WHO Good Reliance Practice and Collaborative Registration Procedure

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World Health Organization

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

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Objectives of the WHO regulatory system strengthening programme

Why reliance?

ML

1 *With some elements of regulatory system*

2 *Evolving national regulatory system*

3 *Stable, well functioning and integrated*

4 *Advanced level of performance and continuous improvement*

ML: *(regulatory system) maturity level*

Total Number of countries = 194

Data as of November 2023

1 - Build regulatory capacity in Member States consistent with good regulatory practices

Good regulatory practices, 2021

2 - Promote regulatory cooperation, convergence and transparency through networking, **work-sharing and reliance**

Good reliance practices, 2021

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

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

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

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

WHO Listed Authorities
Transparent, evidence-based system to define trusted authorities

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.

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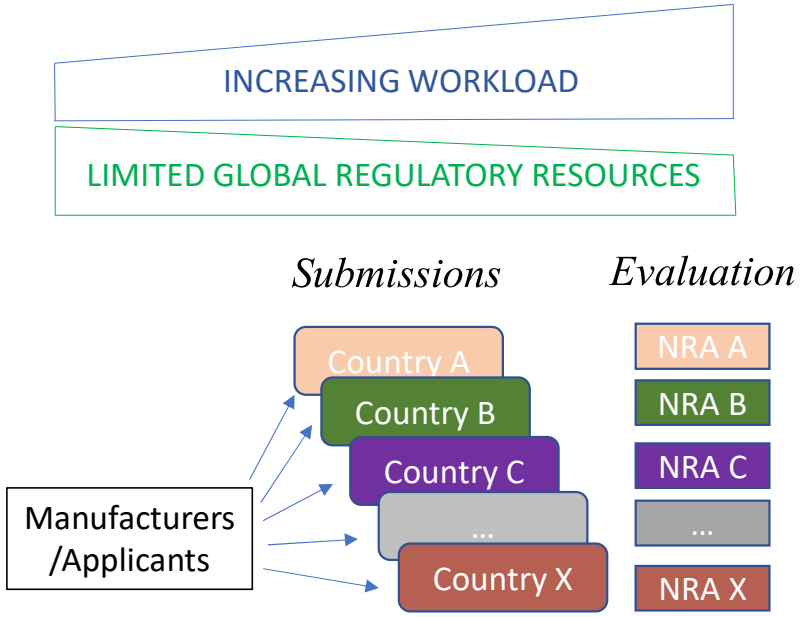
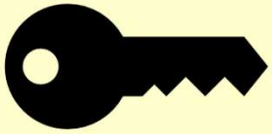
Reliance for a more efficient use of global resources



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

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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

Same principles for life cycle

90 days

Product sameness
Quality Information Summary validated by WHO/SRA

Source of information on reliance

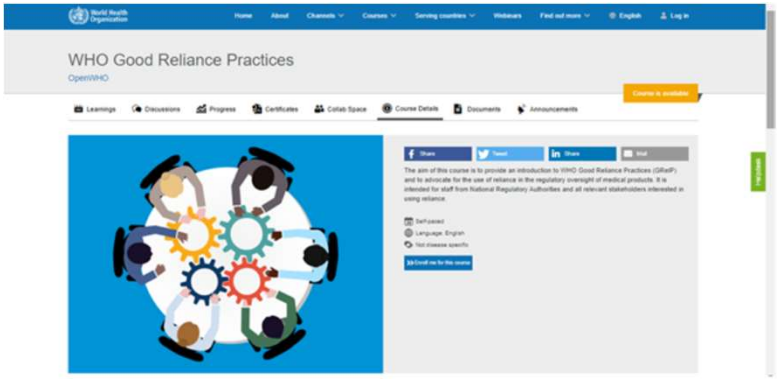
WHO Good Reliance Practices

Annex 10

Good reliance 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



Adopted by WHO Expert Committee on Specification for Pharmaceutical Products in October 2020, published in March 2021 https://www.who.int/publications/i/item/55th-report-of-the-who-expert-committee-on-specifications-for-pharmaceutical-preparations

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

IPRP Questions and Answers document[1] on Reliance
Version dated 30 September 2022

Table of Contents

International Pharmaceutical Regulators Programme
Questions & Answers on Reliance
https://admin.iprp.global/sites/default/files/2022-11/IPRP_RelianceQ%26As_2022_0930.pdf

www.who.int/medicines

Thank you for your attention!

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

Wednesday 22nd 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

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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)

WHAT it is and HOW does it work?

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

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

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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

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WHO PQ CRP : Mechanism

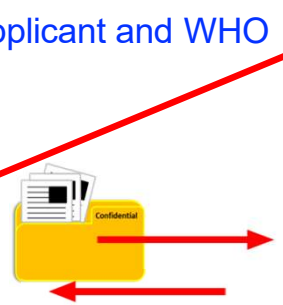
1. Source of Information to rely upon:

WHO FPI

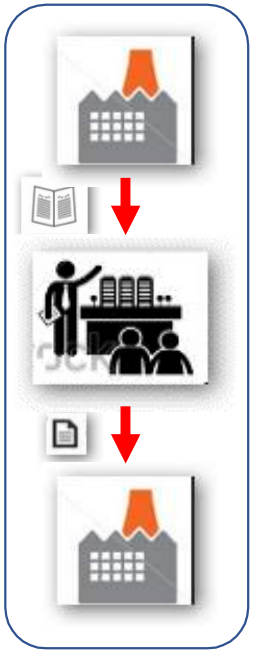
WHO PQT/SRA

2. Documentation to be shared:

Applicant and WHO



a) Full Product Dossier (CTD format) : updated
b) Module 1 : Country specific
c) Detailed Assessment Reports: QOS PD (Initial, add. data) and Variations
d) GMP Inspection Reports (API + FPP)
e) GCP Inspections : CROs



Lifecycle management

3. Actions for different stakeholders

Applicant

Submission

NRA

NRA Review: Recognition or Reliance - 90 working days (regulatory time)

Approval / Rejection

Variations
NRA Review: Recognition or Reliance - 30 working days (regulatory time)

