Innovations in Biologicals: from Concept to Care

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GMP FORUM 2024

Agenda

- What is Bench to Bedside
- The bench to bedside – Stages
- Introduction to Biologicals
- Priority Pathway
- GMP for IMPs
- Clinical Implementation
- Case Study
- Challenges and Solutions
- Future trends

Bench to Bedside

Defining ‘Bench to Bedside’

- Translating laboratory research into clinical treatments
- Importance in medical advancements

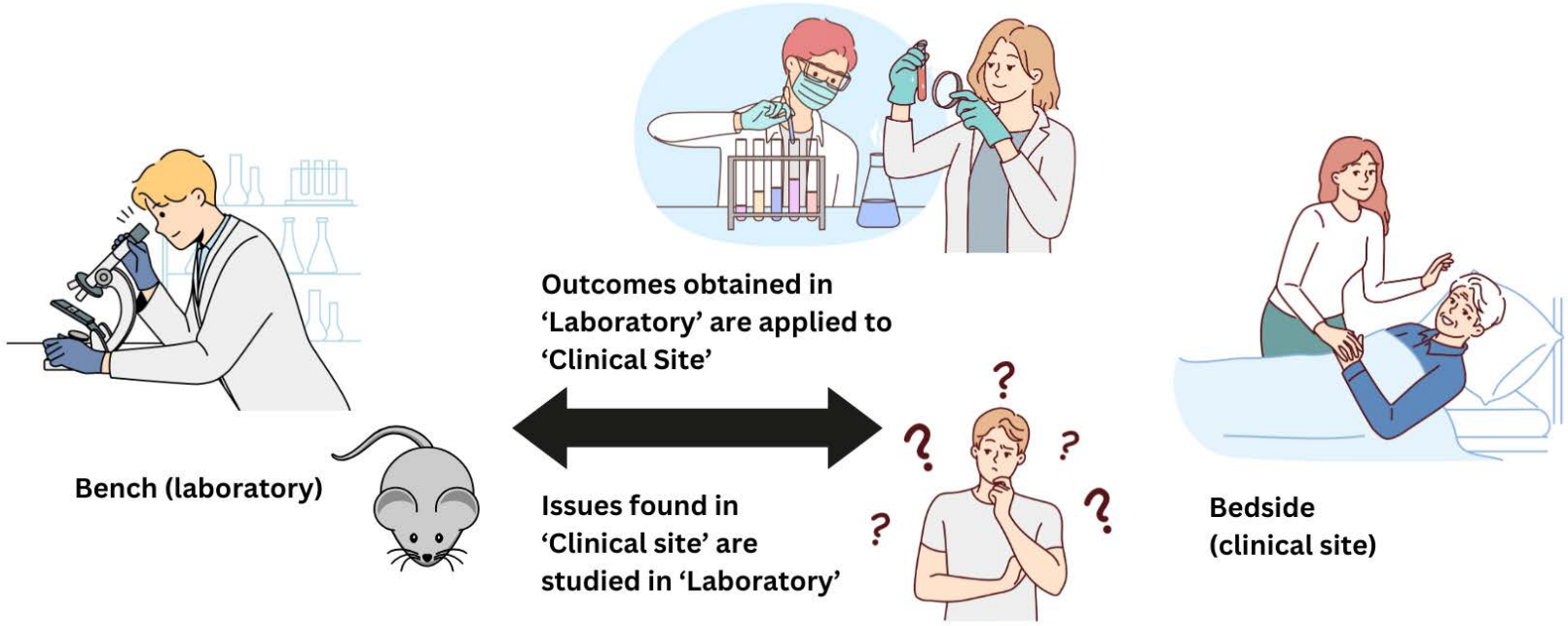
Why it’s important

- A lot of great science ideas come from basic research, but without the collaboration of the industry, clinicians and a lot of luck, it is difficult to reach patients.

The Bench to Bedside Process

Stages

- Basic Research
- Preclinical Research
- Clinical Trials
- Regulatory Approval
- Clinical Implementation



Basic Research

Resourcing

- **Description:**
  - Fundamental scientific discoveries
  - Understanding disease mechanisms
- **Examples:**
  - Genetic studies
  - Cellular and molecular biology

Practical Research

Resourcing

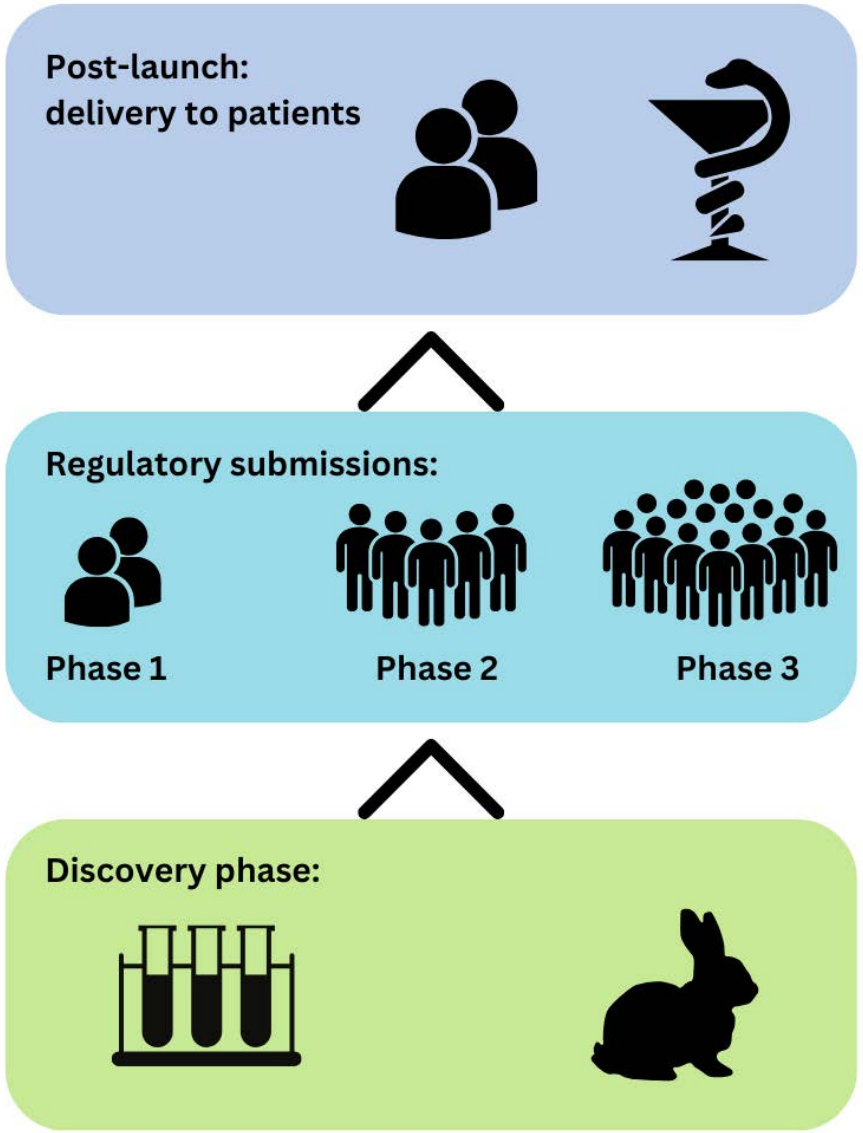
Description

- Testing in cell cultures and animal models
- Assessing safety and efficacy

Examples

- Biological assays
- Toxicology studies

Clinical Trials



Phases

Phase I: Safety and dosage
Phase II: Efficacy and side effects
Phase III: Confirmation and comparison
Phase IV: Post-marketing surveillance

Importance

Ensuring that treatments are safe and effective

Regulatory Framework

Key Legislation

- Therapeutic Goods Act 1989
- Therapeutic Goods Regulations 1990 (Schedule 16)

Key Guidelines

- Good Clinical Practice (GCP)

Clinical trials regulated by the TGA

Clinical trials with biologicals in Australia offer access to new (but unproven) therapies.

