An overview of international initiatives in the regulatory sphere

Cordula Landgraf
Head of Networking, Swissmedic

Do you know what substance this is?
Oxytocin – an elixir to support cooperation?

What recent studies suggest …

- Increase of attention to social stimuli
- Reduction of natural fear of the other
- Promotion of getting closer to others and let us enjoy this “closeness”
- Cortisol
- Last but not least: promotion of building trust and establishing confidence

Research by Markus Heinrichs and Ernst Fehr, University of Zurich

Nobody can do everything alone:

An overview of international initiatives in the regulatory sphere
Outline

1. Background
2. Examples of initiatives
3. Latest developments and achievements
   - Focus on IPRF and ICH
4. Summary & Outlook

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Harmonisation versus Convergence

- Harmonisation of technical requirements for medicines regulation, i.e. legislation, guidelines, procedures, etc. (WHO)
  - The process by which the interpretation and/or application of technical guidelines can be made uniform or mutually compatible. (FDA/CBER)

- Regulatory requirements become more similar or aligned over time as a result of gradual adoption of internationally recognised technical guidance documents and standards
  - Does not represent harmonization of laws and regulations (APEC)
**Reliance and Work Sharing**

- **Reliance**
  - State of being dependent upon or confident in something or someone
  - Having trust
    (The Business Dictionary)

- **Work Sharing**
  - Making use of work products and leveraging resources and expertise of as well as sharing workload between agencies. This includes:
    - **Reliance** on or consideration of work already performed by other agencies
    - "Real-time" work sharing for simultaneous activities ("joint assessments").
      (ACSS Consortium)

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**Levels of regulatory cooperation**

- **Confidence building/harmonisation/convergence**
- **Reliance/work sharing**
  - Benefit for regulators; sharing of workload, but independent decisions
- **Recognition**
  - Based on treaties; «maximal benefit» but partial loss of sovereignty with regard to decision-making
- **Trust**
  - «Foundation», Equivalence of requirements
Levels of regulatory cooperation

Recognition
Examples: Mutual Recognition Agreements (EU, ASEAN); marketing authorisation procedures (EU, GCC); unilateral recognition of marketing authorisations (Mexico);…

Reliance/Work-sharing
Examples: Abridged application routes/reference country model; WHO Pre-Qualification; EAC/MRH joint assessment procedure; ZAZIBONA(S), IGDRP; ACSS Consortium (HSA, TGA, HPFB, Swissmedic); …

Confidence building/harmonisation/convergence
Examples: AMRH; EAC/MRH; PIC/S; ICH; IPRF; IGDRP; IMDRF; RHIs/RECs; WHO trainings and networks, ICDRA; GRPs; Bilateral agreements; …

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### Examples of global initiatives involved in convergence/harmonisation (1)

<table>
<thead>
<tr>
<th>Initiative</th>
<th>Scope</th>
<th>Main objective(s)/areas of work</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICH</td>
<td>Human medicinal products</td>
<td>Harmonisation of requirements for registration for human medicinal products</td>
</tr>
<tr>
<td>VICH</td>
<td>Veterinary medicinal products</td>
<td>Harmonisation of requirements for registration for veterinary medicinal products</td>
</tr>
<tr>
<td>IGDRP</td>
<td>Generics</td>
<td>Promote collaboration and convergence in generic drug regulatory programs in order to address the challenges posed by increasing workloads, globalisation and complexity of scientific issues …</td>
</tr>
<tr>
<td>IPRF</td>
<td>Medicinal products</td>
<td>Support implementation of ICH and other internationally harmonized technical guidelines; identification of need for harmonization or convergence in specific areas; …</td>
</tr>
</tbody>
</table>

