Consortium Internacional ACSS
The ACSS Consortium

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On behalf of and with input from the members of the ACSS Consortium
Overview

- Background and introduction
- Working groups (WG) overview
  - Generics WG
  - NCE WG
  - CHP WG
  - IT WG
- Summary and conclusions
Background and introduction: A global network

... a truly global network!
Background and introduction: Rationale

- Globalised industry sectors
- Rapid emergence of new technologies; increased complexity
- Increasing expectations regarding performance
- Increasing pressure on financial and human resources

Increasing workload for regulators
☞ How to provide for the increasing resource needs?
☞ Which approaches should be applied to address these challenges?
Background and introduction: Approach

Effective information and work-sharing

- Consortium formed in 2007 to explore opportunities for work-sharing between like-minded medium-sized regulatory authorities.
- Basis: Network of bilateral agreements/arrangements between the four agencies.
- Voluntary network to build synergies, enhance effectiveness and efficiency of domestic regulatory systems and capitalize on each country’s area of strength.
Background and introduction: Main objectives

- Providing an effective and efficient alternative to participating regulators working independently on similar scientific and regulatory work
- Enabling participating regulators to draw on the very best scientific and technical data, information, expertise, resources and best practices to better inform regulatory decisions
- Improving each participant’s effectiveness and efficiency as a regulator (domestically)
- Creating or complementing existing communication networks and increasing dialogue
- Exploring new initiatives and regulatory concepts
Background and introduction: Guiding principles

- Trust
- Openness
- Equality
- Transparency
- Flexibility
- Respect
Background and introduction: Key success factors

Each country has something to offer the other countries

Equal status in terms of engagement and decision making

Flexibility with regard to participation: «Opt-in/opt-out» possibility from any work plan activities
Background and introduction: Work-sharing

Work-sharing (and reliance): proposed definitions in the draft WHO Good Regulatory Practices

http://www.who.int/medicines/areas/quality_safety/quality_assurance/GoodRegulatory_PracticesPublicConsult.pdf?ua=1

Work-sharing: a process by which NRAs of a number of jurisdictions share activities. Work-sharing entails exchange of information consistent with the provisions of existing agreements and compliant with each agency's or institution’s legislative framework for sharing such information with other NRAs. Other opportunities for work-sharing include: jointly assessing applications for marketing authorizations or therapeutic product manufacturing sites, joint work in the post-marketing surveillance of therapeutic product safety, joint development of technical guidelines or regulatory standards, and collaboration on information technology (44).

Reliance: the act whereby the NRA in one jurisdiction may take into account and give significant weight to – i.e., totally or partially rely upon – evaluations performed by another NRA or trusted institution in reaching its own decision. The relying authority remains responsible and accountable for decisions taken, even when it relies on the decisions and information of others.
Background and introduction: Scope

In terms of products
- Medicinal products for human use (current scope)

In terms of topics
- Scientific and/or technical requirements related to the efficacy, safety and quality for marketing authorization
- Regulation and policy frameworks
- Regulatory oversight of clinical trials and manufacturing sites
- Electronic data strategies
- Other issues of emerging concern
Background and introduction: Governance

ACSS

Heads of Agencies

Coordinators

WG

WG

WG

WG

WG
Background and introduction: Roles & responsibilities

- Review the progress of the ongoing work and projects
- Define the strategic direction
- Identify and prioritize challenges to be addressed
- Authorize resources in support of advancing the ACSS Consortium’s goals and objectives
- Make decisions on behalf of the Consortium
Background and introduction: Roles & responsibilities

- Management of ongoing business
- Acting as primary contact point
- Preparing and organizing the meetings of the Heads of Agencies
- Ensuring effective communication between the members
- Coordinating the work of the experts in the ACSS Consortium Working Groups (WG)
Background and introduction: Cooperation mechanisms