Each trial has a research purpose, and patients need to provide informed consent.

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Notification under CTN Scheme or application under CTA Scheme required where investigational use of a product involves:

Any product not entered on the ARTG including:

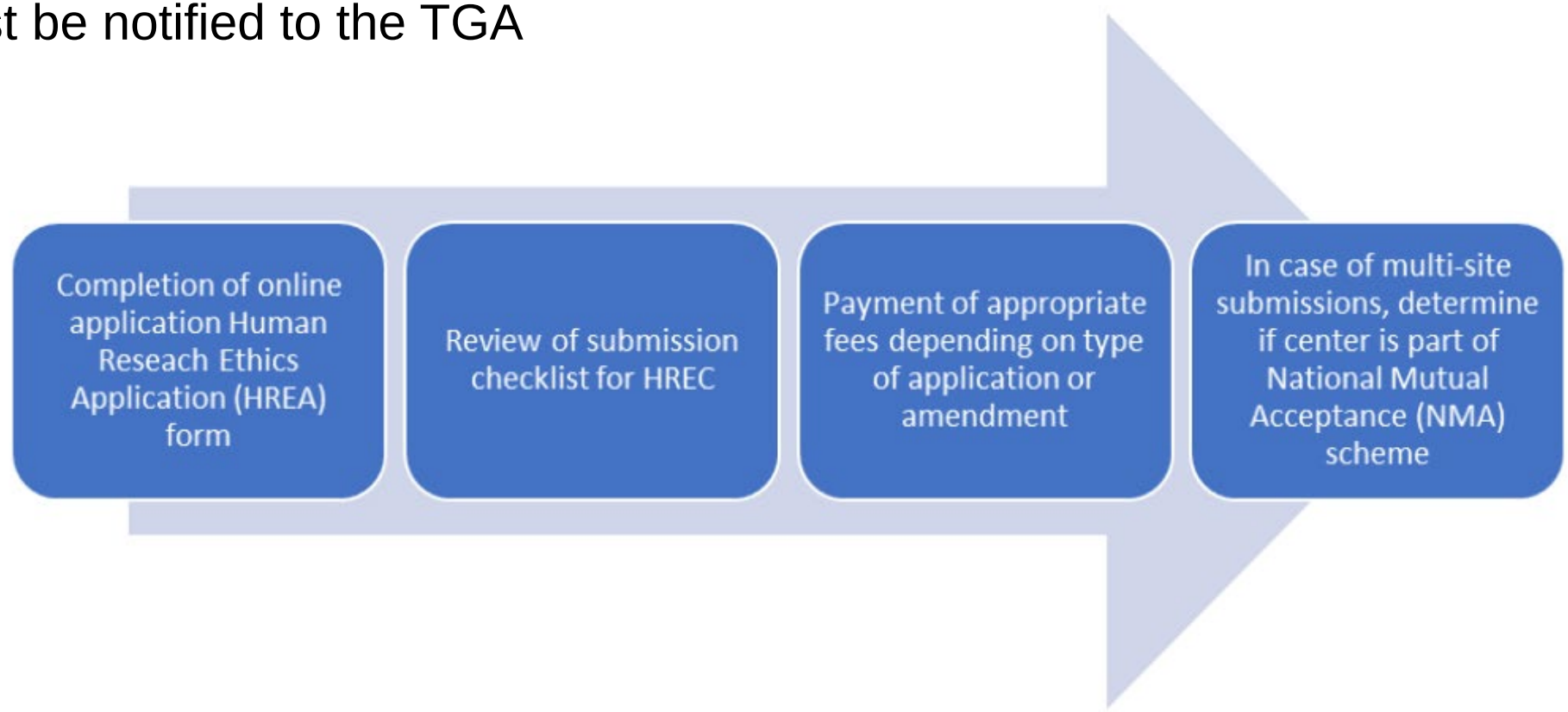
- any new formulation of an existing product
- any new route of administration,
- In the case of an existing biologicals, new technology, new material or a new treatment modality

Use of product beyond the condition of its marketing approval, including:

- New indications extending the use of a medicine to a new population group
- Extension of doses or duration of treatments outside the approved range.

Ethics Approval

- Institutional Ethics Review Board (IERB)
- Required before TGA approval
- All trials must be notified to the TGA



Submission and Review

- TGA Evaluation
  - Trial design, methodology, and safety data
- Investigator qualifications

Your Clinical Trial

Goal

- Propose a new technology to solve a health problem
- Present a mock design of the new technology and plans for a clinical trial to evaluate the technology

Must identify:

- A disease of global health significance
- Current medical technologies to treat the disease
- Limitations of those technologies in a resource challenged setting
- Design constraints of technologies in a resource challenged setting
- A new medical technology to treat the disease
- An appropriate clinical trial design
  - Subjects to be tested
  - Primary and Secondary outcomes
  - Sample size

Must submit

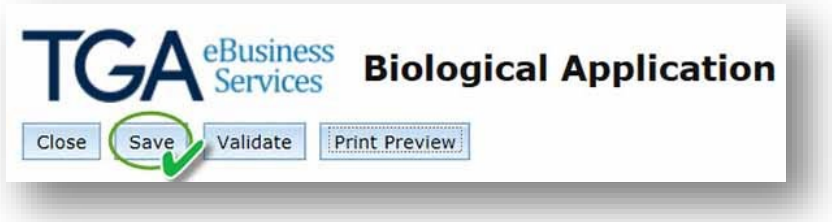
- An illustrative prototype
- A clinical trial research protocol
- An informed consent document
- A presentation of your findings and proposed solution

Reporting

- Adverse Events Reporting
- Immediate reporting of serious adverse events (SAEs)

Post-trial obligations

- Post-trial Reporting
  - Submission of results and data to the TGA



Introduction to Biologicals

What are biologicals?

