Principles for Regulatory Reliance

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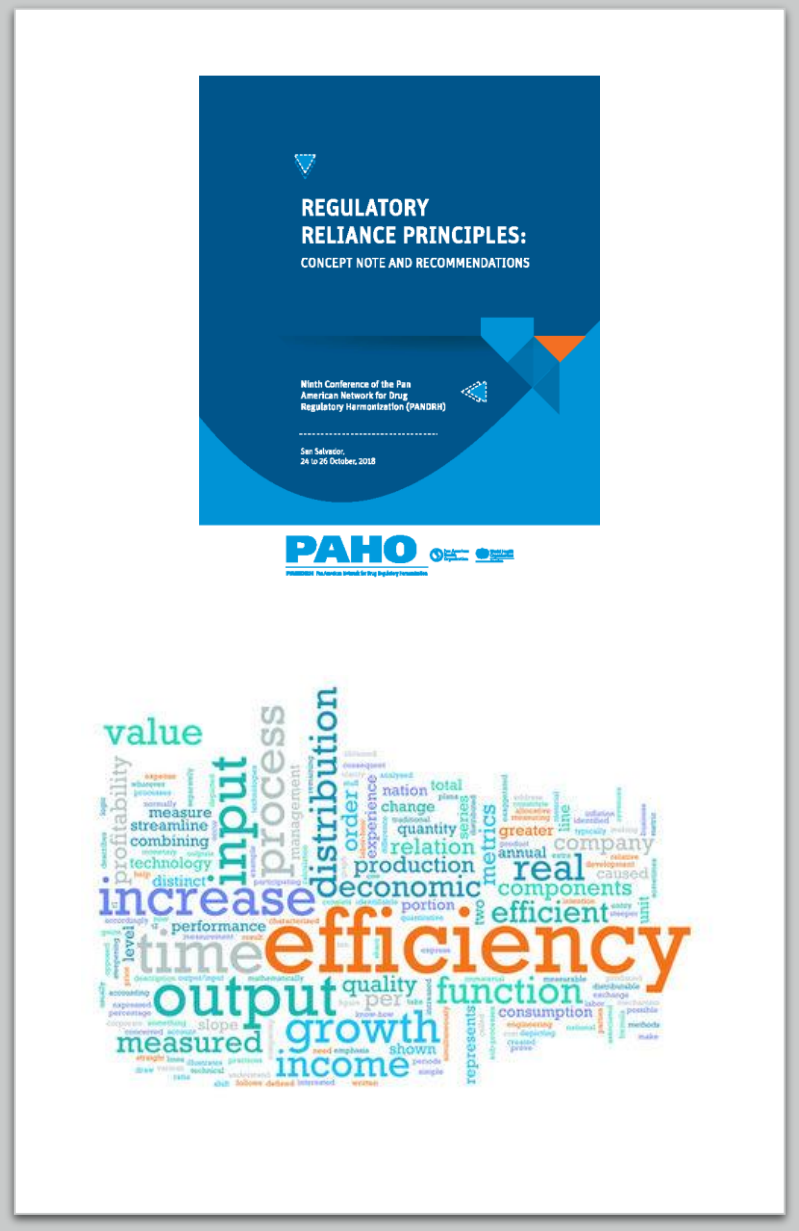
Pan American Health Organization
World Health Organization
Regional Office for the Americas

PAHO

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.

Ref: Regulatory reliance principles: concept note and recommendations: http://iris.paho.org/xmlui/handle/123456789/51549