Working Groups on identified/selected topics/projects chaired by one member

Project Proposals based on mandate and initial work plan

Networks for ongoing exchange and sharing of information (including secure platform for information exchange)
Overview of working groups

New Chemical Entities (NCE) / Benefit-Harm-Risk (B-H-R) Co-chaired by Health Canada and TGA

Generic Medicines
Rotating chair (input for this presentation by HSA)

Complementary Health Products
Chaired by HSA

Information Technology
Chaired by Health Canada
Chair and Secretariat Support – HC and TGA

Teleconference Meetings every 2 months

A number of work items under the work plan have been completed while other items are ongoing:

- Comparison of regulatory framework and technical requirements (completed)
- Benefit/Harm/Uncertainty (completed):
  - Compare respective frameworks
  - Compare agencies’ reviewer tools used for B-H-U assessment (e.g. report templates, standard operating procedures, learning activities, etc.)
New Chemical Entities (NCE)/Benefit-Harm-Risk (B-H-R): work plan

- Two clusters: CNS and Infectious Diseases (ongoing)
- Sharing information on NCE applications under review (ongoing)
- Developing a framework for work sharing of joint-reviews (ongoing) / Pilot of a NCE Submission between HC and TGA
The Working Group (WG) has been actively screening NCE filings to identify suitable candidate submissions for work sharing.

Concrete timelines and deliverables for the development of a work sharing framework for joint-review are in place.

Upcoming face to face meeting on the margins of the DIA in Chicago to finalize framework documents and commence analysis on pilot phase.

Next phase will be a joint-review pilot with Canada and Australia participating in the pilot and Switzerland and Singapore would be the observers.
New Chemical Entities (NCE)/Benefit-Harm-Risk (B-H-R): benefits

Benefits
- Leverage best practices from multiple jurisdictions
- Leverage global expertise and resources
  - ready access to expertise to consult on complex issues with submissions
  - Keep networks active
    - access to international counterparts addressing challenges that are global in scale
New Chemical Entities (NCE)/Benefit-Harm-Risk (B-H-R): challenges

Challenges

- NCEs inherently more challenging than generics due to diverse set of scientific disciplines and complex submission packages and review elements
- Lack of overlapping submissions among all agencies
- External communication strategy is being developed to attract industry participation
Generics: objectives

- Develop true information and work sharing arrangements for the four participating ACSS Consortium members;
- Share best practices and lessons learned on issues relating to the regulation of generic medicines with broader, multi-lateral collaborative initiatives, notably with the International Generic Drug Regulators Programme (IGDRP);
- Demonstrate a model for other collaborations among regulatory authorities;
- Support and inform International Coalition of Medicines Regulatory Authorities (ICMRA) efforts to develop global information and work sharing approaches.
Generics: key milestones and joint achievements

- Summary of Application Elements:
  - Compilation of regulatory requirements and review practices for the identification of potential areas for harmonisation

- Quality Working Group:
  - common assessment report template (drug substance)
  - guideline for quality assessors (drug substance)

- Bioequivalence Working Group:
  - guidance for bioequivalence assessors

- Summary of information on Reference Product:
  - completed in May 2016
Generics: generic medicines work-sharing trial (GMWST)

Applicant

- TGA
- Health Canada
- Swissmedic
- HSA

Reference Regulatory Agency (RRA)

Concerned Regulatory Agencies (CRA)
Generics: generic medicines work-sharing trial (GMWST)

- All dosage forms would be considered for this trial.
- Application can be submitted to at least 2 of the 4 agencies.
- Valuable knowledge is being obtained through this pilot exercise that will inform internal procedures on the effective use of foreign assessment reports as well as collaborative work with our international regulatory partners.
Generics: generic medicines work-sharing trial (GMWST)

**Reference Regulatory Agency (RRA)**
- Lead agency
- Evaluates CTD module 2-5 and provides assessment report (AR)
- Evaluates own module 1

