Progress Report on Recommendations made at the 13th International Conference of Drug Regulatory Authorities, Bern, 2008

Dr Lembit Rägo
Coordinator
Quality Assurance and Safety of Medicines
Essential Medicines and Pharmaceutical Policies
Building mutual trust as a key to access (1)

ICDRA Recommendations
WHO should …
- Undertake WHO Prequalification of Medicines Programme joint assessments of selected applications, using the Model Registration Package.

WHO Comment
- Two product dossiers were jointly assessed by Kenya, Tanzania, Uganda and the WHO Prequalification of Medicines Programme. One of the products has already been prequalified and registered in some EAC countries (presentation in Plenary 4 for more details).
<table>
<thead>
<tr>
<th>ICDRA Recommendations</th>
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<tr>
<td>- In partnership with well-resourced regulatory authorities, establish formal mechanisms for the exchange and use of regulatory information among all authorities, to maximize efficiencies, and facilitate cooperation between small and medium well-resourced regulatory authorities.</td>
<td>- WHO, in collaboration with well-resourced regulatory authorities, has initiated training workshops on implementation of the International Conference of Harmonization (ICH) Common Technical Document (CTD) (CTD – &quot;common language&quot;)</td>
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Regulatory systems in a changing environment

ICDRA Recommendations
WHO should …

- Continue to support and create new activities that stimulate trust building and cooperation among regulatory agencies

WHO Comment

- WHO, in cooperation with the Bill and Melinda Gates Foundation, NEPAD Agency, DFID, William J. Clinton Foundation and the World Bank, has established an African Medicines Registration Harmonization Initiative, aimed at collaboration and streamlining marketing authorization of pharmaceutical products.
Crisis management: safeguarding health (1)

ICDRA Recommendations

WHO should …

- Work further to integrate and coordinate the information and other requirements in the International Health Regulations (2005) with functions and activities of DRAs and related networks. Such integration could include establishing links between the DRAs and their respective National IHR Focal Points, including potential access to the WHO IHR Event Information Site.

WHO Comment

- WHO Medicines and Vaccines programmes have worked with the relevant WHO IHR focal points in providing case studies for inclusion in the WHO Guidance for the Use of Annex 2 of the IHR (2005).
- Work further to integrate and coordinate the information and other requirements in the International Health Regulations (2005) with functions and activities of DRAs and related networks. Such integration could include establishing links between the DRAs and their respective National IHR Focal Points, including potential access to the WHO IHR Event Information Site.

- The WHO Medicines Programme has organized workshops for regulatory authorities and national pharmacovigilance centres to provide training in crisis management, principles of communication in crises and in developing risk management plans for pharmaceutical products.
Good Governance for Medicines (GGM) (1)

ICDRA Recommendations
WHO should …

- Develop, implement and monitor a country GGM implementation framework, including:
  - establishment and implementation of codes of conduct
  - enforcement of anticorruption laws
  - provision of transparency and access to information
  - protection of whistleblowers
  - improvement of inter-institutional collaboration and cooperation
  - provision of guidelines to define and underpin Public-Private Partnerships

WHO Comment

- 11 countries have a national GGM framework.
  Progress in implementation of recommendations includes:
  - National pharmaceutical laws, regulations and procedures revised (GMP, promotion, etc.)
  - Web-based pharmaceutical services (e.g. registration, licensing) and web-based information (e.g. pricing)
  - Conflict of interest policies developed and implemented
Involvement of consumers in medicines surveillance reporting

ICDRA Recommendations

WHO should …

- Increase efforts to include consumers in medicines surveillance reporting by fostering consumer awareness, informing and educating the public and by promoting the programme to consumers

WHO Comment

- A WHO draft guideline has been developed for pharmacovigilance centres for consumer reporting of adverse medicines events. A survey of consumer reporting practices in 11 countries was also carried out by the WHO-UMC led FP 7 Medicines Monitoring Project. The guideline will be finalized in 2011.
WHO stability testing guideline

ICDRA Recommendations
WHO should …

- finalize revision of the stability guideline and apply it in Member States
- provide information about the national long-term conditions to WHO
- WHO to make the data available on their website

WHO Comment

WHO 43rd Expert Committee on Specifications for Pharmaceutical Preparations adopted in 2008 the new WHO guidance on stability testing of active pharmaceutical ingredients and finished pharmaceutical products. It includes a list of requirements as requested by NMRAs.
Regulatory aspects of paediatric medicines (1)

ICDRA Recommendations
WHO should …

- Convene a global paediatric working group of regulators

WHO Comment

- Paediatric Medicines Regulators Network (PmRN) has been established among 26 Authorities

- WHO PmRN web site has been launched with a restricted area and forum.
Regulatory aspects of paediatric medicines (2)

- Work with civil society to mobilize and empower consumers, parents, patient groups and health professionals to advocate for better medicines for children.