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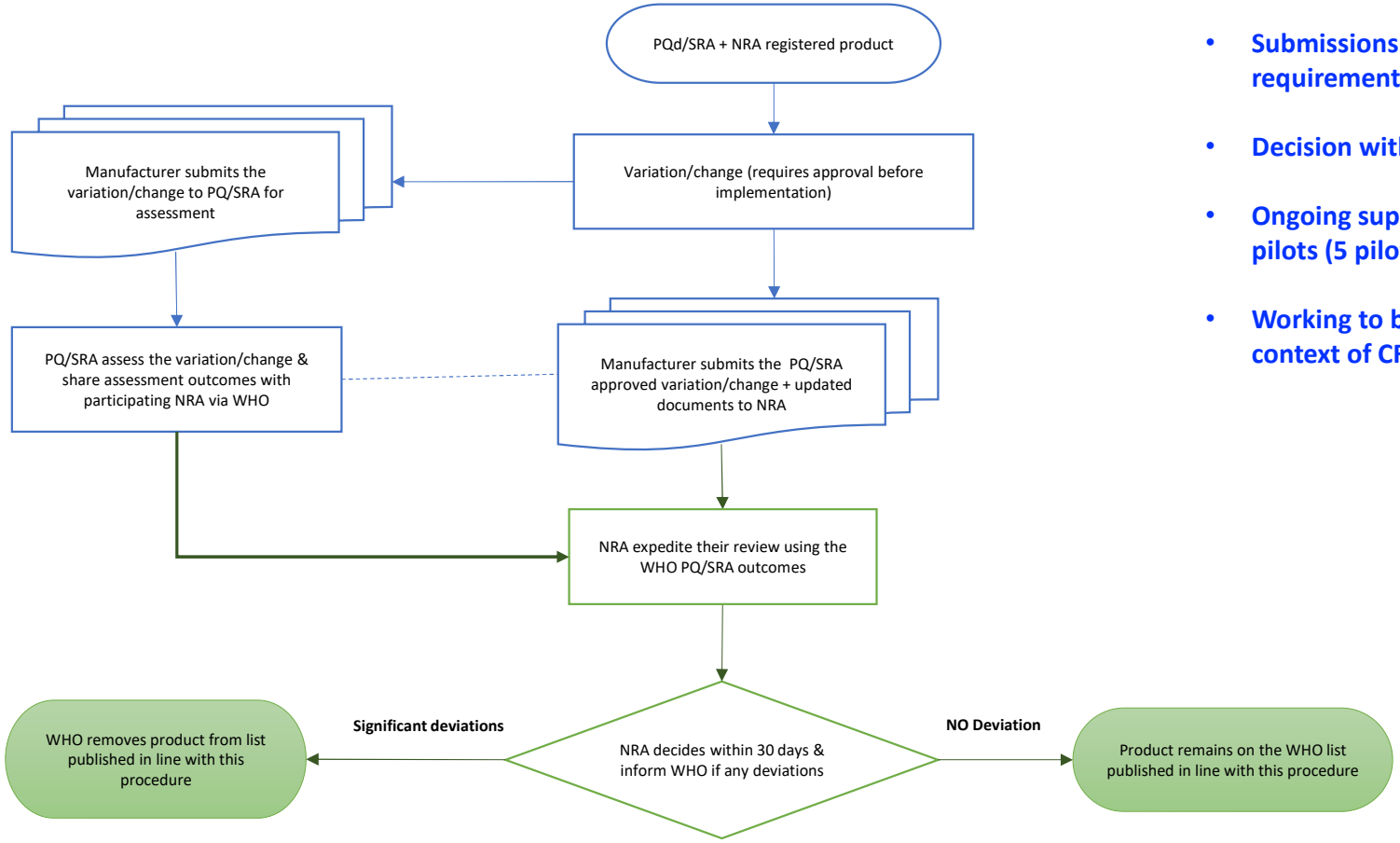
Post-Approval changes in CRP context



- **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**

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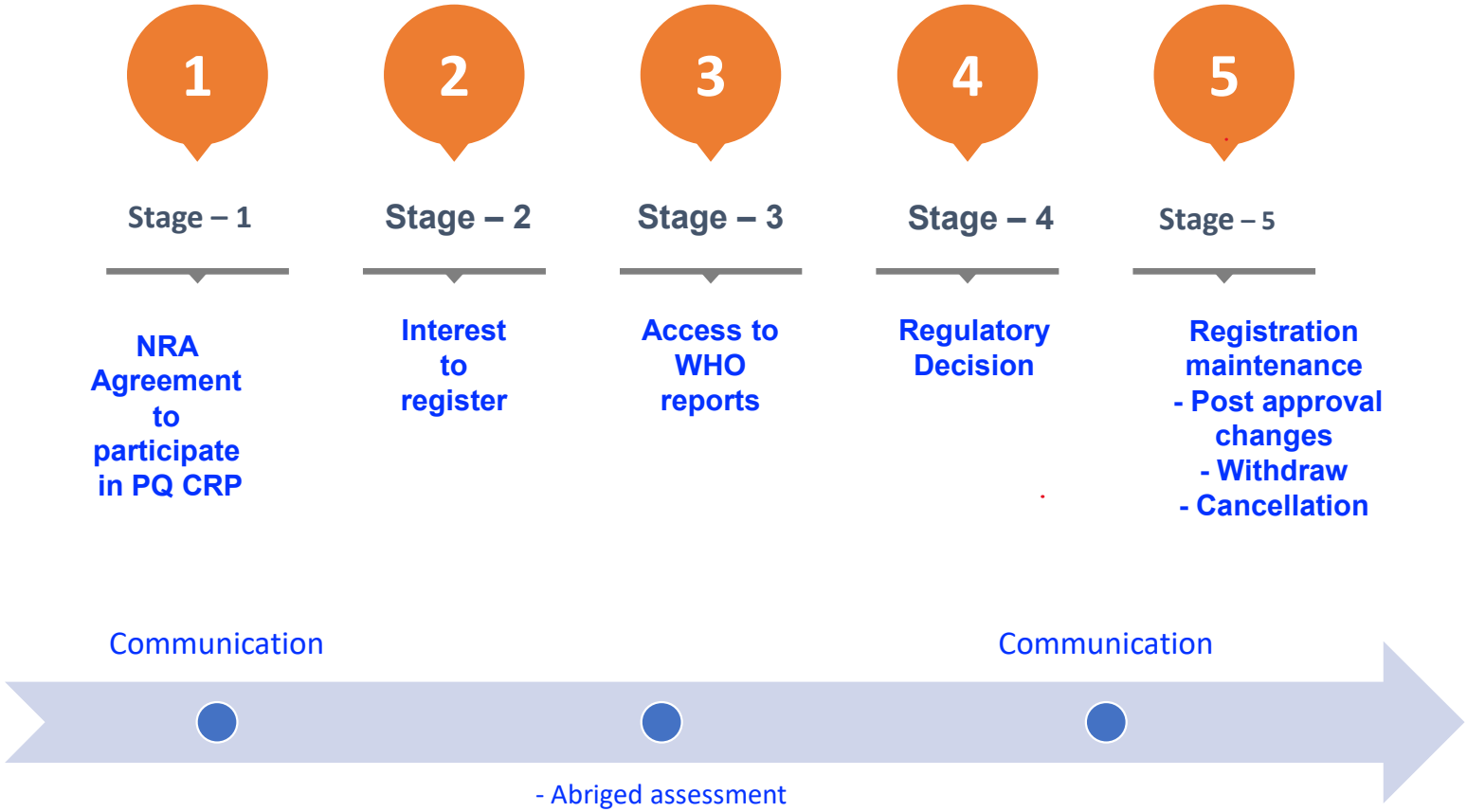
CRP Steps – PQ CRP/SRA CRP