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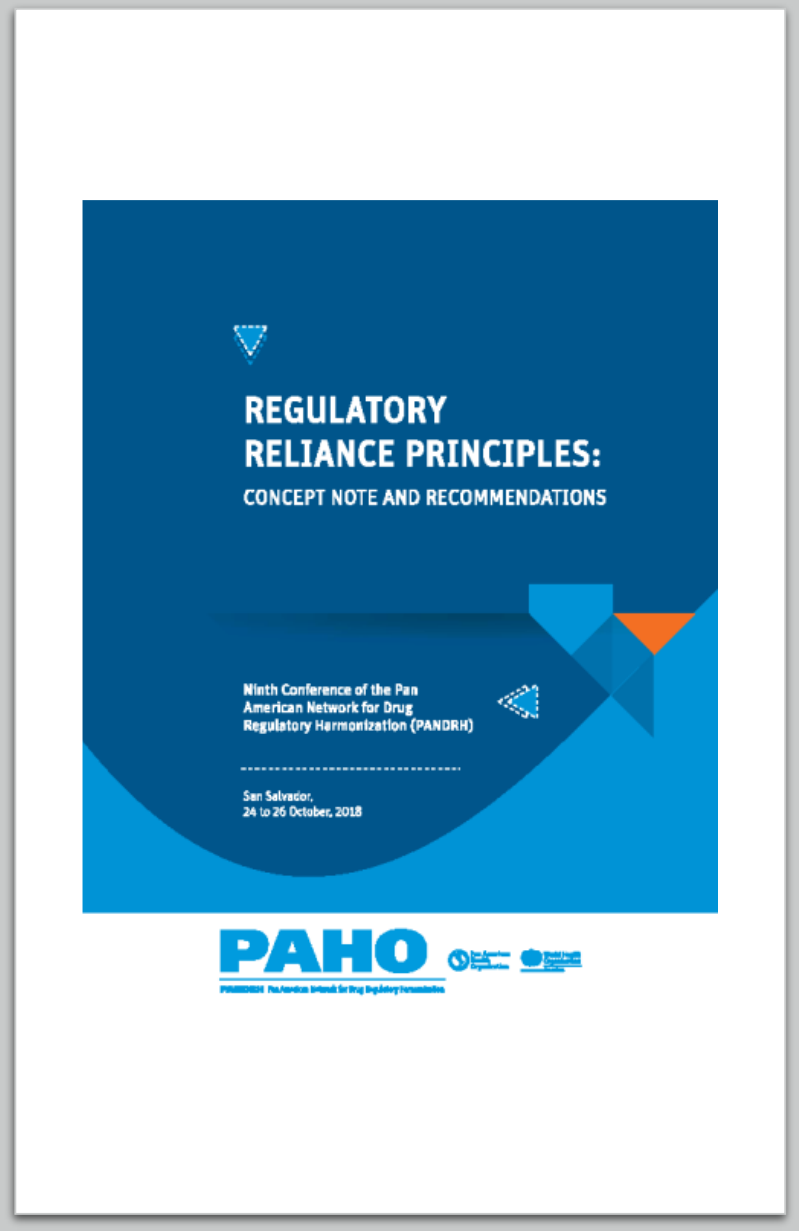
Goal

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



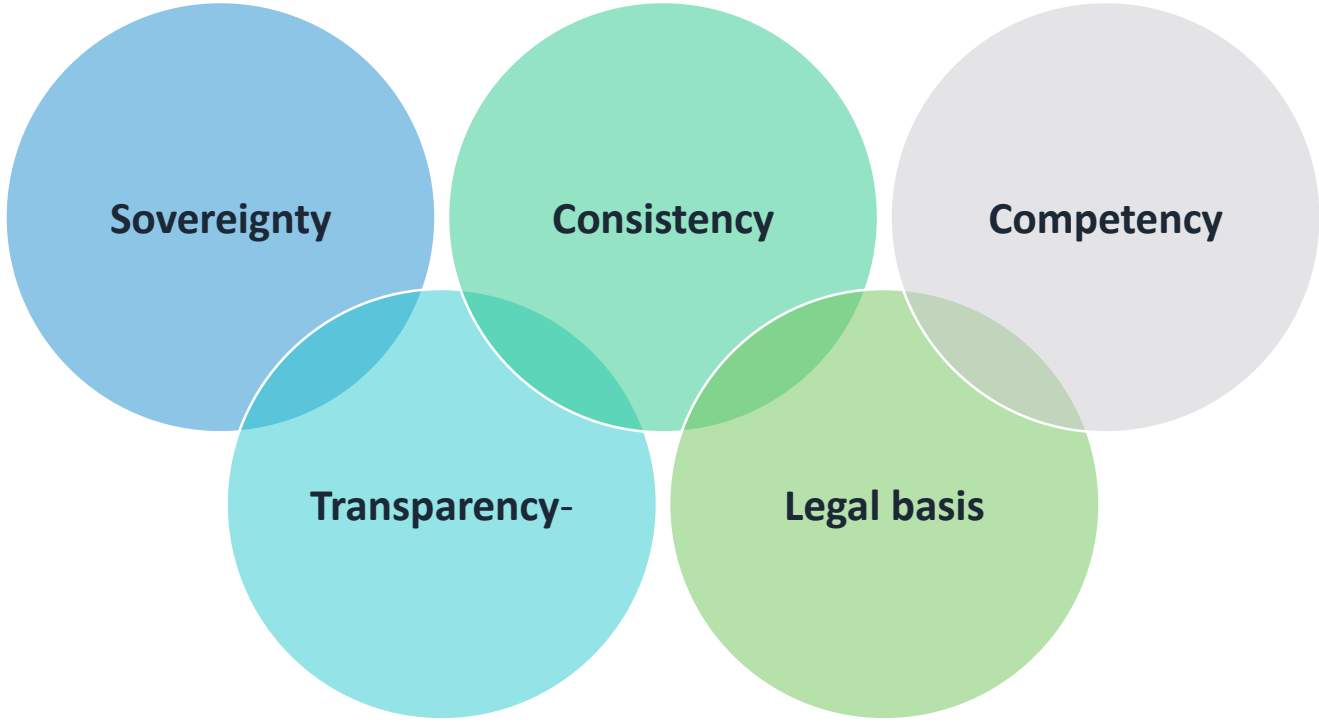
Ref: Regulatory reliance principles: concept note and recommendations: http://iris.paho.org/xmlui/handle/123456789/51549