**Concerned Regulatory Agencies (CRA)**
- Conduct a peer review of assessment report provided by RRA, evaluates CTD module 2-5, and prepares peer review report with any additional questions
- Evaluate their respective module 1

**Output**
- AR by RRA on Module 2-5
- AR Module 1
Generics: generic medicines work-sharing trial (GMWST)

- Submission of Application: 10 days
- Assessment of Application: 55 days
- List of Questions to Applicant: 30 days
- National steps towards decision
- 2nd List of Questions/ Pre-approval letter: 45 days
- Submission of Responses by Applicant

Timelines and milestones currently under review

Timelines expressed in calendar days
Generics: generic medicines work-sharing trial (GMWST)

How to participate:

- Interested applicant informs ACSS agencies (ACSS@health.gov.au) about their intent and proposes their preferred RRA by completing an Expression of Interest form.
- A pre-submission teleconference will be held between the ACSS agencies and the applicant to discuss the requirements and application process for the trial.
- The application (including DMFs) should be submitted to all agencies simultaneously.

Breaking news: The first application has now been approved in Australia, Switzerland and Canada!
Complementary Health Products: background and key objectives

Regulatory challenges with Complementary Health Products (CHP):

- Scope of CHP ingredients is wide and diverse
- “Complementary Health Products” is used as a general term to describe a diverse group of products comprising of traditional medicines, herbal medicines, homeopathic medicines, health supplements, complementary medicines, natural health products, etc.
- Some might have been used in small populations only
- Limited safety information presented by companies
- Rapid emergence of new CHP ingredients
The ACSS CHP WG was formed in February 2015 with the aim to:

- Assess CHP ingredients with safety concern
- Develop methodology framework for safety assessment
- Review appropriate cautionary labelling for CHP
- Share new development in CHPs regulation
- Share evaluation standards/requirements with regard to non-conventional technologies applied in manufacture of CHP ingredients.
Complementary Health Products: key milestones and achievements

- **OCT 2015**
  Pilot Run for safety assessment of 4 ingredients – Cycloastragenol, Annona muricata, Nattokinase & Ginkgo biloba (Completed)

- **FEB 2015**
  ACSS CHPWG 1st meeting

- **JAN 2016**
  Safety Assessment Report Template (Completed)

- **MAY 2016**
  Guidance on the Calculation of the Acceptable Daily Intake (ADI) for Safety Assessment of Complementary Health Product (CHP) Ingredients (Completed)

- **SEP 2016**
  Minimum Data Requirements for Safety Assessment of Complementary Health Product (CHP) Ingredients (Completed)

- **MAY 2017**
  Safety assessment of 2nd batch of 3 ingredients: Ephedra, Areca Catechu, Ibogaine (Completed)
Complementary Health Products: work-sharing model

<table>
<thead>
<tr>
<th>Identification of Ingredients for safety assessment</th>
<th>Joint Safety Assessment</th>
<th>Regulatory Outcomes</th>
<th>Benefits</th>
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</thead>
<tbody>
<tr>
<td><strong>Selection Criteria</strong></td>
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<tr>
<td>• Without well documented safety profiles</td>
<td>Assessment report peer reviewed Assessment Tools</td>
<td>Information Sharing Regulatory decisions based on each country’s frameworks, risk management strategies</td>
<td>• Convergence in assessment methodology</td>
</tr>
<tr>
<td>• Known to have adverse event occurrence</td>
<td>• Safety Assessment Report Template</td>
<td>• Calculation of the Acceptable Daily Intake for Safety Assessment</td>
<td>• Reduction in duplicated efforts</td>
</tr>
<tr>
<td>• New ingredients</td>
<td>• Minimum Data Requirements for Safety Assessment</td>
<td>• Refinement of regulatory approach</td>
<td></td>
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</tbody>
</table>
Member countries propose ingredients of interest