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

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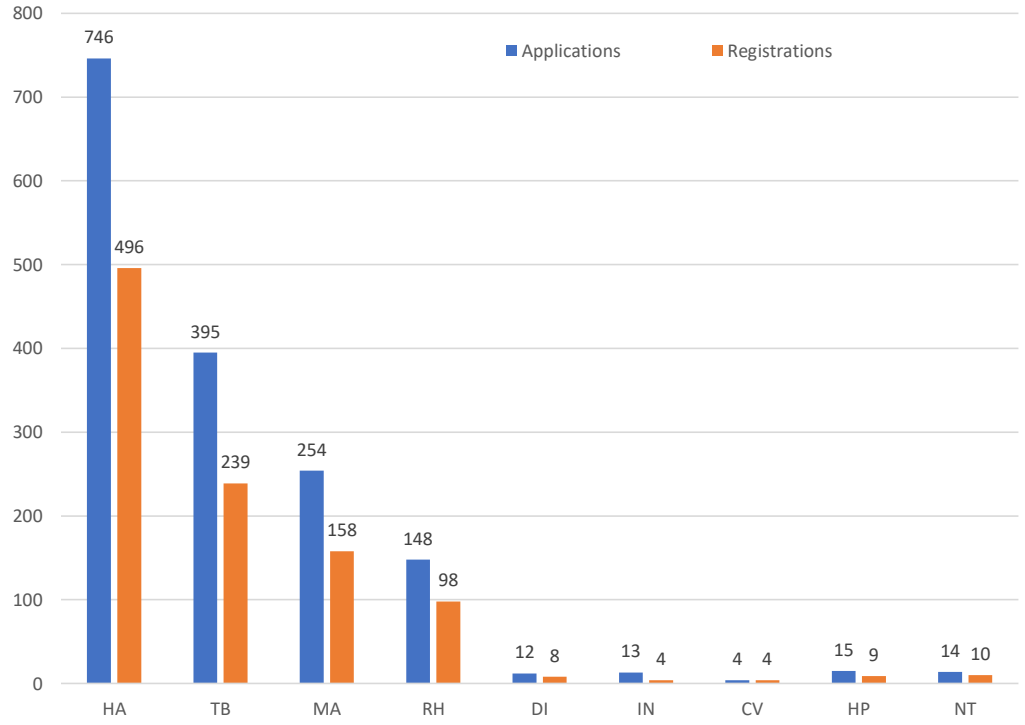
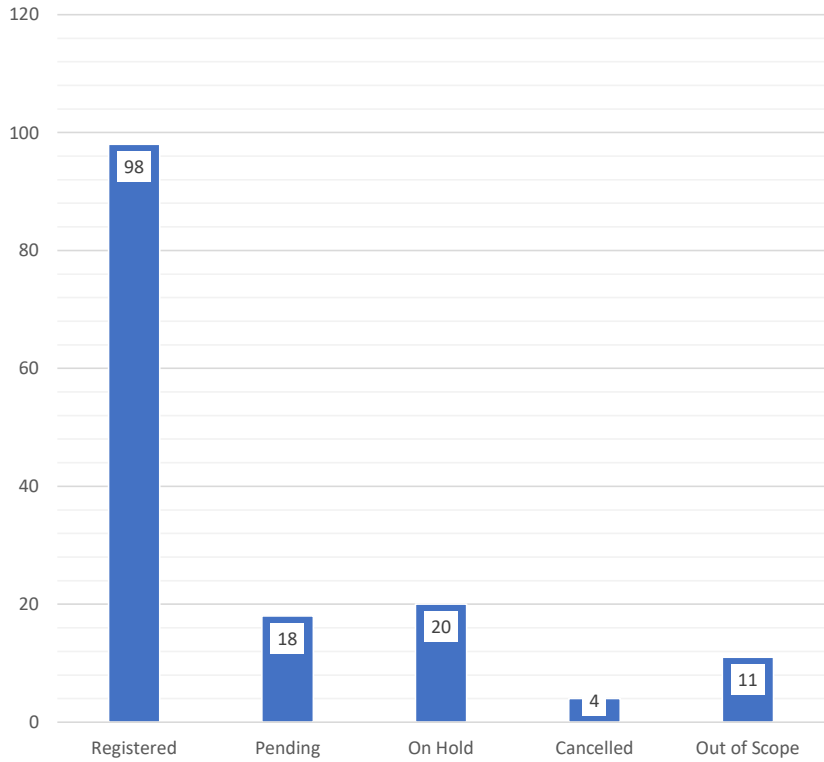
PQ CRP Implementation : WHO Experience

Distribution Across Product Streams: Number of submissions and registrations



Status distribution within Reproductive Health Products: Number of products



HA : HIV/AIDS, TB : Tuberculosis, MA : Malaria, RH : Reproductive Health, DI : Diarrhea, IN : Influenza, CV : Covid 19, HP : Hepatitis B&C, NT : Neglected tropical diseases