PANDRH RECOMMENDATIONS

- (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.

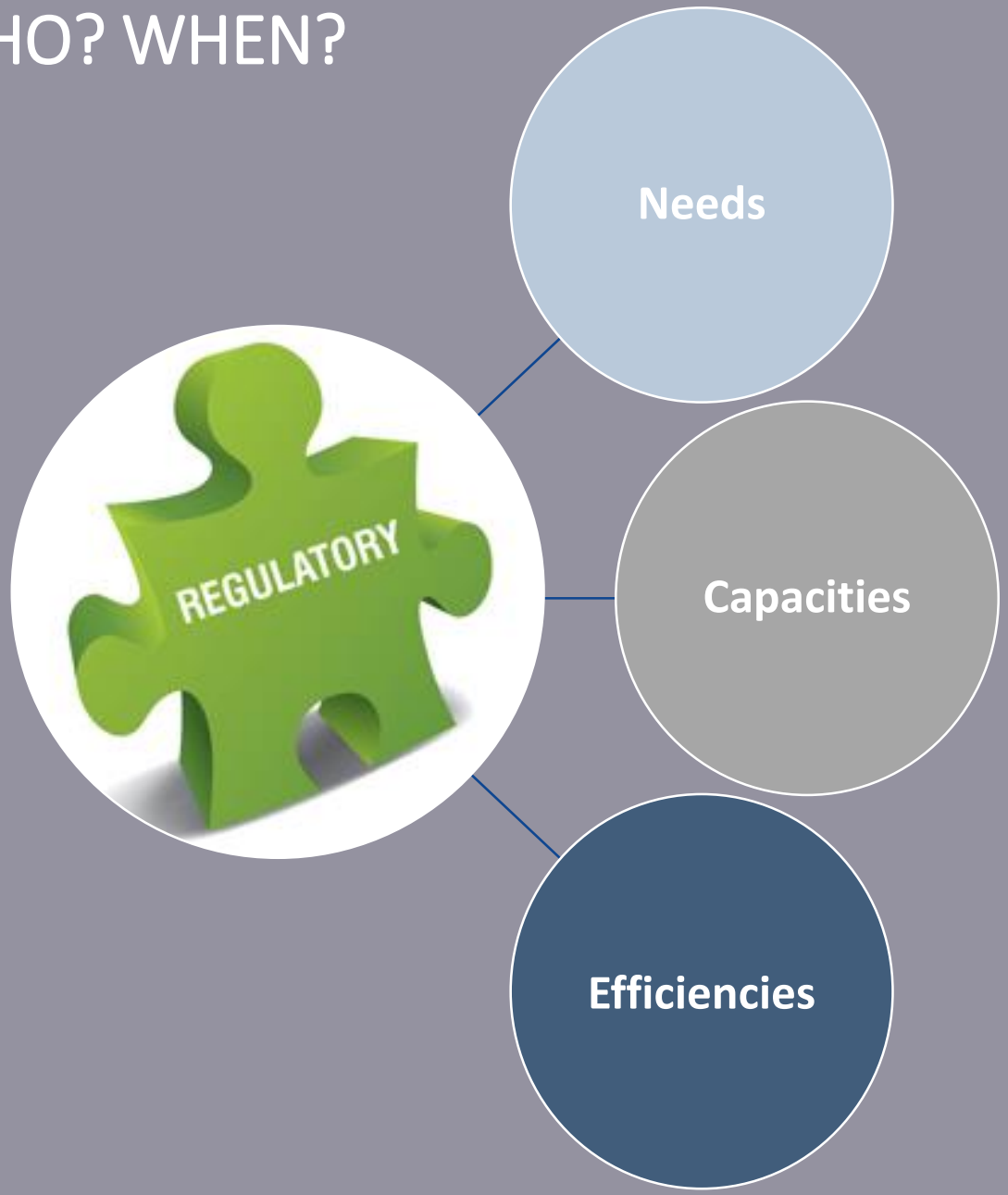
Ref: Regulatory reliance principles: concept note and recommendations: http://iris.paho.org/xmlui/handle/123456789/51549

