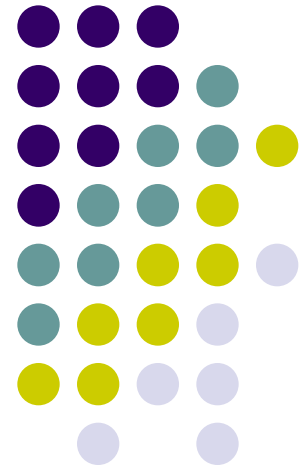


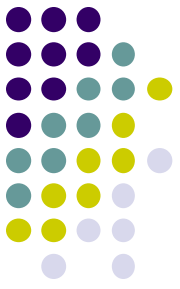
# Access to orphan drugs through a HTA framework

## - *Rare Disease Legislation in Taiwan*

Yi-Wen Tsai, Ph.D.  
Professor/Director  
Institute of Health and Welfare Policy  
National Yang-Ming University, Taiwan

7<sup>th</sup> Asia Pacific Future Trends Forum 2014  
September 12-13  
Malaysia





# Brief Introduction

- **Education**

Ph.D. of Health Services and Policy Analysis, University of California at Berkeley (1994-1998), (*specialty*: health economics)

- **Academic career**

*National Yang-Ming University* (2005 ~ present): Associate Professor, Professor, Director. Institute of Health and Welfare Policy

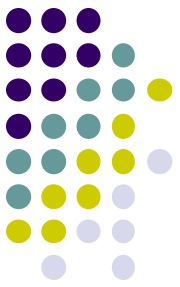
*National Health Research Institutes* (1999-2010): Assistant Principal Investigator, Associate PI. Institute of Population Health

- **Public service**

Academic advisor to National Development Council, Executive Yuan (2010-present); Committee member of Tobacco Control and Health Care Fund Review (2010-present); Committee member of the Actuary committee of National Health Insurance (2009,2010,2011,2012)

- **Research**

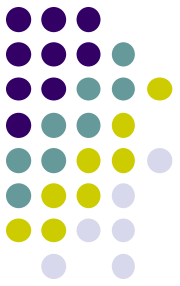
Pharmacoeconomics, pharmacoepidemiology, tobacco control



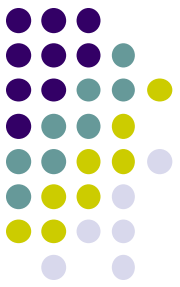
# Outlines

- Regulations of Rare Diseases and Orphan Drugs in Taiwan
- Rare Diseases and Orphan Drugs Under NHI
  - Catastrophic disease
  - Listing and Pricing of New Drugs under National Health Insurance
  - Health Expenditure and Access to New Orphan Drugs
- Key Issues in Orphan Drugs under NHI