In Australia, ‘biologicals’ is the name for cell and tissue therapy products:

- Products in tissue banks
- Stem cell therapy product
- Excludes in vitro fertilisation products
- Excludes blood
- Other countries use different names for these products [advanced therapy medicinal products] (ATMP)

Overview of ATMP

ATMPs are medical products for human use and include:

- Gene Therapy medicinal product
- Somatic cell therapy products
- Tissue engineering products

Where a products contains human cells or tissues, the donation, procurement and testing of those tissues or cells required to comply with Therapeutic Goods Orders (TGOs) 108 and 109

Regulatory approval

Process

- Submission of clinical trial data
- Review and approval

EMA (Europe)

Australian Government
Department of Health and Aged Care
Therapeutic Goods Administration

TGA (Australia)

FDA (USA)

Priority Review Pathway – key factors that influence the process

- Significant improvements in treatments
- Unmet medical need
- Innovative Technology
- Fast track designation
- Clinical evidence
- Public health impact
- Regulatory history

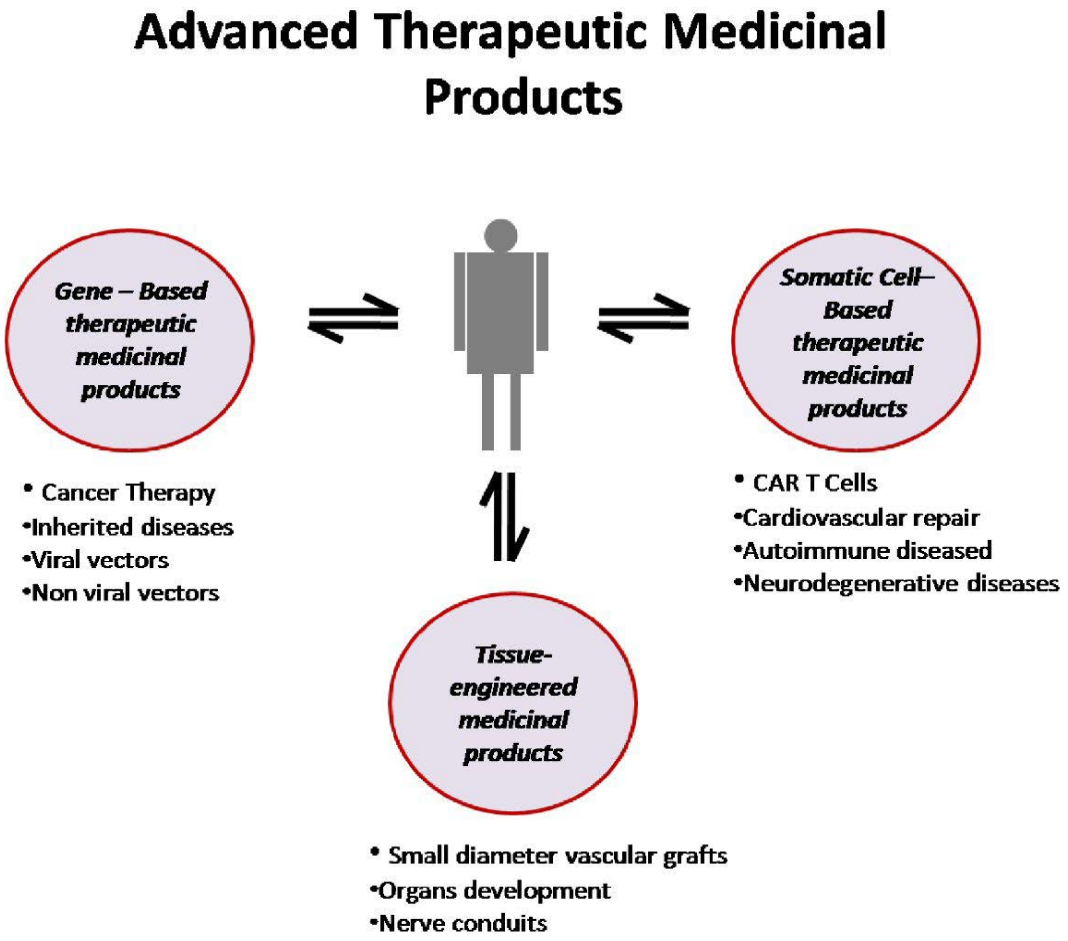
Better Evidence Better Health

Manufacture in accordance with appropriate GMP

- All biologicals accessed through unapproved goods pathways, GMP applies
- unless there is an exemption in place - unapproved biologicals used in first-in-human clinical trials.

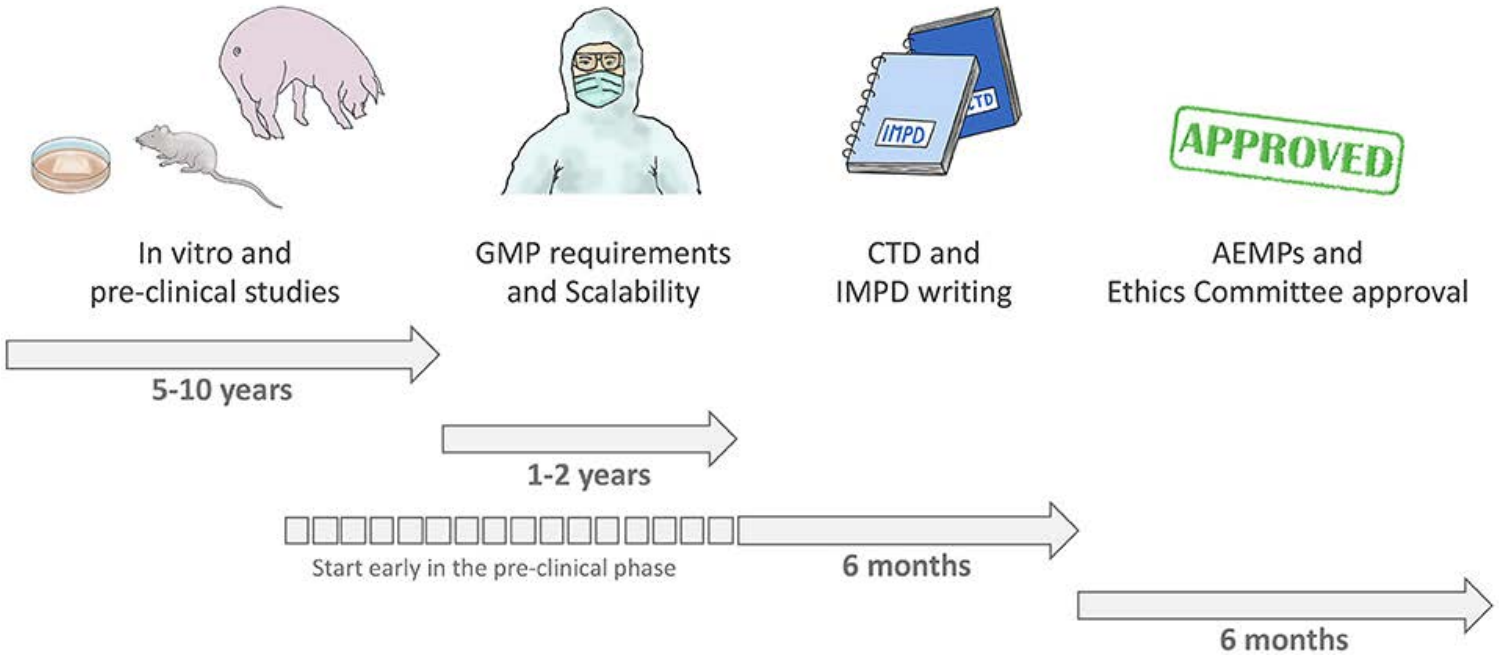
Definition:

- First-in-human: Innovative treatment or therapy, the trial testing a new drug, therapy or medical procedure that has never been used in humans before



