REGULATORY UPDATES FROM WHO AND PARTNERS

SESSION 12 – PLENARY SESSION

5 DECEMBER 2024

Objectives:

- To share expériences of manufacturers`participation in WHO Collaborative Registration Procedure
- To provide update on progress of CRP implementation, including revised and new guidelines and product streams
- To share expériences of NRAs `participation in WHO Collaborative Registration Procedure
- To provide information on WHO PQT support to WHO CRP on Vector Control Products

Panelists

- Sandhya Jadhav - Macleods Pharmaceuticals
- Sunday Kisoma - WHO/FPI
- Deon Poovan - SAHPRA, South Africa
- Worasuda Yoogthong - Thai FDA, Thailand
- Dominic Schuler - WHO/PQT

Session layout

- Introduction, objectives and introduction of speakers and moderator – 3 minutes
- Expérience and perspectives from manufacturers – 15 minutes
- CRP updates and outlook – 15 minutes
- NRA experience and perspectives – 2 NRAs (10 minutes each)
- WHO/PQT support and data sharing, support to CRP VCP – 15 minutes
- Discussion, Questions and Answers – 17 minutes

Experience & Perspective of WHO Collaborative Registration Procedure

By
Ms. Sandhya Jadhav
General Manager- Drug Regulatory Affairs
Macleods Pharmaceuticals Limited, Mumbai, INDIA

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Macleods Pharmaceuticals Limited

Amongst the top 10 Pharmaceutical companies in India

Over 20000 Employees are at service to provide uninterrupted care

Presence & supplies in >170 countries with annual turnover of around USD 1 Bn (FY23-24)

Infrastructure

Vertically Integrated Pharmaceutical Company Developing & Manufacturing APIs to Finished Dosage Forms

Therapeutic Segments

- Operates in >10 therapeutic divisions like Anti-TB, Anti-Malarial, ARVs, Anti-Bacterial, Anti-Diabetic, Anti-Osteoporotic, CNS, CVS, Respiratory, Gastrointestinals & Dermatologicals

Manufacturing Facility

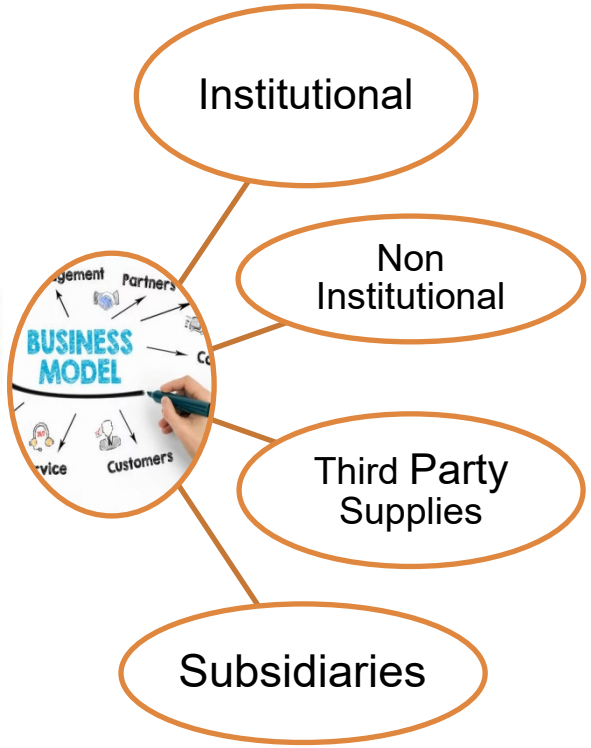
- 8 finished dosage manufacturing sites for various dosage forms
- 3 API Manufacturing sites for small molecules (general products), oncology products and peptides

R&D Bioequivalence Centre

- Supported by state-of-the-art R&D centre & in-house bioequivalence centre

Macleods has strong International Presence with 4000+ products approved by multiple Globally accredited Regulatory bodies

>170
Countries



Approvals from Global Regulators

FDA APPROVED	USA
MHRA	UK
	Europe
ANVISA	Brazil
	South Africa
	WHO Geneva

& many more...