# Regulations of Rare Diseases and Orphan Drugs in Taiwan

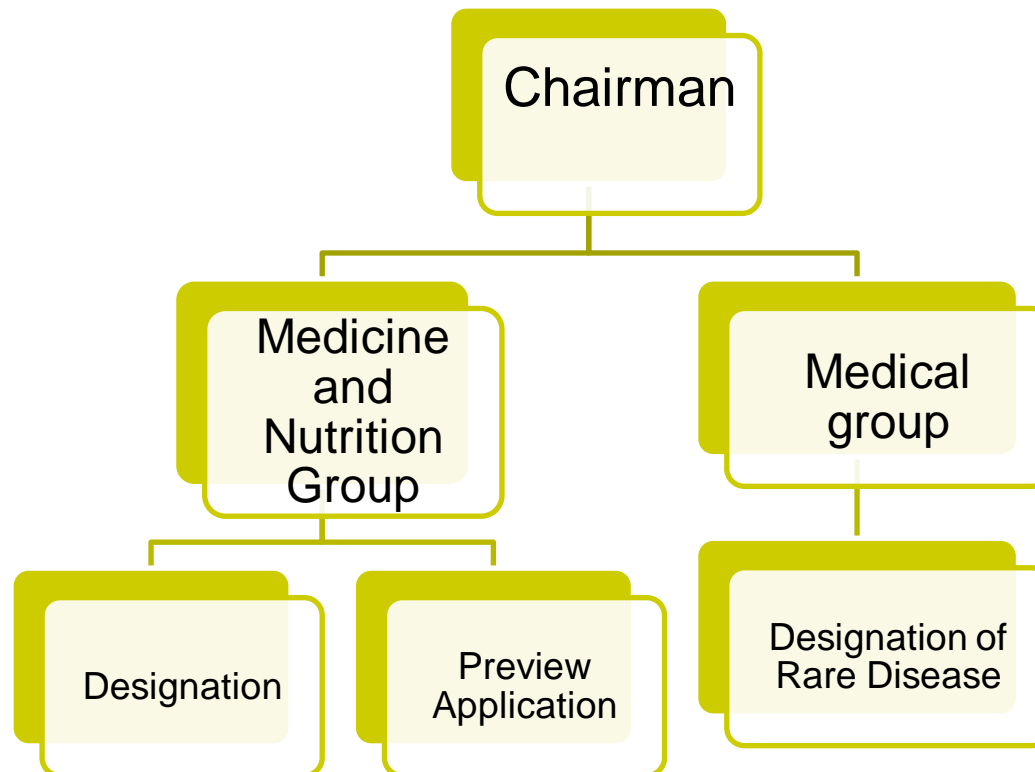


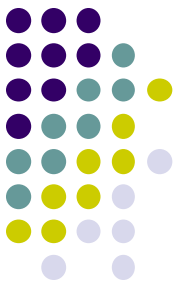
- Rare Disease Control and Orphan Drug Act
- National Health Insurance Act
- Pharmaceutical Affairs Law
- People with Disabilities Rights Protection Act
- Genetic Health Act



# Rare Disease Control and Orphan Drug Act

- Competent Health Authorities: Health Promotion Administration (HPA), MHW (Article 2)
  - Rare Diseases and Rare Disease Drugs Review Committee





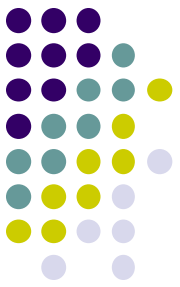
# Rare Disease Control and Orphan Drug Act

- Rare Diseases and Rare Disease Drugs Review Committee
  1. Review on the designation of rare diseases, and counseling on their prevention and control;
  2. Review on the designation of orphan drugs and special nutrient foods essential to the maintenance of life;
  3. Review on the registration and market approval of orphan drugs
  4. Review on the subsidies to and research and development of orphan drugs and special nutrient foods essential to the maintenance of life;
  5. Review, assistance and counseling on international medical cooperation projects for rare diseases;
  6. Review of non-orphan drugs for the treatment of specific diseases;
  7. Counseling on other matters related to rare diseases.

# Rare disease/orphan product system in Taiwan



Rare Disease/ Orphan Product System in Taiwan	
Legal framework	Rare Disease Control and Orphan Drug Act (since 2000)
Authority	Health Promotion Administration and Taiwan FDA (FDA), MHW
Patient advocacy	Taiwan Foundation for Rare Disorders (TFRD)
Criteria for rare diseases	<ul style="list-style-type: none"> <li>• Max prevalence &lt; 1 per 10,000</li> <li>• Heritage genetic disorders (option)</li> <li>• High unmet needs: Difficulty in diagnosis/ treatment for end-of-life diseases (option)</li> <li>• 197 rare diseases (Feb. '13)</li> </ul>
Designation of OD	<p>The term orphan drugs as used in this Act refers to pharmaceuticals with major indications for <i>prevention, diagnosis, and treatment</i></p> <ul style="list-style-type: none"> <li>• Pharmaceuticals (x 79) (Feb. Mar. '13)</li> </ul> <p>(50 orphan drugs specific for rare diseases; 29 drugs used for rare diseases) (2013/2)</p>
<b>Market exclusivity</b>	<b>10 year</b>
Tax credits	Reduction for clinical studies
TFDA assistance	<ul style="list-style-type: none"> <li>• TFDA fee reduction for marketing authorization applications, inspections and post-authorization activities</li> <li>• <b>Fast track</b>: only 2 meeting in 2009, Expected to be better in the future</li> </ul>
Early access (special import)	NHIA orphan drug payment (<0.5~1 M NTD/ mth) before license granted: compassionate use/ nominative base of patients once either FDA/ EMEA approval