RELIANCE PROPOSED PRINCIPLES



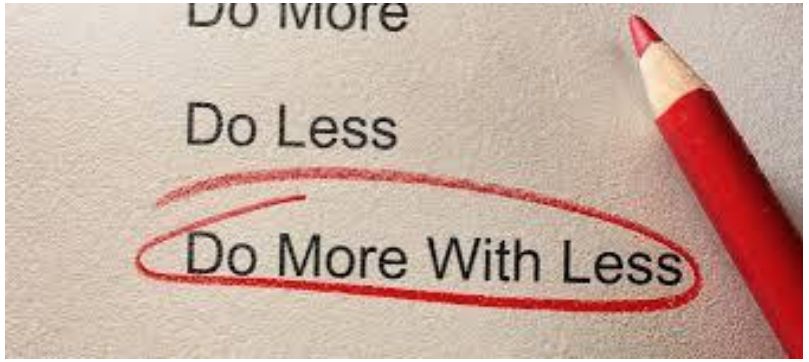
Ref: Regulatory reliance principles: concept note and recommendations: http://iris.paho.org/xmlui/handle/123456789/51549

WHO? WHEN?



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.**



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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!

Reference: https://ascpt.onlinelibrary.wiley.com/doi/epdf/10.1002/cpt.1617

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

U.S. FOOD & DRUG ADMINISTRATION

PAHO

Enablers

TRUST

HARMONIZATION

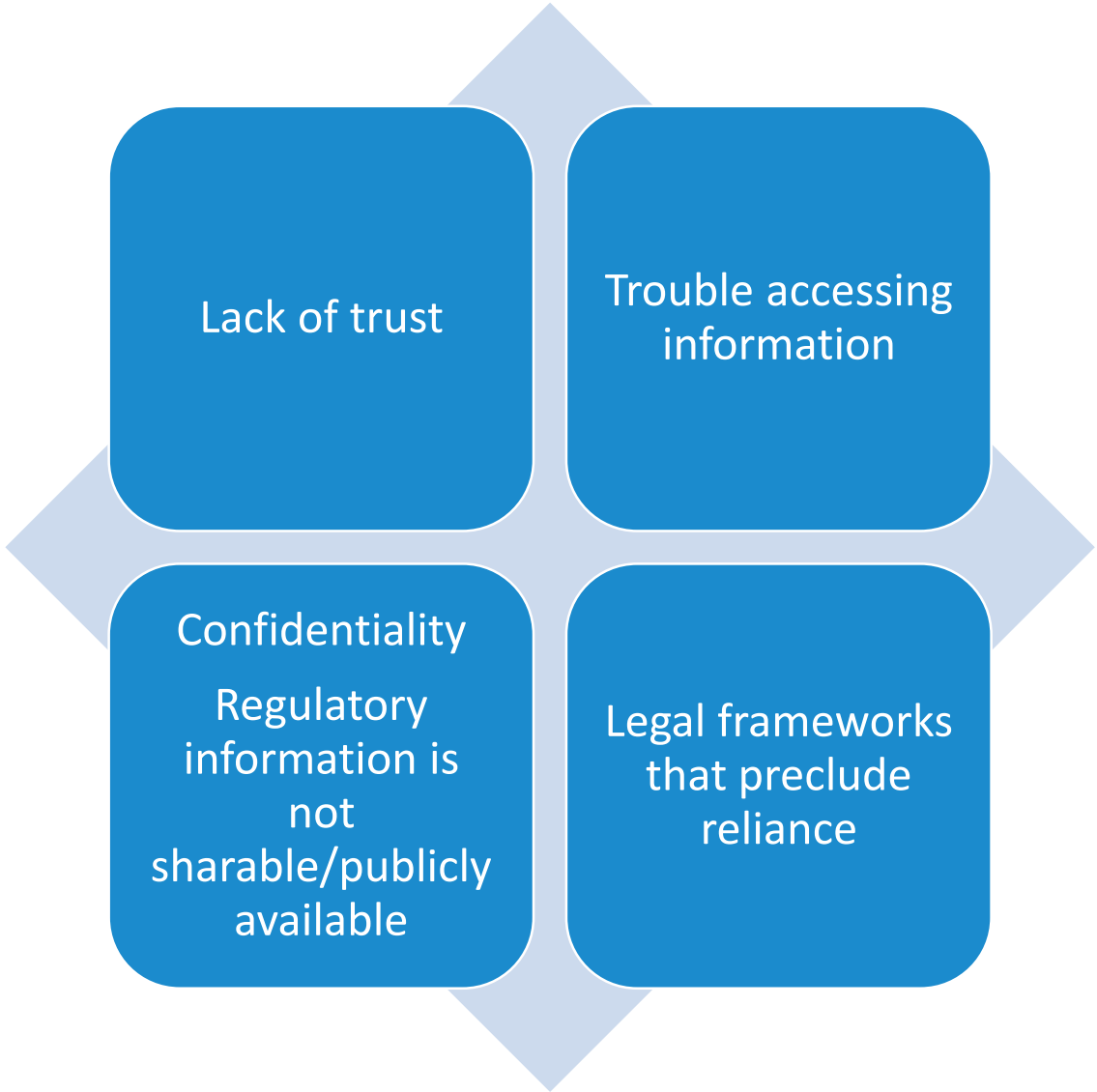
INFORMATION SHARING

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

Outline

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

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

Sharing Product Information

QUALITY	EFFICACY	SAFETY
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**	**THERAPEUTIC EQUIVALENCE** (BIOEQUIVALENCE/ BIOAVAILABILITY STUDIES) OR BIOWAIVER	PERIODIC SAFETY UPDATED REPORT **(PSUR) or PBRER**

- **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

Trastuzumab

Bevacizumab

Sofosbuvir

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

References for images: google images

Isotretinoin

Rituximab

Dengue Vaccine

PV Regional network: Evaluation of PSUR / RMP joint Project (2017-2022)

Executive Summary of the Periodic Safety Updated Report (PSUR)

- Ongoing

References for images: google images

Health Canada Santé Canada

Cofepris
Comisión Federal para la Protección contra Riesgos Sanitarios

Pembrolizumab

Agência Nacional de Vigilância Sanitária

Instituto de Salud Pública
Ministerio de Salud
Gobierno de Chile

