# Robust regulatory systems

***A critical enabler of local pharmaceutical development in Africa***

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# OUTLINE

- What is a robust regulatory system?
- What can a robust reg system deliver for pharma manufacturing?
- Examples - AMRH, Brazil, and Mexico

 

# WHAT IS A REGULATORY SYSTEM?

- A Regulatory System consists, of all organizations, people and actions whose primary intend is to ensure access to essential medicines and other health products of assured quality, safety and efficacy or performance. A regulatory system is therefore more than the pyramid or the institutional arrangements of public institutions that deliver regulatory services but include private providers such as manufacturers or distributors (The Global Fund, 2019)

- A Regulatory system is that specialized part of the health system codified in law to provide oversight for the development, manufacture, storage, distribution (including import export) and use of all medical products, as well as the external actors and networks that facilitate the actions of the legally mandated regulatory institutions (Mukanga, 2020)

 

# WHAT IS A ROBUST REGULATORY SYSTEM?

- Effective, efficient, predictable and transparent approach is critically important in ensuring the quality, safety and efficacy of health products in an increasingly complex global environment

- Recognizes that the regulatory agency is not the only player in the regulatory system, and cannot deliver on the access goal on their own – manufacturer, distributor, local outlets, patients/caregivers

- The regulatory agencies while keeping their oversight role, must work hand in hand with manufacturers, academia, health providers to advance innovation, research and development, and improvement in quality systems

 

# WHAT IS ACCESS?

- What is access? Not just availability – includes affordability, physically accessible, acceptable, informed provider/user



For free is not cheap enough

J. Jannin, WHO

Pictures courtesy of the Swiss TPHI

 

# ROLE OF INDUSTRY REGULATORY AFFAIRS TEAMS

**Table 2.1 Global regulatory affairs**

| Product Development Areas HQ & Regional | CMC, Compliance, Conformance | Policy & Regulatory Intelligence | Promotion & Advertisement | Regulatory Submissions Management | Product Labeling |
|---|---|---|---|---|---|
| • Develop and lead global regulatory strategy<br>• Coordinate with regional regulatory teams for global strategy<br>• Liaison with regulatory authorities<br>• Review regulatory submissions | • Liaise with BOH's on CMC issues<br>• Develop regulatory strategy for manufacturing plans/process<br>• Support site and facility inspections<br>• Conformance<br>• Compliance | • Monitoring for emerging trends, policies, regulations and guidelines<br>• Analyze and communicate<br>• Regulatory intelligence<br>• External industry participation | • Generation of competitive and compliant promotional materials<br>• Regulatory review of promotional copies and publication<br>• Primary liaison to regulatory agency on promotions and advertising | • Electronic publishing and compilation<br>• Document standards<br>• Electronic CTD submissions<br>• Technology management<br>• Assembly of submissions | • Develop product labeling<br>• Ensure compliance and accuracy of product label |
| STRATEGY | | | | | |
| LIAISON | | | | | |
| GATEKEEPER | | | | | |

Source: Ukwu H, Global Regulatory systems A Strategic Primer for Biopharmaceutical Product Development and Registration

# WHAT CAN A ROBUST REG SYSTEM DELIVER FOR PHARMA MANUFACTURING?

- **Access to medicines of assured quality, safety and efficacy by patients** is at the center of a robust regulatory system
- Standards for quality, safe, efficacy – Well regulated markets encourage good companies to flourish
- Promoting use of generic names can have a huge impact on competitiveness of the local industry, and lower prices
- Drive Innovation – scientific advice sessions to align on development program; policies on CTs in-country or region; policy coherence on what needs to be produced locally overtime
- Proactive linkages with other key actors –
  - HTA, procurement agencies to help drive quality considerations
  - Providers to understand product performance, **define unmet need**

 

# ROBUST REGULATORY SYSTEMS - A CRITICAL ENABLER OF LOCAL PHARMACEUTICAL DEVELOPMENT IN AFRICA

## THE AMRH EXPERIENCE

# AMRH

- Benefits of harmonization of technical requirements and processes across the region

- Regional work-sharing, and opportunities to leverage these to cover regional markets
  - Promoting reliance, efficiency and predictability
  - Cutting regulatory and overall timelines
  - Next step is to link these to procurement – regional PQ listing

- Capacity building of regulators and industry
  - Practical talent building natural next step; Dalberg helping us do a landscape on this

 

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## THE BRAZIL EXPERIENCE

**Reforming pharmaceutical regulation: A case study of generic drugs in Brazil**

**Elize M da Fonseca**

Policy and Society Journal, Pages 65-76 | Published online: 03 Mar 2017

# BRAZIL – INN MORE PRONOUNCED THAN BRAND NAME

- Executive issued a presidential decree (793/1993) introducing generic drugs – The font size of brand name could not exceed 1/3 of the font size of the INN; drug retailers should present a list of generic medicine names; and all drugs prescribed and procured by the National Health System should use the generic name