### Examples of global initiatives involved in convergence/harmonisation (2)

<table>
<thead>
<tr>
<th>Initiative</th>
<th>Scope</th>
<th>Main objective(s)/areas of work</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMDRF</td>
<td>Medical Devices</td>
<td>Accelerate international medical device regulatory harmonization and convergence …</td>
</tr>
<tr>
<td>WHO</td>
<td>Health Products</td>
<td>Development of international standards for the manufacturing and regulation of health products</td>
</tr>
<tr>
<td>PIC/S</td>
<td>GMP inspections</td>
<td>Developing and promoting harmonised GMP standards and guidance documents …</td>
</tr>
<tr>
<td>ICMRA</td>
<td>Medicinal products</td>
<td>Regulatory convergence, alignment and standards development; regulatory cooperation and work-sharing; capacity and competence building/technical assistance; regulatory systems comparability criteria and assessment criteria; regulatory science.</td>
</tr>
</tbody>
</table>
Examples of global initiatives involved in convergence/harmonisation (3)

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<tr>
<th>Initiative</th>
<th>Scope</th>
<th>Main objective(s)/areas of work</th>
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<tr>
<td>WHO Prequalification <a href="http://www.who.int/topics/prequalification/en/">http://www.who.int/topics/prequalification/en/</a></td>
<td>Drugs, vaccines, diagnostics</td>
<td>The prequalification process consists of a transparent, scientifically sound assessment, which includes dossier review, consistency testing or performance evaluation and site visits to manufacturers.</td>
</tr>
<tr>
<td>ACSS Consortium</td>
<td>Medicinal products/medical devices</td>
<td>Various collaborative projects ranging from marketing authorisation, post-market surveillance to IT.</td>
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ICH

- **International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)**
- Established as a legal entity (international association based in Geneva, CH)
- Bodies of the association

ICH

- Opening up to new members and observers
- **New regulatory members:**
  - Agência Nacional de Vigilância Sanitária (ANVISA), Brasil
  - CFDA, China
  - MFDS, South Korea
- **Current observers include:**
  - Southern African Development Community (SADC)
  - Gulf Cooperation Council (GCC)
  - Pan American Network for Drug Regulatory Harmonization (PANDRH)
  - Asia-Pacific Economic Cooperation (APEC)
  - Therapeutic Goods Administration (TGA)
  - ...

http://www.ich.org/about/membership.html

Altogether:
- Members 14
- Observers 23
ICH

ICH Assembly Meeting, Montréal, Canada, May/June 2017

Adoption of two new ICH topics

• Guideline on extrapolation of paediatric indications

• E8(R1) General considerations for clinical trials
  as part of the announced GCP renovation

IPRF

• The IPRF has emerged from the “Regulators Forum” in 2013
• Regulators-only platform, meeting twice a year in the margins of the “ICH week”
• Membership quite extensive
  – Australia (TGA)
  – Brazil (ANVISA)
  – EU (EMA/EU Commission)
  – Canada (Health Canada)
  – Japan (MHLW/PMDA)
  – Korea (MFDS)
  – Mexico (Cofepris)
  – Russia (Roszdravnadzor)
  – Singapore (HSA)
  – Switzerland (Swissmedic)
  – USA (FDA)
  – RHI
  – WHO (observer)
The Management Committee (MC) currently oversees the work of five working groups:

- Cell Therapy
- Gene Therapy
- Biosimilars
- Nanomedicines
- IDMP

**Biosimilars Working Group**

- Development of a template for “Public Assessment Summary Information for Biosimilar (PASIB)”
- Development of a “Reflection paper on extrapolation of indications for biosimilars”
  - to be published soon on the IPRF website
- The Biosimilars Working Group has held a workshop with WHO to advance work on developing training material to establish biosimilar comparability
IPRF / IGDRP consolidation

- Principle support by both the IPRF Management Committee and the IGDRP Steering Committee
- Establishment of a joint Implementation Task Group (ITG) to consider various governance models for the joint initiative and to work out an implementation plan
- Joint initiative expected to be launched in January 2018
- First joint f2f meeting planned for June 2018