- A First and Second Partners Meeting on Better Medicines for Children was convened in May 2009 and October 2010 to provide information on activities and identify completing objectives of resolution WHA60.20.
Regulatory aspects of paediatric medicines (3)

ICDRA Recommendations
WHO should …

- Develop strategies for addressing high priority needs with achievable results including: zinc for diarrhoea, *Pneumoniae* treatment, neonatal sepsis, HIV, TB, malaria treatments, and analgesics.

- Improve information on safety of medicines used in children: Infrastructure for pharmacovigilance

WHO Comment

- A two day meeting of interested parties was convened by UNICEF Supply Division and WHO.

- A WHO technical document describes minimum pharmacovigilance requirements and infrastructure for effective capture and exchange of information on safety of medicines.
Regulatory aspects of paediatric medicines (4)

ICDRA Recommendations
WHO should …

- Facilitate the long-term sustainability of networking among NRAs for the joint evaluation and oversight of clinical trials of new vaccines in Africa, and other vaccine regulatory networking initiatives

WHO Comment

- The regulatory forum "AVAREF“, supported by WHO, meets annually, funding has been obtained for a Secretariat and a network. Additional resource mobilization efforts are underway.
Regulatory aspects of paediatric medicines (5)

- Support capacity building to generate post-marketing effectiveness data

- An initiative to improve links between NRAs and National Immunization Advisory Committees has been established, in part to generate such data, and will be reported to ICDRA 14

ICDRA Recommendations
WHO should …

WHO Comment
### Regulatory aspects of paediatric medicines (6)

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<td>- Support vaccine pharmacovigilance through setting standard definitions, development of guidelines, training, and development of networks</td>
<td>- The Brighton collaboration will develop standard definitions. A blueprint project will define minimal capacity for vaccine pharmacovigilance. A network of 12 countries has been established for post-marketing surveillance of newly prequalified vaccines.</td>
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<td>- Provide more detailed information about the quality, safety and efficacy of prequalified vaccines.</td>
<td>- The WHO website provides information on prequalified vaccines.</td>
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**Development of regulation for herbal medicines (1)**

ICDRA Recommendations

- Provide policy and technical support to countries to facilitate integration of traditional medicine into the healthcare system
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WHO Comment

- The World Health Assembly adopted a Resolution on Traditional Medicine referring to the Beijing Declaration and urging integration of traditional medicine into national health systems.
- A series of WHO documents relating to basic training for TM/CAM were published in 2010.
Development of regulation for herbal medicines (2)

ICDRA Recommendations
WHO should …

- Continue to support sub-regional group countries in developing monographs on commonly used medicinal plants through cooperation and in building national research capacity for traditional medicines.

- Provide technical guidance to countries on how to avoid interactions between conventional and herbal medicines.

WHO Comment

- WHO monographs on selected medicinal plants, volume 4, 2009, and WHO monographs on selected medicinal plants commonly used in Newly Independent States (NIS) printed in 2010.

- Development of a new technical document on interaction of herbal medicines with other medicines.
Development of regulation for herbal medicines (3)

ICDRA Recommendations
WHO should …

- Continue to play a coordinating role in International Regulatory Cooperation on Herbal Medicines (IRCH) functions by promoting the network and encouraging member countries of IRCH to incorporate their national lists of registered herbal products into the IRCH library

WHO Comment

- Membership of IRCH has increased to 23 Members.
- Annual meetings of IRCH continue to be held.
- IRCH has established seven working groups.
- WHO continues supporting the MedNet-based information exchange tool for IRCH.
Safety and pandemic preparedness (1)

- Establish, facilitate and intensify international collaboration in safety surveillance of pandemic vaccines and antivirals.

WHO Comment

- PaniFlow™, a computer software for case report management addressing specific needs of vaccine and antiviral safety monitoring in a pandemic situation created (based on the VigiFlow™ software).

- A functional international collaborative network exchanges safety information on vaccines in real-time during the H1N1 pandemic.
Safety and pandemic preparedness (2)

ICDRA Recommendations

WHO should …

- Request the WHO Collaborating Centre for International Drug Monitoring/Uppsala Monitoring Centre, to provide free access to Paniflow (a simplified online reporting form for primary reporters) for all countries who wish to use it, and to develop and implement a tool for rapid signal detection on pooled data and keep all countries informed on findings in a timely manner.

