Medicines Regulation, Regulatory Harmonization, Global Initiatives

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Presentation Outline

• The World Bank’s mandate and strategy
• Good governance and regulation for better health
• Challenges for medicines regulators
• Roadmap for better “division of labor”
• Strengthening regulators in Low Income Countries (LICs)
How the World Bank operates

Overall goal: reduce poverty, increase equity

Financing (IDA, subsidized) → Low-Income Countries

Research, analytics, policy advice → Middle-Income Countries

Financing (market rates) → Middle-Income Countries
Focus on Health Systems

Governance (laws, regulations, standards)

Human Resources

Access to Quality Health Care

Financing and payment systems

Medicines, supplies, infrastructure, technology
The Importance of Regulation

• Indispensable for proper functioning of economies and societies
• Underpin markets, protect the rights and safety of citizens and ensure delivery of public goods and services
• Regulatory policy ensures regulations support economic growth and development, social welfare, environmental sustainability, and rule of law
• Differences in services regulation across countries constitute trade restrictions, standards convergence or international standards can lead to increased services trade

Source: OECD 2011, Regulatory Policy and Governance: Supporting Economic Growth and Serving the Public Interest, OECD Publishing
### Attributes of Effective Regulatory Systems

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Meaning</th>
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</thead>
<tbody>
<tr>
<td>Responsive</td>
<td>Respond rapidly to a crisis Promptly modify policies</td>
</tr>
<tr>
<td>Outcome Oriented</td>
<td>Focus on product safety outcomes</td>
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<tr>
<td>Predictable</td>
<td>Clear framework guaranteeing that decisions are neither arbitrary nor capricious</td>
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<tr>
<td>Proportional (Risk-based)</td>
<td>Allocates control based on threat to public health Products with similar risks regulated similarly</td>
</tr>
<tr>
<td>Independent</td>
<td>Independent of the political process</td>
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</table>

Missing: Market-oriented – ensure conditions that make market attractive a level playing field?

*Source: Adapted from Riviere et Al. Ensuring Safe Foods and Medical Products Through Stronger Regulatory Systems Abroad, Institute of Medicine*
The Case for Medicines Regulation

Strengthening governance, regulations and accountability in the pharmaceutical sector

• Improves patient access to safe, effective, and good quality medicines
• Increases citizen confidence in health system
• Creates stable conditions for pharmaceutical sector trade and contributes to economic development
Challenges for Medicines Regulators

- Growing demands from risk-averse societies
- Pressure from industry
- Growing body of knowledge
- Globalization of trade
- Gaps in export regulation
- Gaps in standards and enforcement
- Budget limitations
- Hiring and retaining qualified staff

Medicines Regulator
## Links between Enforcement of Drug Regulation and Access to Medicines

### Area of Regulatory Weakness | Potential Systemic Effect
--- | ---
Circulation of low-quality drugs and inconsistent enforcement of manufacturing standards | Lack of confidence in drug quality and preference for more expensive branded or imported drugs
Weak licensing process for businesses and products | Fewer products on the market, potential procurement delays in the launch of new drugs
Inadequate reporting of adverse events and inadequate recall mechanism | Reliance on adverse event data from developed countries, with potentially disastrous health impacts
Sale of prescription drugs over the counter | Risk of irrational use of a drug or use in cases where the drug is contraindicated, with negative impacts on individual’s health; drug resistance
Inadequate information provided with drugs | Risk of irrational use of a drug or use in cases where the drug is contraindicated, with negative impacts on individual’s health; drug resistance
Unethical marketing practices | Overuse and inappropriate use of certain drugs and skewed advice to committees that develop drug lists for institutions or health insurance
Lack of oversight for clinical trials | Reduction of in-country clinical trials by drug companies and trial data that is unacceptable to regulatory authorities; harm to patients

Source: Seiter 2010, *A Practical Approach to Pharmaceutical Policy, World Bank*
The global market reality

<table>
<thead>
<tr>
<th>High Income Countries</th>
<th>Competent “stringent” regulators</th>
<th>Consistent quality of products, small share of illicit drugs</th>
<th>Sufficiently high consumer confidence</th>
<th>Generally good conditions for pharm. Sector businesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Middle Income Countries</td>
<td>Varying strength of regulators</td>
<td>Variations in product quality and share of illicit drugs</td>
<td>Variations in consumer confidence, preference for branded drugs</td>
<td>Generally good conditions for pharm. Sector businesses</td>
</tr>
<tr>
<td>Low Income Countries</td>
<td>Weak, under-resourced regulators</td>
<td>High (double-digit) share of illicit drugs in many countries</td>
<td>Low consumer confidence in public sector systems</td>
<td>Challenges for legitimate businesses, unfair competition</td>
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</table>
• Gates Foundation plans to undertake in-depth study of global medicines regulatory situation
• Boston Consulting Group selected to do the study*, details not yet known
• Outcome likely to impact funding availability from Foundation