- This matters a great deal for company marketing strategies and costs. It was then agreed that, in the label of innovator products, the trademark would be displayed in a higher font size and the INN would come right below, with a reduction of 50% compared to the brand name. **On the other hand, all products registered as generic drug could only be commercialised by its INN**

- In 1996, under the administration of Fernando Henrique Cardoso, that Congress approved the IP law, assuring patent protection of pharmaceutical products and processes (Law 92879/1996)

- Impact: local manufacturers share of generic drug market increased, prices dropped

 

# BRAZIL - REQUIREMENTS FOR BIO-EQUIVALENCE

- Requirement for BE testing for generic (legislation in 1999). The medicine's reputation and quality are bound together into the regulatory concept of BE (cf. Carpenter & Tobbell, 2011).
  - While initially opposed, now local generics companies use their BE data to make the case their quality is just as good as the innovator

- Impact: Brazilian pharmaceutical industries account for 88% of the domestic generic drugs market. In 1999, the local pharmaceutical firm EMS was 29th in the ranking of pharmaceutical industries in Brazil, and in less than 10 years it became the market leader in the generic segment

- Debate on dropping BE requirements continues

 

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## THE MEXICO EXPERIENCE

Pen˜alosa, Cepeda, Garza, & Lumpkin
Optimized Medical Product Regulation in Mexico: A Win-Win for Public and Economic Health
Therapeutic Innovation & Regulatory Science 1-7 (2017)

# REFORMS

- Elimination of Requirement for in-Country Manufacturing

- Clinical trials – By requiring a percentage of the test population in multicenter trials be Mexican, COFEPRIS could discard the previous requirement for a certification of marketing in another country prior to acceptance of a marketing application in Mexico. This facilitated quicker submissions of marketing applications with better information about use of the product in the Mexican context

- Use of an online checklist of the dossier requirements to mitigate the submission of incomplete dossiers

- Reliance on information and reports from MAs issued by reference regulatory agencies for both medicines and medical devices

 

# IMPACT

- Prior to 2011, companies requesting marketing authorization of medicines were required to build and operate a manufacturing plant in Mexico. However, in March 2011 this requirement was repealed, resulting in 614 products registrations, which would not have been authorized if the in-country manufacturing site requirement was still in place

- Clinical trial reform - an estimated USD 100 million in new technological investments occurred in 1 year. In 2013, the Mexican pharmaceutical industry registered 86,783 direct jobs

- COFEPRIS accepts certificates of compliance with GMP issued by Australia, Brazil, Canada, Europe, Japan, and the US. These redundant inspections alone has saved COFEPRIS 200 million USD annually

 

