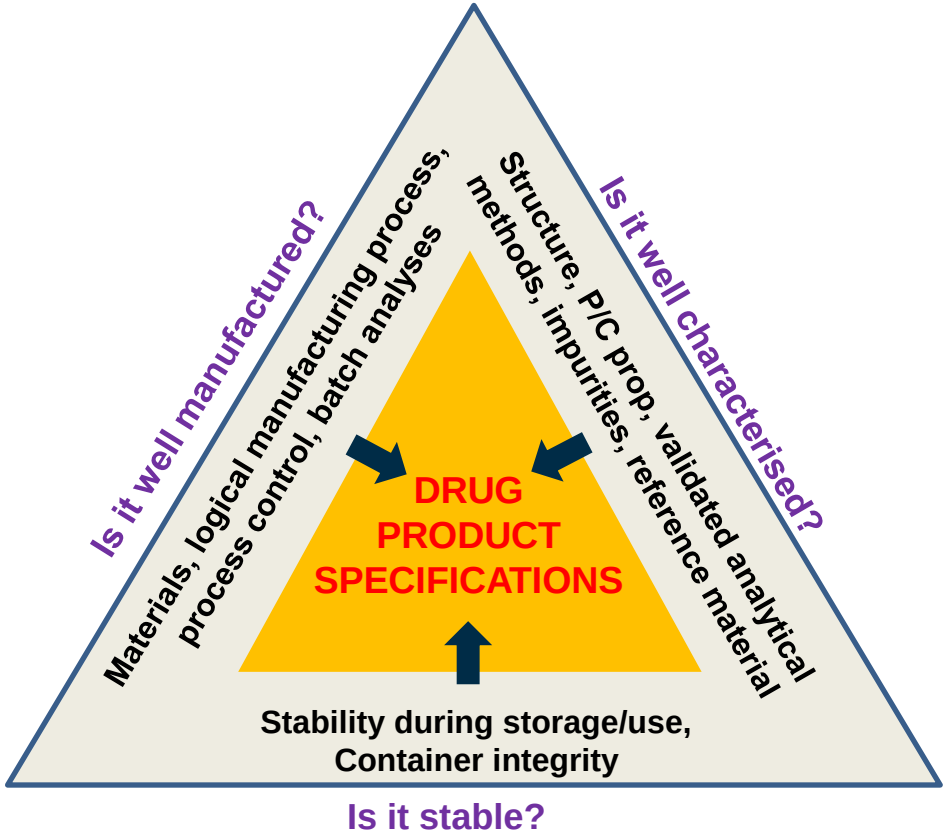
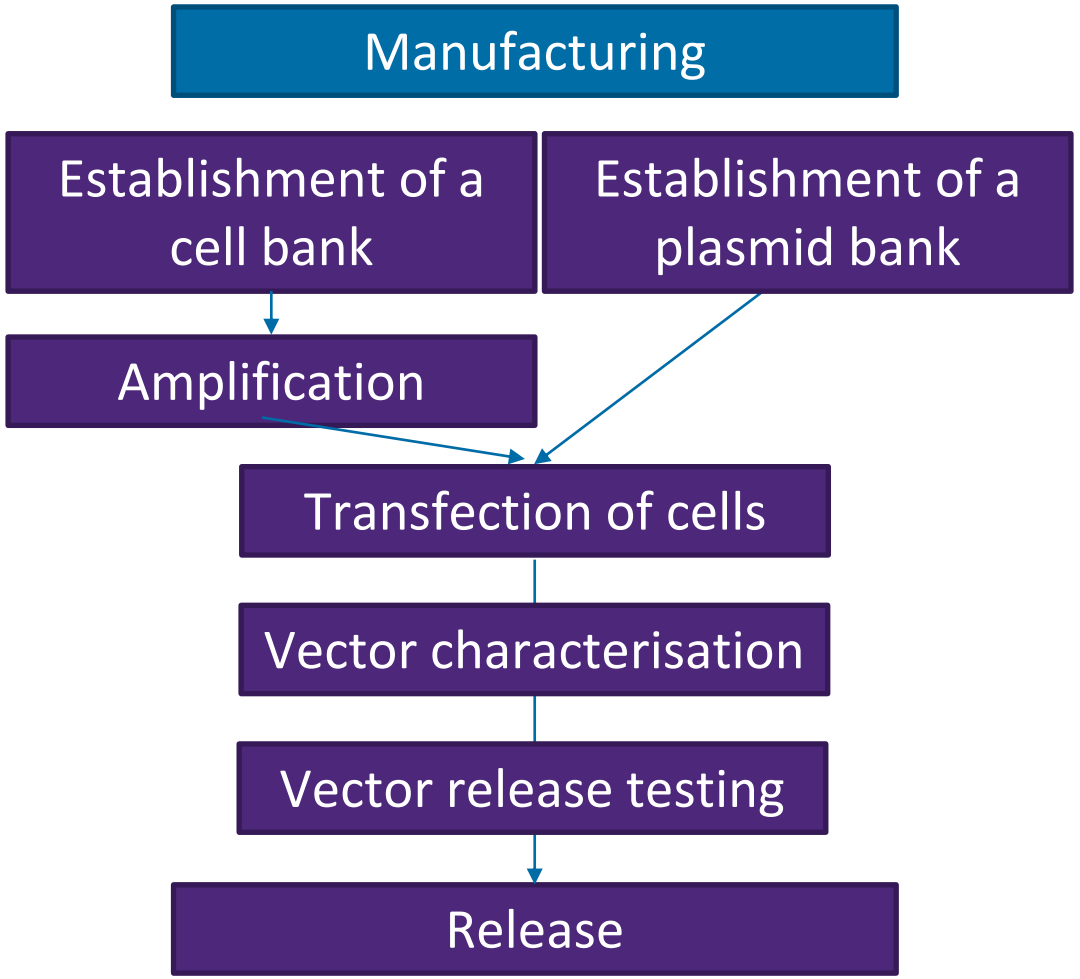
Biological



