# Regulation of Cell and Gene Therapy Products in Taiwan

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衛生福利部
食品藥物管理署
FDA Food and Drug Administration
http://www.fda.gov.tw/

# Outline

- Overview Regulatory of Cell Therapy product
- Current Regulatory Framework
- Legislation update
- Future Prospects

# Approved Cell & Gene Therapy Products in The World

## EMA (8)

- Chondrocelect(2009)
- MACI (2012)
- Glybera (2013)
- Provenge, DC (2013)
- Holoclar (2015)
- Imlygic (2015)
- Strimvelis (2016)
- Zalmoxis(2016)

## Korea(14)

- Chondron (2001)
- Holoderm (2002)
- Kaloderm (2005,2010)
- Keraheal (2006)
- CreaVax-RCC (2007)
- Immuncell-LC (2007)
- RMS Ossron (2009)
- QueenCell (2010)
- CureSkin (2010)
- Hearticellfram-AMI (2011)
- Cartistem, MSC (2012)
- Cupistem (2012)
- Neuronata-R (2014)
- Keraheal-allo (2015)

## Japan (4)

- JACE (2007)
- JACC (2012)
- TEMCELL (2015)
- HeartSheet (2015)

## New Zealand(1)

- Prochymal, MSC

## Canada (1)

- Prochymal, MSC (2012)

## US. (13)

- Carticel (1997)
- Provenge, DC (2010)
- Laviv, fibrocell (2011)
- Hemacord (2011)
- Gintuit (2012)
- HPC, Cord Blood (2012)
- HPC, Cord Blood (2013)
- Ducord (2012)
- Allocord (2013)
- Imlygic (2015)
- Clevecord (2016)
- HPC, Cord Blood (2016)
- Kymriah(2017)

In black: autologous

In green: allogeneic

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# Differences in Regulation

| | Japan | | Korea | US | | EU |
|---|---|---|---|---|---|---|
| **Feature** | **Two regulatory pathway** | | **Regulated as product** | | | |
| **Authority** | MHLW | MHLW/PMDA | MFDS | US FDA | | EMA |
| **Regulatory** | **Act on the Safety of Regenerative Medicine** | **Pharmaceuticals and Medical Devices Act** | Pharmaceutical Affairs Act | **PHS Act<br>FD&C Act<br>21 CFR** | | • **Directive 2004/23/EC**<br>• **Regulation 1394/2007/EC** |
| **Terminology** | • **Medical care**<br>• **Academic research** | **Regenerative medical products** | **CTP<br>Cell therapy products** | **HCT/Ps<br>Human cells, tissues, and cellular and tissue-based products** | | **ATMP<br>Advanced therapy medicinal products** |
| **Scope** | Risk-based category (Class I,II,III) | • IND and NDA application required。<br>• Condition-approval | • As biologics<br>• IND and NDA application required。 | PHS 361<br>*(lower risk)*<br>• Tissue (cartilage, bone, tendon, skin)<br>• Premarket review & approval not required<br>• minimally manipulated<br>• homologous use<br>• no combination<br>• no systemic effect | PHS 351<br>*(higher risk)*<br>• Biologic or Device<br>• BLA application required | • Marketing Authorization by Centralized EMA/CAT<br>• Licensure not required for Hospital Exemption |

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# Regulatory Change on Cell Therapy

## Before TFDA Inauguration

**Medical Practices**

- 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"***.

2010

## After TFDA Inauguration

**Medicinal Products**

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



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# Reasons of Regulatory Change

## Regulatory harmonization

Many countries have considered cells therapy products as one kind of *biologics, medical devices, advanced medicinal products or regenerative products.*

## Altered relevant biological characteristics

Cells *manipulated in vitro* might be not the same with the original cells or genes. It is necessary to establish regulations to ensure manufacturing consistency.