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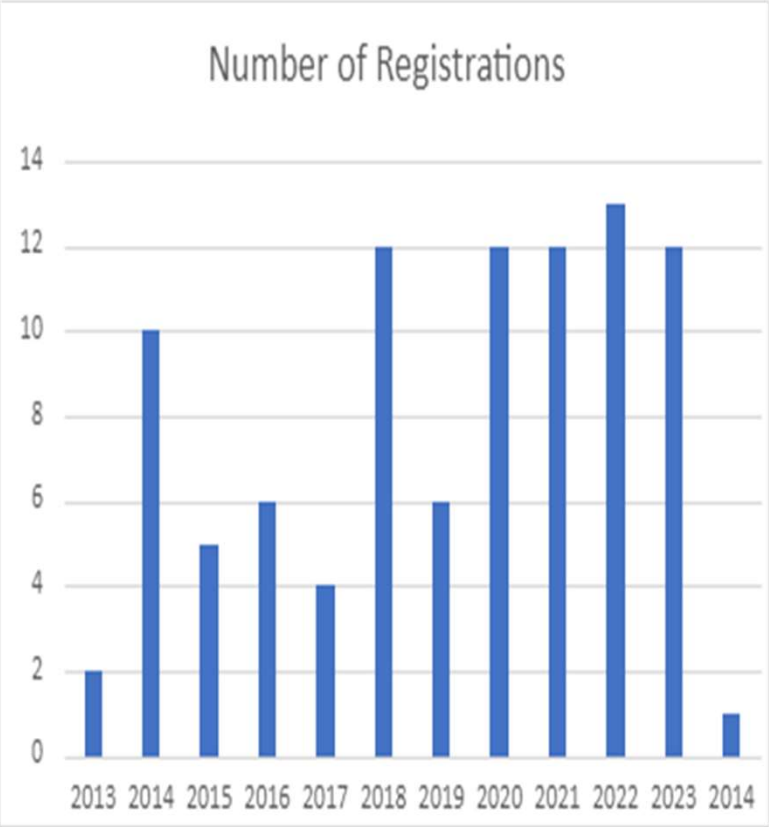
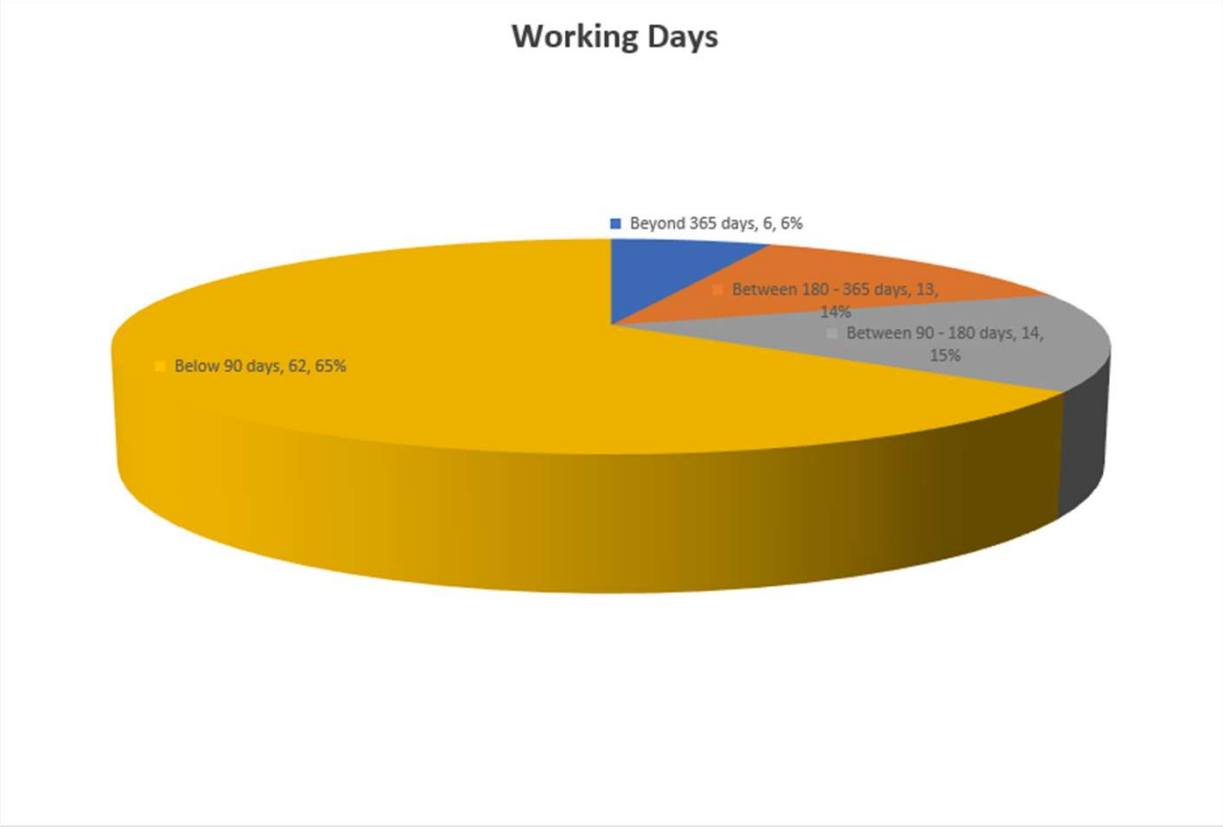
PQ CRP Implementation : WHO Experience





