Development of International Orphan Drug Policies

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Emmanuelle Lecomte
VP, Head International Regulatory strategy

Our purpose
We enable people with life-altering conditions to lead better lives.

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Political frameworks for treatment of rare diseases and development of orphan drugs

- Rare diseases are recognised as an important public health issue and a challenge to medical care.
- Increasing number of identified rare diseases make these a priority for policymakers, researchers, legislators, and health care professionals in many countries
- Important challenge is the lack of qualitative information and a networking system to facilitate interaction among all stakeholders.
- Specific legislation to encourage research of rare diseases and development of orphan drugs has been enacted.
- In recent years, much progress has been made in some parts of the world with the initiation of draft regulatory framework, implementation of legislation and regulations both on rare diseases and orphan drugs.

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Political frameworks for treatment of rare diseases and development of orphan drugs

- Remains a lot of gaps and expectations in many countries to ensure substantial improvement in the availability of orphan treatment to patients

- Main incentives are marketing exclusivity, the setting up of tax credits and financial subsidies for research; regulatory support to development and marketing approval (e.g fast track approval, fee waivers, and protocol assistance)

- comparative analysis of the regulation worldwide to identify the challenges to and future perspectives on promoting research on rare diseases and development of orphan drugs
  - ✓ Definition and classification of rare diseases (life threatening and debilitating illness+prevalence being the main difference)
  - ✓ Incentives for orphan drug research and development
  - ✓ Remaining challenges and expected improvement

- cover the latest political initiatives and ongoing discussion where orphan disease is part of government priorities.

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Orphan Policies in main regions

	USA	Japan	Australia	UE
Legal framework	Orphan Drug Act **(1983)**	Orphan Drug Regulation **(1993)**	Orphan Drug Policy Therapeutic Goods Act and Regulations **(1998)**	Regulation (CE) N°141/2000 **(2000)**
Authorities involved	FDA / OOPD	MHLW/OPSR (Orphan Drug Division)	TGA	EMA / COMP
Prevalence of the disease justifying the orphan status	7,5/10 000	4/10 000	1,2/10 000 <=2,000	5/10 000
Marketing exclusivity	7 years	10 years	5 years (for new molecular entities)	10 years
Tax credit	yes : 50% for clinical studies	yes : 6% for any type of study + limited to 10% of the company's corporation tax	No	managed by the member states
Grants for research	Programmes of NIH and others	Governmental funds	No	'FP7' + national measures
Accelerated MA procedure	Yes	Yes	Yes	Yes
Challenges /required update	Extension of ME	Legislation has room for interpretation. Clarification on requirement of clinically superior data expected	Extension of ME and incentives offered for the development of orphan medicinal products	No similar and limitted tax credit in MS. Full implementation of national plans

Orphan Policies in Asia

	Singapore	South Korea	Taiwan
Legal framework	Medicines Act (Chapter 176, Section 9: (Orphan Drugs Exemption) **(1991)**	MFDS Notification No. 2013/222: Provision on Designation of Orphan Drugs **(1998)** Orphan Drug Provision of designation 2013	Rare Disease Control and Orphan Drug Act **(2000)**
Authorities involved	MoH	MFDS/KFDA	TFDA/DOH
Prevalence of the disease justifying the orphan status	less than 20,000	less than 20,000	1/10 000
Marketing exclusivity	No	No 6 years for data reexamination for NCE	10 years
Tax credit	No	No	No
Grants for research	No	Very few precedent of national funded research programs	Financial subsidies for local R&D for orphan drugs
Accelerated marketing procedure	Yes	Yes	Yes
Challenges /expected updates	Clarification on the OD definition for consistency across designation More incentives, such as marketing exclusivity or subsidies in the orphan drug policy	Long designation process up to 9 months	Local clinical data sometimes required No exemption of manufacturing sites registration which can significantly impact the registration timeline