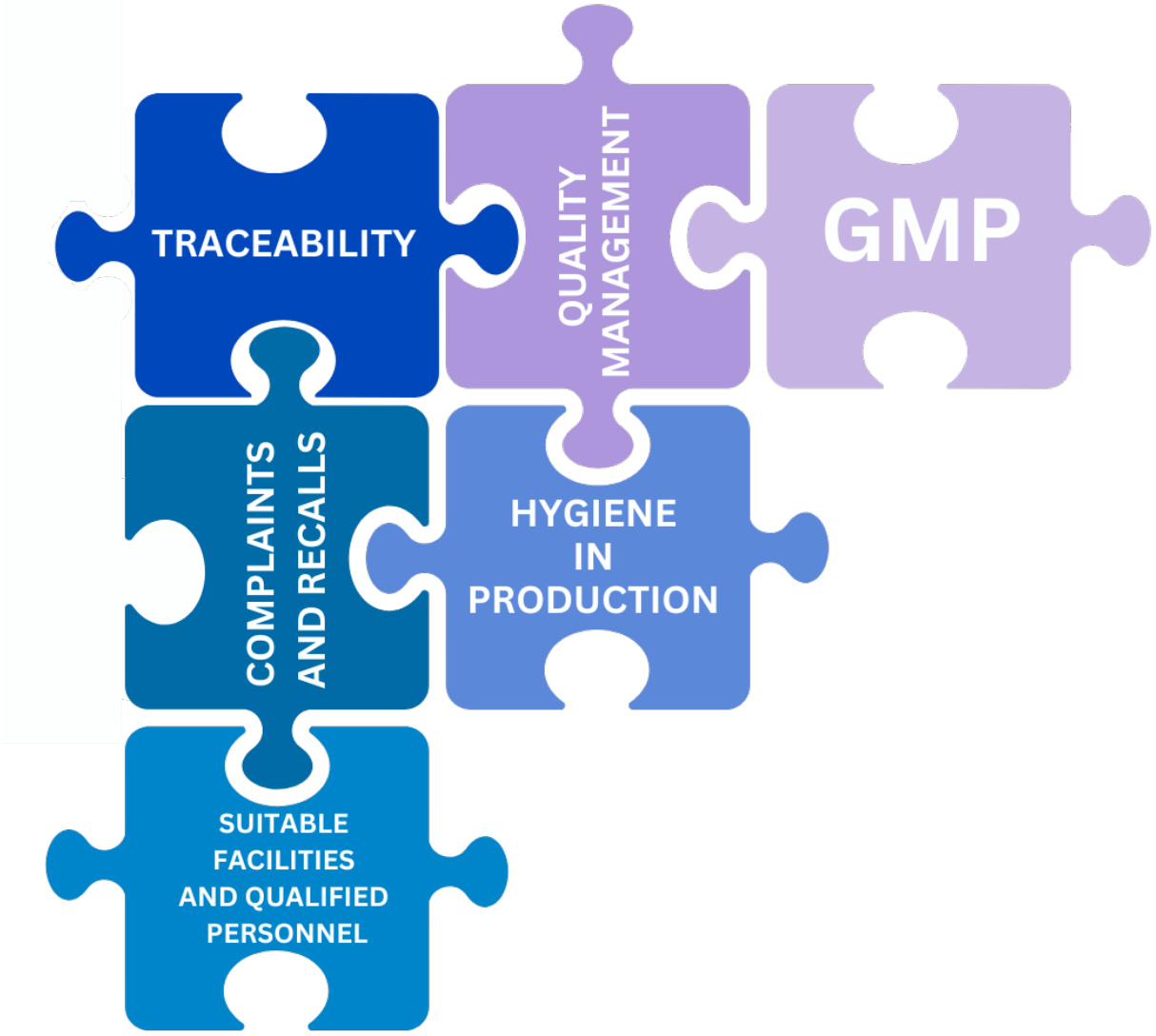
GMP for IMPs: why?

- Protect study participants against risk that may arise from inadequate manufacturing, manipulation, storage and transport
- Make sure that results of clinical trials are not to be influenced by inadequate safety, insufficient quality or changed efficacy because of poor production



Different chapters of GMP

- Quality Management
- Personnel
- Premises and equipment
- Documentation
- Production
- Quality control
- Contract manufacture and analysis
- Complaints and recalls
- Self-inspections



Quality Management Systems

- Structured and organised approach
- Organisation quality policy
- QA appropriate for the manufacture of products
- Deviations
- Change management
- Risk management
- Self-inspections
- Management review
- Regular periodic review

Infrastructure Overview

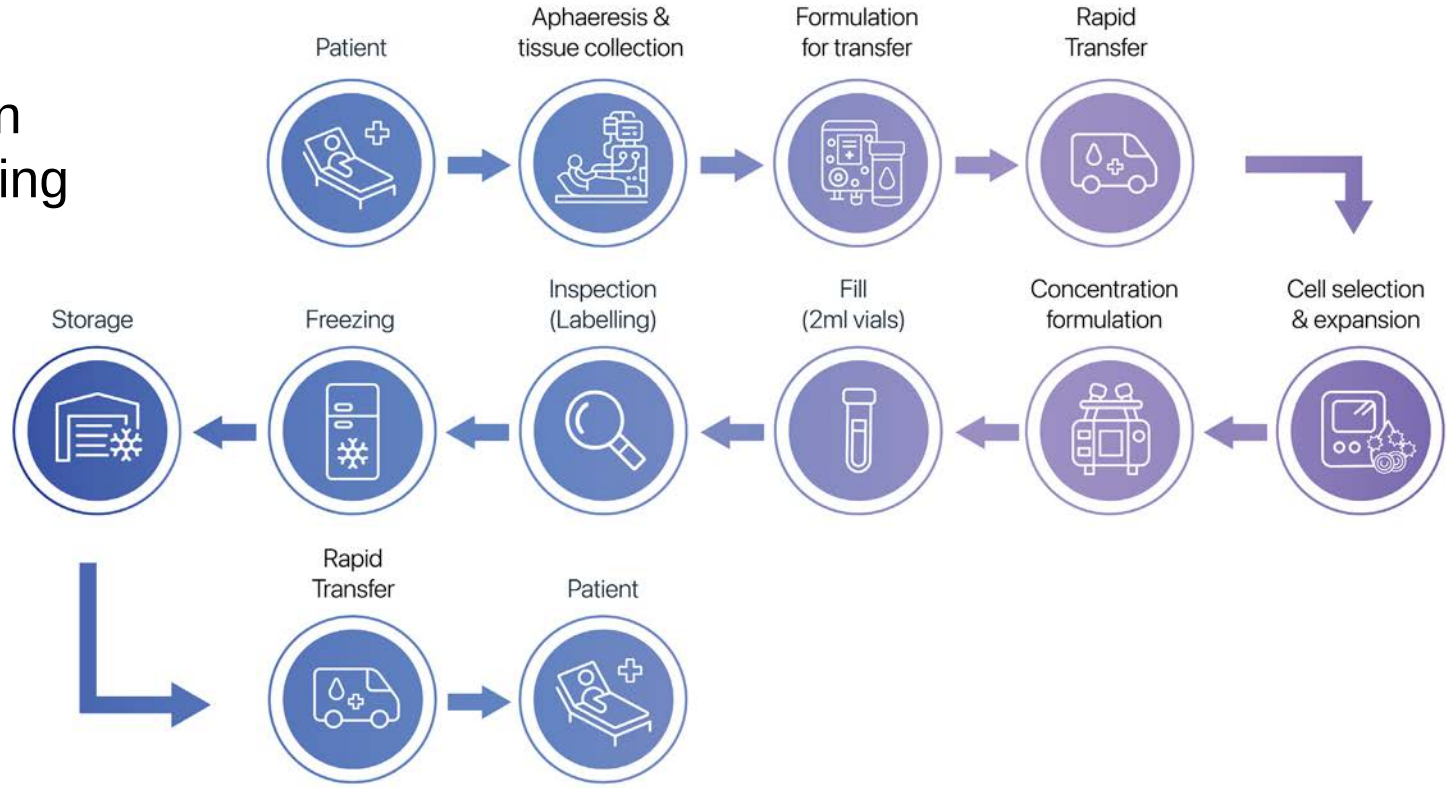
Facility Requirements:

