Future challenges and opportunities for medicines regulation

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* The views stated in this presentation reflect the views of the author and not necessarily those of the World Health Organization.
Content

- Setting the scene
- What is the environment
- Medicines regulation and realities
- Where from now?
- Conclusions
We are all equipped to assess what is around us. But not much regarding medicines as usual perceptions and emotions may not help in making judgements about medicines.
Medicines is a very special category of products

- Consumers, patients and (even) health care workers have limited capacity to judge there
  - SAFETY
  - QUALITY
  - EFFICACY

- And all these have to built in ONE – the medicine
How medicines industry regulation compares with other well regulated industries?

- Pharma industries and their products likely the most regulated industries/products, but ... perhaps aircraft industry regulations have achieved Globally better results.

- Most journeys by air from A to B are very effective and safe (very high % starting the journey reaches from A to B, almost all getting in air land safely as well).

- If the aircraft business would be Globally regulated as good or bad as medicines today:
  - Perhaps quite high % of planes would not take off the ground or would not reach the destination for quality reasons.
  - Not talk about the inherent relative lack of efficacy of many medicines.
    - In case of medicines it is not rare that from 100 starting the journey (treatment) only less than 10 may reach the destination (cure).
Medicines regulation – evidence based science or administrative activity with some scientific input?

- To enable access to good quality, safe and effective medicines the regulation should be based on science and evidence.

Realities – scientific input may be weakened, or get lost in political, economical, administrative, media and other battles.

- If it is science in its own rights then multidisciplinary complex discipline based on many basic and applied sciences.

- So far medicines regulation itself not much object of scientific research.

- Discipline for academia to give more importance?
Shifting the regulatory paradigm during the history (1)

- From elementary quality requirements to safety and efficacy
- From quality control of finished product to control of quality of manufacturing (inspection)
- From quality control of finished product and inspection of manufacturing sites in general to more understanding the general processes, and product specific processes involved
- From rigid limits to agreed upon beforehand set of limits which can be used by manufacturers in a more flexible manner
- Refocusing from pre-marketing assessment on effective risk management during the whole life cycle of a medicines.

......
Shifting the regulatory paradigm during the history (2)

- Increased role of science – new molecules, new advanced therapies and combination therapies (device + medicine, etc)
- From national to international – not a single regulator today can work meaningfully in isolation and not using other regulators experience/knowledge/information
- Increasing need to decide what regulatory functions priorities nationally and what expertise/capacities to build
- Increasing need for harmonization, collaboration and cooperation
- Regulatory capacities – is gap between well resourced and less resourced regulators increasing?
Medicines regulation lives in a rapidly changing environment (1)

- Economic landscape – new emerging economies on economical rise and budget deficits in "old economies"
- Emerging economies – "emerging" regulators?
- R&D based industries changing (mergers, R&D staff in house decreasing, out sourcing)
- Declining numbers of new medicines and increasing R&D costs
- Clinical research globalizing, pre-clinical R&D likely following the trend
Medicines regulation lives in a rapidly changing environment (2)

- Pharmaceutical manufacturing follows more Global market and business logics - Globalization is ongoing and likely there is no alternative
- Development of new technologies – from genome research to nanotechnologies, from stem cell research to high tech diagnostics solutions
- From "population" treatment to more "personalized" treatment
- Relative efficacy of drugs: an emerging issue between regulatory agencies and third-party payers – more interaction and cooperation with health technologies assessment?
Medicines regulation lives in a rapidly changing environment (3)

- Increasing public concerns about safety
- Increasing concerns about access (and price)
- Increasing demands for more transparency and patients involvement
- Need for better communication strategies to the public
- But …
Old problems continue

- Relative lack of regulatory capacity in many countries
- In spite of some progress in developing regulatory capacities the gap between well resourced and less resourced regulators may have increased
- Quality still remains the problem
- Pharmacovigilance systems development has progressed but still lacks behind
- Market control and supply chain security remains outstanding issue
Where we are with medicines regulation today?