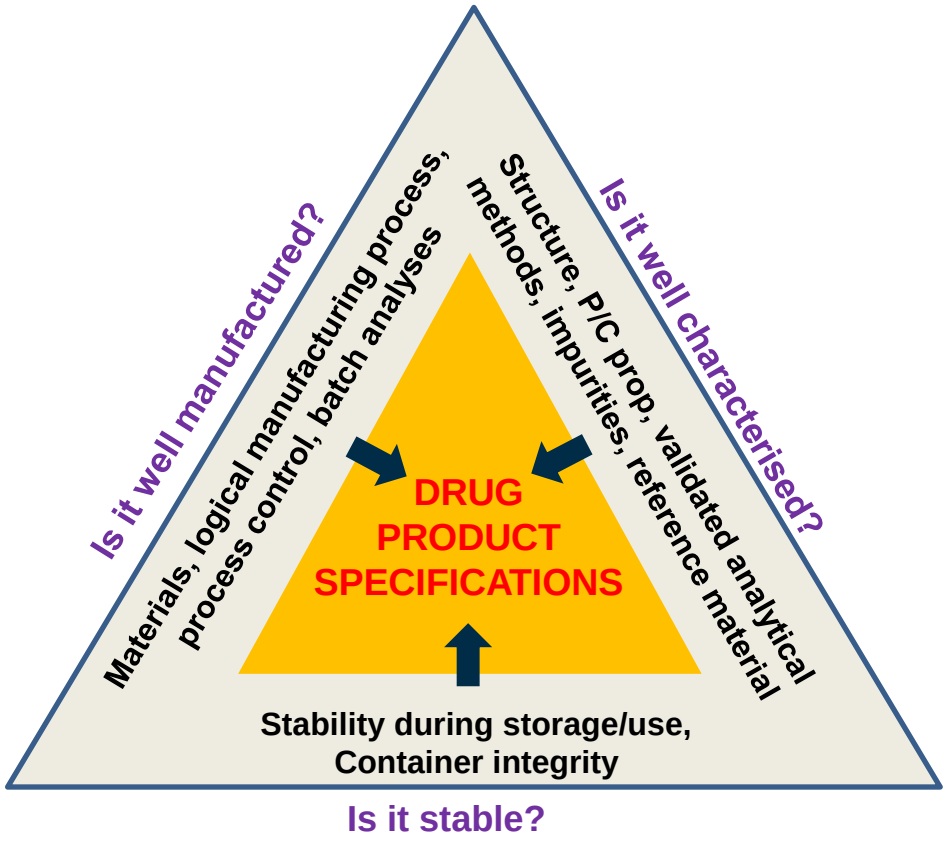
Biological medicine

Quality review of viral vector production



