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Medicines Harmonization and Regulatory Convergence

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Summer Program on Emerging Issues in Food and Drug Law

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Should sovereignty matter for the approval of medicines?

Just one example: a drug is developed in Germany, tested for toxicology in US, clinical trials for marketing in Europe were carried out in UK where Phase 1 trial resulted in a disaster.

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- Does this example make the case that traditional governance is no longer effective?
- Are patients so different that national differences require national medicines regulation to be exclusive?

- New ways of regulating the safety and effectiveness of drugs have are being used and explored.

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Without harmonization

- Every drug and medical device and any other product that must be approved before being placed on the market, must be approved in every country where it is to be sold or dispensed.

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- Makes supply chain management very difficult; example HIV medicines and PEPFAR PFSCM.
- Costs and time related to registration delays entry to markets.
- Is registration a technical barrier to trade?

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Why harmonization at all in any area of law?

"Conceive the security and peace of mind of the ship owner, the banker, or the merchant who knows that in regard to his transaction in a foreign country the law of contract, of moveable property, and of civil wrongs is practically identical with that of his own country."

Lord Justice Kennedy, "The Unification of Law", Journal of the Society of Comparative Legislation, vol. 10, (1909), 212 et seq. (241-15).

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Advantages of law harmonization

- Facilitates commerce by lifting barriers.
- Creates a legal framework that disregards differences in domestic regulation.
- Can fill a legal vacuum by providing rules where national law was non-existent.
- Substitutes a single law rather than a proliferation of national laws;
  - Dispenses with need to use conflicts of law rules,
  - Avoids forum shopping.
- Reduces transaction costs.
- Increased predictability and legal certainty.
- Harmonization can bring law reform and modernization and can increase likelihood of resolving thorny issues.

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Disadvantages of harmonization

- Negotiations and drafting can be lengthy and costly process
- Different legal traditions may result in only the common denominator
- States do not negotiate as equal partners.
- Ratification and implementation must be accomplished
- No guarantee that harmonized law will be interpreted or implemented in a harmonized manner.

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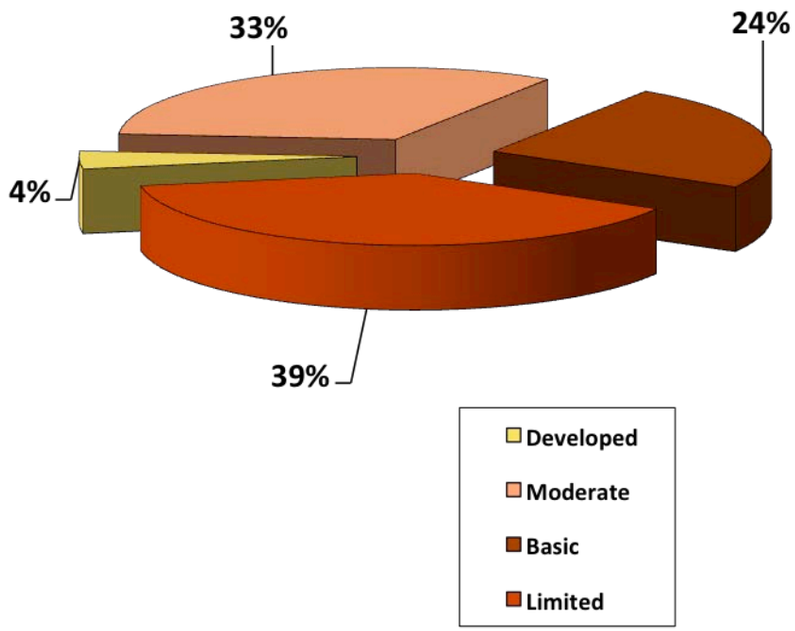
Why harmonization or regulatory convergence?

- Our first example
- Every country on earth imports finished or unfinished products; medicines business is international trade.
  - Half of the sales of the fifty largest drug companies are made outside their respective countries.
  - Pharmaceutical research, manufacturing and distribution regularly cross frontiers all over the world.
- Why in Africa?
  - 11% world population,
  - 60% of general global population of people with HIV/AIDS, TB, malaria, diarrheal disease, lower respiratory track infections,
  - 70% of medicines used are imported, 30% local manufactured, and
  - Non-transparent process for medicines registration.