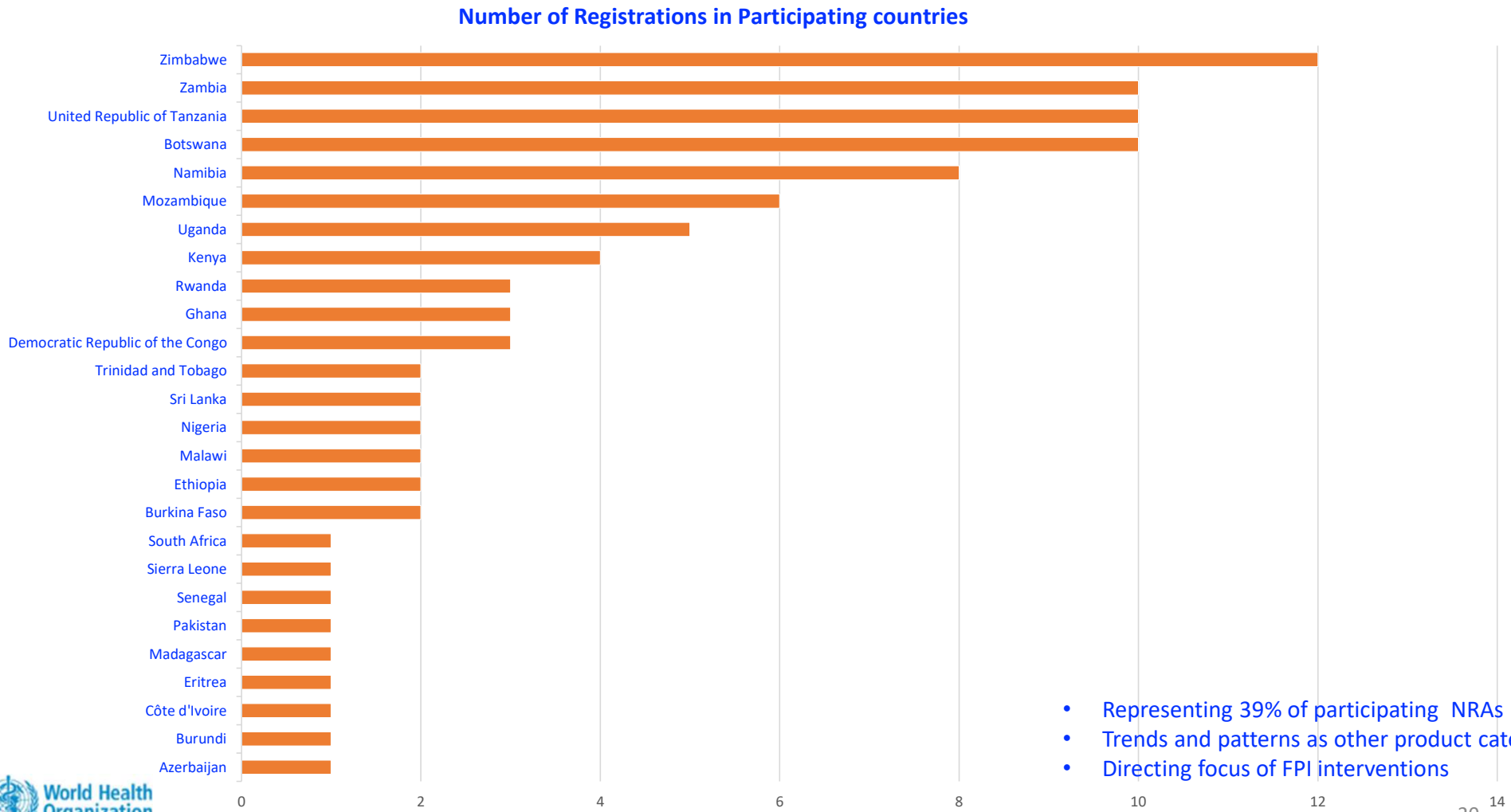
2015-2024

- 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)

KS2

PQ CRP Implementation : WHO Experience



- Representing 39% of participating NRAs
- Trends and patterns as other product categories
- Directing focus of FPI interventions

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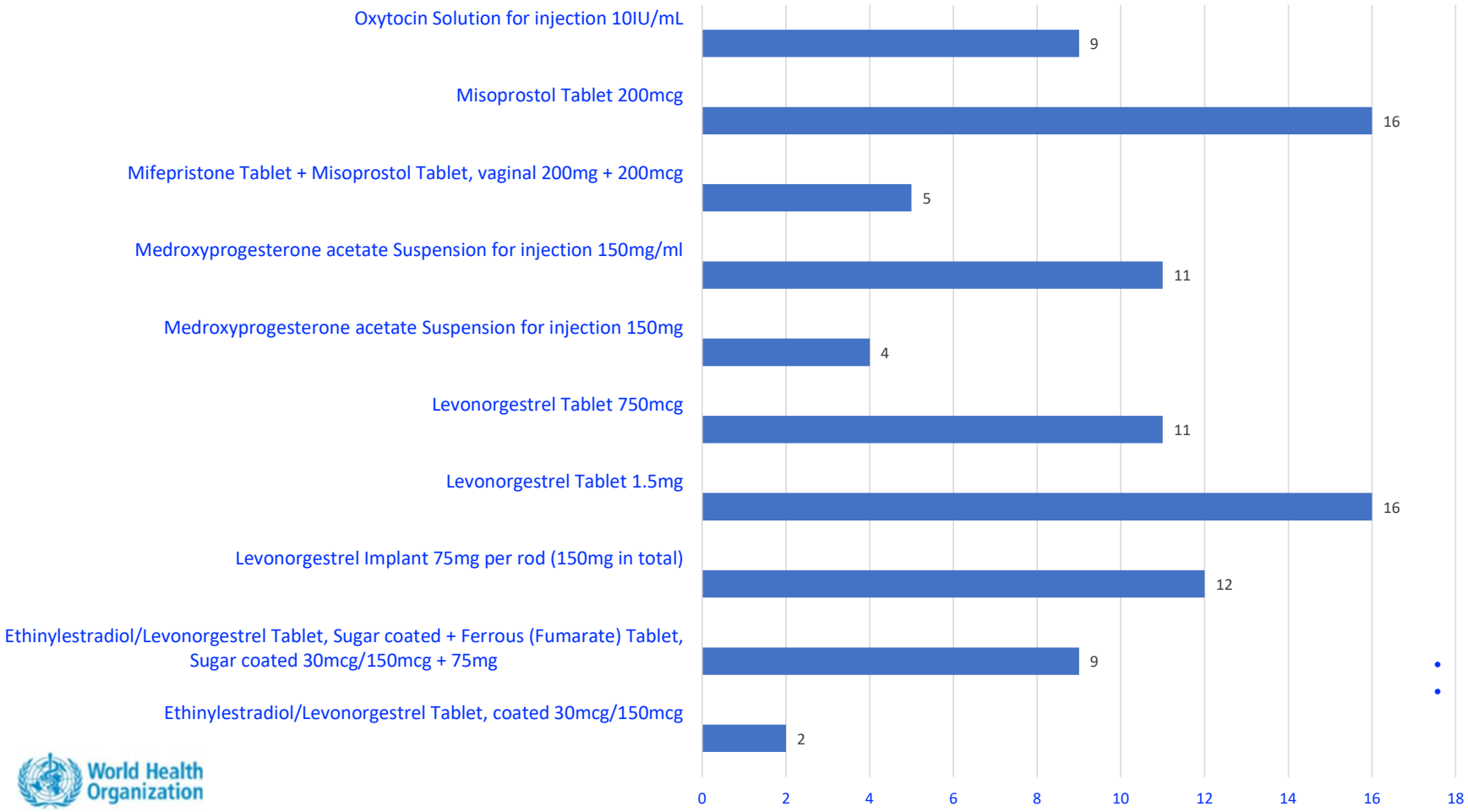
PQ CRP Implementation : WHO Experience