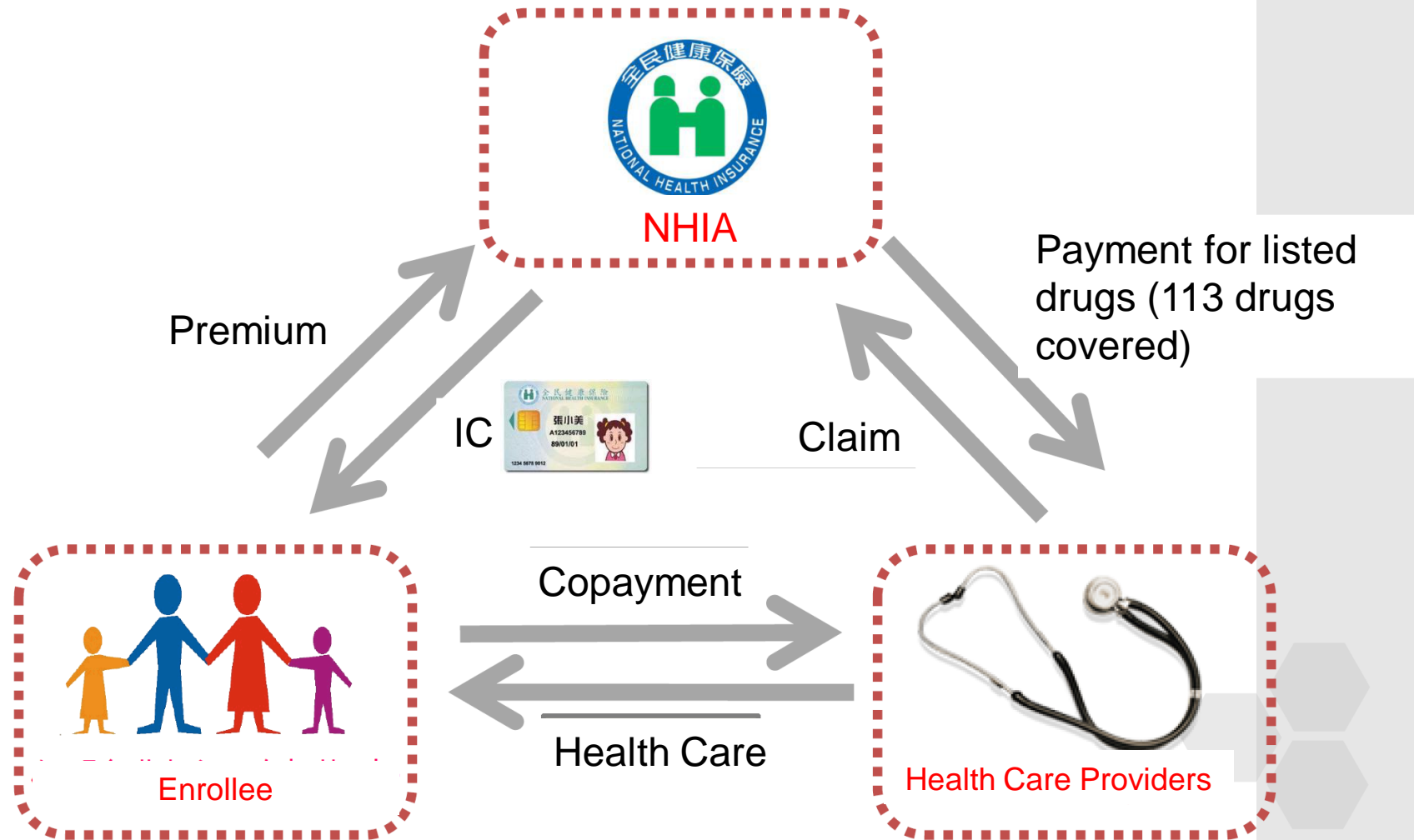


# Outlines

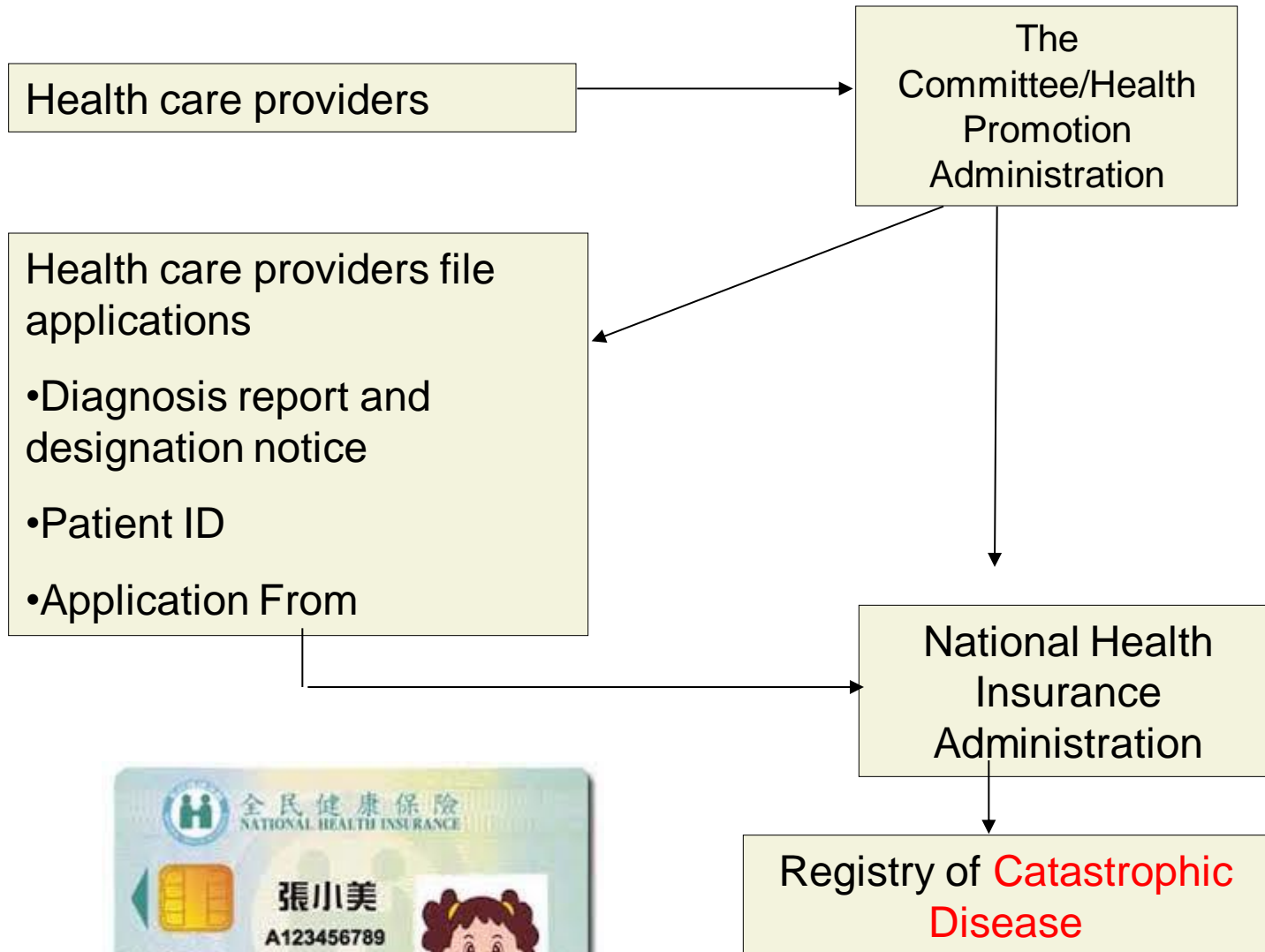
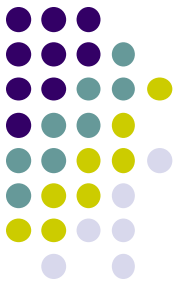
- Regulations of Rare Diseases and Orphan Drugs in Taiwan
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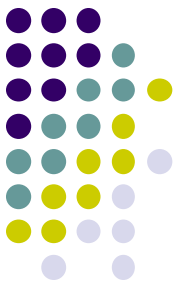


# Health Care System Under NHI



# Patients: Registry of Catastrophic Diseases

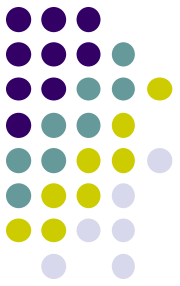




# Protections of patients with rare diseases

- **Catastrophic disease (category #31):** No copayment or any cost-sharing requirements for health care covered by NHI (Article 36, NHIA)
- **An earmarked budget:** the medical expenditure for rare diseases is not regulated by the global budget of NHI (cap ceiling) payment system.
- **Subsidy** from Health Promotion Administration (HPA, MHW) for the health expenditure not covered by NHI (Article 33, RDCODA)
  - Ceiling: 80% of the expense
  - Poverty: 100%

# Orphan Drugs to Health Care System under National Health Insurance



## Designation

- **Legislation:** Rare Disease Control and Orphan Drugs Act
- **Competent health authority:** HPA, MHW
- **Technical Review:** Rare Disease and Rare Disease Drugs Review Committee (HPA)

