Regulation of Regenerative Medicine in Taiwan

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Introduction

Regulatory development for cell and gene therapy products

New regulatory framework for regenerative medicine

Future prospects
Organization of TFDA

MOHW
Bureau of Medical Affairs

Director-General
Deputy Director-General
Chief Secretary

TFDA

Administrative Office
Secretariat
Personnel
Accounting
Service Ethics
Information Management

Center of Regional Administration
Northern
Central
Southern

Operational Division
Planning & Research Development
Food Safety
Medicinal Products
Medical Devices & Cosmetics
Controlled Drugs
Research & Analysis
Risk Management

Task Force
Factory for Controlled Drugs
Decision Support Center

Collaborative Institute
Center for Drug Evaluation (CDE)
Taiwan Drug Relief Foundation (TDRF)

Technical document review and consultation

Regulatory Science and review of drugs and biologics

GLP, GTP, GMP compliance
Different regulatory approaches

Before TFDA Inauguration

- Cell therapy was regulated as “**New Medical Practices**“ by Bureau of Medical Affair (BMA).
- After human trials, “new medical practices” would have the opportunity to turn into “**Routine Medical Practice**”.

After TFDA Inauguration

- Regulation of cell therapy was transferred to TFDA in 2010.
- The regulatory approach was changed to “**Medicinal Products**”.

Comparison table:

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<tr>
<th>Before TFDA Inauguration</th>
<th>After TFDA Inauguration</th>
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<td>GTP Inspection</td>
<td>Medicinal Products</td>
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<td>Review for applications</td>
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<td>Phase I</td>
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<td>NDA</td>
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<td>GCP, GTP Inspections</td>
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Currently, TFDA has not yet approved any human cell or gene therapy products on marketing, but numerous clinical studies are ongoing. The majority are from academia.
The first and successful clinical application of cell therapy product in Taiwan

Color powder explosion at a water park in Taiwan (June 27, 2015)

- Burn injured: 484
- Burn surface > 40%: over 200
- Burn surface > 80%: 24
- Deceased: 15

Japanese Medical service team arrived within one week.
American Burn Association provides the consultation.

First clinical use of cell therapy product in Taiwan
JACE (autologous cultured epidermis)
ReCell (autologous cell transplantation)
Patient voice from the Public Policy E-plateform

- E-Participation Platform for Public Policy was launched on Feb. 2015.
- It’s a platform to allow people to join public policy and propose their concerned issues on it ([http://join.gov.tw](http://join.gov.tw)).

### The first successful proposal from the E-platform (Sep.24, 2015)

- **Proposer:** Caspar Wang (with a terminal stage of Nasopharyngeal carcinoma)
- **Propose:** To introduce the Immune Cell Therapy Amendment Bill to the Legislation before by the end of December 2015.
- **Supported by over 5000 people.**

### Short-term

- Proposal Accepted
- MOHW: Regenerative Medicine Development Advisory Council
- Amendment of the Regulations on Human Trials (treatment protocol)

### Mid to Long-term

- MOHW: Regenerative Medicine Development Advisory Council
- Amendment of the Regulations on Human Trials (treatment protocol)
- To promote a reform bill and develop cell therapy product regulations.
Regulatory development of regenerative medicine

- 2002: Good human Tissue Practice (GTP)
- 2007: GTP inspection
- 2010: TFDA
- 2011: Guideline for the application of investigational human cell therapy products
- 2014: Amendment of the Regulations on Human Trials (treatment protocol)
- 2015: Guideline for the application of investigational human cell therapy products
- 2016: Guideline for donor eligibility evaluation of human cell therapy products
- 2017: Guideline for the registration of human cell therapy products
- 2018: Regulations for Cell therapy techniques

- Act of cell and gene therapy products (Draft)
- Regenerative Medicinal Product Act (Draft)
Treatment Protocol (2015)

Amendment of the Regulations on Human Trial

- Expand access to investigational cell therapy products for treatment use
- For individual patients, including emergency use
- For intermediate-size patient populations

**Objective**

- **Serious** condition and **no alternative treatment**
- Based on the **pre-approved clinical trial protocols**
- Medical institution-initiated
- With **adequate safety data**

**Scope**

- **Patient may have to pay** for using the investigational cell therapy products for treatment

**Subjects**

**Payment**

Medicinal Product v.s. Medical Techniques

**Pharmaceutical Affairs Act**

- **Regenerative Medicinal Product Act (Draft - Oct 2018, under legislative process)**

**Pharma**

- Product
  - Pharmaceutical Industry
  - GMP

- Manufacturing site
  - GMP

**Medical institute**

- Cell therapy technique
  - GTP

- Performed by registered physician in recognized medical institute

**Regulation Governing the Application of Specific Medical Examination Technique and Medical Device (RASMET) (Amended - Sep 2018)**