FPP formualtion registered under CRP



- **Prepresenting 30% of EOI**
- **CRP can effectively bridge the gap for the remaining 70%**

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SRA CRP Participation : 59 NRAs + 1 REC (CARICOM)

- Angola
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- 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)
- 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

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List of SRAs as per WHO Guidelines

TRS 1003 - 51st report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations

WHO Technical Report Series 1003

14 June 2017 | Technical document

Overview

The WHO Technical Report Series makes available the findings of various international groups of experts that provide WHO with the latest scientific and technical advice on a broad range of medical and public health subjects. Members of such expert groups serve without remuneration in their personal capacities rather than as representatives of governments or other bodies; their views do not necessarily reflect the decisions or the stated policy of WHO.

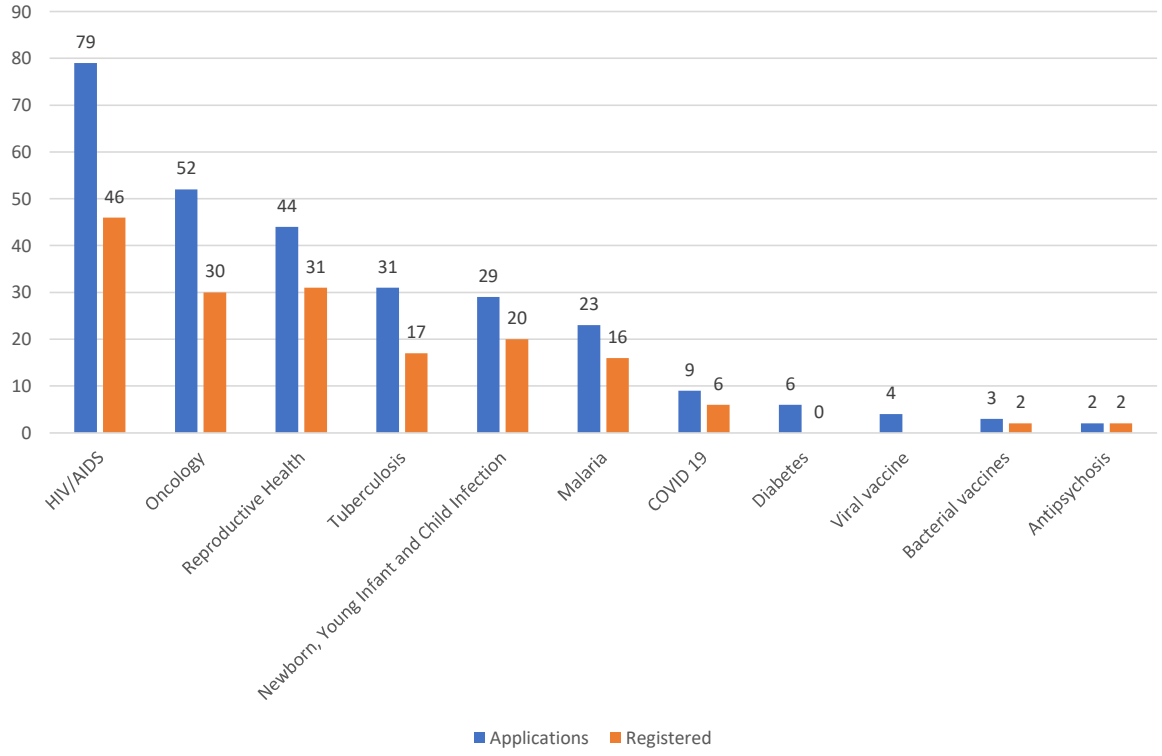
Based on the above interim definition, the following is the list of the countries whose NRAs are designated as SRAs.

Australia	Germany	Netherlands
Austria	Greece	Poland
Belgium	Hungary	Portugal
Bulgaria	Iceland	Romania
Canada	Ireland	Slovakia
Croatia	Italy	Slovenia
Cyprus	Japan	Spain
Czech Republic	Latvia	Sweden
Denmark	Liechtenstein	Switzerland
Estonia	Lithuania	United Kingdom
Finland	Luxembourg	United States of America
France	Malta	Norway