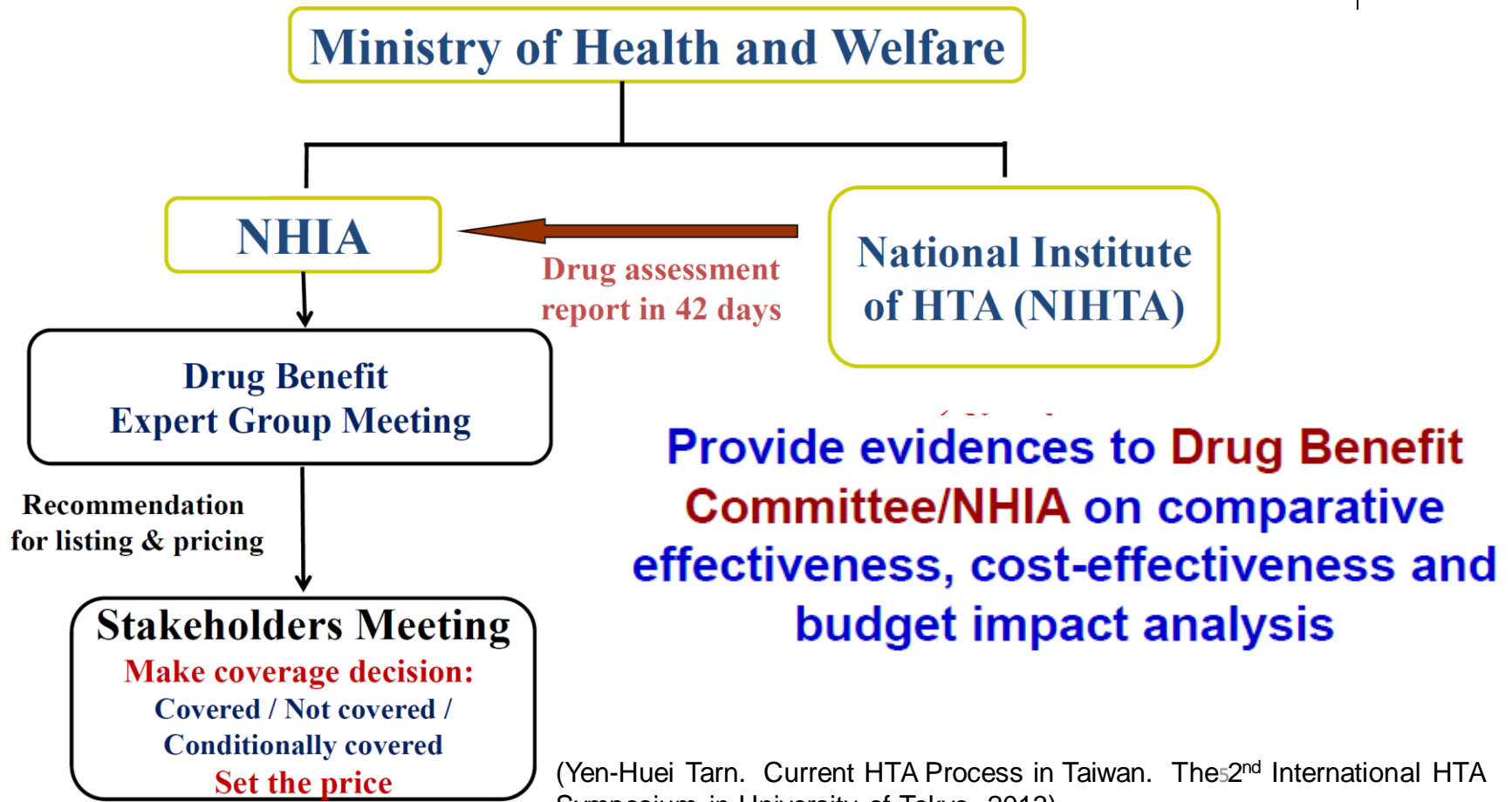
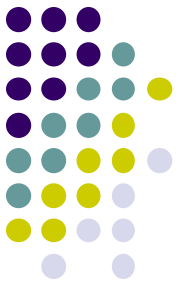
## Market approval

- **Legislation:** Pharmaceutical Affairs Laws
- **Competent health authority:** Taiwan FDA (TFDA), MHW
- **Appraisal:** Drug Advisory Committee, TFDA, MHW