Cleanrooms: standards (ISO 14644, Annex 1 PIC/s GMP and WHO)

- Controlled environments for cell culture and manipulation.
- Quality control laboratories

Technology

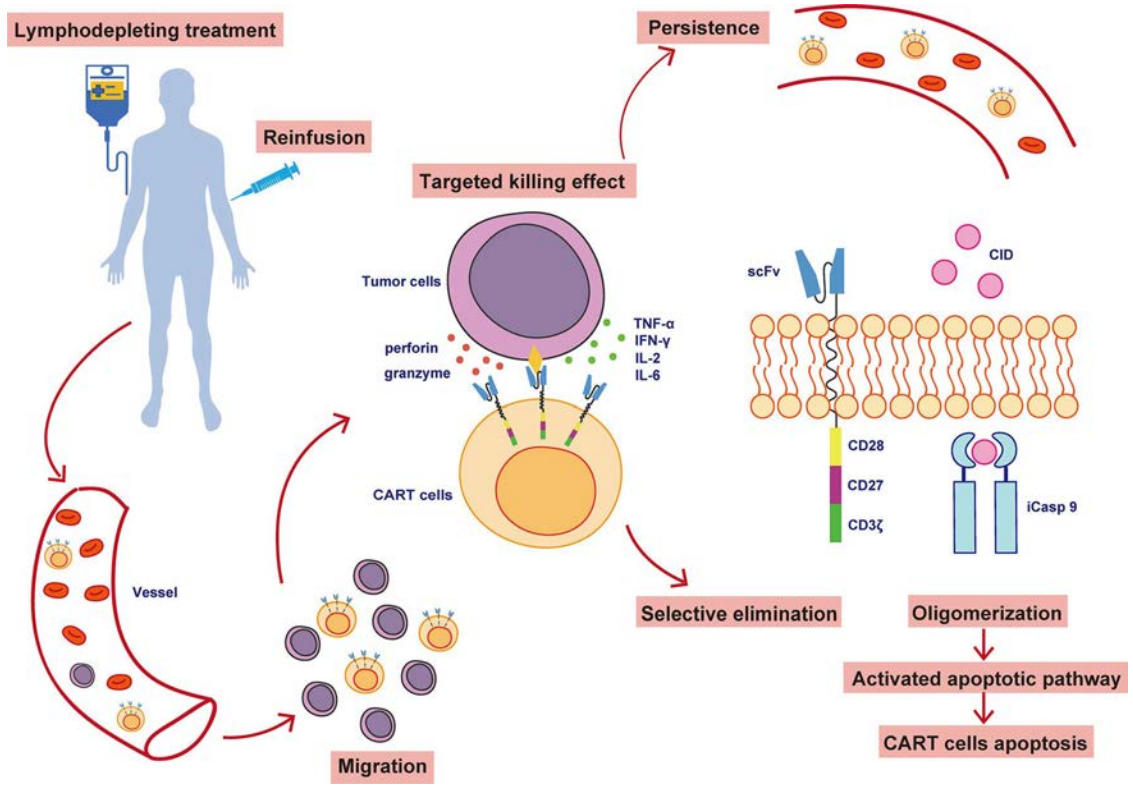
- Bioreactors for cell expansion
- Automation tools for processing
- Data management systems for compliance and traceability.



Manufacturing process

Stages of production

- Cell Sourcing: Collection of cells (donor derived (autologous or allogeneic)
- Cell Expansion: Methods (for example: adherent vs. suspension cultures).
- Product formulation: Processes to ensure therapeutic efficacy.
- Quality control: testing for sterility or product microbial contamination testing, potency and viability.
- Regulatory compliance: Adhering to GMP and relevant regulations



Personnel Requirements

Competent personnel

- Scientists and researcher for R&D
- Quality assurance and quality control specialists
- Manufacturing technicians

Training

- Continuous education on new technologies and regulatory requirements

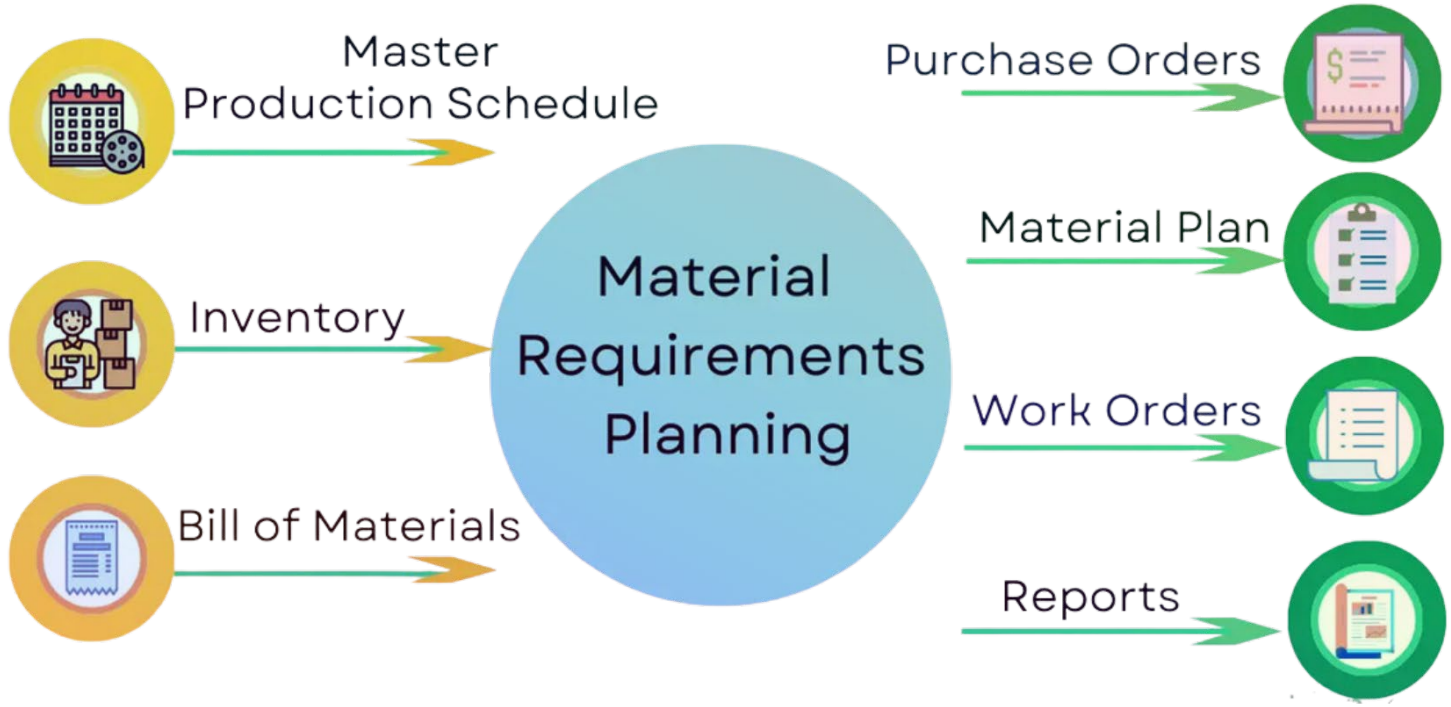
Material Requirements

Raw Materials

- Cell lines, growth factors, culture media
- Ancillary materials: single use or multi-use materials, reagents, disposables and consumables

