Regulatory reliance and work sharing
Objectives

- Definitions of regulatory reliance and work-sharing
- Examples of how these approaches have been used
- Implementation of reliance and work-sharing for COVID-19 vaccine pharmacovigilance
What is regulatory reliance?

1. The act whereby the national regulatory authority (NRA) in one jurisdiction may take into account and give significant weight to assessments performed by another NRA or trusted institution, or to any other authoritative information in reaching its own decision.

2. The relying authority remains independent, responsible and accountable regarding the decisions taken, even when it relies on the decisions and information of others.
Why do we need Reliance

About one third of National Regulatory Agencies globally have limited capacity to perform core regulatory functions

Regulatory capacity gap between different countries (low- and high-income) exists in terms of:

- Human and financial resources
- Regulatory functions effectively performed
  - Expertise available for fulfilling regulatory functions
  - Availability of proper systematic training for regulators
  - Applying quality management principles.
WHO Good Reliance Practices

Promote a more efficient approach to regulation, thereby improving access to quality-assured, effective and safe medical products
Options to facilitate good quality regulatory decisions – reliance in the focus

- Unilateral or mutual recognition: mutual recognition is based on treaties or equivalent, providing maximal benefits but partial loss of sovereignty with regard to decision-making.
- Reliance on regulatory decisions performed by other competent and trusted agencies and/or cooperation/collaboration with other regulators to reduce the workload, with independent final decision-making.
- NRA makes independent decisions based on its own reviews or inspections.

Regulatory cooperation based on convergence/harmonization to improve the quality of decision-making process.
WHO Good Reliance Practices - Scope

Covers reliance activities in the field of regulation of medical products (i.e. medicines, vaccines, blood and blood products and medical devices including in vitro diagnostics)

Addressing all regulatory functions as defined in the Global Benchmarking Tool (registration and marketing authorization, vigilance, market surveillance and control, licensing establishments, regulatory inspection, laboratory testing, clinical trials oversight, and NRA lot release) - spanning the full life cycle of a medical product.
Improving efficiency based on reliance

- Independent decisions based on its own reviews and/or inspections
- Leveraging regulatory work performed by other competent and trusted authorities to reduce the workload, with independent final decision-making
- Regional reliance mechanisms centralized evaluation conducted for a group of countries
- Unilateral or mutual recognition based on treaties or equivalent, providing maximal benefits

Increasing level of reliance

- Standard processes
- Work-sharing including joint activities, abridged pathways using reliance
- Regional reliance mechanisms
- Unilateral recognition
- Mutual recognition

Building trust towards establishment of equivalence
Two Types of Reliance Activities are possible In Pharmacovigilance

Reliance on processes, tools and methods developed by others
- This involves regulatory authorities adopting common processes and standards, e.g. templates for safety reporting, templates for study protocols and reports, signal detection methods, platforms for epidemiological studies.

Reliance on product-specific regulatory activities.
- These can cover the entire life cycle of the product.
- May include participation in a joint assessment committee for marketing authorization approval and variations and for safety assessments.
- May include reliance on product information approved by another NRA or
- Reliance on the assessment of post-authorization safety study protocols and results required by others.

This level of reliance requires that the products concerned are the same or are sufficiently similar in terms of composition, indications, conditions of use, etc.
Definition of work-sharing

**Process**

- A process by which NRAs of two or more jurisdictions share activities to accomplish specific regulatory tasks.

**Opportunity**

- jointly assessing applications for authorization of clinical trials;
- marketing authorizations or good practices inspections;
- joint work in the post-marketing surveillance of medical product quality and safety;
- joint development of technical guidelines or regulatory standards, and collaboration on information platforms and technology.

**Information exchange**

- Work-sharing also entails exchange of information consistent with provisions of existing agreements and compliant with each agency’s or institution’s legislative framework for sharing such information with other NRAs.
Reliance on Global PV Data

Around 140 Member States report safety events to the WHO global database of individual case safety reports - VigiBase

Member States rely on this resource (and thereby, on each other’s data), to confirm or validate signals of adverse events

Regional pharmacovigilance databases, as a subset of VigiBase, can also help regulators from the region share and use safety data on products that are specific for their region/groups of countries
Reliance for product and MAH information

• Under Article 57 of EU pharmaceutical legislation: manufacturers submit and update information on authorized medicines to EMA.

• Regulators of all EU Member States can access the information.

• This helps regulators to:
  • Identify the company’s qualified person for pharmacovigilance (QPPV);
  • Submit coordinated enquiries to companies;
  • Organize joint PV inspections etc.
<table>
<thead>
<tr>
<th><strong>Article 58: Reliance on EMA scientific opinions by non-EU countries</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. <strong>EMA provides scientific opinions on high priority medicines &amp; vaccines for markets outside EU</strong></td>
</tr>
<tr>
<td>2. <strong>The evaluations are carried out by EMA in cooperation with WHO and “target” non-EU NRAs;</strong></td>
</tr>
<tr>
<td>3. <strong>The relying regulatory authorities can use the risk management plan (RMP) proposed by EMA for specific products</strong></td>
</tr>
<tr>
<td>4. <strong>But, benefit-risk assessment is focused on the intended non-EU population and indication(s).</strong></td>
</tr>
<tr>
<td>5. <strong>Procedure facilitates patient access to essential medicines ad vaccines in low- and middle-income countries (LMICs), especially for neglected diseases and diseases such as HIV/AIDS, malaria and tuberculosis.</strong></td>
</tr>
</tbody>
</table>
Regional reliance for PV (example 1)

- The Caribbean Regulatory System (CRS) provides an example of a regional reliance mechanism;
- Many small states in the Caribbean Community (CARICOM) submit in-country adverse reaction reports to VigiBase through CRS;
- Good example of leveraging the regional capacity for post-market surveillance.
Regional reliance for PV (Example 2)

- The AVAREF provides an example of a regional reliance mechanism
- Many states in the Region participate
- Good example of leveraging the regional capacity for post-market surveillance.
Reliance in the context of COVID19 vaccines accessed through WHO PQ process

A group of countries, or a regional economic community could identify a reference country to join (and represent the region/ community in) the WHO PQ assessment process.

For example, representatives from the reference LMIC could participate as assessors for the WHO PQ/EUL of COVID19 vaccine:
- to review the Risk Management Plans and PV activities in the dossiers;
- to ensure relevance of the PV plans for their region.

All other countries in the region would then be able to rely on the WHO PQ decision.

The reliance approach could be used also for PV inspections. For WHO-prequalified products, WHO inspection outcomes would be used by all countries.
Work-sharing in the context of pharmacovigilance of COVID-19 vaccines

1. COVID-19 vaccines could be conducted by a regional regulatory system or by a group of NRAs.

2. A regional review committee should be established to facilitate cooperation and coordination, as well as oversee the process in reaching valid regulatory decisions that will serve as a reference for relying NRAs.

3. Activities that could be carried out through work-sharing include:
   - joint review of periodic safety update reports/periodic benefit-risk evaluation reports (PSURs/PBRERs);
   - joint review of safety data from regional multi-centre studies.
References


• Vigibase: https://www.who-umc.org/vigibase/vigibase/