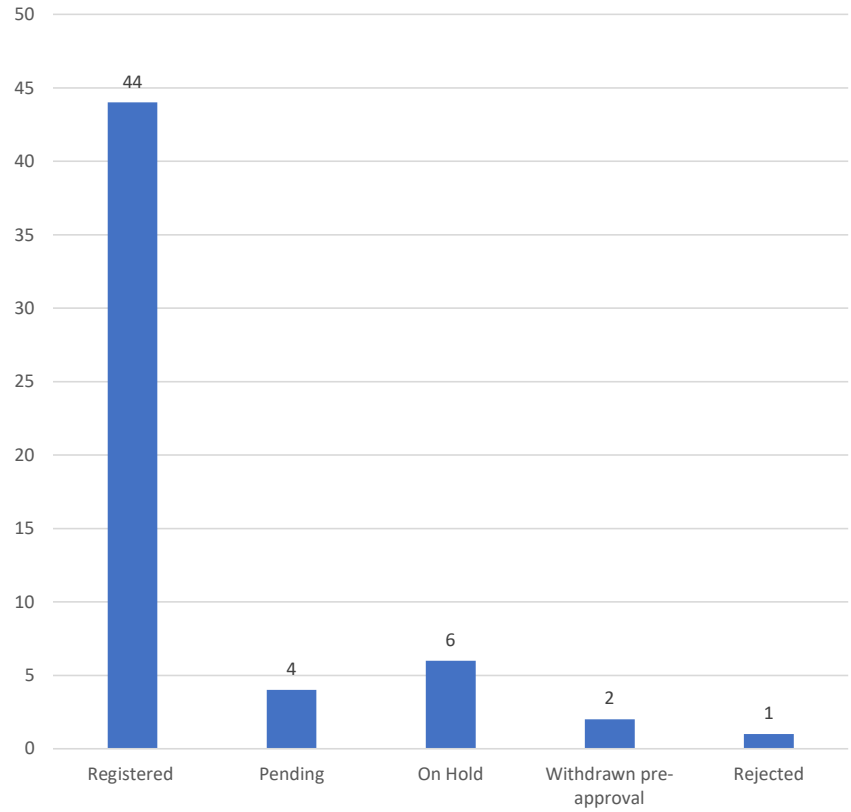
+ EMA

SRA CRP Implementation : WHO Experience

Distribution Across Product Indications: Number of submissions and registrations



Status Reproductive Health Products under SRA CRP: Number of products



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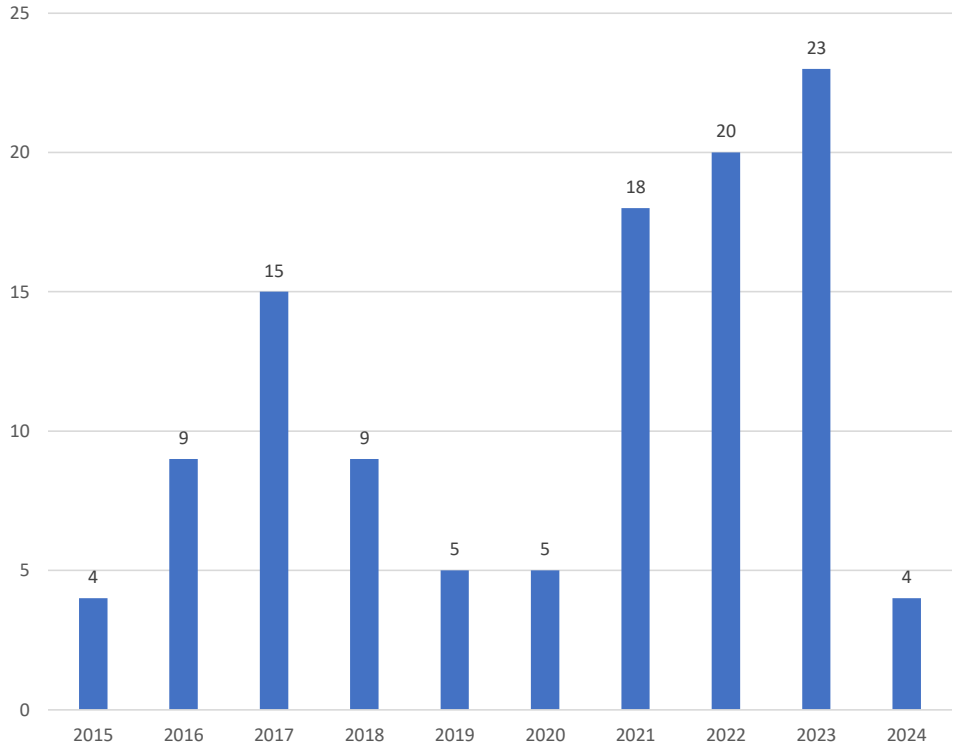
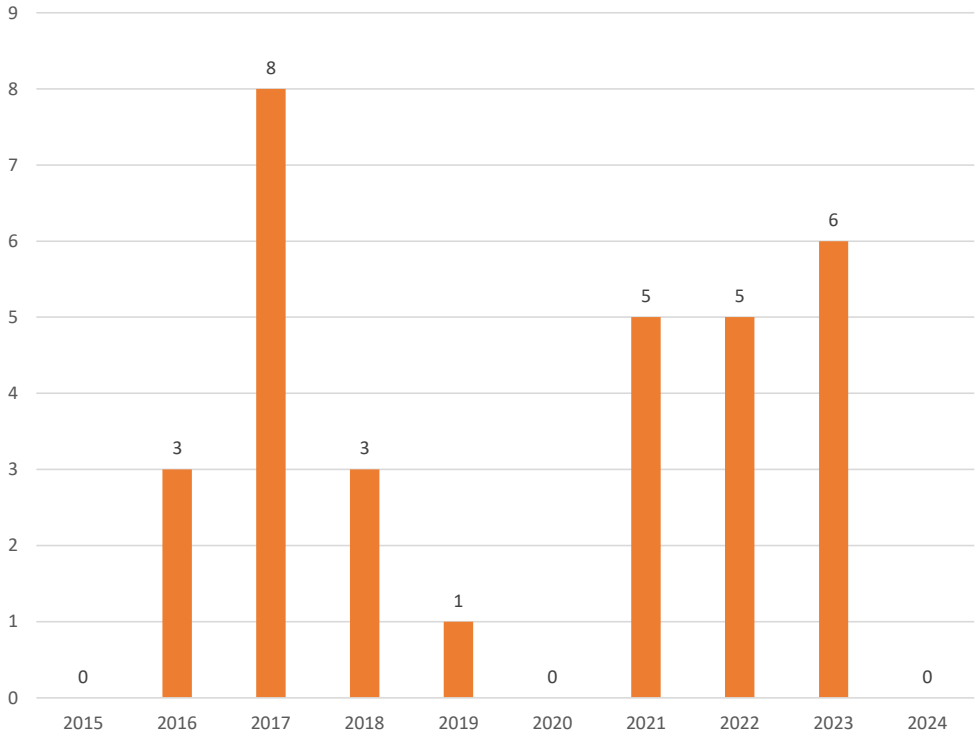
SRA CRP Implementation : WHO Experience

