11th Joint Conference of Taiwan and Japan

Regulatory Updates for Regenerative Medicine in Taiwan

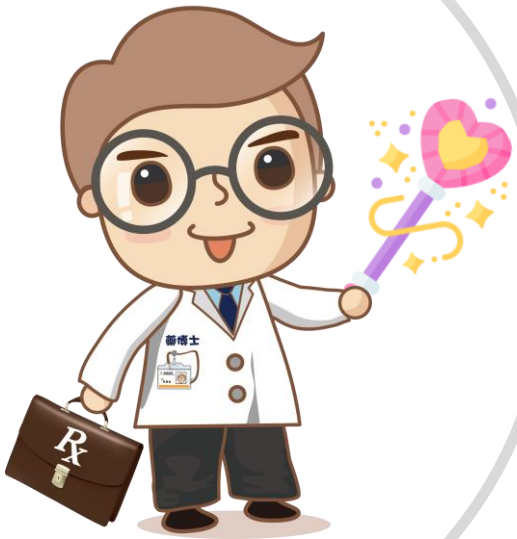
Mei-Chen, Huang
Senior Technical Specialist
Division of Medicinal Products
Taiwan Food and Drug Administration (TFDA)
Ministry of Health and Welfare (MOHW)

October 5, 2023

衛生福利部
食品藥物管理署
Taiwan Food and Drug Administration

http://www.fda.gov.tw/

Outline



1. Current Regulatory Framework in Taiwan
2. Approved Regenerative Medicine
3. Challenges and Future Expectations

Current Regulatory Framework in Taiwan

Dual-track pathway Since 2018

Regulation Governing the Application of Specific Medical Examination Technique and Medical Device (RASMET)

Regenerative Medicine (RM)

Pharmaceutical Affairs Act (PAA)

Medical Practice (Therapy)

Treatment protocol Approval

Medicinal Products (Biologics)

Marketing Authorization

衛生福利部 食品藥物管理署 Taiwan Food and Drug Administration

Regenerative Medical Practice vs Medicinal Products

Department of Medical Affairs, MOHW

RM

Taiwan Food and Drug Administration

	Regenerative Medical Practice	Regenerative Medicinal Products
Character	Personalized	Commercialized
Applicant	Medical institute	Pharmaceutical company
Requirement	Treatment protocol	IND、NDA dossier
Standard	**GTP**	**GMP、GDP、GCP compliance**
Approval	Performed by registered physician in recognized medical institute	Marketing Authorization

Regulation for Regenerative Medical Practice

Regulation Governing the Application of Specific Medical Examination Technique and Medical Device (RASMET)

- **Treatment protocol**
  - ✓ Cell type & indication
  - ✓ Patient selection
  - ✓ Treatment plan
  - ✓ Cell product (preparation, QC, CMC…)
  - ✓ Transportation & storage
  - ✓ Contraindication
  - ✓ Combination therapy
  - ✓ Follow-up
- **Qualified physicians**
- **Certified CPU (GTP)**
- **Patient information and consent form**
- **Quality control data of cell processing, storing and delivering**

Reviewed by Department of Medical Affairs

Approval

- ✓ **Up to 3 years** approval
- ✓ Must provide **annual report**
  - Number of treated cases
  - Treatment outcome
  - Adverse events or incidence
  - Other information required
- ✓ Treatment plan with poor performance would be **terminated or not allowed extension approval period**

Information Disclosure

- ✓ Name of medical institute, qualified physicians and CPU
- ✓ Cell type & indication
- ✓ Treatment fee and method of charge
- ✓ Valid period

Regulations Regarding Regenerative Medicinal Products

Law

Pharmaceutical Affairs Act

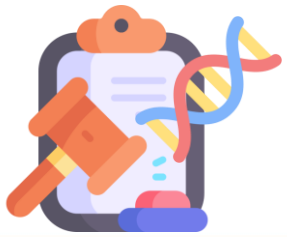
Manufacture, import, clinical trials and marketing authorization

Regulation

- Regulation on Medical Products Registration
- Regulation on Good Clinical Practice (GCP)
- Regulation on Good Manufacture Practice (GMP)

Guidance

- Guidance on NDA for Gene Medicinal Products
- Guidance on NDA for Cell Medicinal Products
- Guidance on IND for Gene Medicinal Products
- Guidance on IND for Cell Medicinal Products
- Guidance on Informed Consent
- Guidance on Trace and Tracking
- Guidance on Donor Recruitment
- Guidance on Donor Eligibility Determination
- Guidance on Bridging Medical Practice to Medicinal Products



福 利 部
物 管 理 署
nd Drug Administration

Review Timeline for IND (Clinical Trials)