Each member country chooses prioritised ingredient for assessment

A member country conducts the first assessment review

Assessment report will be peer-reviewed by another member country

Peer-reviewed assessment reports will be forwarded to remaining countries for further comments

Finalised reports are uploaded to common Sharepoint platform for future reference

Complementary Health Products: review process for joint safety assessments
Complementary Health Products: key learnings from pilot run

- Despite different regulatory framework and controls for CHPs, the WG is able to identify a work area of common interest and further the work on sharing of safety assessment.
- Better understanding of the other members’ existing regulatory approaches in CHP safety assessment.
- General principles and approaches adopted for safety assessment are similar.
Complementary Health Products: key learnings from pilot run

- Some differences in technical parameters applied e.g. Acceptable Daily Intake (ADI) calculation. → Need to standardise assessment parameters and minimum data requirements.
- Identification of information needed in safety assessment report to facilitate peer reviews.
- Regulatory decisions may vary depending on the risk mitigation measures applied by each agency.
Complementary Health Products: conclusions

- Convergence of assessment reports and methodologies will improve regulatory efficiency as agencies are able to work and share their efforts in safety assessment of CHP ingredients.
- Greater robustness in the decisions of safety assessments as well as to improve regulatory efficiency.
- Sharing of safety assessment information will allow further fine-tuning of the risk based regulatory approaches
- Next step, the group is exploring to broaden the scope of collaboration to include efficacy assessment.
Information technology: key activities and deliverables

- **September 2016**: Microsoft Dynamics Expert Session
- **October 2016**: Digitisation Expert Session
- **February 2017**: IDMP Expert Session
- **June 2017**: IDMP Policy Paper completed

**2015**
- December 2015: Big Data White Paper completed

**2016**
- October 2016: Digitisation Expert Session

**2017**
- June 2017: IDMP Policy Paper completed
At each quarterly meeting, members share their regional IT priorities and updates providing a valuable opportunity to learn about issues and initiatives impacting our respective IT areas.

Members have shared a wide variety of updates such as:

- Legislative changes impacting future IT direction at Swissmedic;
- Innovative projects such as HSA’s new mobile apps for consumers or Health Canada’s Drug and Health Product Register;
- TGA’s plans for re-working their operational model.
IT WG was tasked with authoring a White Paper on Big Data providing information on the following topics: 1. What is big data 2. Relevant definitions 3. Regulatory context and implications for our work with health products 4. Challenges with big data 5. Opportunities for multi-lateral cooperation and partnership across the ACSS partners.

Document was completed in December 2015.

Future work on Big Data has been transferred to the International Coalition of Medicines Regulatory Authorities (ICMRA) project.
IDMP importance was recognized at the ACSS Management Committee meeting in October 2016.

IT WG was tasked with drafting a Policy Paper on IDMP implications and implementation considerations for the ACSS regions.

The Policy Paper has been endorsed by the ACSS Heads of Agencies at their meeting on 20 June 2017.

The ACSS partners also participate in and share information with the IDMP WG at the International Pharmaceutical Regulators Forum (IPRF).
ACSS IT WG hosts expert sessions on topics of mutual interest to working group members

Purpose of expert sessions is to share expertise, best practices, and lessons learned on topics that are common to the ACSS agencies:

- Microsoft Dynamics (September 29, 2016)
- Digitisation (October 18, 2016)
- Identification of Medicinal Products (February 23, 2017)
- Cybersecurity (date to be determined)
- Processing Automation (date to be determined)
Summary and conclusions

- The ACSS Consortium is a long-standing and successful collaborative initiative.
- It has received continued high-level support and attention from the participating Agencies’ Heads.
- Work-sharing has been in the focus from the beginning, and is seen as providing the ultimate benefit for the partners.
- Ad hoc exchanges and information-sharing in the WGs provide additional benefit (lessons learned, best practices).
- The future direction of the ACSS Consortium is currently under consideration by the Heads of Agencies.
Thank you for your attention!

Acknowledgement:
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