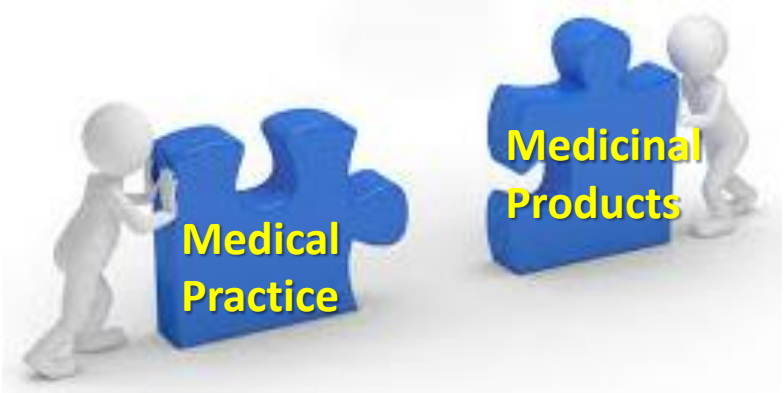
# Controversial Issues

- **Autologous processes?**

  *(Autologous cells graft used in the same graft procedure)*

- **Academia clinical research?**

  *(GMP Compliance)*




**regulatory cooperation to accelerate medical innovation and patient access**

◆ **Risk-based approach**

Relevant factors includes the origin of cells, level of cell manipulation, indication, combination product, etc.

# Advisory Committee for Cell Therapy



**TFDA**

- Since 2014.08
- Review of clinical trials and product approval

**MOHW**

- Since 2015.11
- Policy and new technology development

# Law, Regulation and Guidance


| Regulatory Framework of Cell Therapy Products | |
|---|---|
| **Law** | Pharmaceutical Affairs Act |
| **Regulation** | Regulation for Registration of Medicinal Products<br>Regulations on Human Trials<br>Regulation on Good Clinical Practice (GCP)<br>Regulation on Good Manufacture Practice (GMP) |
| **Guidance** | Guidance on Investigational Cell Therapy Products<br>Guidance on Cell Therapy Products Application<br>Guidance on Donor Eligibility Determination<br>Guidance on Good Tissue Practice (GTP) |

# Timeline of Guidance for Cell Therapy Products

***Human cell therapy products*** are the autologous or allogeneic cells used to treatment, prevent or diagnose diseases.

2002/12/13

**Guidance on Good Tissue Practice**

To prevent the transmission or spreading of communicable diseases and establish reliable quality assurance systems

2014/09/17

**Guidance on Investigational Cell Therapy Products**

To provide review consideration for applicant with IND submission

2015/07/13

**Guidance on Cell Therapy Products Registration Application**

To provide review consideration for applicant with NDA submission

2015/10/02

**Guidance on Donor Eligibility Determination**

Based on donor screening and testing for relevant from communicable disease agents and diseases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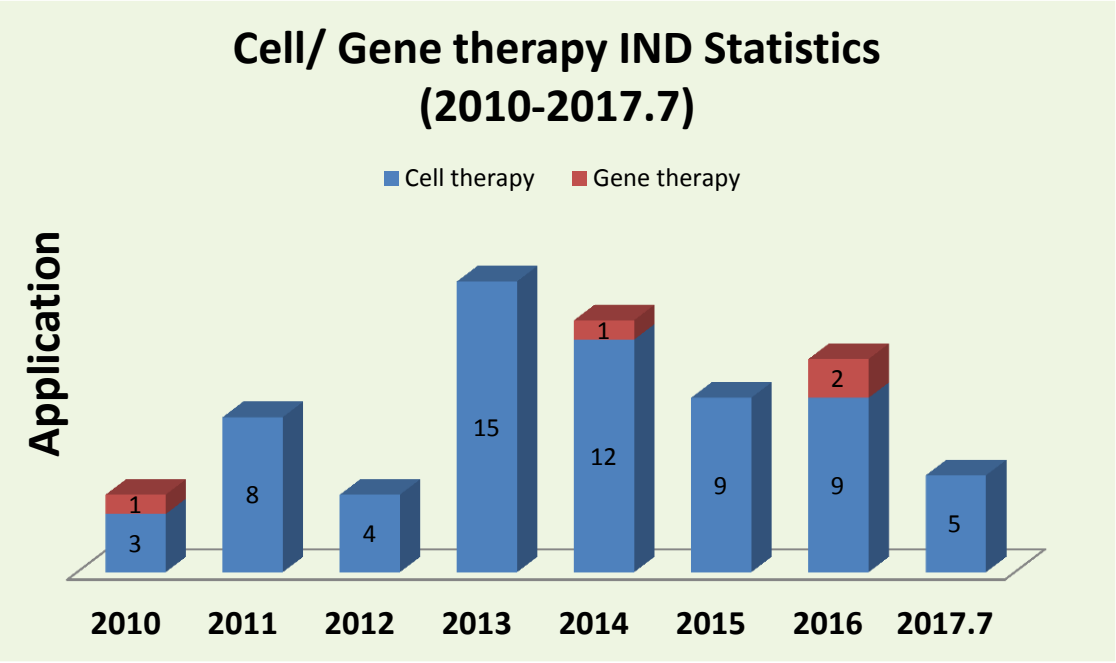
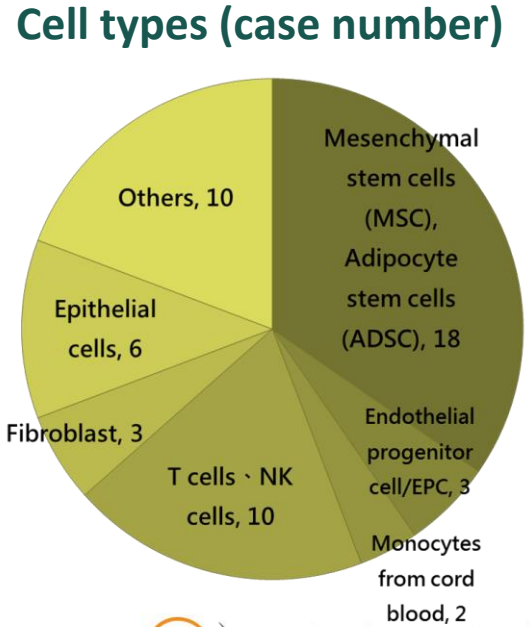
# Current Status