Review Track for Cell/Gene Therapy Products IND

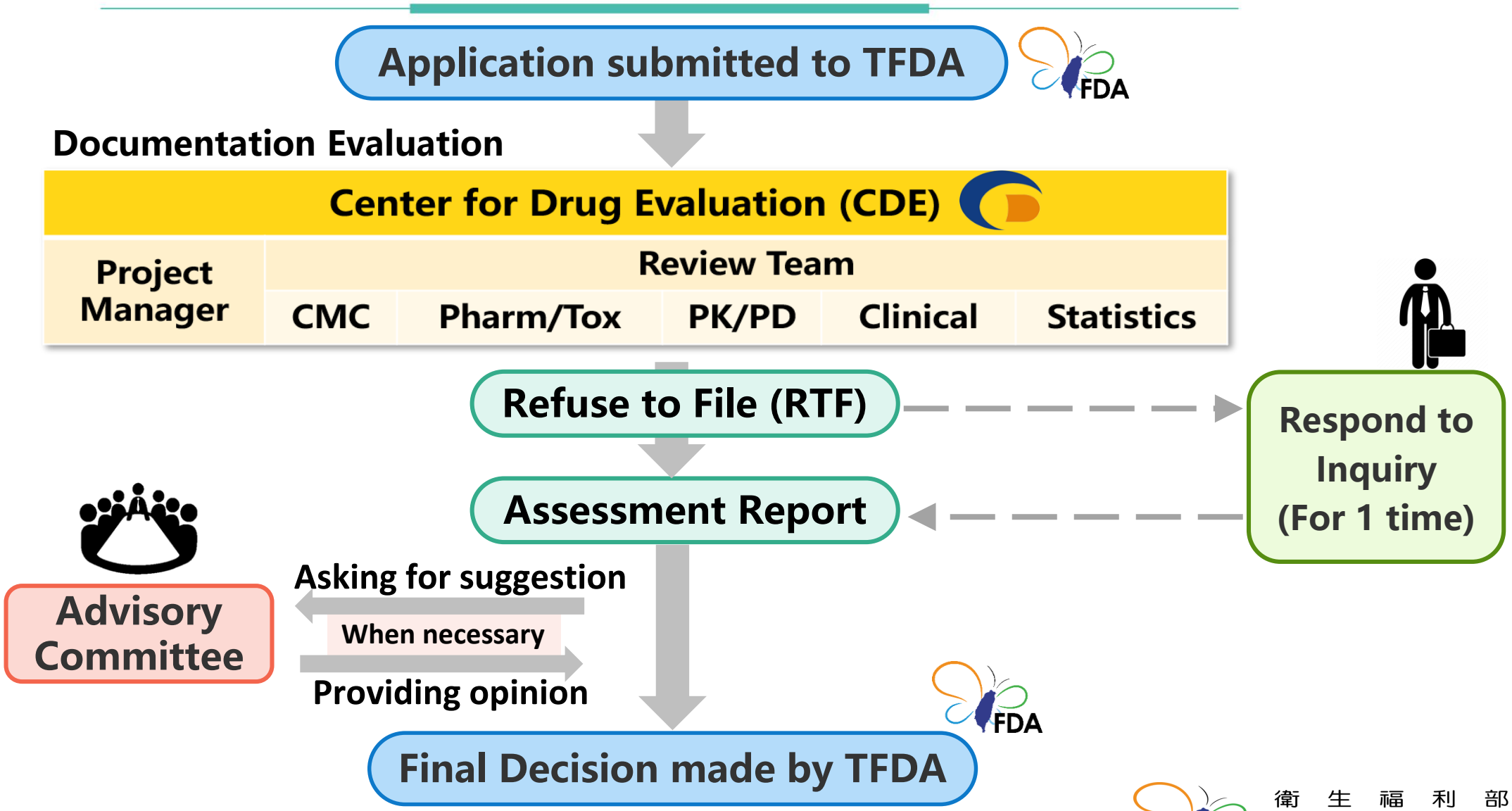
Need AC	Standard	Fast Track
150 days	45 days	30 days

Criteria

1
- Non-first in human clinical trial
- MRCT (include A10 countries)