Health Canada Santé Canada

Ocrelizumab

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

References for images: google images

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World Health Organization
PAHO

Global Vaccine Safety and Multi Country Collaboration Network- AEFIs Surveillance

Enhancing global vaccine pharmacovigilance: Proof-of-concept study on aseptic meningitis and immune thrombocytopenic purpura following measles-mumps containing vaccination

Silvia Perez-Vilar[1,2,*], Daniel Weibel[1,3], Miriam Sturkenboom[1,3], Steven Black[3,4], Christine Maure[5], Jose Luis Castro[6], Pamela Bravo-Alcántara[7], Caitlin N. Dodd[1], Silvana A. Romio[1,8], Maria de Ridder[1], Swabra Nakato[1], Helvert Felipe Molina-León[9], Varalakshmi Elango[10], Patrick L.F. Zuber[5], and the WHO Global Vaccine Safety-Multi Country Collaboration[11]

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	Other sites out of the Region
Argentina (6 sites)	Albania
Chile (4 sites)	Australia (2 sites)
Peru	China
Uruguay	India
Costa Rica	Iran (2 sites)
Honduras	Singapore
Colombia	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

- Regulatory reliance principles: concept note and recommendations. http://iris.paho.org/xmlui/handle/123456789/51549
- 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
- *Are the European Medicines Agency, US Food and Drug Administration, and Other International Regulators Talking to Each Other? available at:* https://ascpt.onlinelibrary.wiley.com/doi/epdf/10.1002/cpt.1617
- Images: google images

Special thanks to the PAHO Medicines and other Health Technologies team for their contributions to this presentation

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