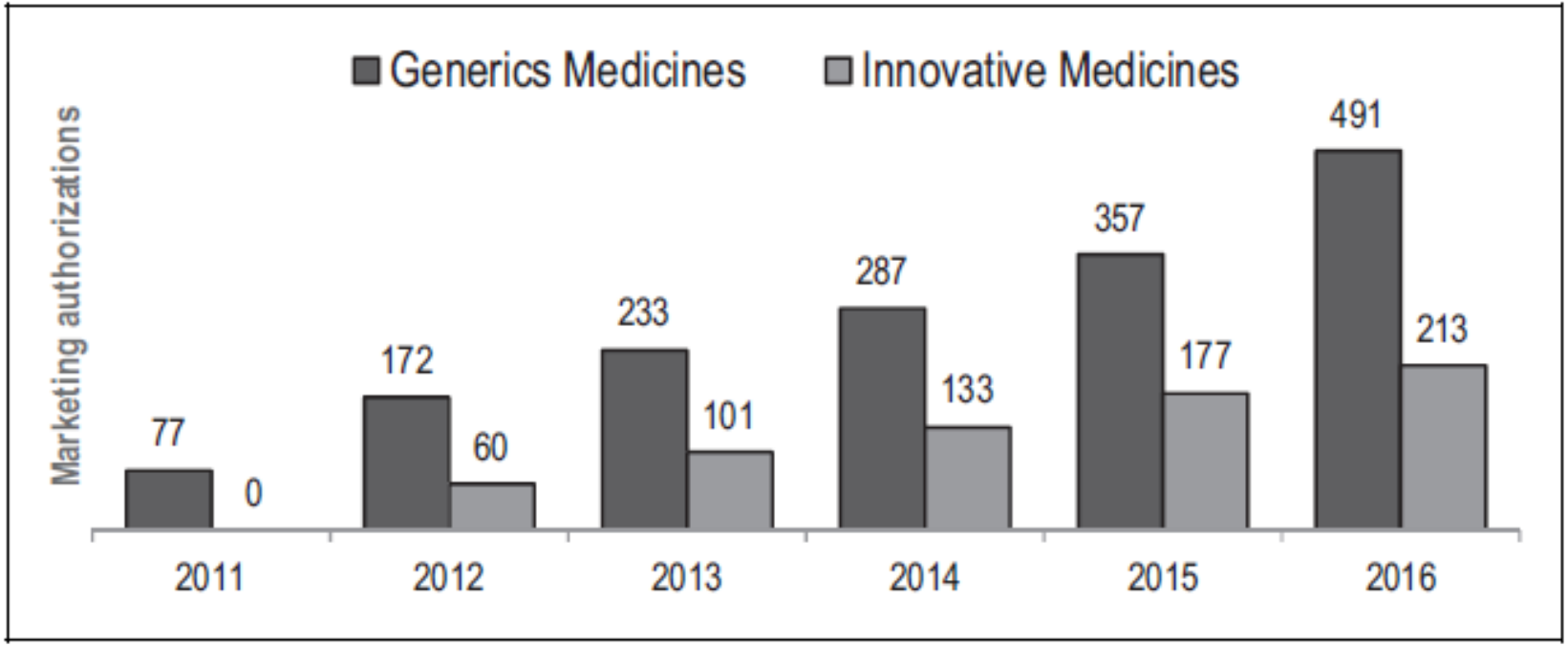


**Figure 1.** Cumulative registrations for new innovative and generic medicines in Mexico.

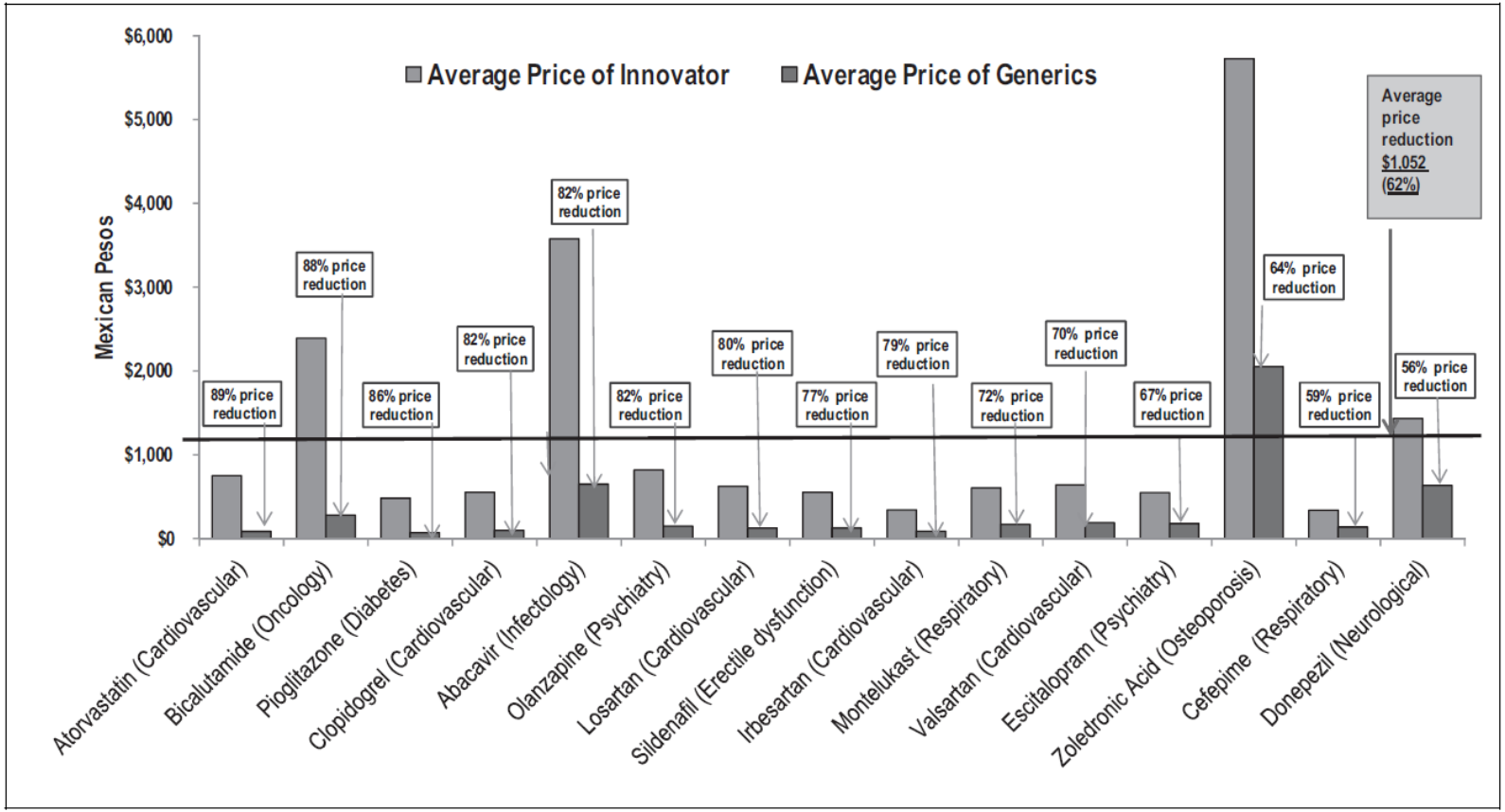


**Figure 2.** Reduction in the market price with introduction of generic versions of these medicines in Mexico.


THANY YOU