Quality Assurance

- Sourcing from reputable and qualified suppliers
- Ensuring compliance with regulatory standards



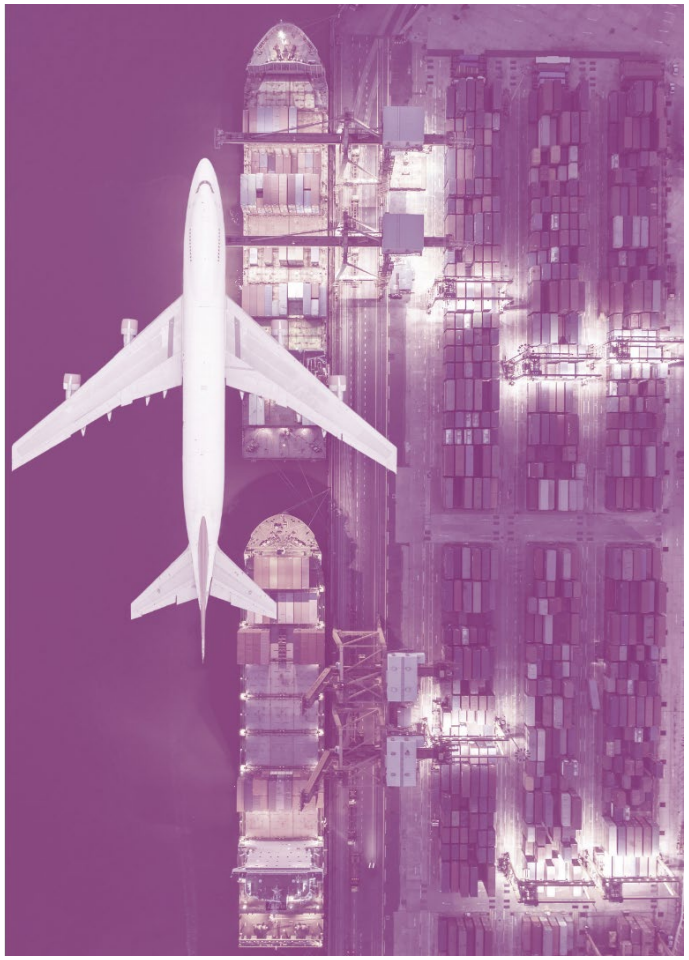
Logistics Management

Supply Chain Management

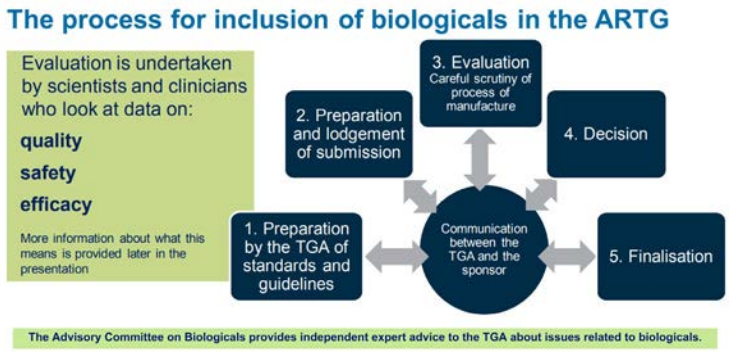
- Procurement of raw materials and components
- Starting materials
- Inventory management to avoid shortages or excess.

Release for Supply and Distribution

- Cold chain logistics for temperature-sensitive products.
- Regulatory considerations for transportation of Biologicals



Submission and Review

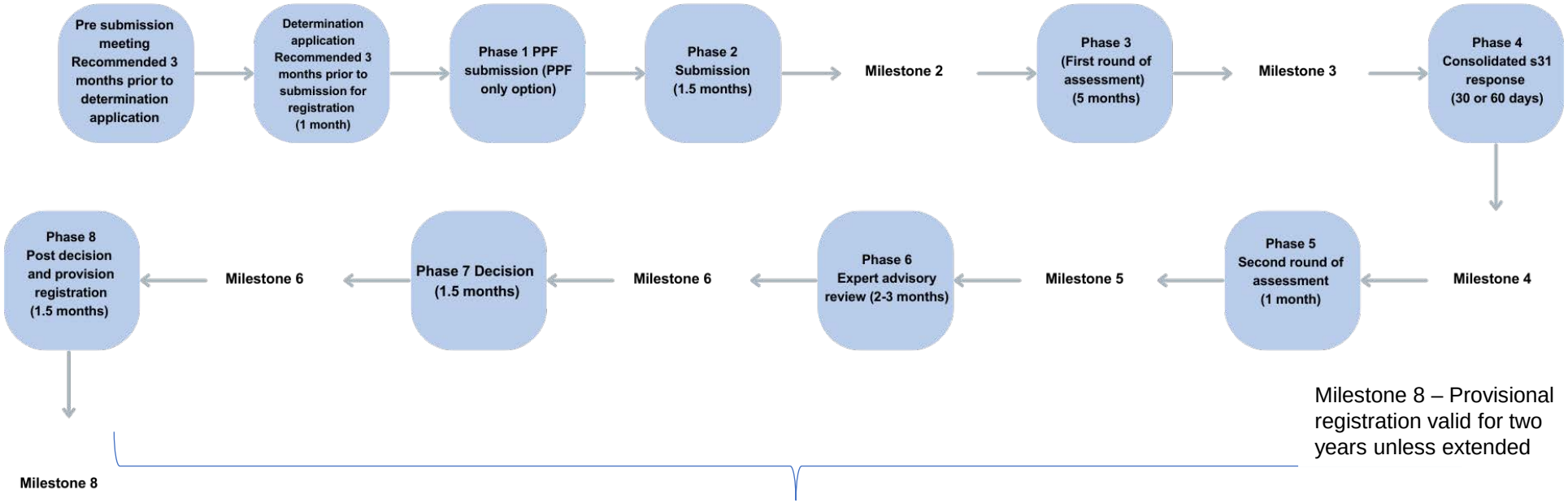


From phase 3 to Phase 7 – **Rolling submissions of clinical data accepted** with stop clock if not submitted by the agreed date (approximately 220 working days)

From phase 5 to phase 7 – Timeframes for final evaluation report, sponsor response and the delegate's overview are as per standard process