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Summary

- Initiatives with the focus on harmonisation/convergence are well under way
- Increasing participation from regulators in multilateral/global initiatives
- Consolidation of initiatives has started to avoid overlap and duplication (IPRF/IGDRP)

Summary

- Increasing number of initiatives focussing on reliance and work sharing
  "even the largest agencies cannot do everything themselves"
- Reliance accepted in the "developed world" (e.g. GMP inspections, sharing of assessment reports)
- WHO increasingly and successfully promotes reliance and work sharing models in developing countries
Interested to read more?
See our article “Swissmedic emphazises international cooperation”

Questions?
Contact Information
Cordula Landgraf
Head of Networking
Swissmedic
Tel.: +41 58 462 0478
E-mail: networking@swissmedic.ch
<table>
<thead>
<tr>
<th>Abbreviation</th>
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<tbody>
<tr>
<td>ACSS</td>
<td>Australia-Canada-Singapore-Switzerland (“Consortium”)</td>
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<tr>
<td>AMRH</td>
<td>African Medicines Regulatory Harmonisation</td>
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<tr>
<td>ANVISA</td>
<td>Brazilian Health Surveillance Agency</td>
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<tr>
<td>APEC</td>
<td>Asia-Pacific Economic Cooperation</td>
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<tr>
<td>ASEAN</td>
<td>Association of Southeast Asian Nations</td>
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<tr>
<td>BIMHMI</td>
<td>Federal Institute for Drugs and Medical Devices</td>
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<td>BfArM</td>
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<tr>
<td>CBER</td>
<td>Centre for Biologics Evaluation and Research</td>
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<td>CFDA</td>
<td>China Food and Drug Administration</td>
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<tr>
<td>EAC</td>
<td>East African Community</td>
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<td>EAC-MRH</td>
<td>EAC Medicines Regulatory Harmonisation</td>
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<td>EMA</td>
<td>European Medicines Agency</td>
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<tr>
<td>EU</td>
<td>European Union</td>
</tr>
<tr>
<td>GCC</td>
<td>Gulf Cooperation Council</td>
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<tr>
<td>GRP</td>
<td>Good Regulatory Practices</td>
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<tr>
<td>HPFB</td>
<td>Health Products and Food Branch</td>
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<tr>
<td>HPRA</td>
<td>Health Products Regulatory Authority</td>
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<tr>
<td>HSA</td>
<td>Health Sciences Authority</td>
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<td>MEF</td>
<td>Medicines Control Council, has transitioned into the South African Health Products Regulatory Authority</td>
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<tr>
<td>MOH</td>
<td>Ministry of Health</td>
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<tr>
<td>MHLW</td>
<td>Ministry of Health, Labour and Welfare</td>
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<tr>
<td>MNU</td>
<td>Memorandum of Understanding</td>
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<tr>
<td>OECD</td>
<td>Organisation for Economic Co-operation and Development</td>
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<tr>
<td>PANDRH</td>
<td>Pan-American Network for Regulatory Harmonisation</td>
</tr>
<tr>
<td>PEI</td>
<td>Paul Ehrlich Institute</td>
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<tr>
<td>PIC/S</td>
<td>Pharmaceutical Inspections Cooperation Scheme</td>
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<tr>
<td>PNdA</td>
<td>Pharmaceticals and Medicines Agency</td>
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<tr>
<td>REC</td>
<td>Regional Economic Community</td>
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<tr>
<td>RHIA</td>
<td>Regional Harmonisation Initiative</td>
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<tr>
<td>TGA</td>
<td>Therapeutic Goods Administration</td>
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<tr>
<td>US-FDA</td>
<td>United States Food and Drug Administration</td>
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<tr>
<td>WHO</td>
<td>World Health Organisation</td>
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<tr>
<td>ZAZBONA</td>
<td>Zambia-Zimbabwe-Botswana-Namibia (Collaborative medicines registration process)</td>
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