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

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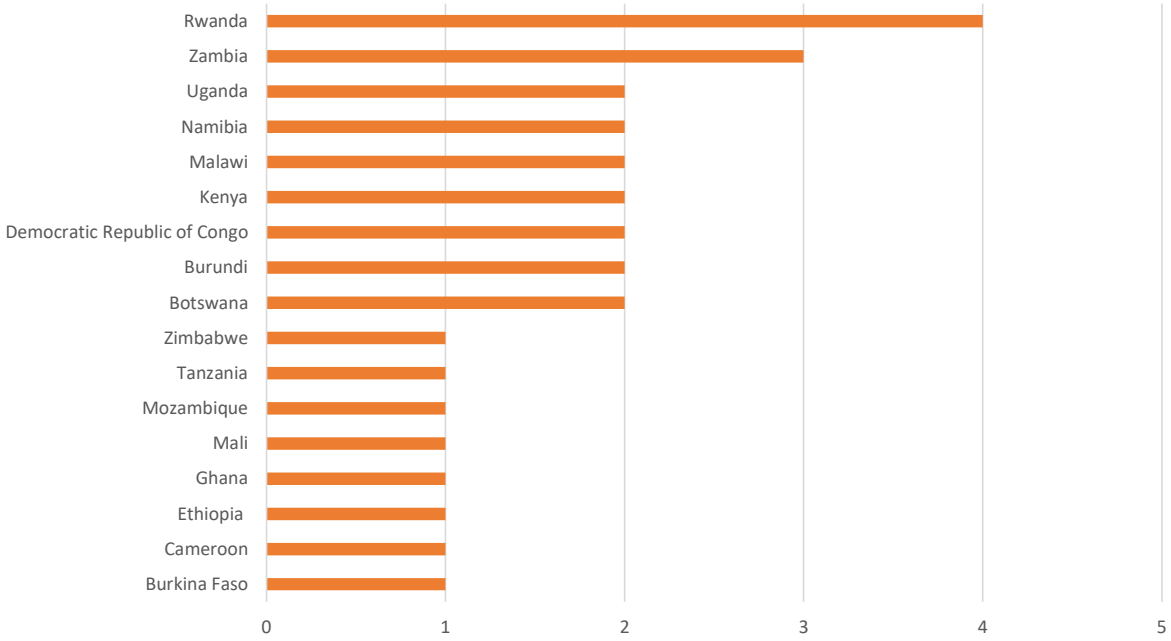
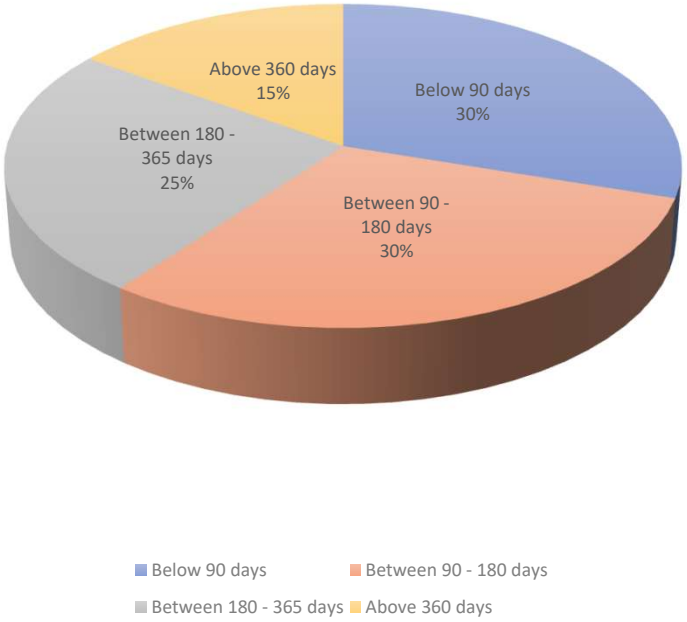
SRA CRP Implementation : WHO Experience

Number of Registrations in Participating Countries



Registration timelines (Working Days)



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- 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

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 buidling
- 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

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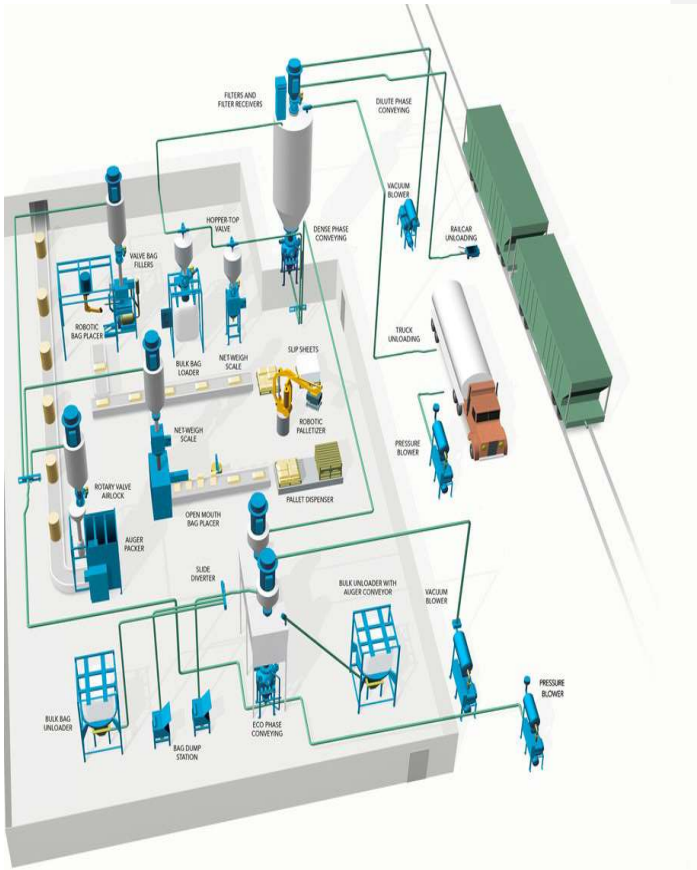
Take Away messages



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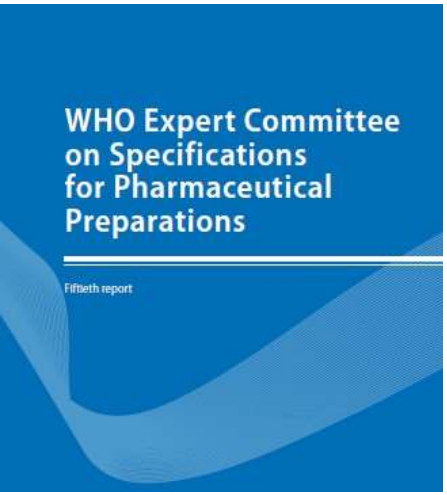
- Evidence over 10 years demonstrating reliance in assessment and MA in action : 1000+ MA facilitated
- CRP works effectively in all product streams : stakeholders to utilize this validated reliance mechanism
- Short timelines vs standard national process : access to patients, quick product introduction
- Supports harmonization and streamlining the submissions, predicted assessment styles and cycles
- Can facilitate reliance in PAC management : reduce manufacturers regulatory burden
- Consideration to expanding to wider product scope and formulations

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

https://iris.who.int/bitstream/handle/10665/255338/9789241209960eng.pdf?isAllowed=y&sequence=1#page=277&zoom=auto,-344,680

SRA CRP

Annex 11

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

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

Thank you

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