Some highlights from released for 14th ICDRA report

- Note. Each study published is out of date in certain details and progress has been made since in several countries
What about post-marketing surveillance and market control? (26 country study in Africa)
Registration (MA)

Figure 6: Resources for Medicines Registration

- **Legal basis (outline)**: Adequate
- **Guidelines (tech. detail)**: Existing but inadequate
- **SOPs for assessment**: Not existing
- **Assessors**: Existing but inadequate
- **Secure filing space**: Adequate
- **IT system**: Not mentioned in country report

Department of Essential Medicines and Pharmaceutical Policies

World Health Organization
Inspections

**FIGURE 7: RESOURCES FOR INSPECTIONS**

- **Legal basis**: Adequate
- **Published GMP text**: Existing but inadequate
- **SOPs**: Existing but inadequate
- **QMS**: Not existing
- **Inspectors**: Adequate
- **Logistics**: Adequate

Department of Essential Medicines and Pharmaceutical Policies

World Health Organization
Also good news. Regulatory transparency increasing

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*The list of countries for 2001 has been adjusted to be the same as the 2009 list.

Regulators and access to medicines

- Regulators seen by many parties as obstacle to access
- Regulatory approvals (registration, MA)
  - Based on science – not easy to understand
  - Need considerable capacity, if done properly
  - Relative lack of transparency
  - Take time
- Regulatory approvals (marketing authorization) and market control – what comes first?
What are the issues?

- Can all national regulators assess and inspect all the *new innovative products* that come to their markets?
- Can and should all the regulators assess and inspect all the *generic medicines*?
- Does *repetitive* assessment and inspections give *added value*?
- How to build confidence in scientific assessments/inspections carried out by other parties?
- How regulators can best contribute to the public health with the resources they have?
Does repetitive assessment and inspection give added value?

- YES, provided the previous assessment has been based on different (lower) set of standards, or missed important issues (due to different qualifications, scientific views)
- Usually NO, if the same standards are used
- Usually NO, if the capacity for assessment is not present, or does not equal to the one of the first assessment
- Duplicate efforts, or trust colleagues? That is the question! Or is it?
Can all national regulators ...

... fully assess and inspect all the (new innovative) products that come to their markets?

- In theory, and only in theory, YES
- But who can pay the bill?
- Thus, in practice, NO

- Reality is that "regulatory bodies" range from staff point of view virtually from 1 person up to 3000+!
- Most WHO Member States are ...small, or very small countries
How to build confidence in scientific assessments carried out by other parties?

- Regulatory science - risk assessment, risk management, risk communication?

- Why not to apply the same principles? Assess, manage, communicate and collaborate

- Collaboration is also confidence building –
  - one way traffic - FAILURE
  - two way traffic - SUCCESS
Is there anything new under the sun?

- Some tools for information exchange have been created long time ago – WHO Certification Scheme - CPP
- Regulators are increasing transparency – more information available in public domain (but is it used?)
- In EU setting not necessarily all national regulators are actively involved but still recognize the outcomes scientific assessments/inspections – and products get to the national markets (e.g. centralized procedure, mutual recognition procedure)
- Exchange of assessment and inspection reports – opportunities and challenges but several initiatives to learn best practices
- Bi- and multilateral arrangements for mutual recognition (e.g. for inspections etc.)
Harmonization of regulatory requirements is important

- Objective of drug regulation: TO IMPROVE AND PROMOTE PUBLIC HEALTH

- Harmonization creates "common language", can facilitate cooperation and access to medicines

- In case of harmonization of regulations the main objective should be:
  - MEASURABLE PUBLIC HEALTH GAINS

- There may be other gains, but these should be in the centre
What is WHO doing?

- Normative activities (setting norms and standards)
- Assisting countries by
  - Providing nomenclatures, regulatory guidelines, norms and standards, including reference standards
  - Assessing regulatory systems
  - Facilitating information exchange and cooperation
  - Promoting and facilitating harmonization
  - Helping implementation of norms and standards through capacity building and training
  - Prequalifying essential medicines, vaccines and diagnostics
Regulatory requirements for multisource (generic) medicines

In short a generic medicine must:

1. contain the same active ingredients as the innovator drug
2. be identical in strength, dosage form, and route of administration
3. have the same use indications
4. be bioequivalent (as a marker for therapeutic interchangeability)
5. meet the same batch requirements for identity, strength, purity and quality
6. be manufactured under the same standards of Good Manufacturing Practice (GMP) as required for innovator products
Essential Medicines and Pharmaceutical Policies

Our vision is that people everywhere have access to the essential medicines they need; that the medicines are safe, effective and of assured quality; and that they are prescribed and used rationally. Visit "About us" to learn more.