*personal information from the Foundation, no official confirmation yet
A Roadmap for More Global Cooperation
Peer-to-Peer Collaboration

• The weakest regulators are the most isolated ones
• Transaction costs: Collaboration requires initially more resources
• A minimum of common standards and terminology is needed for meaningful collaboration
• First step: information sharing
Division of Labor

- Requires common standards, trust, legal agreements
- Typically initiated within a regional economic bloc
- High initial costs
- First step: unilateral adoption of outputs from larger, more competent agencies (e.g. abridged registration procedure)
Global Medicines Regulatory Harmonization (GMRH)

- World Bank administered multi-donor trust fund initiative established in 2011 with an initial contribution of US$ 12.5 million from the Bill & Melinda Gates Foundation.
- Falls under a larger partnership program in the Bank which focuses on Pharmaceutical Governance and Regulation.
- Main objective is to promote the harmonization of medicines regulations as a means to improve access to essential and quality medicines by strengthening governance and regulatory systems of the pharmaceutical sector.
- Partners include WHO and New Partnership for African Development.
- Initial focus on the Africa region: African Medicines Regulatory Harmonization.
Harmonizing registration addresses resource constraints, enabling accelerated product approval and access

How would harmonization impact the registration process?

**Today's current environment**

- ~50 National Medicines Regulatory Authorities (NMRAs) governing drug registration across Africa
- Paperwork, technical requirements, and other registration steps differ across NMRAs
- Manufacturers must invest significant time and effort in each registration, so a limited set of countries are targeted
- No clear timelines for a drug to clear registration and be ready for the marketplace
- Little transparency before or during the process

**A harmonized future environment**

- 9 regional economic communities (RECs) covering the entire African continent
- Common documentation, procedure, and decision-making framework across all RECs
- Low cost to register in each additional country, so coverage is more broad and equitable
- Streamlined process that is faster and easier... starting first with generics
- Clear understanding of the process by all parties involved
Regulatory harmonization contributes over time to many public health and development goals

<table>
<thead>
<tr>
<th></th>
<th>Prevention and treatment of diseases</th>
<th>Enhanced access to new health technologies</th>
<th>Broad economic development in the region</th>
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</thead>
<tbody>
<tr>
<td><strong>Short term</strong></td>
<td>Increased access to generics treating many important diseases</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Intermediate term</strong></td>
<td>Broader, more rapid access to vaccines and other therapies</td>
<td>More efficient launches for vaccines and other PDP products</td>
<td>Level playing field for pharm. industry will stimulate investment</td>
</tr>
<tr>
<td><strong>Long term</strong></td>
<td>Drug quality, safety and efficacy with extension to all regulatory functions</td>
<td>Greater impact of new life-saving technologies</td>
<td>Healthier, more productive workforce</td>
</tr>
</tbody>
</table>
Regional Economic Communities (RECs) in Africa

COMESA
- Libya
- Arab Jamahirya
- Egypt
- Eritrea
- Djibouti
- Ethiopia
- Kenya
- Rwanda
- Seychelles
- Burundi
- Madagascar
- Mauritius
- Réunion

IGAD
- Sudan
- Uganda
- Ethiopia
- Djibouti
- Somalia
- Kenya

UEMOA
- Senegal
- Mali
- Niger
- Benin
- Togo

EAC
- Uganda
- Rwanda
- Burundi
- Kenya
- The Democratic Republic of the Congo
- Zambia
- Zimbabwe
- Swaziland

SADC
- Angola
- Zambia
- Zimbabwe
- Botswana
- Namibia
- South Africa
- Swaziland
- Lesotho

UMA
- Morocco
- Mauritania
- Algeria
- Tunisia
- Libyan Arab Jamahiriya

ECOWAS/WAHO
- Senegal
- Cape Verde
- Gambia
- Guinea-Bissau
- Guinea
- Sierra Leone
- Liberia
- Côte d'Ivoire
- Mali
- Burundi
- Mali
- Niger
- Nigeria
- Benin
- Togo
- Ghana

OCEAC
- Cameroon
- Chad
- Equatorial Guinea
- Gabon
- Congo
Global Medicines Regulatory Harmonization (GMRH) Project Status

- East African Community Project launched in March 2012
- Includes Burundi, Kenya, Rwanda, Tanzania, Uganda, Zanzibar
- Project steering committee for EAC Project has met twice
- 4 Technical Working Groups close to finishing drafting:
  - Medicines Evaluation and Registration
  - Good Manufacturing Practices and Inspection
  - Information Management Systems
  - Quality Management Systems
- Stakeholder consultations beginning early 2013
- Small, exploratory projects planned in other regions (Latin America, Middle East and North Africa, South Asia, South East Asia)
## Asian Pacific Economic Community (APEC)