WHO Comment

- The PaniFlow™ software and required technical support is being provided to 95 countries receiving H1N1 vaccine donations from WHO.
- PaniFlow™ software was made available to countries. For A/H1N1 vaccines, UMC's Vigibase received reports from more than 23 countries.
Regulatory approaches to proving interchangeability

- Promote mutual trust and international cooperation mechanisms in order to recognize MRA inspections of CROs that have been conducted based on internationally acceptable standards.

WHO Comment

- WHO’s Expert Committee on Specifications for Pharmaceutical Preparations adopted the WHO Additional guidance for organizations performing in vivo bioequivalence studies.

- The WHO revised procedure for prequalifying medicines facilitates recognition of CRO inspections conducted by a stringent regulatory authority.
Strategies to fight counterfeit medicines (1)

WHO should further assist MRAs to strengthen their capacity to detect and combat counterfeit medical products and to exchange information at the international level.

WHO Comment

- Ongoing action through regulatory support of quality assurance programmes.
Strategies to fight counterfeit medicines (2)

WHO should further promote a harmonized definition of a counterfeit medical product that is based on the 1992 definition of counterfeit medicine, that focuses on the protection of public health, and takes into account the need to safeguard legitimate generic medicines.

- Survey carried out and posted on the web.
Strategies to fight counterfeit medicines (3)

**ICDRA Recommendations**

- WHO should develop and implement initiatives aimed at disseminating awareness and triggering political will to combat counterfeit medical products.

**WHO Comment**

- An open Forum about IMPACT was carried out and preparations for intergovernmental working group organized.
## Emerging regulatory issues concerning biosimilars and biologicals (1)

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<td>- Develop guidance for regulatory evaluation of similar biological products that includes clarification of the scientific basis for the reduction, wherever possible, of non-clinical and clinical data requirements for such products.</td>
<td>- Guidance on regulatory evaluation of similar biotherapeutic products was adopted by the Expert Committee on Biological Standardization at its 2009 meeting.</td>
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Emerging regulatory issues concerning biosimilars and biologicals (2)

ICDRA Recommendations

WHO should …

- Assist regulators in implementing globally agreed regulatory principles into national regulations and, where appropriate and feasible, develop support mechanisms such as regional centres of excellence in regulatory evaluation of similar biological products.

WHO Comment

- Regional WHO workshops on the implementation of the new WHO guidelines on similar biotherapeutic products have been run in Seoul, Korea and also in the Dominican Republic. WHO also supported a workshop run by the International Association of Biologics, immediately prior to the start of ICDRA 14.
Emerging diseases: regulating blood products (1)

ICDRA Recommendations
WHO should …

- Take steps to further develop and strengthen national and regional blood regulatory authorities and promote cooperation among them.

- Promote introduction of WHO recommended plasma standards by NRAs

WHO Comment

- The World Health Assembly Resolution on availability, quality and safety of blood products (WHA 63.12) was adopted in May 2010.

- The “Achilles” project will increase availability of safe blood derived products for developing countries by applying WHO standards on plasma. A resource mobilization plan is now in process.
Emerging diseases: regulating blood products (2)

ICDRA Recommendations

WHO Comment
- A set of criteria for assessment of national blood regulatory systems has been developed.
Emerging diseases: regulating blood products (3)

**ICDRA Recommendations**

- Take full account of existing assessment tools in use by NRAs by: a) convening a consultation of NRAs to review the assessment tool, and b) ensuring coordination with related WHO guidance documents

**WHO Comment**

- The Assessment criteria for national blood regulatory systems will be discussed during Workshop A on blood and blood products.
Emerging diseases: regulating blood products (4)

- Prioritize development of guidelines on good manufacturing practices (GMP) for blood establishments

- WHO guidelines were adopted by the WHO Expert Committee on Biological Standardization on 22 October 2010.
**Update on harmonization initiatives (1)**

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<tr>
<td>- Encourage and facilitate Member States’ use of the assessment tool for drug regulatory authorities as an important step in promoting effective International Harmonization regulatory strategies and harmonization efforts.</td>
<td>- The WHO Assessment Tool was further revised and used to conduct assessments of Medicines Regulatory Systems in more than 10 countries.</td>
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<td>- The WHO Assessment Tool was further revised and used to conduct assessments of Medicines Regulatory Systems in more than 10 countries.</td>
<td>- East African Community Partner States NMRAs conducted an assessment of the regulatory functions using the WHO tool, in the framework of the African Medicines Registration Harmonization Initiative.</td>
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### Update on harmonization initiatives (2)

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<td>- Facilitate the adoption by Member States of a common format for marketing applications as a means of promoting a common regulatory language that supports the sharing of information, good review practices and access to medicines.</td>
<td>- WHO conducted a series of the workshops on the implementation of the Common Technical Document (CTD) in Francophone and Anglophone countries in Sub-Saharan Africa as a preparatory step in the implementation of the African Medicines Registration Harmonization Initiative.</td>
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Role of regulators in clinical trial approval (1)

ICDRA Recommendations
WHO should …

- Promote regulation of clinical trials by supporting countries to establish robust legal and regulatory frameworks and systems to register and publish ongoing trials to achieve transparency.