- Medical institute
  - Cell Processing Unit
  - GTP

- Cell, Gene or Tissue engineering product w/ marketing authorization
Regenerative Medicinal Product Act
(Under legislative process)

General
- Purpose, Scope, Definition, Authority
- Registration, Changes, Extension of approval

Conditional Approval
- Conditional Approval, Criteria and Requirements
- Evaluation of donor eligibility, Informed consents, Manufacture and Distribution

Post-Approval Management
- Pharmacovigilance, Product and source traceability
- Drug injury relief, Administrative injunction, Implementation date

Others
- Registration
- Manufacture, Distribution
- Others
<table>
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<tr>
<th>Cell Therapies</th>
<th>Indication</th>
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<tr>
<td><strong>CD34+ Selected Autologous Peripheral Blood Stem Cell Transplantation</strong></td>
<td>• Hematological malignancies&lt;br&gt;• Leukemia (Except CML chronic phase)&lt;br&gt;• Lymphoma&lt;br&gt;• Multiple myeloma&lt;br&gt;• Chronic ischemic stroke&lt;br&gt;• Severe lower limb ischemia</td>
</tr>
<tr>
<td><strong>Autologous cellular immunotherapy (adoptive T cell therapy including CIK, NK, DC, DC-CIK, TIL, gamma-delta T)</strong></td>
<td>• Hematologic malignancy failed standard treatment&lt;br&gt;• Stage 1-stage 3 solid tumor failed standard treatment&lt;br&gt;• Stage 4 solid tumor</td>
</tr>
<tr>
<td><strong>Autologous Adipose Tissue Stem Cell Transplantation</strong></td>
<td>• Chronic or non-healing wound last for 6 months&lt;br&gt;• More than 20% BSA burn or traumatic skin injury&lt;br&gt;• Subcutaneous and soft tissue damage&lt;br&gt;• Degenerative arthritis and knee chondral injury&lt;br&gt;• Combination or adjuvant treatment with other skin minimally invasive surgery</td>
</tr>
<tr>
<td><strong>Autologous Fibroblast Transplantation</strong></td>
<td>• Skin defects: wrinkles, dents and scars repair&lt;br&gt;• Subcutaneous and soft tissue damage&lt;br&gt;• Combination or adjuvant treatment with other cutaneous minimally invasive surgery</td>
</tr>
<tr>
<td><strong>Autologous Bone Marrow Mesenchymal Stem Cell Transplantation</strong></td>
<td>• Degenerative arthritis and injured cartilage of knee&lt;br&gt;• Chronic ischemic stroke&lt;br&gt;• Spinal cord injury</td>
</tr>
<tr>
<td><strong>Autologous Chondrocytes Transplantation</strong></td>
<td>Injured cartilage of knee</td>
</tr>
</tbody>
</table>

*First approved application: CIK cell therapy for hematologic malignancy (May 2019)*
A new regulatory framework for regenerative medicinal products and medical practice

Cell therapy as medical practice

Cell therapy

New cell therapy

Clinical data

Time-limited permission

Specific Medical Technique

Routine evaluation

The Council

Safety confirmed

Safety and primary efficacy confirmed

Safety and clinical data collected could be used as supportive data for applying clinical trials and registration of the cell products.

Regular medical practice

Efficacy confirmed

Extend validity

Efficacy uncertain

No-efficacy

Cancellation

Conditional Approval (5yr)

NDA

Phase III

Phase II

Phase I

Pre-clinical

RM Product

Regenerative medicinal products

Pharmaceutical Affairs Act

Regenerative Medicinal Product Act (Draft)

(dot line: drafting)
Summary

- **Advantage of the new regulatory framework**
  - Service for unmet medical needs
  - Accelerate the development of regenerative medicine in Taiwan

- **Challenges**
  - Evaluation of clinical outcome (risk-benefit)
  - Linkage between products and practices
  - Pricing (Value-based pricing)
  - Approve of the first regenerative medicinal product in Taiwan.
Future Prospects

To Enhance International Collaboration

To Establish Training Programs and Scientific Workshop
GTP, GMP, and Specificity of cell production process, animal model, clinical trial design

To Improve Consultation Mechanism

To enact “Act of Regenerative Medicinal Products”
To define and better regulate the cell therapy and gene therapy products

To continue establishing specific guidance
Registration requirements, Traceability, GMP for regenerative medicinal products, etc.

Better Products, Better Life

Regulatory support and accelerate development of cell therapy products
Incentives for small and medium sized enterprises
Thank you for your attention!