- Currently, TFDA has not yet approved any human cell therapy on marketing, but numerous clinical studies of cell therapy products are ongoing.
- The majority are from academic research.

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# Platform for Public to Join Government policy


*Proposer：Caspar Wang , 2015-09-24*
*Propose：Introduce the Immune Cell Therapy Amendment Bill to the Legislation before by the end of December 2015, and accelerate the passage approval of new cancer drugs.*

## Short Term

1.Revising the "Regulations on Human Trials and implement **"Treatment Protocol".**

2.The MHLW has convened **a "Regenerative Medicine and Cell Therapy Development Advisory Council".**

## Medium to Long Term

1.Immune cell therapy should be listed as a **conventional medical treatment** or regulated as a **specific cell product**.

2.MHLW will promote a reform bill and **develop cell therapy product regulations.**

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# Current regulation Framework

## Cell Therapy Product or Medical Practices

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醫事司

| Cell Therapy Product | Medical practices |
| --- | --- |
| IND & NDA application | IND & NDA not required |

# Compassionate Use

## (treatment protocol)

**Objective**

Expanded access to investigational cell therapy products for treatment use

**Scope**

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

**Subjects**

- ✓ For individual patients, including emergency use
- ✓ For intermediate-size patient populations

**Payment**

Patients may have to pay for using the investigational cell therapy products for treatment

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# Regulation of Cell Therapy Products in Taiwan

Pre-marketing | Post-marketing

Product Development → IND Clinical trials → NDA Market licensing → Production → Marketing

**Consultation**
**2011.08.02**

**Guidance on Donor Eligibility Determination**
**2015.10.02**

**Guidance on Investigational Cell Therapy Products**
**2014.09.17**

**Guidance on Good Tissue Practice (GTP)**
**2002.12.13**

**Guidance on Cell Therapy Products Application**
**2015.07.13**

**Cell and Gene Therapy Product Management Act (draft)**
**2017.7.26**


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# Cell and Gene Therapy Medicinal Product Management Act (Draft)-1

| | Description | Article |
|---|---|---|
| 1. | General Information | Article 1-4 |
| 2. | Registration &market approval | Article 5-6 |
| 3. | Manufacturing standards | Article 7 |
| 4. | obligation of the license holders | Article 8 |
| 5. | Advertisement management | Article 9 |
| 6. | Measures establishment | Article 10 |
| 7. | Penal provisions | Article 11-13 |
| 8. | others | Article 14-15 |