Orphan Policies in Russia, Ukraine and Kazakhstan

	Russia	Ukraine	Kazakhstan
Legal framework	Federal Law N 323-FZ **(2011)** refers to rare diseases +list of 24 diseases (2013)	Regulation Order of the MoH N°3 **(2013)**	Order of the MoH N°735 **(2009)**
Authorities involved	Ministry of Health (MoH) and Roszdravnadzor (RZN) (Registration and Review expertise)	MoH state expert center	MOH National Center for Medicines, Medical Devices, and Medical equipment expertise
Prevalence of the disease (per 10,000 individuals), justifying the orphan status	<10 per 100,000 population	<5 in 10'000 persons	No more than 10'000 individuals
Marketing exclusivity	No	No	No
Tax credit	No	No	No
Grants for research	No	.No	Inclusion of a product on the List of Orphan Drugs allow government to allocate funds for state procurement of the product
Accelerated marketing procedure	No	Yes 90 D	No
Challenges /expected updates	Lack of clarity about orphan drug registration process. Next expected draft amendments are currently being discussed. Proposals for ME, Details in the definition of orphan drugs Any accelerated registration for orphan drugs, possibility of recognition of results of preclinical and clinical trials performed outside Russia	More incentives including ME	More incentives including ME and accelerated approval

CANADA:
Proposed Regulatory Framework for OD under Food and Drugs Act

Objective:

- Health Canada also announced in 2012 plans to develop a framework for orphan medicinal products
- To include the development, designation, authorisation and monitoring of OD and foster innovation and research in Canada.
- Align Canadian regulatory activities with international partners.
- Proposal suggests a Life-Cycle approach – from designation to post-approval.

OD criterias

- Prevalence not more than 5 in 10,000 persons
- drug is intended for the diagnosis, treatment, mitigation or prevention of a life-threatening, seriously debilitating, or serious and chronic disease
- or condition and is necessary because there is no existing therapy for the rare disease; or, if there is an existing therapy for the rare disease, the drug would provide substantial therapeutic benefit for the patients

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CANADA:
Proposed Regulatory Framework for OD under Food and Drugs Act

Incentives

- Scientific and clinical protocol advice
- Priority review
- Fee reductions for small to medium companies

Challenges

- No specific market exclusivity for orphan but current data protection 8 years system, +6 months for pediatric studies
- No Tax incentives

Timelines:

- Initial Draft Discussion Document was released publicly on December 13, 2013 for review and comment . Final revisions ongoing and it is expected to be published by Q3 2014.

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New Zealand

- A proposal has been submitted to the National Health Committee for the development of a rare diseases action plan for New Zealand.

- Orphan Drug Policy has been included as one of the TGA/Medsafe Joint Agency (ANZTPA) Harmonization Activities:
  - Primary goal is to provide an appropriate mechanism to facilitate access to safe and effective orphan drugs.
  - Secondary goal is to minimize the likelihood that the orphan drug process could be misused for products that are commercially viable.

- The implementation pathway for orphan drugs that is reflective of the approved policy decision is anticipated by Q2 2014

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Turkey

- National Draft Guideline for Orphan Medicines issued in 2010, including incentives for the development and registration of orphan drugs. MOH updated the draft guideline in 2013 but did not share information on proposed changes. Publication of the final National Guideline is not expected before the end of 2014.

- The limit for the definition of a rare disease will be within the EU-defined limit of no more than 5 in 10’000 individuals.

- Only 30% of drugs for rare diseases have marketing authorization in Turkey, with another 30% imported into Turkey via Turkish Pharmacists’ Association (TEB), subject to approval by the Ministry of Health on a case-by-case basis. The remaining 40% of these drugs are not available in Turkey.

- Pricing incentives: Orphans are exempted from the reference pricing policy, MOH different criterias when such a product is indicated for the treatment of diseases for which the etiology is not clearly defined and diseases which affect no more than 1 in 100’000 individuals.

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Brazil

- No current regulation related to registration of orphan drug products. However, a possibility of request expedite review for drugs designated to treat rare diseases (Resolution 28/2007).
- First Ibero-American Congress on Rare Diseases (CIADR), organised by the Associação MariaVitoria (AMAVI) on 25 September 2013 in Brasília
- Minister of Health committed to the creation of the Technical Group for Rare Diseases (finalised during the event of World Rare Disease Day in February 2012). AMAVI promised to seek the necessary actions in the future that will contribute to integration of Brazil in more advanced discussions on rare diseases.
- In January 2014, the MoH issued a law establishing assistance and guidance for patients with rare disease in the Public Health System (PHS) (P. 199/2014).

  This Order establishes the Brazilian Rare Disease National Policy (Health Policy for the Integrated Attention to People with Orphan Diseases), to assure people with orphan diseases be properly diagnosed and treated as soon as possible.

