WHO Good Reliance Practice and Collaborative Registration Procedure

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Reproductive Health Supplies Coalition Webinar on WHO Collaborative Registration Procedure (CRP)
Wednesday 22nd May 2024
Reliance is not a new concept...

Long history of improving efficiency through reliance e.g. Certificate of Pharmaceutical Products Scheme

“Regulate through reliance” as the hallmark of a modern and efficient regulatory authority.

Increasing role of reliance

Promoting “informed” reliance

WLA a new transparent and evidence-based system

COVID-19 response as a strong accelerator for the use of reliance

Flexibility/new ways of working
Objectives of the WHO regulatory system strengthening programme

Why reliance?

1. Build regulatory capacity in Member States consistent with good regulatory practices
2. Promote regulatory cooperation, convergence and transparency through networking, work-sharing and reliance

Data as of November 2023
Reliance at the core of a more efficient use of global resources

70% of countries have weak national regulatory systems
Need to facilitate access to quality-assured medical products and to build capacity

Implementation
Voluntary participation, change mindset, start small, learning by doing, harmonization facilitator but not pre-requisite

Evolving science and regulatory challenges
Globalization of markets and clinical trial programmes, complexity of supply chains, rapid evolution of science, transparency and growing public expectations etc.

Reliance to promote better use of limited resources and to strengthen global regulatory oversight

Apply a risk-based approach, avoid duplication where possible, full range of reliance options (work sharing, abridged pathways, etc.)

WHO Listed Authorities
Transparent, evidence-based system to define trusted authorities
Reliance for a more efficient use of global resources

INCREASING WORKLOAD
LIMITED GLOBAL REGULATORY RESOURCES

Manufacturers/Applicants

Country A
Country B
Country C
...
Country X

SOLUTIONS

Work-sharing,
Joint assessment,
Abridged pathways,
Strengthened collaboration,
etc.

Implementation of reliance

Voluntary participation
Change mindset
Start small, learning by doing
Harmonisation facilitator but not pre-requisite

Are we using the global regulatory resources as best as we can?
WHO support to facilitated registration procedures

WHO Collaborative Registration Procedure

Global Health Products Procedures (EU-M4all, Swissmedic MAGHP)

Regional Joint assessments (e.g. ASEAN, Regional economic communities in Africa, etc.)

EU-M4all: European Union Medicines for all  
MAGHP: Marketing Authorisation for Global Health Products  
ASEAN: Association of Southeast Asian Nations
WHO Collaborative Registration Procedure - Overview

Promote informed reliance

Source of information:
- WHO PQ
- SRA/WLA

Dossier application to NRA, provision of assessment & inspection reports from PQ/SRA

90 days

Product sameness
Quality Information Summary validated by WHO/SRA

Same principles for life cycle
Source of information on reliance

WHO Good Reliance Practices

Annex 10

Good reliability practices in the regulation of medical products: high level principles and considerations

Background

WHO supports reliance on the work of other regulators as a general principle in order to make the best use of available resources and expertise. This principle allows leveraging the output of others whenever possible while placing a greater focus at national level on value-added regulatory activities that cannot be undertaken by other authorities, such as, but not limited to: vigilance, market surveillance, and oversight of local manufacturing and distribution. Reliance


Short eLearning Module of main principles and examples of reliance (Oct 2022) [https://openwho.org/courses/good-reliance-practices](https://openwho.org/courses/good-reliance-practices)

International Pharmaceutical Regulators Programme

Questions & Answers on Reliance

Thank you for your attention!

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Reproductive Health Supplies Coalition Webinar on WHO Collaborative Registration Procedure (CRP)

Wednesday 22\textsuperscript{nd} May 2024

Overview of Collaborative Registration Procedure for WHO Prequalified medicines and SRA approved medicines and vaccines

Sunday Kisoma,
Technical Officer, Facilitated Product Introduction,
WHO/MHP/RPQ/REG/FPI
Outline

Collaborative Registration Procedure: Overview and scope

Participating NRAs and SRAs

CRP Implementation: WHO experience

Challenges and opportunities

Take away messages
Collaborative Registration Procedure (CRP)

CRP facilitates exchange of information to accelerate national registrations in countries through the provision to NRAs of detailed assessment and inspection reports generated by reference NRAs/WHO PQ

WHAT it is and HOW does it work?