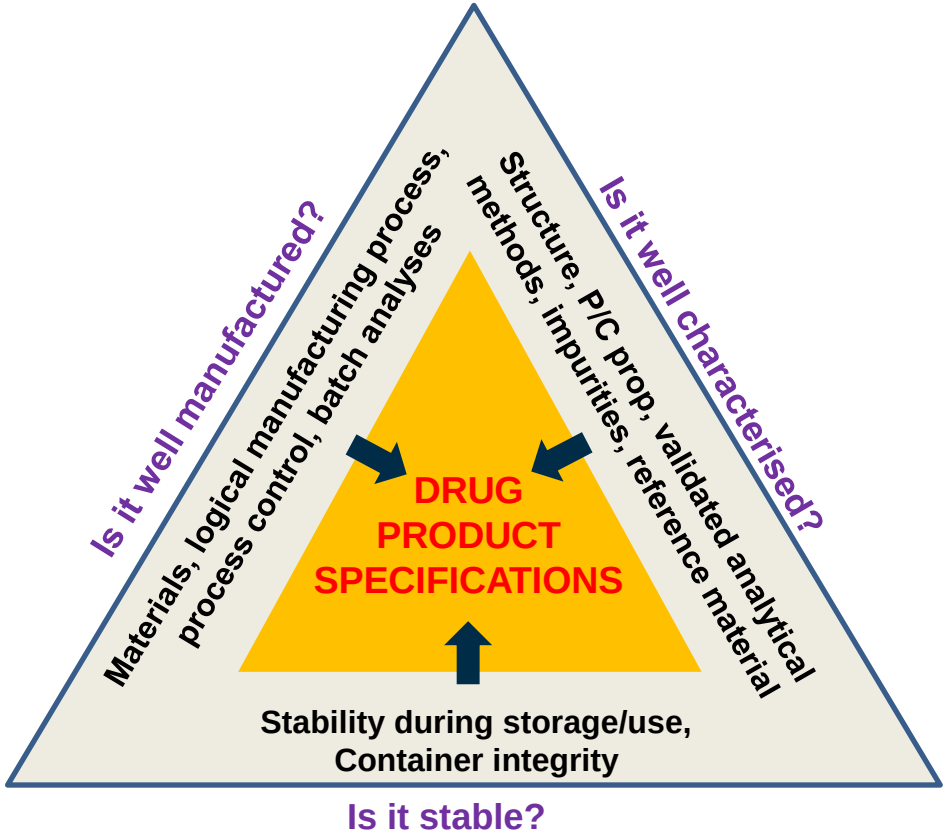


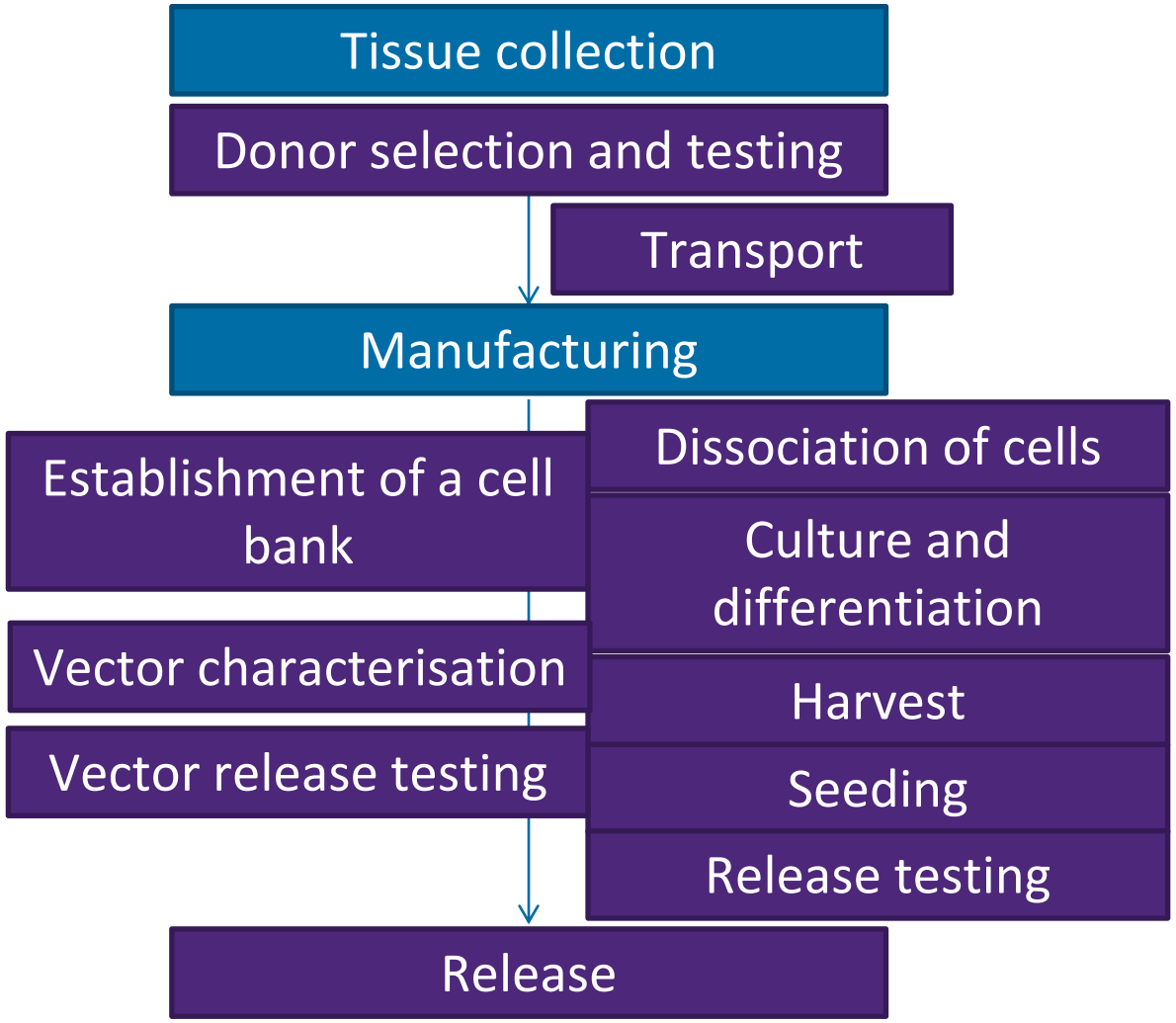
Quality review of viral vector production