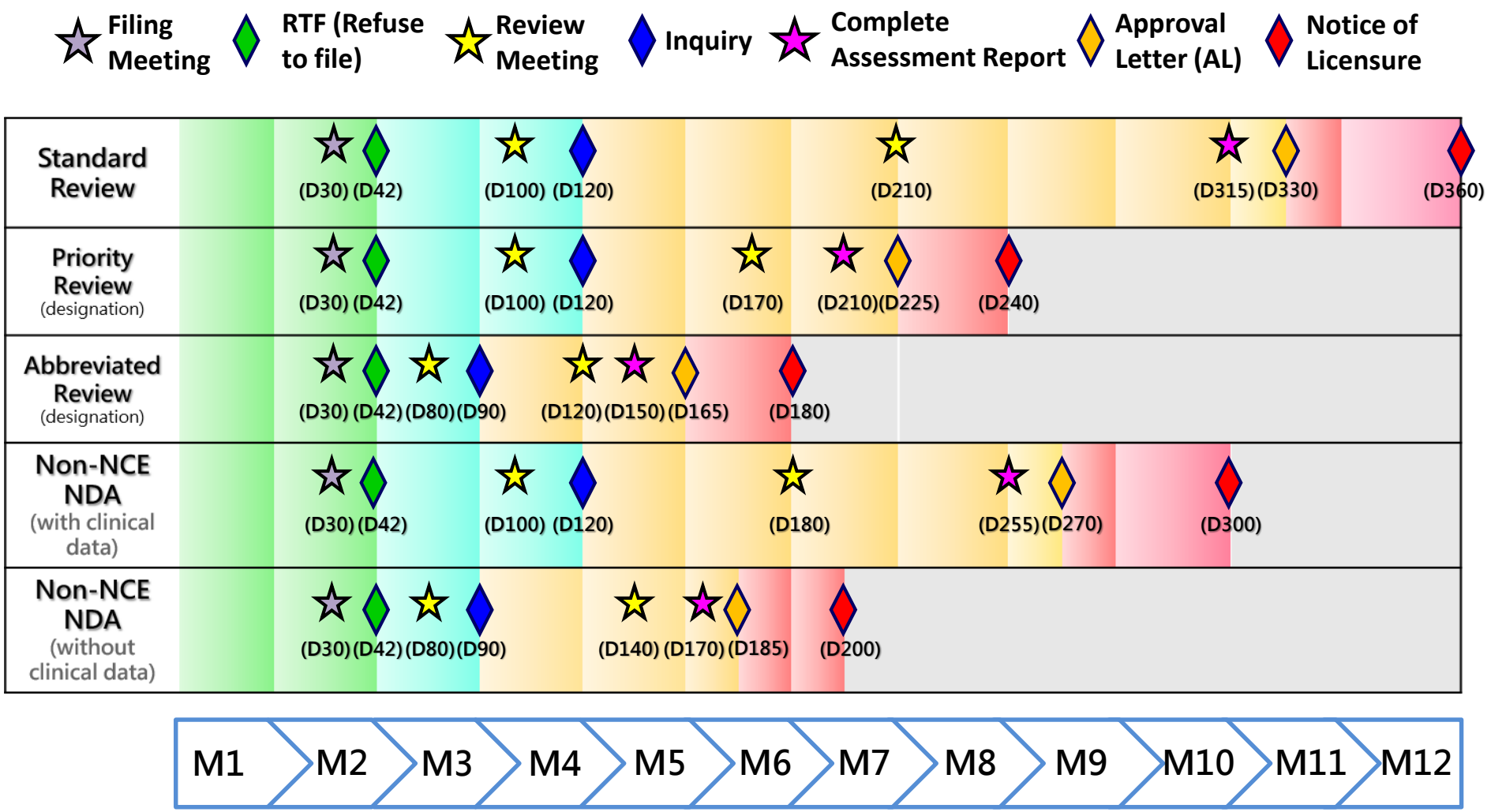
2
- Cell/gene therapy products which are produced by the same laboratory with the same manufacturing process
- With approved IND in Taiwan
- For investigator-initiated clinical trials
- Pivotal trials can not be applied