Recommendation Collecting

**Website for public：http://www.fda.gov.tw/TC/newsContent.aspx?cid=3&id=22304**

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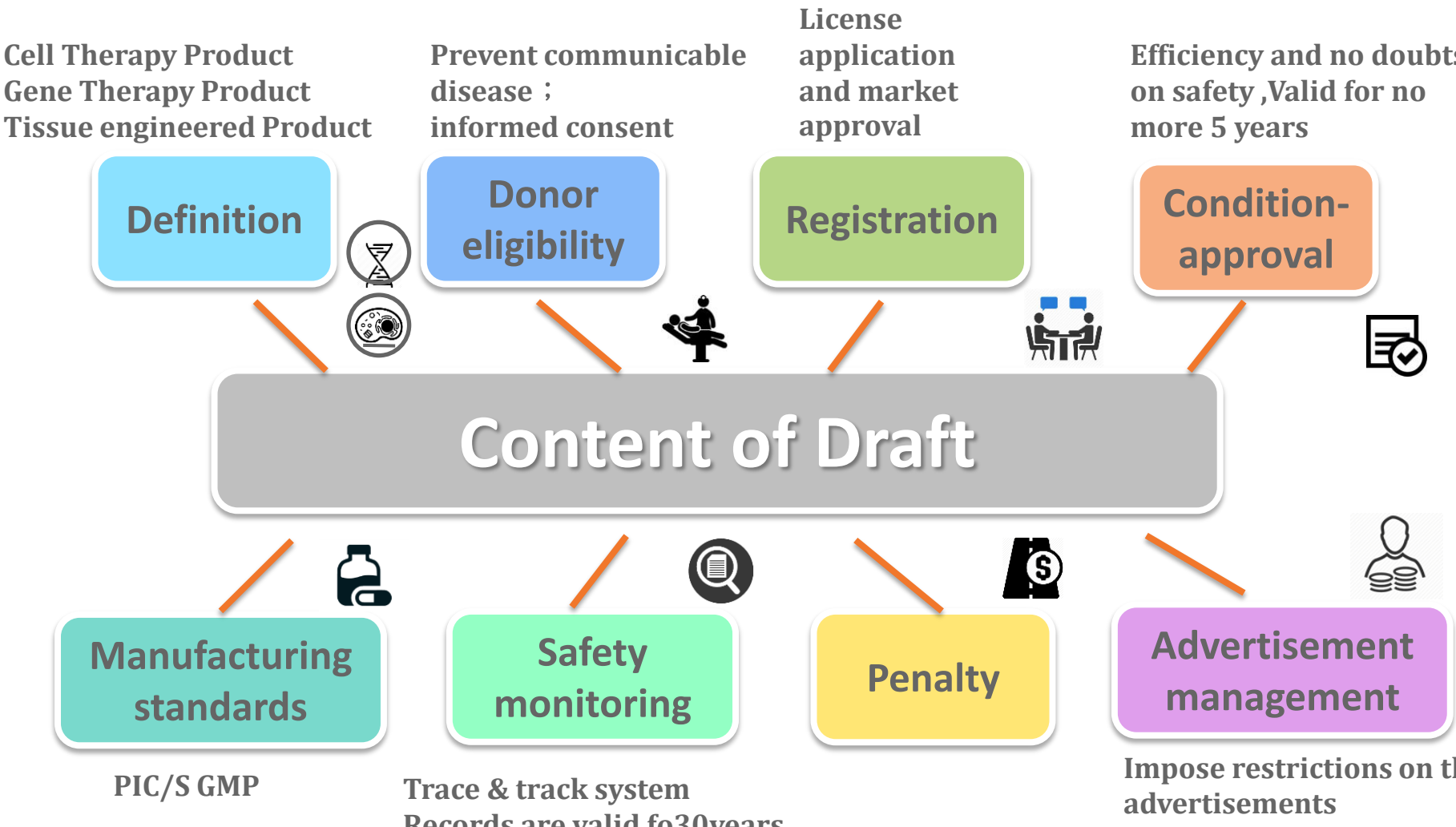
# Cell and Gene Therapy Medicinal Product Management Act (Draft)-2



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# Follow-up Plans

Cell and Gene Therapy Medicinal Product Management Act (Draft)

**Regulations for Registration of Cell and Gene Medicinal Product**

To regulate the relevant review procedures for registration and market approval.

**Regulation for Donor Eligibility Determination**

To ensure the cell or gene therapy products meet the safety requirements and have no risk of infectious diseases.