Applicant

Single product dossier

+ Prod. Assessment Reports from SRA/WHO PQ

To multiple CRP participating country(s)

Accelerated assessment and registration of quality-assured products in countries

Faster access to priority quality-assured products by the population

World Health Organization
CRP mechanisms and product scope

PQ CRP - products prequalified by WHO via full assessment:

- Medicines
- Vaccines
- Biotherapeutics
- IVDs

- Applies to therapeutic areas in the scope of PQ

PQ CRP (Mx and Vx): https://extranet.who.int/prequal/medicines/accelerated-registration-prequalified-fpps

PQ CRP (IVDs): https://extranet.who.int/prequal/vitro-diagnostics/collaborative-procedure-accelerated-registration

SRA CRP - any product assessed or approved by an SRA:

- Innovative and generic products (chemicals or biologicals): Medicines/Pharmaceuticals, multisource/generics, vaccines, biosimilars, biotherapeutics, etc.
- Products Prequalified by WHO via Abridged review (SRA approved)
- Products approved by special routes or provided with positive scientific opinion: EU M4-all and Swissmedic Marketing for Global Health Products.
- Applies to any therapeutic area

SRA CRP: https://extranet.who.int/prequal/medicines/accelerated-registration-fpps-approved-sras
WHO PQ CRP: Mechanism

1. Source of Information to rely upon:
   - WHO
   - FPI
   - WHO PQT/SRA

2. Documentation to be shared:
   - Applicant and WHO
   - Full Product Dossier (CTD format): updated
   - Module 1: Country specific
   - Detailed Assessment Reports: QOS PD (Initial, add. data) and Variations
   - GMP Inspection Reports (API + FPP)
   - GCP Inspections: CROs

3. Actions for different stakeholders
   - Applicant
     - Submission
   - NRA
     - NRA Review: Recognition or Reliance - 90 working days (regulatory time)
   - Variations
     - NRA Review: Recognition or Reliance - 30 working days (regulatory time)
   - Lifecycle management
Post-Approval changes in CRP context

- Submissions to NRA: In line with national requirements
- Decision within 30 days
- Ongoing support to industry driven PAC reliance pilots (5 pilots to date)
- Working to better define PAC management in context of CRP
CRP Steps – PQ CRP/SRA CRP

1. Stage – 1
   - NRA Agreement to participate in PQ CRP

2. Stage – 2
   - Interest to register

3. Stage – 3
   - Access to WHO reports

4. Stage – 4
   - Regulatory Decision

5. Stage – 5
   - Registration maintenance
     - Post approval changes
     - Withdraw
     - Cancellation

Communication - Abriged assessment
PQ CRP Participation: 65 NRAs + 1 REC (CARICOM)

- Angola
- Armenia
- Azerbaijan
- Bangladesh
- Belarus
- Benin
- Bhutan
- Botswana
- Burkina Faso
- Burundi
- Cabo Verde
- Cameroon
- Caribbean Community (CARICOM)
- Central African Republic
- Chad
- Comores
- Côte d'Ivoire
- Democratic Republic of the Congo
- Eritrea
- Ethiopia
- Gabon
- Gambia
- Georgia
- Ghana
- Guinea (Republic of)
- Kazakhstan
- Kenya
- Kyrgyzstan
- Lao People's Democratic Republic
- Lesotho
- Liberia
- Madagascar
- Malawi
- Malaysia
- Maldives
- Mali
- Mauritania
- Mozambique
- Namibia
- Nepal
- Nigeria
- Pakistan
- Papua New Guinea
- Philippines
- Republic of Congo
- Republic of Moldova
- Rwanda
- Sao Tome and Principe
- Senegal
- Sierra Leone
- South Africa
- Sri Lanka
- Sudan
- Tanzania (Mainland)
- Tanzania (Zanzibar)
- Timor-Leste
- Thailand
- Togo
- Türkiye
- Uganda
- Ukraine
- Uzbekistan
- Yemen (Sana'a)
- Yemen (Aden)
- Zambia
- Zimbabwe

CARICOM: Antigua and Barbuda, Bahamas, Barbados, Belize, Dominica, Grenada, Guyana, Haiti, Jamaica, Montserrat, Saint Lucia, St. Kitts and Nevis, St Vincent and the Grenadines, Suriname, Trinidad and Tobago
PQ CRP Implementation: WHO Experience

