Principles for Regulatory Reliance

Alexandra Guta, B.Pharm, M.Sc
Specialist QMS, Medicines and Other Health Technologies
PAHO/WHO
Outline

• Context for reliance
• PANDRH recommendations
• Principles
• Examples of reliance
• Impact and responsibilities of actors
Regulatory convergence, harmonization and reliance

Strengthening regulatory systems for medicines and other health technologies remains a critical priority for well-functioning health systems that want to achieve *Universal Health*.

The globalization of health technologies markets has pushed regulatory systems to act internationally to ensure the safety, quality and effectiveness of the products that are consumed locally.

Countries need to consider the merits of strategies to strengthen regulatory systems and that may help gain efficiencies and effectiveness.
Goal

To improve understanding of how reliance practices can help regulatory systems strengthening and establish the principles to ensure effective use.

Outlines key examples and principles for implementing reliance practices

• (a) to adopt the phrase “use of regulatory decisions of other jurisdictions” to describe reliance;

• (b) to share the concept note on regulatory reliance principles with Member States to ensure that it helps decision making to improve their regulatory efficiencies;

• (c) to consider following the principles proposed in this document when applying and adopting regulatory reliance strategies for processes, products and/or practices;

• (d) to recommend the inclusion of reliance-related provisions and language in legal documents, where appropriate, for registry, inspection, laboratory testing, etc.;

• (e) to encourage Member States to use reliance to increase efficiencies and in particular, states with limited resources which are seeking fast improvements in regulatory capacities; and

• (f) to request that PAHO and its Member States monitor and evaluate the impact of regulatory reliance across the Region.

RELIANCE PROPOSED PRINCIPLES

- Sovereignty
- Consistency
- Competency
- Transparency
- Legal basis

Ref: Regulatory reliance principles: concept note and recommendations:
http://iris.paho.org/xmlui/handle/123456789/51549
Reliance is a strategy that seeks a better use of resources, thus, it should not be limited to low capacity systems but should be considered as a good strategy to improve capacities in all a wide range of regulatory settings.

While reliance may offer more clear advantages to developing regulatory systems, it is a strategy that should be considered for any regulatory body in search of efficiencies.
Reliance should translate into...

...and lead to...

Trustful, transparent, adaptative and efficient regulation

- Informed regulatory decision-making

- Improved oversight of regulated industry (inspections, data integrity)

- Strengthened regulatory processes NOT the mere outsourcing of regulatory processes!
Reliance is a daily activity!

Enablers

TRUST        HARMONIZATION       INFORMATION SHARING       ECONOMIC INTEGRATION       LEGAL       SHARED RESPONSIBILITY AND ACCOUNTABILITY
Barriers

- Lack of trust
- Trouble accessing information
- Confidentiality
  - Regulatory information is not sharable/publicly available
- Legal frameworks that preclude reliance
Examples of reliance mechanisms in PAHO and the Region of the Americas

• PAHO Revolving Funds (access)
• Caribbean Regulatory System (pre-market entry)
• Pharmacovigilance network (post market entry)
PAHO Revolving Fund uses reliance for vaccine procurement for 41 countries and territories

<table>
<thead>
<tr>
<th>WHO Prequalification</th>
<th>NRAs of reference</th>
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<tbody>
<tr>
<td>Freeze-dried BCG vaccine</td>
<td>ANMAT (Argentina), ANVISA (Brazil), BGTD (Canada), CECMED (Cuba), COFEPRIS (Mexico), EMA (Europe), FDA (USA), KFDA (Korea) or TGA (Australia)</td>
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<td>Inactivated oral cholera vaccine</td>
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<td>DTaP</td>
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<td>DTwP-Hib</td>
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<td>Tdap</td>
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<td>DPwT-Hep B-Hib (Pentavalent)</td>
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<td>DTaP-IPV-Hep B – Hib (Hexavalent)</td>
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<td>Hepatitis A</td>
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<td>Hepatitis B (recombinant DNA)</td>
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<td>Hib</td>
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<td>HPV</td>
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<td>Influenza (seasonal)</td>
<td>Tdap – IPV</td>
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<tr>
<td>IPV</td>
<td>DTaP-IPV-Hib</td>
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<td>Meningo ACYW-135</td>
<td>Pneumococcal conjugate vaccine (23 valent)</td>
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<td>MR</td>
<td>Varicella</td>
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<td>MMR</td>
<td>Canine Rabies</td>
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<tr>
<td>OPV</td>
<td>Immunoglobulins Human and Equine origin</td>
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<td>PCV</td>
<td>Tuberculin Purified Protein Derivative (PPD)</td>
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<tr>
<td>Rabies</td>
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<tr>
<td>Rotavirus</td>
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<tr>
<td>Typhoid (conjugate) and (polysaccharide Ty2 strain)</td>
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<tr>
<td>Varicella</td>
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<tr>
<td>Yellow Fever</td>
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## QUALITY