WHO > Programmes and projects > Medicines

TECHNICAL AREAS

- Medicine Information and Evidence for Policy
  - Information and Publications
  - Medicines Policy
  - Monitoring and Evaluation
  - Technical Briefing Seminars

- Medicine Access and Rational Use
  - Antimicrobial Resistance
  - Better Medicines for Children
  - Controlled Medicines
  - Pricing and Financing
  - Good Governance for Medicines
  - Rational Use
  - Selection

- Traditional Medicine
  - Traditional, Complementary and Herbal Medicine

- Prequalification of Medicines
  - WHO-UNICEF-UN Project

- Quality and Safety of Medicines
  - Blood Products and Related Biologicals
  - Counterfeit Medicines
  - International Nonproprietary Names
  - Quality Assurance
  - Regulatory Support
  - Safety and Efficacy
  - The International Pharmacopoeia

More information: www.who.int/medicines/en/
Setting norms and standards for quality

NB! 57
CURRENT official WHO guidance texts and guidelines
Quality Assurance and Safety: Blood Products and related Biologicals

Since the middle of the 20th century, medical science has found ways to prepare therapeutic products derived from human blood and plasma for the treatment of many life threatening diseases, as well as for complex surgical procedures.

Processing blood into various types of medicines or products is a highly specialized process because blood products and biological technologies are inherently variable due to the nature of the source materials as well as the methods used to test them. The overall goal of the National Regulatory Authorities is to ensure that only blood products of demonstrated quality, safety and efficacy should be used. Yet, experience with regulatory authorities indicate that many countries have significant difficulties in fulfilling their responsibilities in this field.

WHO is responding to immediate needs by providing technical guidance and quality assurance tools to Medicines Regulatory Authorities, National Control Laboratories and manufacturers to support implementation of quality and safety systems for the production and control of blood products and related in vitro diagnostic devices worldwide.

The development of International Reference Materials and Guidelines to support the technical capacity of National Regulatory Authorities and to assure the compliance of manufacturers to quality and safety measures form the basis of our Mission. These contribute to technology transfer and global harmonization of quality assurance regulations.

Challenges and Issues:

- To strengthen National Regulatory Authorities on quality assurance systems for the control of quality and safety of blood products and in vitro diagnostic devices.
- Need to assure quality and safety of blood and plasma globally to prevent transmission of bloodborne viral diseases via blood products.
- Need to prioritize the development of WHO International Reference Materials of interest in Regions and countries with limited resources.
- To facilitate access to and appropriate use of WHO International
The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) - http://www.ich.org

Welcome to the official web site for ICH

The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) is a unique project that brings together the regulatory authorities of Europe, Japan and the United States and experts from the pharmaceutical industry in the three regions to discuss scientific and technical aspects of product registration.

The purpose is to make recommendations on ways to achieve greater harmonisation in the interpretation and application of technical guidelines and requirements for product registration in order to reduce or obviate the need to duplicate the testing carried out during the research and development of new medicines.

The objective of such harmonisation is a more economical use of human, animal and material resources, and the elimination of unnecessary delay in the global development and availability of new medicines whilst maintaining safeguards on quality, safety and efficacy, and regulatory obligations to protect public health. This Mission is embodied in the Terms of Reference of ICH.

The ICH Secretariat can be contacted on admin@ich.org
How regulators can best contribute to the public health with the resources they have?

- Ask the question how YOU can best contribute to the patients in your country setting with the resources you have.
- Avoid doing things that do not give added value, concentrate on things that do **give added value**.
- Concentrate on high risk areas/products.
- Be pragmatic – *Nice to know – forget it, need to know – get it!* And learn making difference between the two.
Conclusions

- Sharing of information, collaboration and harmonization can help optimize workload and improve overall regulatory performance but initially more resources may be needed.

- Cooperation and harmonization can help to direct the expert knowledge and resources to performance of the functions that can improve public health and facilitate access to essential medicines.

- Formation of effective networks between regulatory authorities nationally and internationally may facilitate sharing of scarce resources and eliminate duplicating of activities.

- Collaboration and harmonization may contribute in building regulatory capacity and trust, which is an important achievement in its own right.

- WHO has supported and continues to support collaboration and harmonization initiatives. These can be a win-win situation to all concerned parties when public health gains are kept in focus.
PS. Cooperation and collaboration needs also human resources!

Which one of these empty chairs can collaborate more efficiently?
PPS. How we collaborate during forthcoming two days?

- Workshops
- Moderators
- Speakers
- Support (WHO staff)
- Expected outcomes