Registrations & Approvals

API DMF /CEP Application

US :- Filed **111** API DMFs

EU :- CEP application: **50** APIs and Received**: 46** CEP approval

USA Filing

Filed **208** ANDAs, Received **122** approvals

Europe Filing

201 Products filed through DCPs, National and MRP procedure and Received 146 Approved

Canada Filing

Filed **55** , Received **51** approvals

Around **3700 + Registrations** all around the globe in Rest of the Countries **(ROW)**

Macleods: WHO-PQ Registrations

Macleods filed its first dossier to WHOPQ in **2005**

So far around **103** dossiers Products have been filed

74 product approved & remaining products are under evaluation

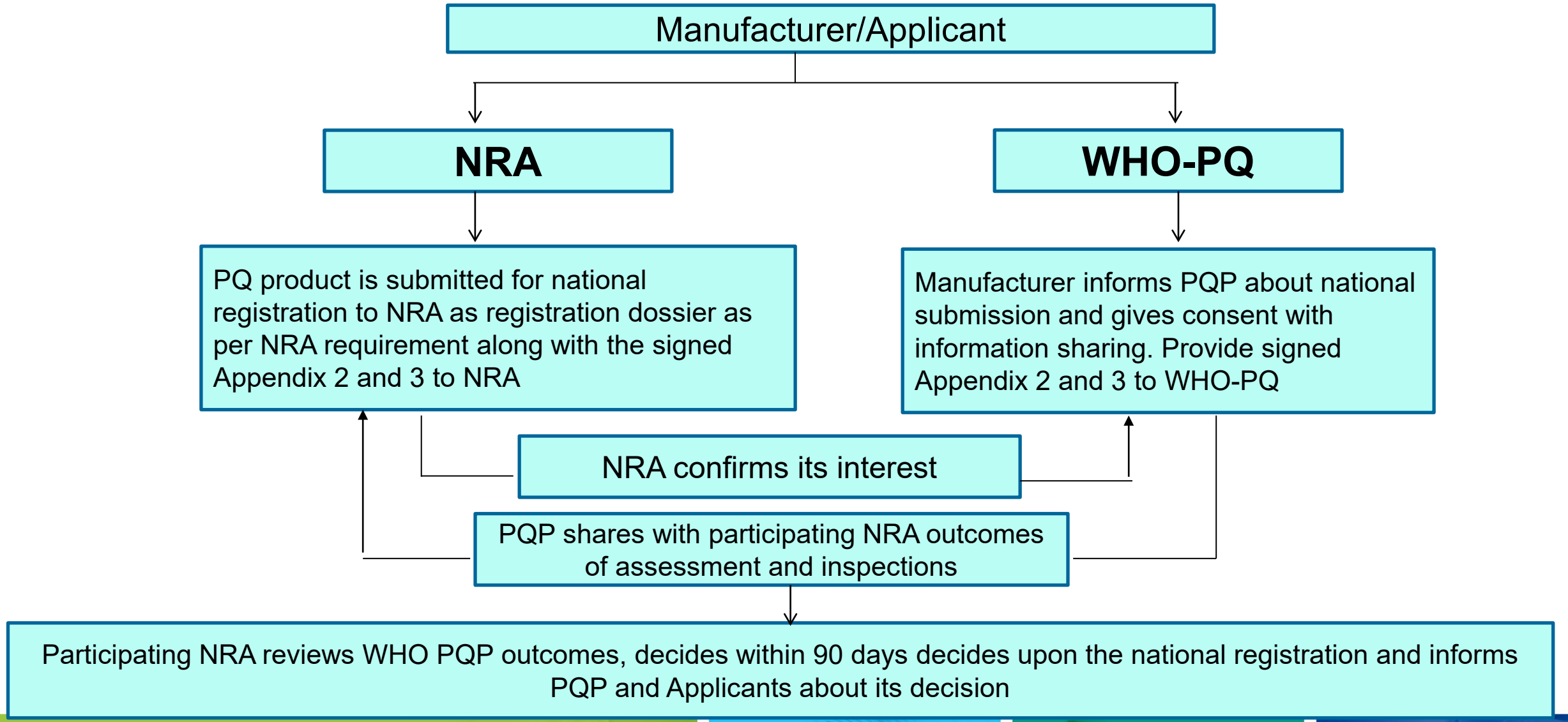
It gives access to global organizations **like Global Drug Facility, Global Fund, IDA, UNICEF, UNDP, UNAIDS, PAHO, CHEMONICS, UNOPS**