- RESPONSIBLE NRA FOR LOT RELEASE OF FINISHED PRODUCT AND PLASMA POOL RELEASE (if applicable)
- MANUFACTURING SITES
- GMP CERTIFICATES FOR ALL SITES
- CURRENT FINISHED PRODUCT SPECIFICATIONS
- CERTIFICATE OF ANALYSIS
- SUMMARY PROTOCOL OF MANUFACTURING AND CONTROL
- STABILITY STUDIES (LONG-TERM AND ACCELERATED)
- PRODUCT INSERT AND PACKAGING

## EFFICACY

- THERAPEUTIC EQUIVALENCE (BIOEQUIVALENCE/ BIOAVAILABILITY STUDIES) OR BIOWAIVER

## SAFETY

- PERIODIC SAFETY UPDATED REPORT (PSUR) or PBRER

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**WHO PQ LETTER**

**PROOF OF REGISTRATION AND MARKETING AUTHORIZATION IN ELIGIBLE NRA (CPP, REGISTRATION CERTIFICATE, MA)**

Reference: Standard quality related components for pharmaceuticals and biologicals ITBs and RFQs for the PAHO Revolving Funds
Caribbean Regulatory System: a regional reliance mechanism and registration of cholera vaccine in Haiti

• CRS is a fast-track, regional reliance mechanism for CARICOM
• WHO PQ or NRA of reference approved products
• Sameness
• MOU CRS - NRA of Haiti maintaining sovereignty, responsibility and accountability
• Cholera vaccine dossier assessment, share of information (report) and capacity building for trust
• NRA access to WHO PQ regulatory documents through the WHO collaborative procedure
• Euvichol and Euvichol-plus registered in Haiti
• PMS and PV activities channeled through CRS (Vigicarib)

http://new.carpha.org/What-We-Do/Programmes-and-Projects/CRS/Caribbean-Regulatory-System
Reliance and “SAMENESS”

- Regulatory reliance supports and promotes sameness and access to same quality products

- Reliance mechanisms to address existing weaknesses such as limited regulatory capacity in small markets (CARICOM market)

- Ensure same standards and procedures are applied (GMP)

- Ensure molecule, dose, presentation destined to highly regulated markets are the same as the ones destined to markets with lower regulatory capacity thus ensuring access with same quality, efficacy, safety product specifications

- A matter of equitable access and transparency
PV Regional network: Evaluation of PSUR / RMP joint Project (2017-2022)
Executive Summary of the Periodic Safety Updated Report (PSUR) shared between focal points of specific NRAs on regulatory platform PRAIS
PV Regional network: Evaluation of PSUR / RMP joint Project (2017-2022)
Executive Summary of the Periodic Safety Updated Report (PSUR)
- Ongoing
PV Regional network: Evaluation of PSUR / RMP joint Project (2017-2022)

Executive Report of the Risk Management Plan (RMP) shared between focal points of specific NRAs
Objective: Assess the Network capacity to evaluate the association of rare AEFIs such as aseptic meningitis (AM) and idiopathic thrombocytopenic purpura (ITP) with measles mumps rubella (MMR) vaccine

Inclusion
Children 9 - 23 months of age hospitalized with AM or ITP during study period

Results and conclusions ...
Network integration in routine monitoring of vaccine adverse events in the Region.
Unique vaccine integrated active surveillance system could be applicable to other vaccines and diseases, save technical and financial resources and share final PV conclusions for other countries with similar or less regulatory capacity.

Conducted in 25 sites, 16 countries

Region of the Américas
- Argentina (6 sites)
- Chile (4 sites)
- Peru
- Uruguay
- Costa Rica
- Honduras
- Colombia

Other sites out of the Region
- Albania
- Australia (2 sites)
- China
- India
- Iran (2 sites)
- Singapore
- South Africa
- Spain

References: (1) Publication in Vaccine Building capacity for active surveillance of vaccine adverse events in the Americas: A hospital-based multi-country network
(2) Publication Enhancing global vaccine pharmacovigilance: proof-of-concept study on aseptic meningitis and immune thrombocytopenic purpura following measles mumps containing vaccination
Roles and responsibilities

Industry’s role?
NRA’s role?

Shared responsibility!!

What will be your “enabling reliance” success story at the next DCVMN meeting?
REFERENCES

PAHO

- Standard quality related components for pharmaceuticals and biologicals ITBs and RFQs for the PAHO Revolving Funds (internal document PAHO)

Caribbean Regulatory System:  
http://new.carpha.org/What-We-Do/Programmes-and-Projects/CRS/Caribbean-Regulatory-System

Publications:

- Building capacity for active surveillance of vaccine adverse events in the Americas: A hospital-based multi-country network. available at: https://doi.org/10.1016/j.vaccine.2017.04.069
- Enhancing global vaccine pharmacovigilance: proof-of-concept study on aseptic meningitis and immune thrombocytopenic purpura following measles mumps containing vaccination. available at: https://doi.org/10.1016/j.vaccine.2017.05.012
- Images: google images
Special thanks to the PAHO Medicines and other Health Technologies team for their contributions to this presentation

Alexandra Guta
Specialist, Quality Management Systems
Health Systems and Services/Medicines and Health Technologies
PAHO/WHO | gutaa@paho.org