Part of the determination process

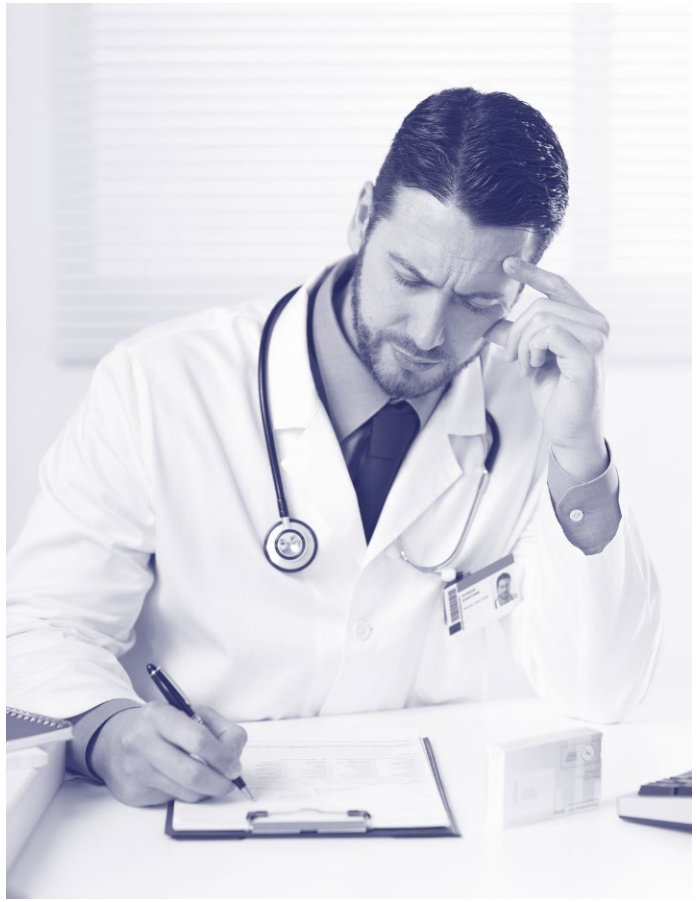
No more than 6 months (unless determination extension granted)



Milestone 8 – Provisional registration valid for two years unless extended

Clinical implementation

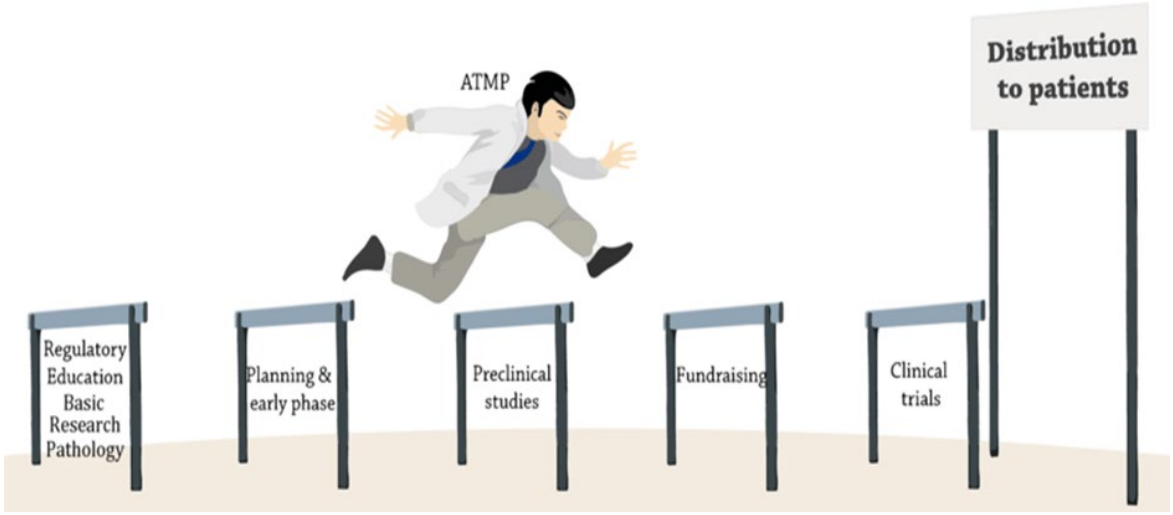
	Steps	Integrating new treatments into clinical practice Training healthcare professionals
	Challenges	Cost Accessibility

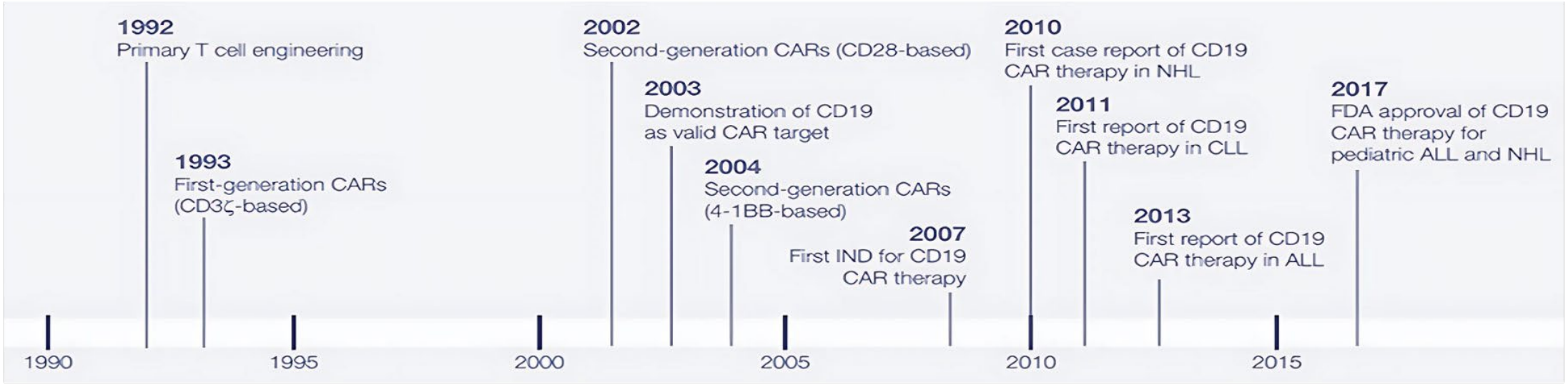


Case Study

Example

- A specific biological (ATMP) that successfully went from bench to bedside
- Key milestones and outcomes