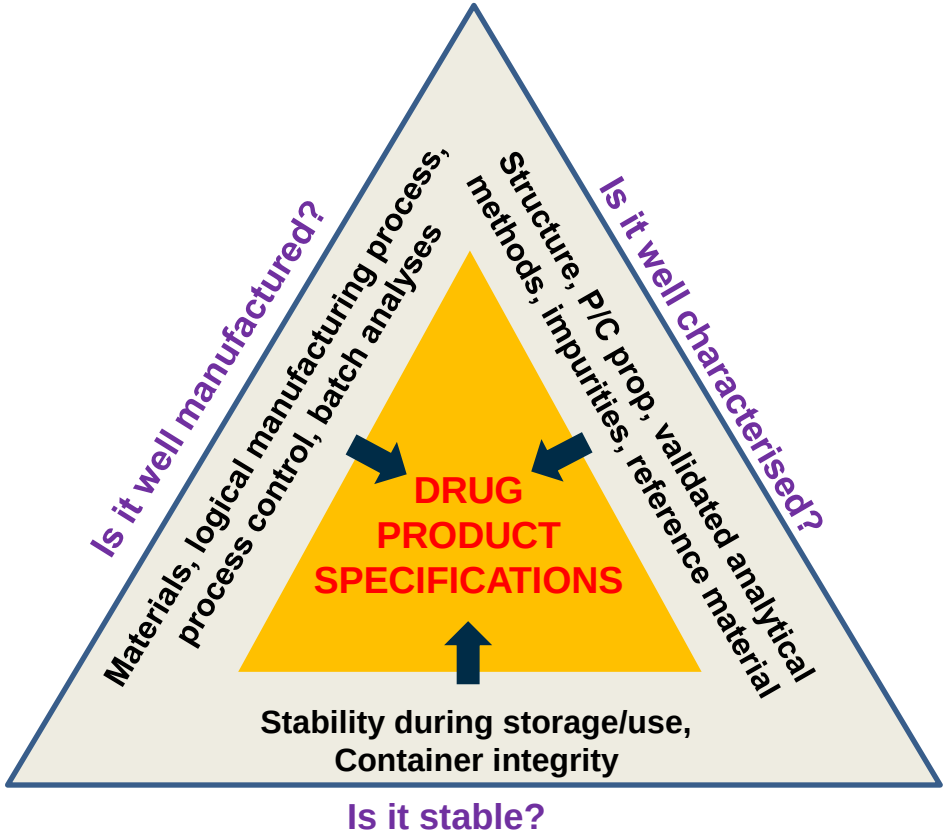
- For a viral gene therapy we would expect evidence of:
  - Most parameters met with therapies examined so far
- Issues with some analytical methods
  - e.g. Lack of a meaningful potency assay
  - Ultimately considered acceptable based on risk analysis and balance of other analytical data
- Interest in manufacturing process evolution
  - Looking for comparability between early and late batches
    - Especially in regard to those used for clinical trials

Quality review of cell therapy production





Quality review of cell therapy production



- Cell therapies have many more steps which are difficult to control
- CAR-T cells as an example
  - Starting materials inherently different
  - Batch analysis difficult
  - Lack of appropriate reference material
  - After transduction multiple active ingredients
  - Limited material to establish test methods
  - Appropriate potency assay

Reducing regulatory burden

- Autologous cellular therapies have a reduced risk of infectious disease transmission compared to others
- Current Australian legislation for donor selection mandates testing, medical history and deferral requirements
- We are proposing to exempt these requirements in certain autologous settings
  - Criteria which compromise quality, safety and efficacy must be considered
  - GMP required for appropriate manufacturing to prevent potential contamination

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