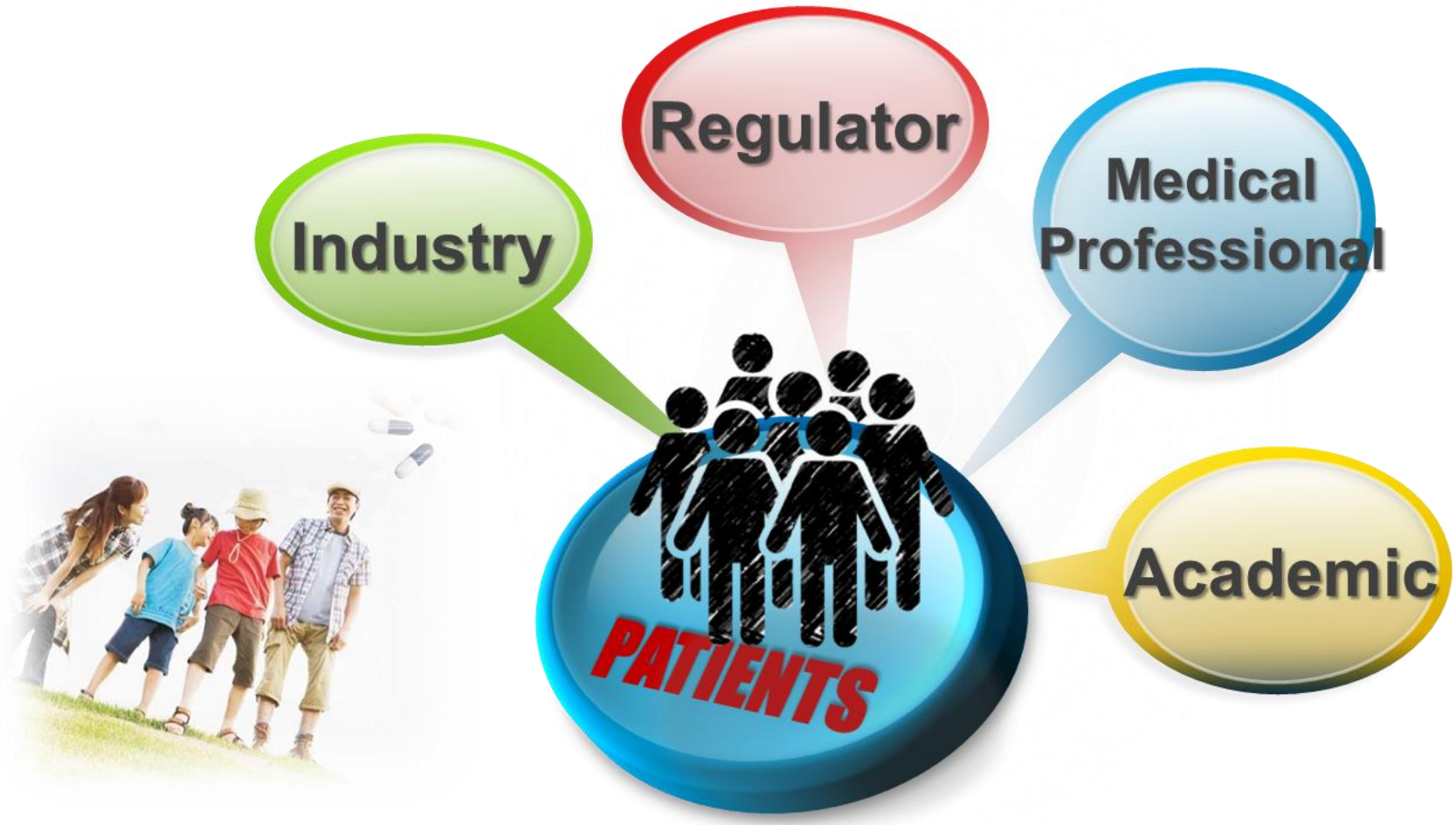
**Guidance on Informed Consent of Recipients and Donors**

To clearly informed the involved relevant of rights and risks.

**Guidance on Post-Approval Surveillance**

To follow-up the Safety & Efficacy for public.

# Win-Win Situation



# For more information

Website is at: http://www.fda.gov.tw








***Thank You for Your Attention***

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