Regenerative Medicinal Products NDA Review Process

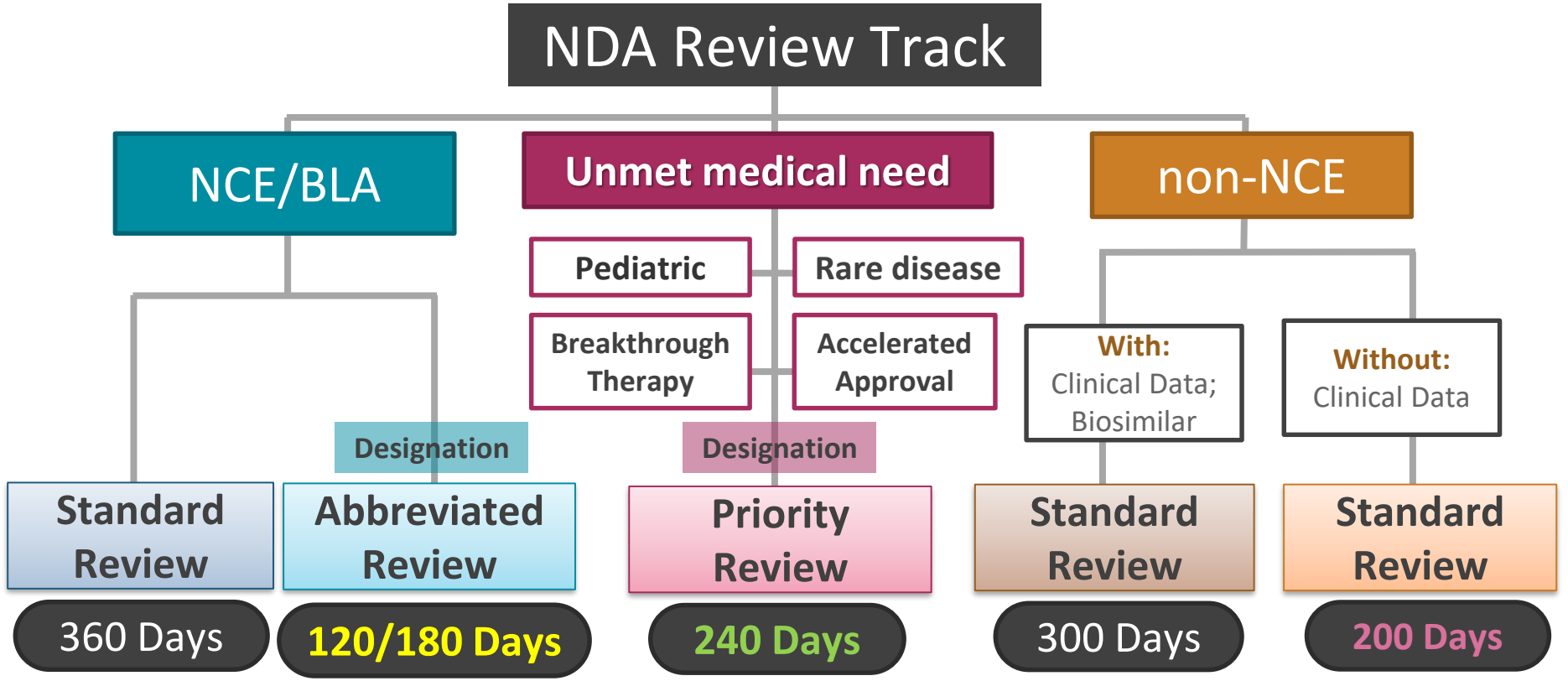


Review Process and Timeline Management for NDA

2021.10 update



Expedited Review Pathway



- **Pediatric designation**: Serious diseases that mainly affect children's ethnic groups.
- **Rare disease designation**: Serious disease with prevalence rate less than 5/10,000.

Review Considerations for Regenerative Medicinal Products

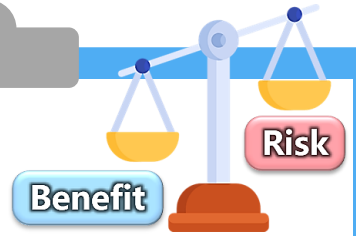
Quality

- Entire manufacturing process
- Acceptance criteria and CoA
- Adventitious agents evaluation
- Identification, Purity, Potency, Microorganism, Endotoxin, Bioburden
- Shelf-life and storage condition
- Complete traceability

Non-Clinical

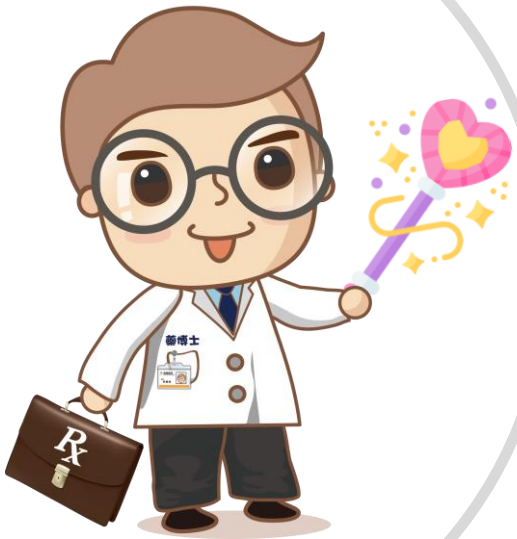
- Primary and secondary pharmacodynamics
- Safety pharmacology
- Biodistribution, persistence, shedding study, interactions
- Single and repeated dose toxicity study
- Tumorigenesis study
- Genotoxicity study
- Reproductive study
- Immunogenicity

Clinical



- Randomized controlled and blinded confirmatory trial
- Surrogate endpoints may be considered
- Risk management plan
- Long-term follow-up study
  - For integrating vectors, virus vectors with establishing latency, microbial vectors with persistent infection or genome editing products, they may require at least 15 years follow-up