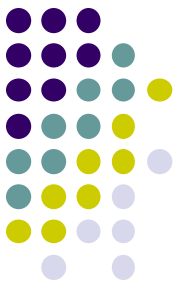
## Listing and pricing under NHI

- **Legislation:** National Health Insurance Act
- **Competent health authority:** NHIA, MHW
- **Assessment:** HTA/CDE
- **Appraisal:** Stakeholders Meeting

# Drugs Listing and Pricing of Pharmaceutical under NHI

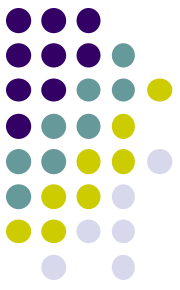


(Yen-Huei Tarn. Current HTA Process in Taiwan. The 2<sup>nd</sup> International HTA Symposium in University of Tokyo, 2013)



# Listing and Pricing of New Drug under NHI

Classification	Definition	Pricing
<b>Category 1 ND</b> (Breakthrough innovative product)	Via head-to-head comparison or indirect comparison indicates substantial improvement of the therapeutic value	<ul style="list-style-type: none"><li>• <b>Median price</b> of international ten ref. countries</li><li>• Efficacy and safety clinical trial in Taiwan, <b>add 10%</b>.</li></ul>
<b>Category 2 ND</b>	<b>Category 2A</b> : moderate improvement in comparison with the best comparator <b>Category 2B</b> : Similar effectiveness in comparison with the best comparator	<ul style="list-style-type: none"><li>• median of prices in ten international countries is the ceiling price</li><li>• Have efficacy and safety clinical trial in Taiwan, <b>+10%</b>.</li><li>• <b>Have PE study in Taiwan, + &lt;=10%</b></li><li>• <b>methods</b> : the lowest of the international ten, prices at the original country, international price ratio, etc.</li></ul>



# Pricing for Orphan Drugs

Reference to the international price of the drug or similar items:

- Monthly amount less than NT\$ 500,000: A-10 median plus 20% as ceiling price
- Monthly amount between NT\$ 500,000 to NT\$ 1 million: A-10 median plus 10% as ceiling price
- Monthly amount higher than NT\$ 1 million: A-10 median as ceiling price

Based on the product cost:

- Imported product based on import cost (including transportation, storage, custom duties, clearance fee and insurance) plus 25% as ceiling price
- Local manufactured product base the manufacture cost (exclude research cost) plus 25% as ceiling price

# NHI Reimbursement for Rare Diseases and Orphan Drugs



Unit: million USD

year	patient	growth %	Medical care (\$)	growth %	Total drug (\$)	Orphan drugs (earmarked\$)	growth %
2008	6,681	--	65	--	47	43	
2009	7,368	10.3%	74	12.5%	54	48	12%
2010	7,884	7.0%	82	11.2%	61	55	15%
2011	8,465	7.4%	96	17.1%	73	66	20%
2012	9,056	7.0%	116	20.8%	92	82 96 (2013)	26% (16%)

**+35%**

**+78%**

**+95%**

**+90%**

(Exchange rate of the Taiwanese Dollar against US\$ = 31.642 in 2010)





# Top 10 Orphan Drug Expenditure

(unit: million USD)

Rare Diseases	2008		2009		2010		2011		2012	
	visits	Orphan drugs (M\$)	visits	Orphan drugs (M\$)	visits	Orphan drugs (M\$)	visit	Orphan drugs (M\$)	visit	Orphan drugs (M\$)
Fabry Disease	20	5.03	31	6.45	61	8.28	66	16.28	84	22.95
Pompe disease	26	6.80	33	8.25	37	9.51	45	10.87	48	12.96
Sanfilippo Syndrome	5	2.56	9	3.89	9	4.93	17	8.09	17	8.91
Primary Pulmonary Arterial Hypertension	149	4.27	171	4.87	179	5.31	215	6.38	223	8.22
Gaucher disease	37	6.61	20	4.84	21	5.63	43	2.37	22	7.24
Mucopolysaccharides (type 6)	9	4.84	9	5.12	9	5.15	10	6.07	10	6.54
Multiple Sclerosis	332	3.54	350	4.01	387	4.46	423	4.71	492	5.21
Niemann-Pick disease			7	0.47	9	1.11	8	1.45	9	1.55
Mucopolysaccharidoses (type 1)	10	1.58	5	1.36	4	1.33	4	1.17	3	1.04
Porphyria	25	0.44	23	0.63	27	0.82	26	0.88	31	0.98