WHO Comment

- The AVAREF forum has provided support to countries for regulatory oversight (19 countries in Africa). A new global training course on regulatory legislation is being developed and AVAREF countries have committed to make registration in a primary clinical trial database a pre-condition to acceptance of a clinical trial application for review.
Role of regulators in clinical trial approval (2)

- Facilitate the establishment of confidentiality provisions that will allow communications and cooperation between regulatory agencies from manufacturing and trial host countries.

- Discussions have been initiated, but not yet concluded.
Building regulatory capacity: best practices for the future

ICDRA Recommendations
WHO should …

- Systematically inform ministries of health of outcomes of NRA assessments.
- Evaluate ways for improving benchmarking activities within the assessments.
- Strengthen NRAs in regulatory self-assessment approaches.

WHO Comment

- Reporting on the outcome of NRA assessments is part of the standard operating procedure.
- Criteria to assess performance are being developed within the vaccines NRA assessment tool.
- Country self-assessments have been increasingly used as a first step in the vaccines NRA assessment process.
## GMP inspections: impact of information sharing and risk management

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<td>- Promote and enable networking and information sharing among national, regional and other relevant authorities involved in inspections.</td>
<td>- In 2009, WHO signed a cooperation agreement with the Pharmaceutical Inspection Cooperation Scheme.</td>
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<td>- medicines prequalifying programme can disclose inspection related information to regulatory authorities of WHO Member States as well as regulatory authorities that are members of the Pharmaceutical Inspection Cooperation Scheme (PIC/S).</td>
<td>- Platform and procedures for sharing inspection reports has been created</td>
</tr>
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Conclusion

- ICDRA remains an important forum of regulators which recommendations are followed up and implemented
- A big THANK YOU to all regulators for the excellent collaboration with WHO
WORLD HEALTH DAY 2011

Committing to combat ANTIMICROBIAL RESISTANCE

Stopping the threat to the control of tuberculosis, malaria, HIV and other infectious diseases
WORLD HEALTH DAY 2011
Antimicrobial Resistance
Burden and Threat

TB
• 440,000 new MDR-TB cases annually
  and XDR-TB reported in 58 countries so far

Malaria
• Emergence of Artemisinin resistance
  linked to ongoing use of monotherapies

HIV
• With expanded use of ARVs, resistance now a concern
  • Lethal MRSA is a significant threat in hospitals
  • Pathogens such as E. coli and K. pneumoniae resistant
    to multiple drugs on the rise
  • Increasing resistance in Gonorrhoea and Shigellosis
WORLD HEALTH DAY 2011
Antimicrobial Resistance
Global Policy Response To Date

World Health Assembly Resolutions
1998 – Emerging and other communicable diseases AMR
2005 – Improving the containment of AMR
2009 – Prevention and control of MDR-TB and XDR-TB

WHO Regional Committee Resolutions
(e.g. AFRO, SEARO, PAHO)

WHO Global Strategy for Containment of AMR (2001)

Surveillance systems and response strategies being pursued
Task forces and informal networks at global and regional levels

Despite progress, the strategy for AMR containment has not been widely implemented
WORLD HEALTH DAY 2011
Antimicrobial Resistance
The Challenges

1. Complex problem requiring a comprehensive response
   - within and across Member States
   - across different sectors

2. Actions needed are clear
   - but there is a failure of commitment, implementation and accountability

3. Preventing AMR is a "public good" and a contribution to health security
   - but financing is far from sufficient
WORLD HEALTH DAY 2011
Antimicrobial Resistance
Partners Engaged To Date

• The Bill & Melinda Gates Foundation
• The Government of Sweden
• ECDC (European Centre for Disease Control)
• CDC (US Centers for Disease Control and Prevention)
• CGD (Center for Global Development)
• TATFAR (Trans-Atlantic Task Force on Antimicrobial Resistance)
• ReACT (Action on Antibiotic Resistance)
• APUA (Alliance for the Prudent Use of Antibiotics)
• IFPMA (Int. Fed. of Pharmaceutical Manufacturers Associations)
• FIP (International Pharmaceutical Federation)
• The Global Fund, Stop TB Partnership
• WHONET
WHO wishes to inform regulators about the WHD 2011 topic

WHO invites regulators to join the efforts to fight antimicrobial resistance

Consultations will follow with regulators how best to benefit from their expertise and ongoing activities