Distribution Across Product Streams: Number of submissions and registrations

Status distribution within Reproductive Health Products: Number of products

PQ CRP Implementation: WHO Experience

- Steadily increasing trends
- Consistent with number of submissions and PQT output
- Collaboration: NRAs, Manufacturers, WHO to enhance the trend

- Timelines (NRA + manufacturers)
- High conformance to CRP requirements
- Over 80% registrations within 6 months
- 94% registration within 12 months
- Much lower vs Average registration times (250 days)
PQ CRP Implementation: WHO Experience

- Representing 39% of participating NRAs
- Trends and patterns as other product categories
- Directing focus of FPI interventions
## PQ CRP Implementation: WHO Experience

FPP formulation registered under CRP

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Number</th>
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<tbody>
<tr>
<td>Oxytocin Solution for injection 10IU/mL</td>
<td>9</td>
</tr>
<tr>
<td>Misoprostol Tablet 200mcg</td>
<td>16</td>
</tr>
<tr>
<td>Mifepristone Tablet + Misoprostol Tablet, vaginal 200mg + 200mcg</td>
<td>5</td>
</tr>
<tr>
<td>Medroxyprogesterone acetate Suspension for injection 150mg/ml</td>
<td>11</td>
</tr>
<tr>
<td>Medroxyprogesterone acetate Suspension for injection 150mg</td>
<td>4</td>
</tr>
<tr>
<td>Levonorgestrel Tablet 1.5mg</td>
<td>11</td>
</tr>
<tr>
<td>Levonorgestrel Tablet 750mcg</td>
<td>11</td>
</tr>
<tr>
<td>Levonorgestrel Tablet 1.5mg per rod (150mg in total)</td>
<td>16</td>
</tr>
<tr>
<td>Ethinylestradiol/Levonorgestrel Tablet, Sugar coated + Ferrous (Fumarate) Tablet, Sugar coated 30mcg/150mcg + 75mg</td>
<td>12</td>
</tr>
<tr>
<td>Ethinylestradiol/Levonorgestrel Tablet, coated 30mcg/150mcg</td>
<td>9</td>
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- Prepresenting 30% of EOI
- CRP can effectively bridge the gap for the remaining 70%
SRA CRP Participation: 59 NRAs + 1 REC (CARICOM)

- Angola
- Bangladesh
- Benin
- Bhutan
- Botswana
- Burkina Faso
- Burundi
- Cabo Verde
- Cameroon
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- Central African Republic
- Chad
- Comores
- Côte d’Ivoire

- Democratic Republic of the Congo
- Eritrea
- Ethiopia
- Gabon
- Gambia
- Georgia
- Ghana
- Guinea (Republic of)
- Jordan
- Kazakhstan
- Kenya
- Lao People’s Democratic Republic
- Lesotho
- Liberia
- Madagascar

- Malawi
- Malaysia
- Maldives
- Mali
- Mauritania
- Mozambique
- Namibia
- Nepal
- Niger
- Nigeria
- Pakistan
- Papua New Guinea
- Republic of Congo
- Rwanda

- Sao Tome and Principe
- Senegal
- Sierra Leone
- South Africa
- Sri Lanka
- Tanzania (Mainland)
- Tanzania (Zanzibar)
- Timor-Leste
- Thailand
- Togo
- Türkiye
- Uganda
- Ukraine
- Yemen (Sana’a)
- Yemen (Aden)
- Zambia
- Zimbabwe

CARICOM: Antigua and Barbuda, Bahamas, Barbados, Belize, Dominica, Grenada, Guyana, Haiti, Jamaica, Montserrat, Saint Lucia, St. Kitts and Nevis, St Vincent and the Grenadines, Suriname, Trinidad and Tobago
List of SRAs as per WHO Guidelines

<table>
<thead>
<tr>
<th>Australia</th>
<th>Germany</th>
<th>Netherlands</th>
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<tbody>
<tr>
<td>Austria</td>
<td>Greece</td>
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<td>Finland</td>
<td>Luxembourg</td>
<td>United States of America</td>
</tr>
<tr>
<td>France</td>
<td>Malta</td>
<td>Norway</td>
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Based on the above interim definition, the following is the list of the countries whose NRAs are designated as SRAs.
SRA CRP Implementation: WHO Experience