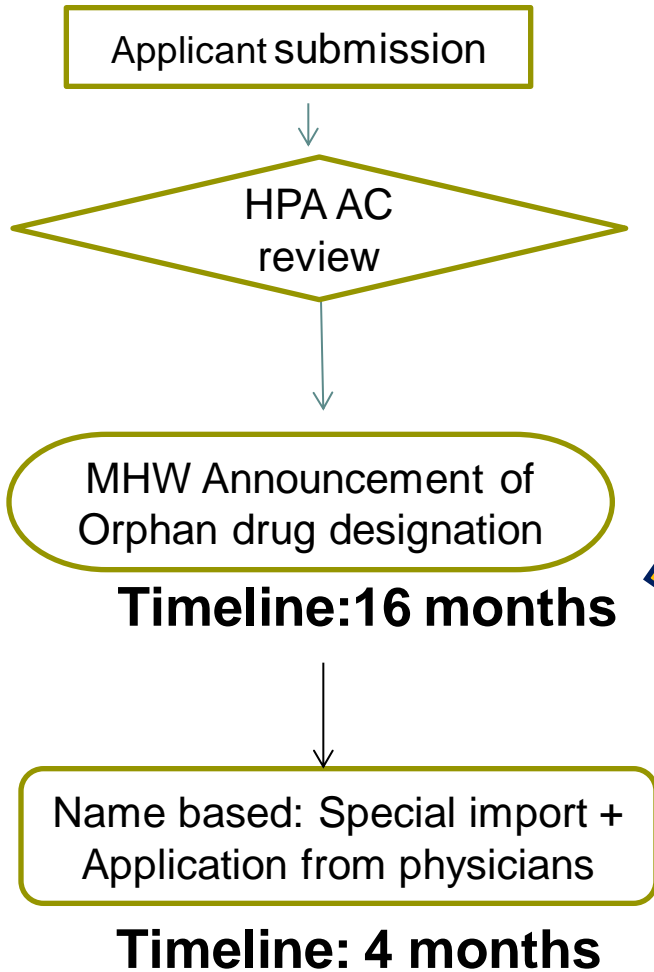
(Exchange rate of the Taiwanese Dollar against US\$ = 31.642 in 2010)

# Orphan Drug Designation, Registration and Listing

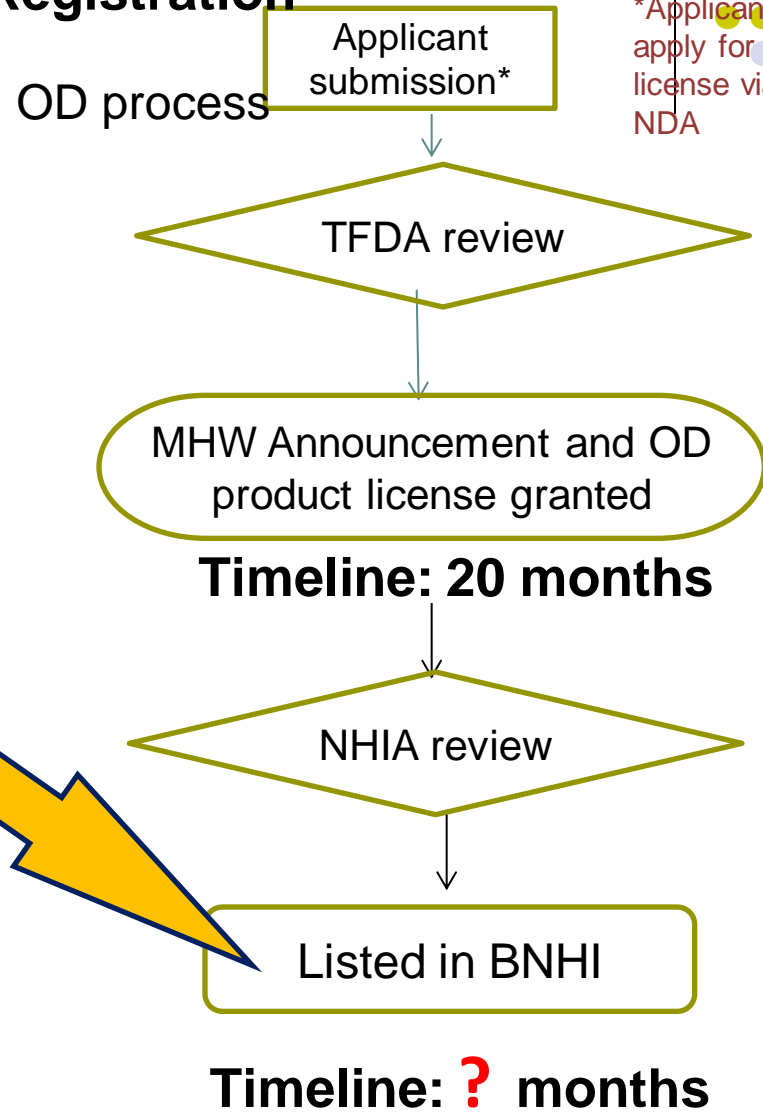
*parallel submission of designation and registration is acceptable*