Macleods is one of the Global leaders in supply of **Anti –TB & ARV & Anti Malarial.**

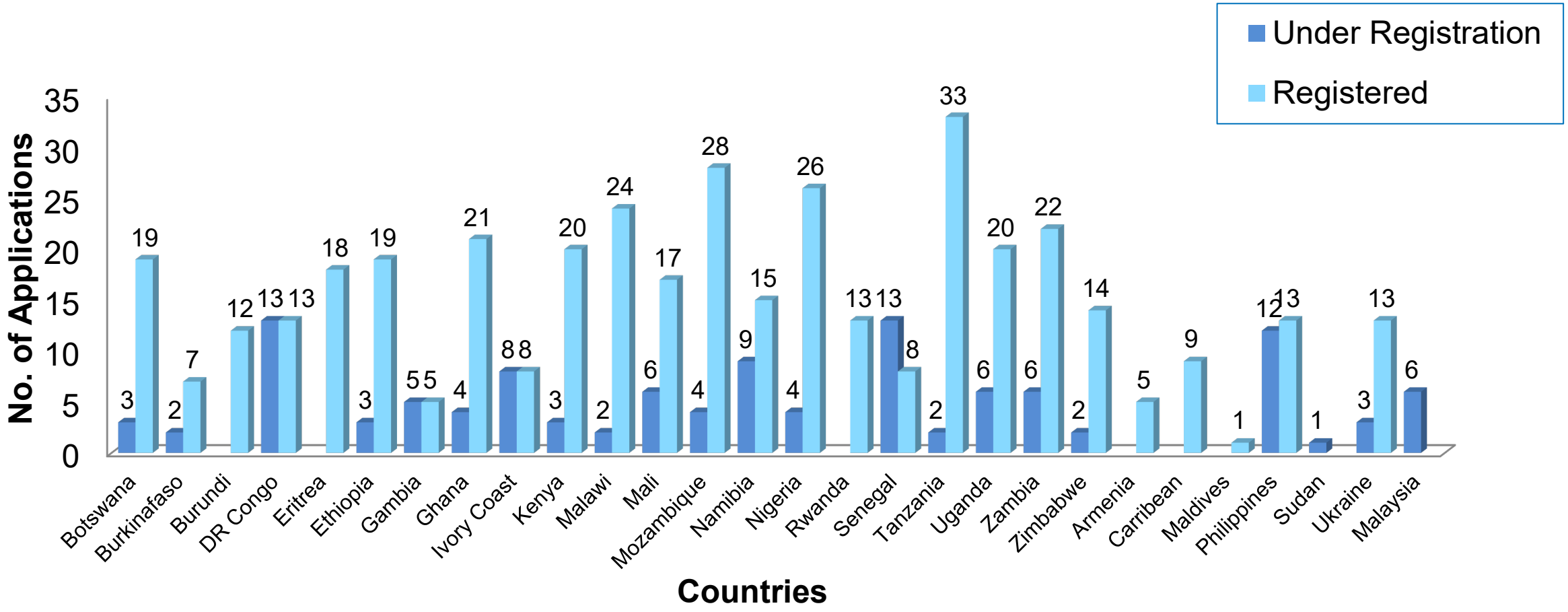
Collaboration Registration Procedure

- **What it is ?**
  It is Accelerated Registration Procedure of the Prequalified Products
- **How does it works ?**
  It works on Reliance
- **How Many Countries are involved so far ?**
  Number of Countries Participated so far : **66 Countries**
- **How Long Does it takes ?**
  90 to 120 Days
- **How Many Registrations so far by using CRP, in Macleods ?**
  403 Registered and around 117 are coming soon
- **What it the Procedure to use CRP ?**