Outline



1 Current Regulatory Framework in Taiwan

2 **Approved Regenerative Medicine**

3 Challenges and Future Expectations

RASMET Listed Cell Therapies

Types of Therapies	Indications	Approved (~6/2023)
CD34+ Selected Autologous Peripheral Blood Stem Cell Therapy	• Chronic ischemic stroke • Severe lower limb ischemia	0
Autologous cellular immunotherapy (adoptive T cell therapy including CIK、NK、DC、DC-CIK、TIL、gamma-delta T)	• Hematologic malignancy (standard treatment failed) • Stage 1 -stage 3 solid tumor (standard treatment failed) • Stage 4 solid tumor	132
Autologous Adipose Tissue Stem Cell Therapy	• Chronic or non-healing wound last for 6 months • More then 20% BSA burn or traumatic skin injury • Subcutaneous and soft tissue damage • Degenerative arthritis and knee chondral injury	37
Autologous Fibroblast Therapy	• Skin defects: winkles, dents and scars repair	4
Autologous Bone Marrow Mesenchymal Stem Cell Therapy	• Degenerative arthritis and injured cartilage of knee • Spinal cord injury	10
Autologous Chondrocytes Therapy	Injured cartilage of knee	10

Approved Cell and Gene Therapy Products and Trials

Approved Products

Zolgensma (2020)

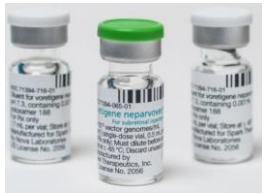
Treatment of children less than 2 years old with spinal muscular atrophy (SMA)

Kymriah (2021)

Immunotherapy for patients with relapsed or refractory B-cell acute lymphoblastic leukemia (ALL), diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL)

Luxturna (2022)

Treatment of patients with vision loss due to inherited retinal dystrophy (IRD) caused by confirmed biallelic RPE65 mutations and who have sufficient viable retinal cells



Upstaza (Eladocagene exuparvovec) (Orphan Drug Designation)

Treatment of aromatic L-amino acid decarboxylase (AADC) deficiency with a severe phenotype

Cell therapy IND

93 trials

- Phase I: 52
- Phase I/II: 19
- Phase II: 16
- Phase III: 6

Gene therapy IND

39 trials

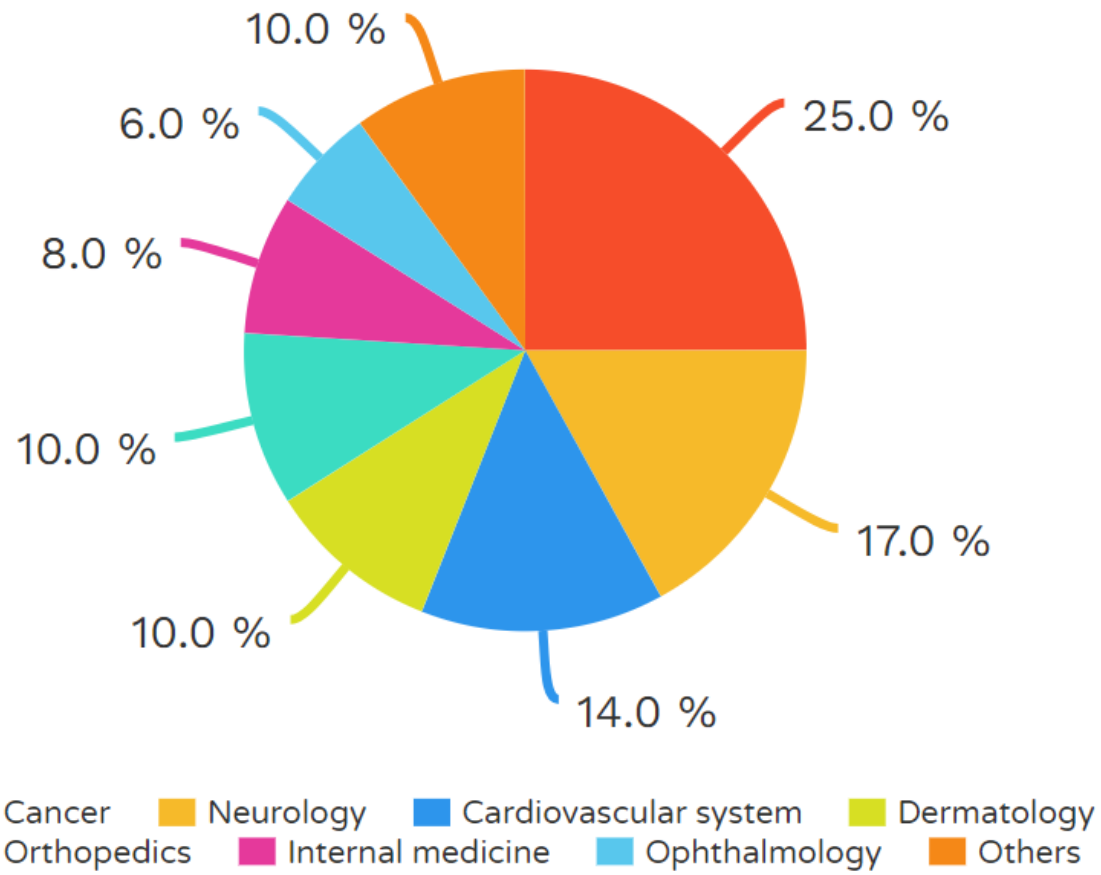
- Phase I: 5
- Phase I/II: 7
- Phase II: 7
- Phase III: 14
- Phase IV: 3
- Others: 3