  There is not yet any reference of treatment for each disease, which should be included case by case.

Mexico

- No official procedure for obtaining registration of orphan drugs in Mexico.
- In 2010 an agreement was signed between the representatives of the Pharmaceutical Industry and the COFEPRIS, with the purpose of establishing the necessary requirements for the allocation of orphan product status, but the regulation has not changed yet further to the agreement.
- General Law of Health published in 2012 states orphan definition: "*Orphan medicines destined to the prevention, the diagnosis or the treatment of rare diseases, are those that have a prevalence of not more than 5 people by each 10 thousand inhabitants*".
- A document called "Letter of recognition" (*Oficio de reconocimiento)* for the orphan product is currently issued (different to a Marketing Authorization). This import application is an emergent measurement till the modification to the Regulation of Health Sector Products is published with requirements for registration of Orphan products.

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Argentina

- 29 June 2011 publication of rare diseases national law establishes the definition and the requirements to market orphan medicinal products (*enfermedades poco frecuentes).* A disease will be considered as rare when it affects less than 1 people in 2 000.

- Orphan application will be evaluated by a specific Commission to Assign and Evaluate the Medicinal products "Under Special Conditions"

- A central multidisciplinary committee is to be created in order to coordinate these actions and will include patient organisations.

- A national registry of patients and neonatal screening programme will be elaborated, along with educational, social and support activities that are all mentioned in the law.

- Significant milestones have been taken but all of these activities need governance and must be coordinated before being able to measure its effect.

Peru & Columbia

Peru

- first national law referring to patients with rare diseases was enacted in 2011 (Law 29698). It promotes treatments for rare conditions and includes reference to a national strategy (diagnostics, surveillance, prevention, care, and rehabilitation).
- No precise definition based on prevalence
- No regulation on orphan drug

Columbia

- An Orphan Disease Law was ratified in July 2010.
- Second National Forum of Orphan Diseases in the Health System of Colombia was held in 2011.
- No precise definition based on prevalence
- No regulation on orphan drug

China

- Recognition of the concept of rare diseases part of Drug Registration Regulation in 1999, but rare diseases and orphan drug have not been defined by legislation
- A definition of rare diseases was proposed by a group of medical experts on 17 May 2010. This definition is of prevalent in fewer than 1/500,000 or has a neonatal morbidity of fewer than 1/10,000. An initial list of 23 rare diseases has been proposed.
- China neither has established “orphan drug program” nor special funding for orphan drug research.
- The launch of the Chinese Rare Disease Research Consortium (CRDRC) was formally announced on 14 September 2013, during the 1st Chinese Rare Disease Symposium to establish a national rare disease registry and provide access to harmonized data.
- Current legislation only sets forth general criteria for accelerated approval and possible CT exemption for a category of innovative drugs with unmet therapeutic needs, such as those for rare diseases, but detailed rules have yet to be implemented and further incentives have not been proposed until now.

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The Future of ‘Orphan Drug’: Increase awareness

- Governments should regard rare diseases as a public health priority and take action to put in place:
  - ✓ legislation to confirm the definition and classification of rare diseases,
  - ✓ assembling accurate epidemiological data on rare diseases,
  - ✓ define orphan drug criteria in homogeneous way
  - ✓ provide attractive incentives to encourage industry to develop orphan drugs
  - ✓ appropriate support system to ensure access to orphan drugs,
  - ✓ promote international cooperation in research on rare diseases and development of orphan drugs

- Patient Association and various organisations are creating awareness on rare diseases and are also pushing governments in bringing legislation acts for better quality of life

- It can be expected that the orphan drug market growth will remain positive as more and more governments are taking action to promote this sector, especially in Asia.

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The Future of ‘Orphan Drug’: An International Dimension

- In recent years, much progress has been made in EU, US and some parts of Asia, including Australia, Japan, South Korea, and Taiwan, with the enactment of legislation and accompanying regulation.
- Some countries are actively promoting the regulation of rare diseases and orphan drugs but still lags far behind above mention countries with orphan drug legislation.
- With more countries adopting similar legislation, it can be expected that innovative drugs to treat rare disease will increase.
- There is still a lot of challenges including rare diseases awareness, need for more partnership and work on future perspectives to give access to all patients around the globe

Thank you!

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