Collaboration Registration Procedure

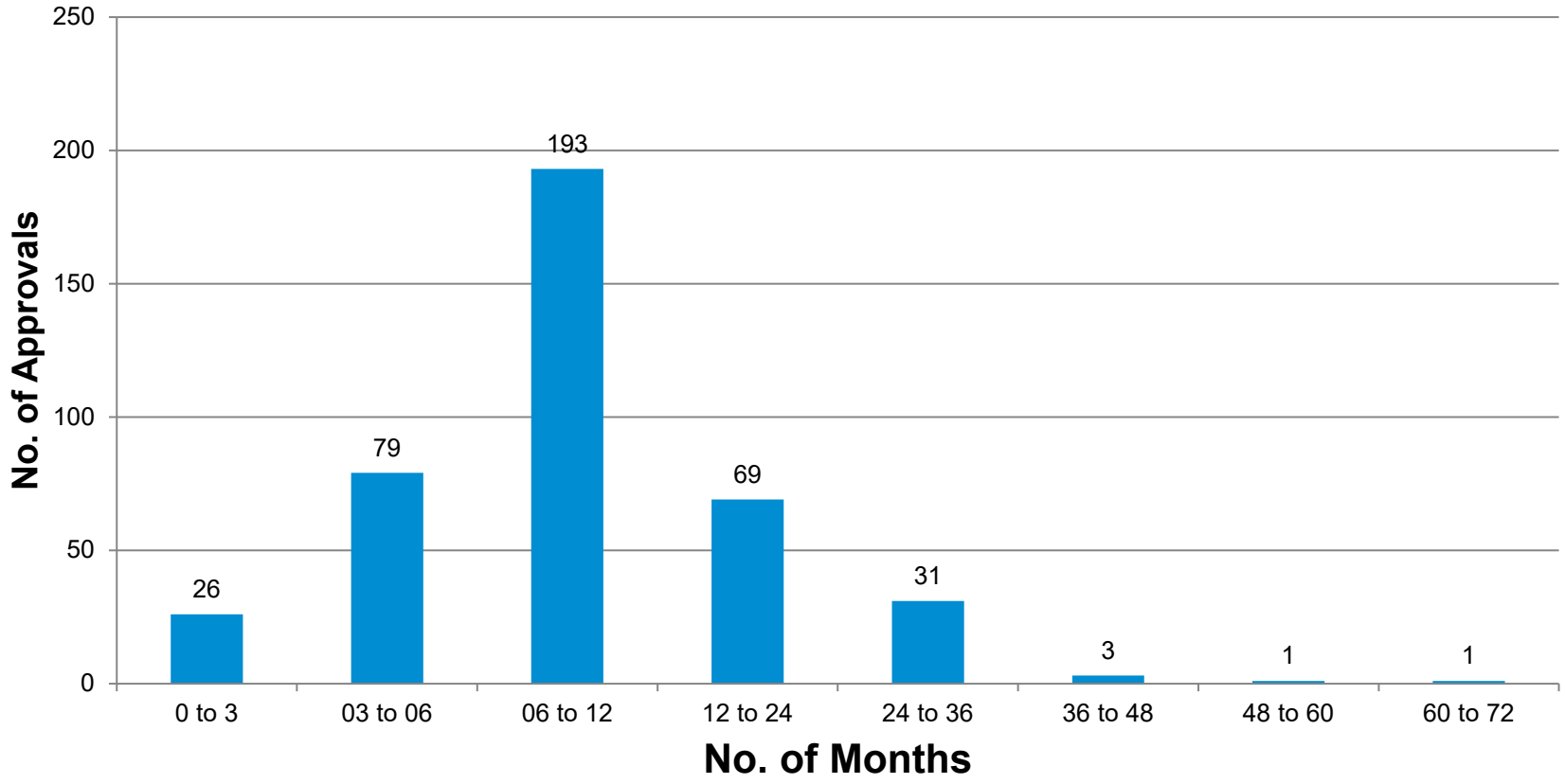


Registered & Under registration Product overview in different Countries



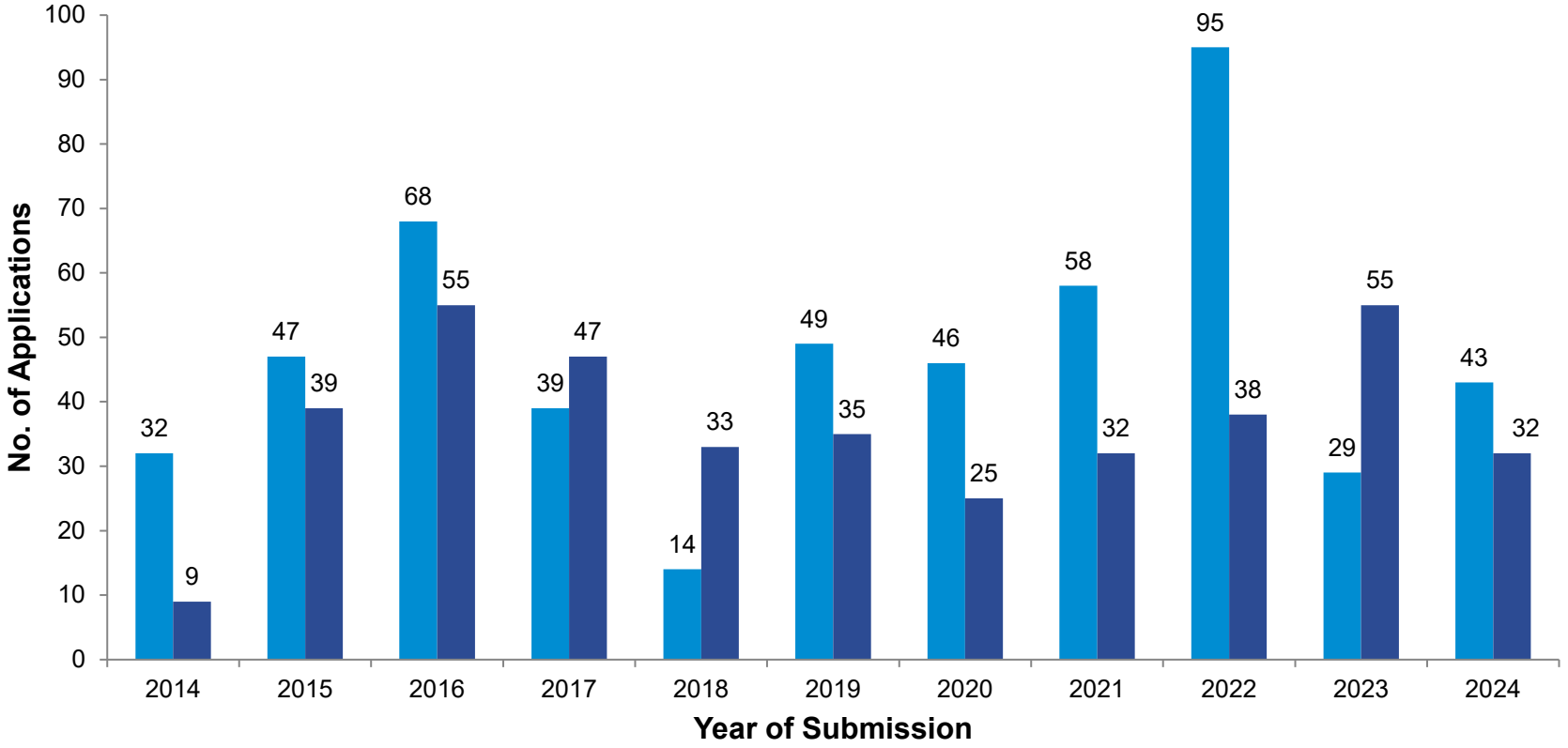
Time taken for Registration by CRP in Months

No. of Approvals	Time Taken in Months
26	0 to 3
79	03 to 06
193	06 to 12
69	12 to 24
31	24 to 36
3	36 to 48
1	48 to 60
1	60 to 72
403	



Year wise filling and Registration

Year	No of Submission	No of Registration
2014	32	9
2015	47	39
2016	68	55
2017	39	47
2018	14	33
2019	49	35
2020	46	25
2021	58	32
2022	95	38
2023	29	55
2024	43	32
	520	**403**



Advantages Of Collaborative Registration Process

1) Manufacturers

- Faster registration process than the general NRA registration procedure (within 90 - 120 days)
- Simple procedure and less No. of Queries as compared to the regular process
- Access to fast approval in listed 66 Countries (As on date)
- Harmonized data for PQ and national registration
- Accelerated and more predictable registrations
- Lab Analysis is waived in few countries, which fasten the process further.

2) Procurers

- Procurement of Essential Medicines can be more faster and wider availability of Prequalified Quality medicines.
- **Assurance about 'the same Quality' medicine as is prequalified**

Advantages Of Collaborative Registration Process

3) NRA

- Availability of WHO assessment and inspection outcomes to support national decisions and save internal capacities/Resources.
- Assurance about registration of 'the same Quality' medicine as is prequalified.
- Faster availability of prequalified medicines in the Country.