Distribution Across Product Indications: Number of submissions and registrations

Status Reproductive Health Products under SRA CRP: Number of products
SRA CRP Implementation: WHO Experience

Number of Registrations per Year all Therapeutic Areas

- Increasing update of SRA CRP
- Increasing clarity among stakeholders

Number of Registrations per Year RH

- Positive trends for RH products
- Focused interventions on pending applications
SRA CRP Implementation: WHO Experience

Number of Registrations in Participating Countries

Registration timelines (Working Days)

- Trends and patterns as other product categories
- Directing focus of FPI interventions

- Timelines (NRA + manufacturers)
- High conformance to CRP requirements – based on complexity of products
- Over 60% registrations within 6 months
- 85% registration within 12 months
- Much lower vs Average registration times (250 days)
Challenges and Interventions

- Relatively Low uptake for RH products
- Lack/low responsiveness from NRAs
- Information sharing and exchange
- National regulatory requirements
- Post Approval Changes management
- National RH policies

- Manufacturers workshop, CRP Annual meetings, 1-on 1 meetings on regulatory pathways and specific NRA requirements
- Regional workshops, CRP annual meeting, individual NRA trainings on reliance practices, assistance on NRA guidelines and procedures
- Centralized information sharing and exchange under dedicated platform (ePQS). NRA and manufactures training expected from Q3
- Assist in review of national requirements (guidelines and procedures) to enhance more reliance and minimize specific national requirements, communications with manufacturers, training and capacity building
- Collaborating with stakeholders on reliance on PACs, support to specific PAC management initiatives, guideline to better define PAC in the context of CRP
- Multiple stakeholders dialogue and involvement
### Take Away messages

<table>
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<tr>
<th>Icon</th>
<th>Message</th>
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<tbody>
<tr>
<td>🔍</td>
<td>Evidence over 10 years demonstrating reliance in assessment and MA in action: 1000+ MA facilitated</td>
</tr>
<tr>
<td>👯‍♂️</td>
<td>CRP works effectively in all product streams: stakeholders to utilize this validated reliance mechanism</td>
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<tr>
<td>⌚️</td>
<td>Short timelines vs standard national process: access to patients, quick product introduction</td>
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<td>📄</td>
<td>Supports harmonization and streamlining the submissions, predicted assessment styles and cycles</td>
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<tr>
<td>✅</td>
<td>Can facilitate reliance in PAC management: reduce manufacturers regulatory burden</td>
</tr>
<tr>
<td>🌍</td>
<td>Consideration to expanding to wider product scope and formulations</td>
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Relevant Tools and Resources

PQ CRP

Annex 8
Collaborative procedure between the World Health Organization (WHO) Prequalification Team and national regulatory authorities in the assessment and accelerated national registration of WHO-prequalified pharmaceutical products and vaccines

1. Definitions
2. Background information
3. Principles of collaboration
4. Steps in the collaboration for national registration of a pharmaceutical product or a vaccine
5. Collaboration mechanisms for post-prequalification and/or post-registration variations
6. Withdrawals, suspensions or delistings of prequalified pharmaceutical products or vaccines and national deregistrations

References

Appendix 1 National regulatory authority participation agreement and undertaking for national regulatory authority focal point(s)
Appendix 2 Consent of WHO prequalification holder for WHO to share information with the national regulatory authority confidentially under the Procedure
Appendix 3 Suspension of import into national regulatory authority (NRA) in the assessment and accelerated national registration, acceptance by NRA and notification of Procedure
Appendix 4 Report on post-registration actions in respect of a product registered under the Procedure

SRA CRP

Annex 11
Collaborative procedure in the assessment and accelerated national registration of pharmaceutical products and vaccines approved by stringent regulatory authorities

1. Background information
2. Glossary
3. Principles of collaborative procedure
4. Medicines
5. Collaboration mechanisms for management of post-registration variations

References

Appendix 1 National regulatory authority participation agreement and undertaking for national regulatory authority focal point(s)
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https://iris.who.int/bitstream/handle/10665/255338/9789241209960eng.pdf?isAllowed=y&sequence=1#page=277&zoom=auto,-344,680

https://iris.who.int/bitstream/handle/10665/272452/9789241210195eng.pdf?isAllowed=y&sequence=1#page=367&zoom=auto,-284,680
Thank you

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