- **Oncology (25%)** accounted for the majority therapeutic area of the approved cell therapy IND.
- **Rare diseases (42%)** and **Oncology (41%)** accounted for the majority therapeutic area of the approved gene therapy IND.

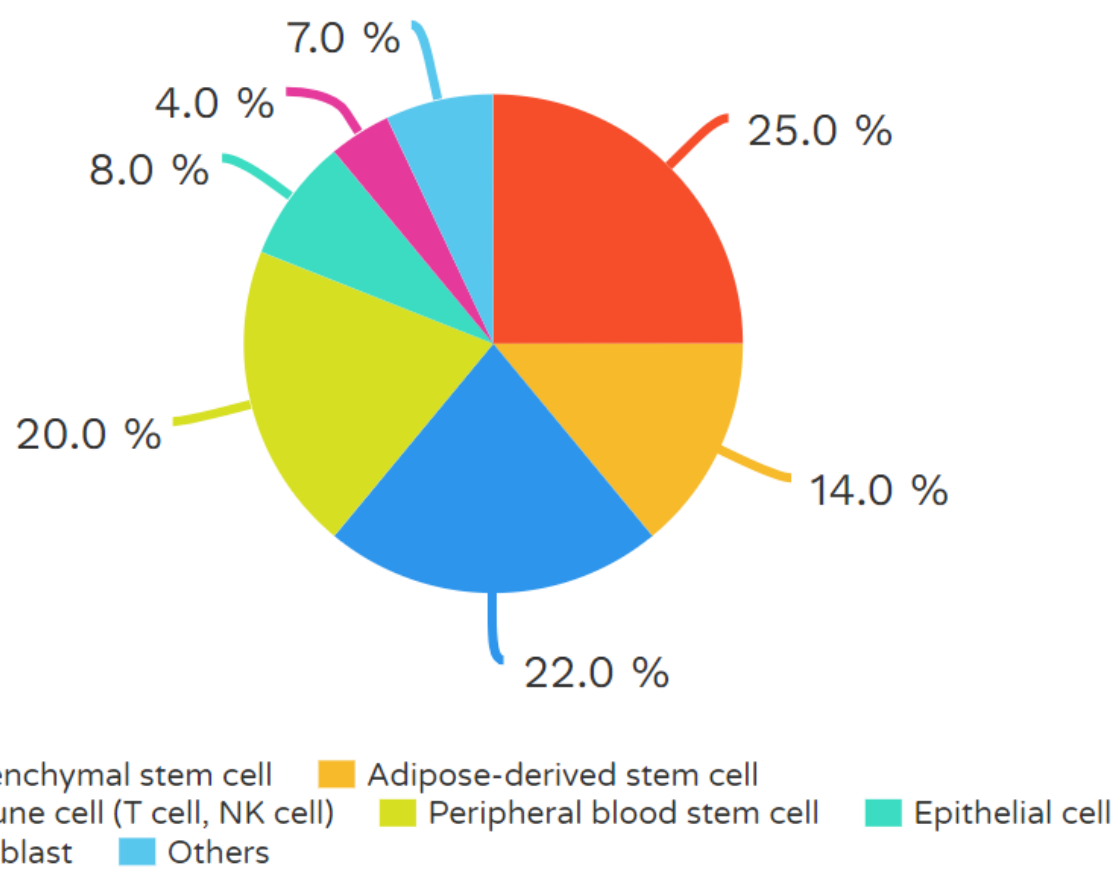
Data as of August 2023

Analysis for Approved Cell Therapy Clinical Trials

Therapeutic Area

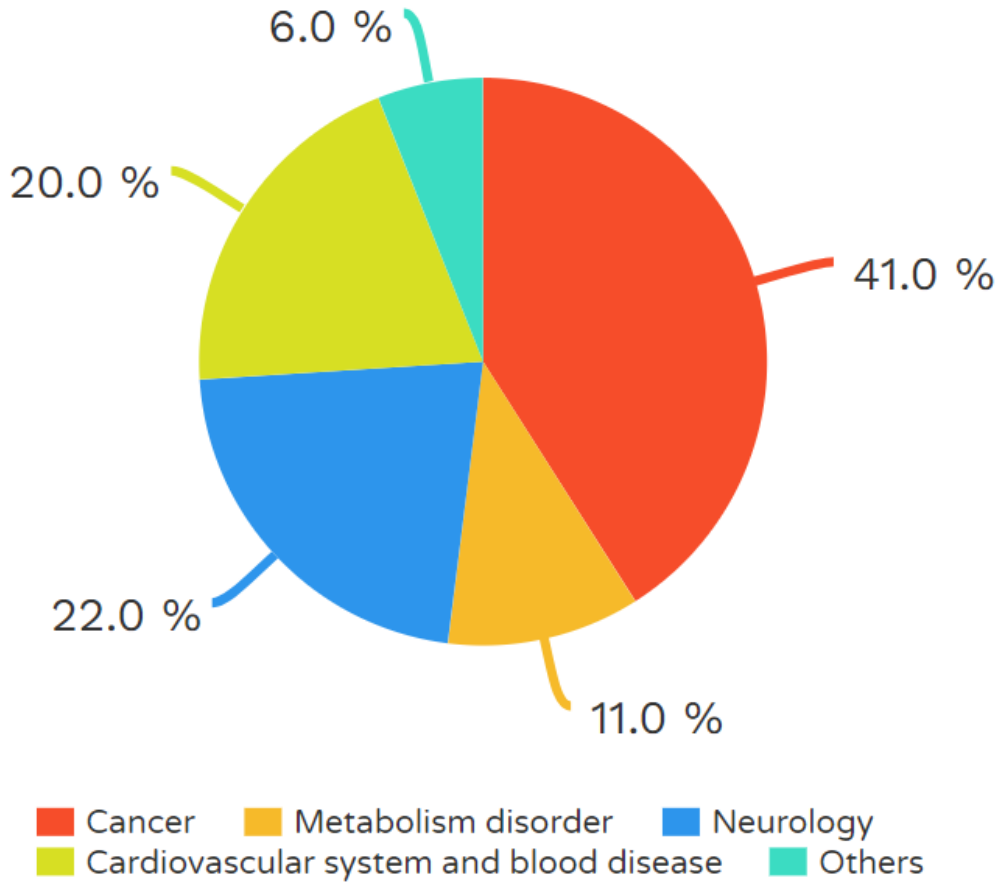


Cell Types

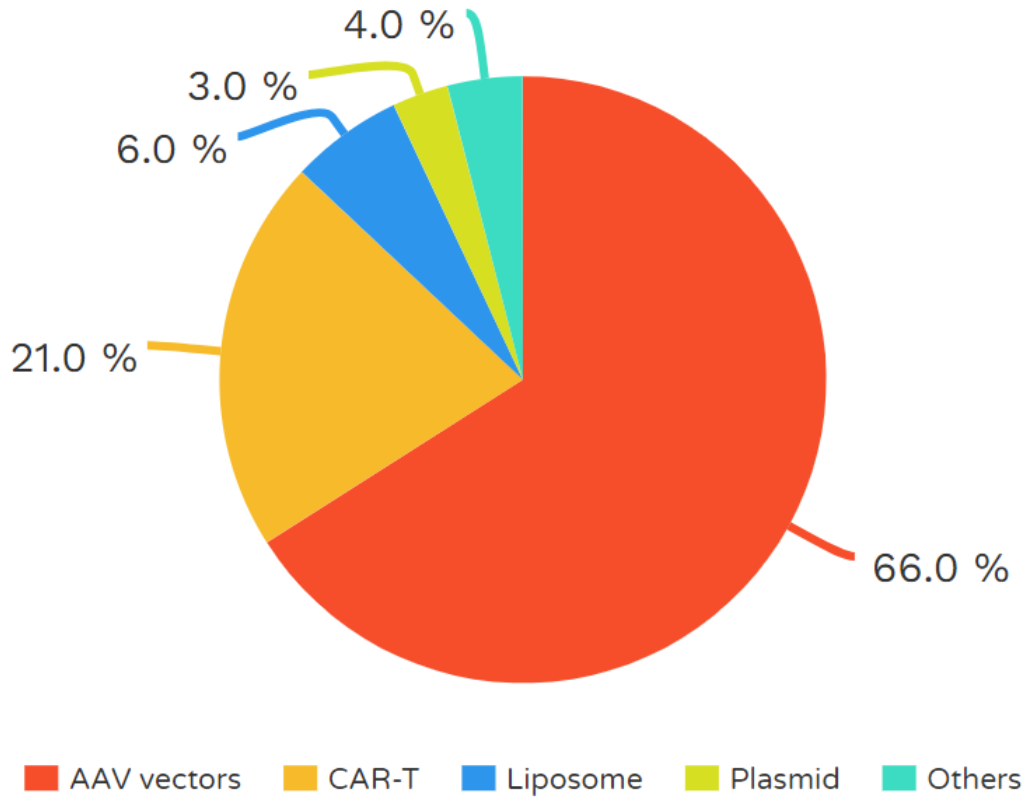


Analysis for Approved Gene Therapy Clinical Trials

Therapeutic Area



Vector Types



Post-Marketing Requirements for Approved Products

Zolgensma

- RMP include Medication Guide, Communication Plan, Product Registry, and Routine Pharmacovigilance Activities. The registry study report shall be submitted in every 2 years.

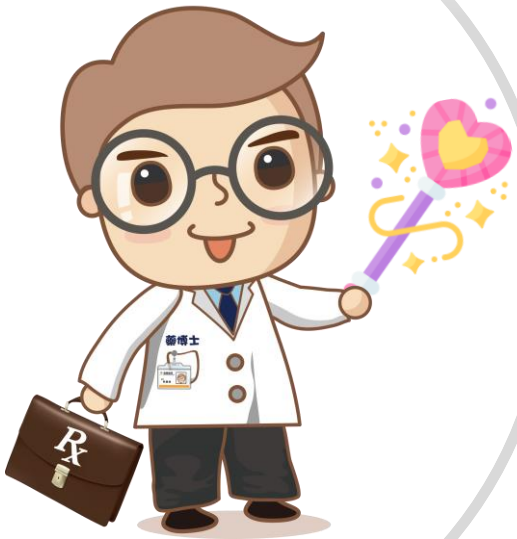
Kymriah

- RMP include global long-term follow-up Study with at least 10 Taiwanese patients being enrolled and followed for 15 years.

Luxturna

- Luxturna-treated patients in Taiwan should be enrolled in the global post-authorization safety Study.

Outline



1. Current Regulatory Framework in Taiwan
2. Approved Regenerative Medicine
3. **Challenges and Future Expectations**