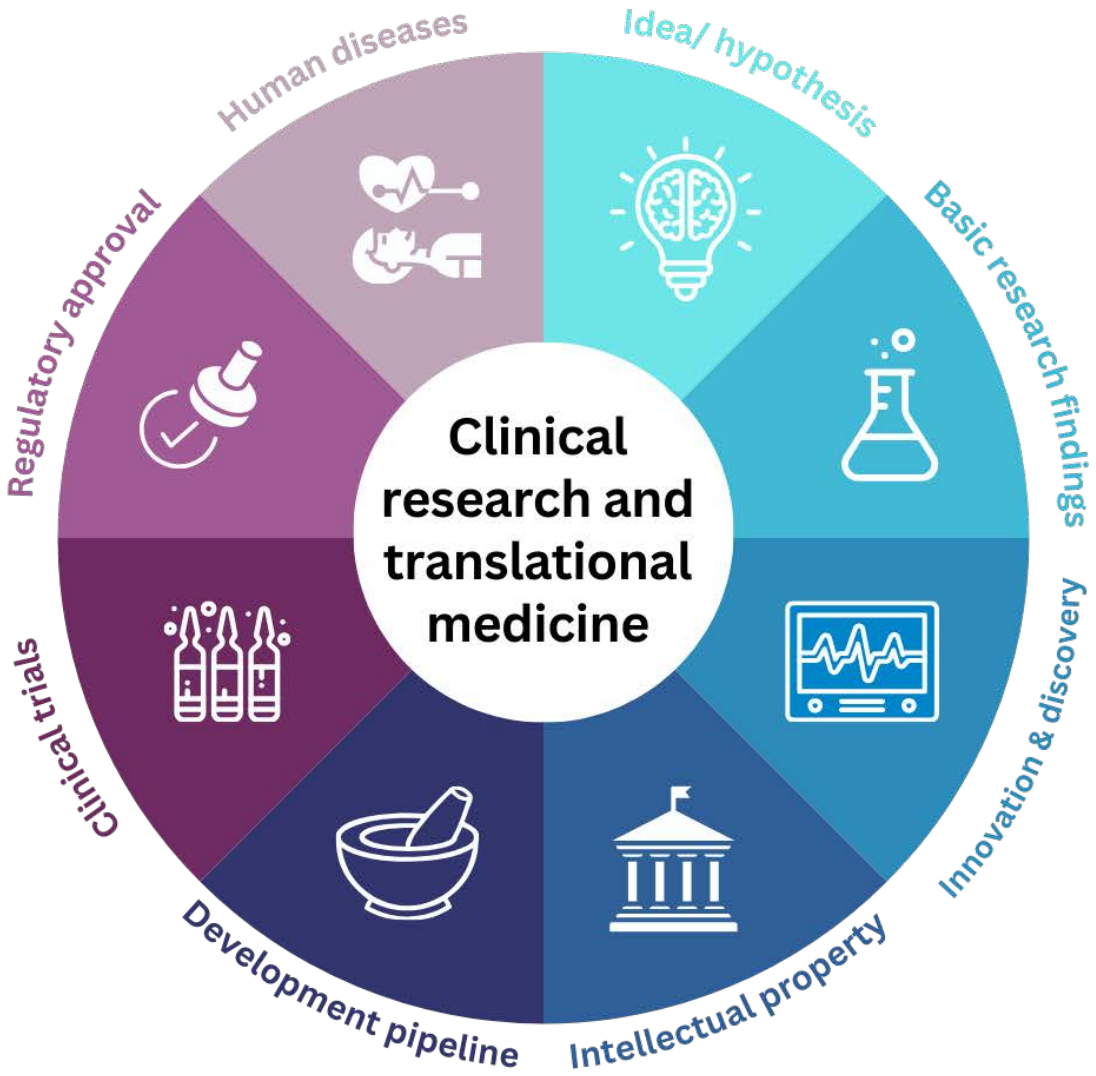




Source: Scienceofsingularity.com

Challenges and Solutions

	Challenges	Funding Time Regulatory hurdles
	Solutions	Collaborative research Public-private partnership



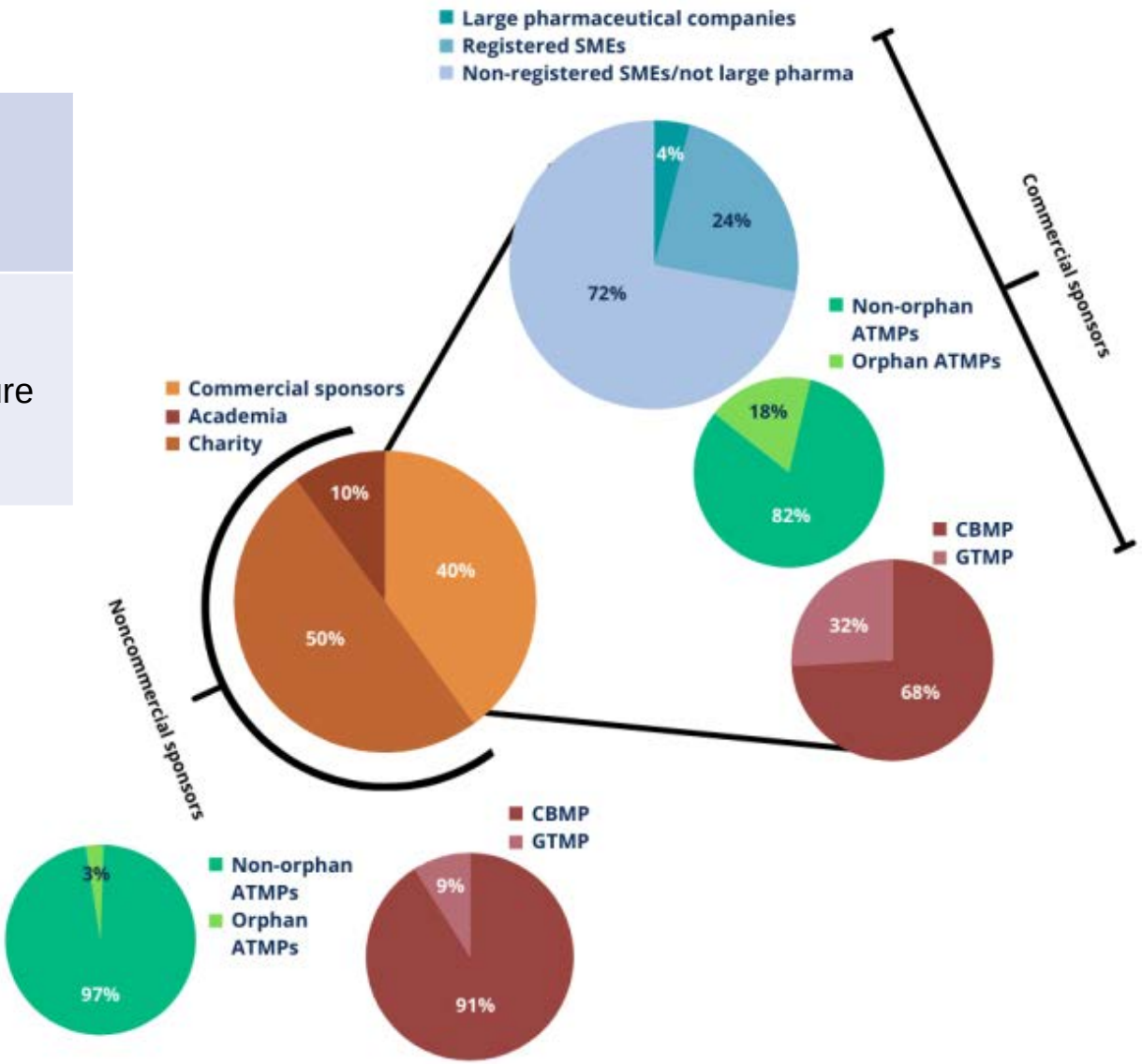
Source: Monash.edu.au

Future trends in biological manufacturing

	Innovation	Advances in bioprocessing technologies
	Personalised medicine	Tailoring therapies to individual patient needs
	Sustainability	Eco-friendly practices in manufacturing processes

Conclusion

	In summary	Concept to commercialization
	Solutions	Collaborative research Investment in technologies for future advancements.



Questions?

Scan this QR code with your device to submit a question

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Department of Health and Aged Care

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