Differences in regulatory capacity in WHO African Region

Due to chronic shortages of human, technical, financial and other resources many National Medicines Regulatory Authorities (NMRAs) in Africa don't have the full capacity to perform **most core regulatory functions**

Medicines Regulatory capacity in 46 WHO AFRO Member States:



Source: *WHO/AFRO/EDP/04.5: Availability of Drug Regulatory and Quality Assurance Elements in Member States of the WHO African Region, 2004, Brazzaville.*

World Health Organization

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Regulatory Functions

- Registration
- Licensing of pharmaceutical establishments
  - Manufactures.
- Inspection and market control
- Promotion control
- Clinical trials
- Selection
- Procurement
- Distribution
  - Importers, warehouses, transport, intermediaries

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Harmonized or converged functions

- Marketing Authorization
- Acceptance of Clinical data
- Conduct Joint inspections and evaluations
- Sharing of laboratory resources
- Reliance on reference or accredited laboratories
- Information sharing

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The means of harmonization of law and regulatory convergence

Hard law

- Legislation (national and international) conventions, bilateral treaties, directives.
- Conflicts of law.
- Standard form contracts.

Soft law

- Lex mercatoria; commercial customs, usages of trade and trade terms such as Incoterms or Uniform Customs and Practice for Documentary Credits.
- International (scholarly) restatements of law, model laws.
- Standards.
- Commissions, forums, schemes, arrangements, cooperation, commitments, MOU, initiatives, work plans, task forces, conferences(ICDRA)

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Is regulatory convergence soft law?

- Regulatory convergence represents process whereby regulatory requirements across economies become more aligned over time as a result of the adoption of internationally recognized technical guidance, standards and best practices. Does not require the harmonization of laws and regulations and is a broader concept than "harmonization"

Example: Good Review Practices

- Established common practice has the effect of legal harmonization.
- Extra-legal standards. E.g.. USP
- Soft harmonization is open-ended and provides for a flexible and effective convergence between different legal systems.

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U.S.-Japan Deregulation Initiative

Market-Oriented, Sector-Selective Agreement US-Japan

- Focus pricing, approval process, and the acceptance of foreign clinical data for pharmaceutical products and medical devices.
- Sets standard period for processing new drug or medical device approvals.
- Acceptance of clinical data gathered outside Japan.
- Increased transparency - Japan agreed to make their instructions for drug approval available to the public.

Regulatory convergence or harmonization?

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ICH - International Conference on Harmonization

- "Project" experts from regulatory authorities of US, Europe and Japan.
- Discuss the "scientific and technical aspects of product registration."
- Focus on methods to eliminate the need for duplicate testing during R&D phase for new drugs and medical devices.
- National law is often designed after ICH guidelines.

  Example: The E6 ICH guideline on Good Clinical Practice, some parts seem to be copied and pasted in the European Directive 2001/20/EC on Good Clinical Practice.

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Global Harmonization Task Force

- GHTF: Japan, US and European Union.
- Purpose of this voluntary organization is to "encourage convergence in regulatory practices related to ensuring the safety, effectiveness/performance and quality of medical devices, promoting technological innovation and facilitating international trade.
- Achieved by publication and dissemination of harmonized guidance documents on basic regulatory practices.

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European Medicines Agency

- Central authorization of medicines: compulsory for some drugs.
- Safety monitoring of medicines of medicines it authorizes.
- Referral procedures to assess nationally authorized medicines.
- Inspections.
- Telematics.
- Stimulating innovation.
- Is the hub of the European Medicines Network.

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Europe's Four Systems

1. Centralized Community Authorization, Council Regulation 2309/93/EEC for whole of EC and Iceland, Liechtenstein and Norway
2. Decentralized Authorization: this helps to authorize drugs in all member states of the EC, once it has been permitted in at least one of them.
3. Mutual recognition
4. National systems
5. Maybe five? nCADREAC

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nCADREAC authorization procedure

- Can be used by any nCADREAC drug regulatory authority (DRA),
- Jan. 2006 New Collaboration Agreement between Drug Regulatory Authorities in Central and Eastern European Countries (nCADREAC)
- For granting a marketing authorization of a medicinal product which has been authorized in European Union (EU) following the Centralised Procedure