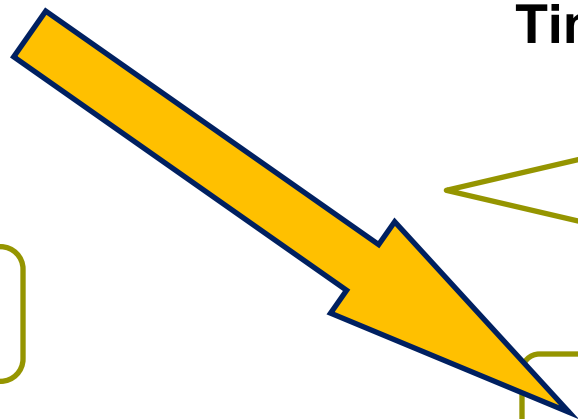
## Designation



## Registration

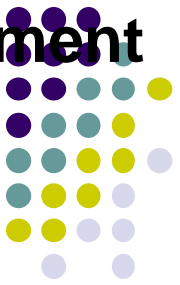


\*Applicant can apply for regular license via normal NDA



# Orphan Drug Designation, Registration and Reimbursement

*parallel submission of designation and registration is acceptable*



## Designation

## Registration

Name based: Special import +  
Application from physicians

Listed in BNHI

**Timeline: 4 months**

**Timeline: ? months**

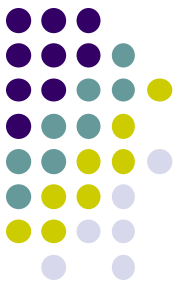
2001-2012

795 new drugs applying for listing

48 orphan drugs

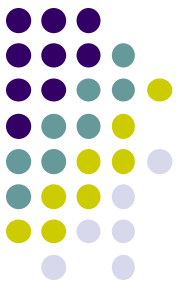
44 listing (91.7% vs. 83% of the other drugs)

Time lag of NHI listing: median 10.69 months vs.  
11.83 months.



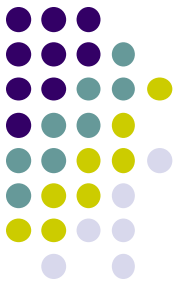
## Key Takeaways”

- Patients with rare diseases are under the protection of [Rare Disease Control and Orphan Drug Act and NHI](#): access to essential drugs, no copayment, financial aid. However, the time lag is still a big concern.
- [Rare Diseases and Rare Disease Drugs Review Committee](#): 197 rare diseases (2013/2), 79 drugs (50 orphan drugs specific for rare diseases; 29 drug used for rare diseases) (2013/2)
- [National Health Insurance](#): 97 catastrophic diseases; 113 drugs covered by NHI (with or without drug permit licenses)
- Orphan drugs hold advantages of market exclusivity for 10 years
- HTA evidence is not the critical concern in the current appraisal of new drug (orphan drugs)
- Orphan drugs can bypass the designation and NHI appraisal for listing and pricing to get into health care market.
- Fast growth of orphan drug expense.

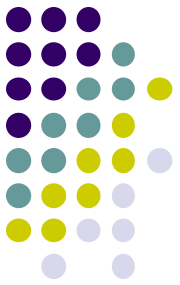


# Next Steps

- Loopholes or incentives of not filing for registration or NHI listing: review and integrate the systems of market approval, NHI listing and earmarked budget policy.
- Efficiency of orphan drug provision: assess the time lags of adoption, designation, and listing.
- Dilemma between the equality of health right and the fairness of resource allocation: welfare system and national health insurance system



Special thanks to  
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National Health Insurance Administration  
in making available of some slides  
in this presentation



Thank you  
**ywtsai@ym.edu.tw**