### Organization | APEC
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**Project** | APEC Harmonization Center
**Objective** | Increase regulatory harmonization among member states with the goal of supporting access to best practices, information exchange and clinical trials that meet international standards and improve quality, safety and efficacy of medical products to enhance health outcomes and facilitate international trade.
**Activities** | Research on harmonization policies and best practices
| Education and training including fellowship programs
| Establish strong information exchange networks
| Maintain online publications
| Develop and disseminate harmonization models
| Support international cooperation
**Where** | Asia Pacific
## ASEAN ACCSQ Pharmaceutical Product Working Group

<table>
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<tr>
<th>Organization</th>
<th>ASEAN</th>
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<tbody>
<tr>
<td><strong>Project</strong></td>
<td>ACCSQ Pharmaceutical Product Working Group</td>
</tr>
<tr>
<td><strong>Objective</strong></td>
<td>The harmonization of pharmaceutical regulations to facilitate the goals of the ASEAN Free Trade Area, particularly eliminating technical barriers to trade, without compromising the quality or safety of medicines.</td>
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</table>
| **Activities** | GMP Training  
Implementation of common technical requirements  
Mutual recognition agreements for GMP Inspections  
Shared postmarket surveillance information  
Vaccine regulation capacity building |
<p>| <strong>Where</strong> | Southeast Asia |</p>
<table>
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<tr>
<th>Organization</th>
<th>FDA</th>
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<tbody>
<tr>
<td>Project</td>
<td>Office of International Programs, Technical Cooperation and Capacity Building</td>
</tr>
<tr>
<td>Objective</td>
<td>Defines regulatory capacity, the ability of national regulatory authorities to perform regularly their core functions to ensure the availability of high-quality and safe food and medical products, as part of the FDA mission to ensure safe products in the United States</td>
</tr>
<tr>
<td>Activities</td>
<td>Strengthen information and evidence so the FDA can make informed decisions about how to use its resources Transfer its expertise and identify efforts globally that do not require the use of FDA resources Encourage global information networks to strengthen detection, surveillance, and assessment systems Support surveillance and tracking efforts for global supply chains Support pharmacovigilance capacity</td>
</tr>
<tr>
<td>Where</td>
<td>Worldwide</td>
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Global Division of Labor

• ICH, PIC/S, etc.
• WHO Prequalification – limited scope
• But who can help secure a common, acceptable standard for (generic) drugs traded between countries with weak regulators?
• Challenge for health systems and donors: procuring effective, quality generics for large public sector programs
• Procurement agents take on quasi-regulatory function, often bypassing (undermining) the official regulator
• Can we envision a global network of regulators who back up their smaller national peers with a WHO-PQ alike system for all essential medicines?
Supporting LIC Regulators

• Use high level (inter-ministerial) diplomacy to highlight importance of strong regulatory agency
• Mentoring/twinning arrangements, exchange programs
• Academic partnerships between schools of pharmacy/regulatory sciences (NEPAD Agency as potential facilitator)
• Pooled funding from industry may be available for capacity building initiatives – acceptable?
• Donation of equipment is generally useless if not embedded into a comprehensive capacity building program with a clear results framework
Sustainable Financing for Medicines Regulatory Agencies

- Ongoing Cambridge Executive MBA project, supported by World Bank, first output by late 2012
- How can fee basis be strengthened? Example: 2% release fee for all imports (FOB price as basis) – income will grow with market
- Reducing internal costs at manufacturer level by eliminating duplication, making process predictable and transparent
- Savings potential 40% (EAC industry estimate) of internal costs
- Industry feedback: significant increase in fees acceptable if “value for money” can be demonstrated (need for metrics!)
- Particular concern: PMS = cleaning up the market and shutting down “grey” imports that undermine legitimate players
Conclusion

• Medicines regulation and strong regulatory systems are an essential part of health systems strengthening and assuring access to safe and effective medicines

• The current global and national systems have significant gaps, in particular affecting the poor in Low and (to a lesser extent) Middle Income Countries

• Better regional and global cooperation and “division of labor” can help improve the situation. Some innovative thinking is needed for additional resource mobilization

• The World Bank is actively supporting regulatory harmonization and capacity building through financing (Trust Fund), project management, stakeholder engagement and knowledge sharing
A Practical Approach to Pharmaceutical Policy discusses the wide range of challenges facing policy makers, presents the current know-how, and provides specific examples of policy packages that can be used in defined circumstances. The book, which focuses on developing countries, equally addresses the issues faced by low-income and middle-income countries. It concludes with a prognosis of how things might evolve in the longer term, assuming convergence toward models that work to reduce the fragmentation of policies and enhance regulatory and economic efficiencies. Such an evolution to a sustainable platform would benefit all stakeholders, but particularly those who, as patients, do not have reliable access to effective and safe medicines.

A Practical Approach to Pharmaceutical Policy will be of interest to pharmaceutical policy makers and advisers in developing countries; people in related fields such as health financing, health service delivery, and health insurance management; representatives of the pharmaceutical industry and associations; academics and students of public health policy, pharmacy, and health economics; and undergraduate and graduate students in related fields.