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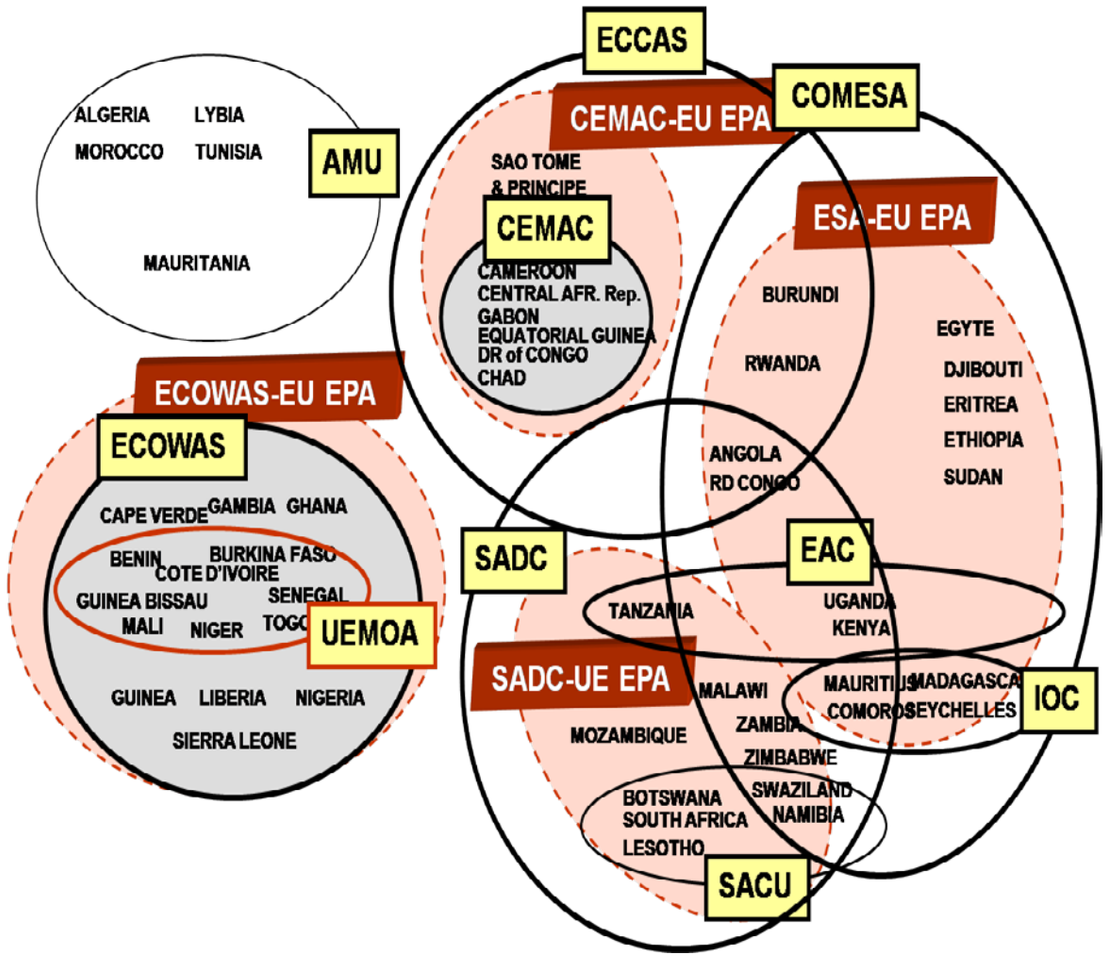
Harmonization Experience in Africa

- OHADA – Organization for the Harmonization of African Business Law created by treaty in 1993 with revisions in 2008. 17 members
  - Institutions and structure to harmonize contract law, business organizations, securities and bankruptcy and arbitration,
  - A Common Court of Justice and Arbitrage

- African Union – 54 countries (sauf Morocco)
- Many regional and economic groupings
  - Sahel – Saharan, CEN-SAD, COMESA, EAC, ECCAS, ECOWAS, IGAD, SADC
  - Some countries are members to more than one

Why Regional Economic Communities (RECs) - based approach?

- But.. a number of overlaps and politically complicated environment substantially affect the situation…



World Health Organization

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African Medicines Plan

AU plan for African continent-wide pharmaceutical manufacturing plan

EAC pilot - started in March 2012

- Use of harmonized policies, legislation, guidelines, standards
- Gradually move towards a system of mutual recognition of regulatory functions and decisions within the regional bloc

West African Medicines Regulation Harmonization (SRCMRH) project (WAHO and WAEMU)

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AMRHI Activities and Plan

- Situation Analysis
- Model Law
    - Draft
    - Consultations with health/justice ministers, AU policy organs, REC/stakeholders July 2014-June 2015
    - Presentation to AU Parliament
- Ratification process through local and regional systems
- Implementation

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Thank you!

Questions? Comments?

Enjoy your week!

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