New Regulations for Regenerative Medicine in Taiwan

Since Jan 2022
(Currently under legislative process)

Medical Practice (Therapy)

Regenerative Medicine (RM)

Medicinal Products (Biologics)

NEW

Regenerative Medicine Therapies Act (Draft)

NEW

Regenerative Medicinal Products Act (Draft)

Regenerative Medicine Therapies Act (Draft)

Regulate regenerative medical practice in medical institutions

To intensify quality management of regenerative medicine therapies

Cell and tissue management (3)

Donor eligibility,
CPU quality management

Perform regenerative medicine (2)

Medical institutions, Physician qualification, Patient informed consents, Documentation and patient registry

General (1)

Purpose, Scope, Definition, Authority, Advisory committee, Policy promotion

Human trials (4)

Restrictions on research,
Subsidies and incentives

Supervision and prevention (5)

Advertisement for regenerative medicine therapy and donor recruitment, Report of treatment outcome, Report of AE, Insurance

Others (6)

Penalties

Regenerative Medicinal Products Act (Draft)

A special law under Pharmaceutical Affairs Act

To strengthen the whole lifecycle management for regenerative medicinal products

General

Purpose, Scope, Definition, Authority, Advisory committee

Registration, Post-approval Changes, Extension of approval

Registration

Conditional Approval

Conditional Approval, Criteria and Requirements

Donor eligibility, Donor consents, Manufacture and Distribution

Manufacture, Distribution

Post-Approval Management

Pharmacovigilance, Product traceability, Documentation

Drug injury relief, Recruitment advertisement, Penalties

Others

衛生福利部 食品藥物管理署
Taiwan Food and Drug Administration

Future Prospects

Pharmaceutical industry and academy

Regulatory agency

- Since the guidelines and regulations often lag behind the updated scientific knowledge, regulatory agencies also need to **cooperate** with pharmaceutical industry and academy to ensure establishing appropriate regulatory framework while not impeding patient access to innovative regenerative medicine.
- TFDA encourages pharmaceutical companies in Taiwan and Japan to **share the experience** with us and create a win-win situation together.




Thank You
For Your Listening!

For more information, please refer to
http://www.fda.gov.tw


衛 生 福 利 部
食 品 藥 物 管 理 署
Taiwan Food and Drug Administration