4) Patients

- Faster access and availability of prequalified medicines to the one who is in need.

Challenges

1. Delayed Responses by few NRAs
2. Irrespective of the base of reliance, manufacturer has to follow the country specific requirement in few countries like,
    - I. Country Specific Pharmacopoeial compliances
    - II. Country specific Reference product comparison (CDP)
    - III. Stability requirements are not in line with ICH guidelines
    - IV. Post approval Variations strategies/Guidelines are different
    - V. WHO filed retrospective data is not considerable
3. WHO inspections are not considered, and PICS GMP or SRA GMP is mandatory.
   Or Country Specific GMP Inspection required

Recommendations

1. Reduce Approval Timelines; conforms to the timelines in the guidance
2. Use of Single Harmonized Dossier format of international Standards with minimum or without Country specific Requirements
3. Harmonisation of Variation Guidelines for Post approval changes
4. Consideration of WHO Inspected facility GMP standards
5. Consideration of Bio waiver based on WHO approval

So the conclusion is…..

Take the benefits of

1. *Collaborative registration Procedure*
2. *WHO facilitation and the technical assistance during the assessment process*
3. *WHO Team's excellent Support and further follow-ups with NRAs towards getting registration faster.*


thank you
danke
рахмат
謝謝
ngiyabonga
teşekkür ederim
Баярлалаа
спасибо
faafetai lava
mersi
barka
welalin
tack
vinaka
спасибі
blagodaram
dank je
misaotra
matondo
paldies
grazzi
gracias
kiitos
dankie
dhanyavad
tapadh leat
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asante
manana
obrigada
enkosi
bedankt
dziękuję
hvala
mauruuru
köszönöm
djiere dieuf
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дякую
mamnun
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gratias ago
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sulpáy
go raibh maith agat
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мерси
kam sah hamnida
감사합니다
xièxie
ευχαριστώ
merci

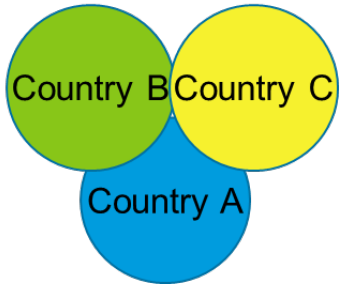
COLLABORATIVE REGISTRATION PROCEDURE (CRP): Updates and Outlook

Sunday KISOMA
Technical Officer
Facilitated Product Introduction Team
WHO/MHP/RPQ/REG/FPI

Reliance : Scope and Practices

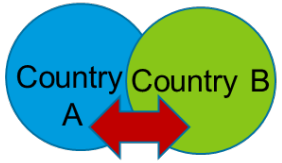
"The act whereby the regulatory authority in one jurisdiction **takes into account and gives significant weight** to **assessments performed by another regulatory authority or trusted institution**, or to any other authoritative information, **in reaching its own decision**. The relying authority remains **independent, responsible and accountable** for the decisions taken, even when it relies on the decisions, assessments and information of others."

Work-sharing



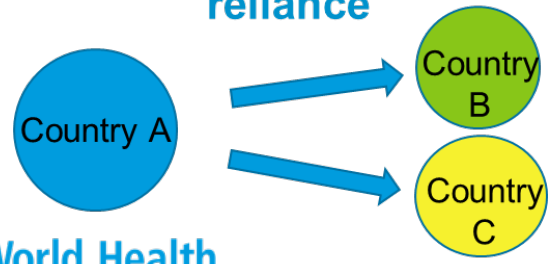
Recognition

Unilateral



Mutual recognition

Abridged pathway using reliance



- Sovereignty maintained;
- More efficient use of global regulatory resources;
- Decrease duplication, increase trust and collaboration.

WHO Collaborative Registration Procedure

Applicant

Single product dossier

+

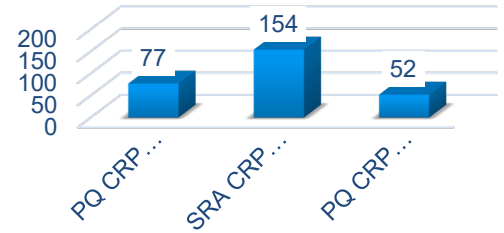
Prod. Assessment Reports from SRA/WHO PQ

To multiple CRP participating country(s)

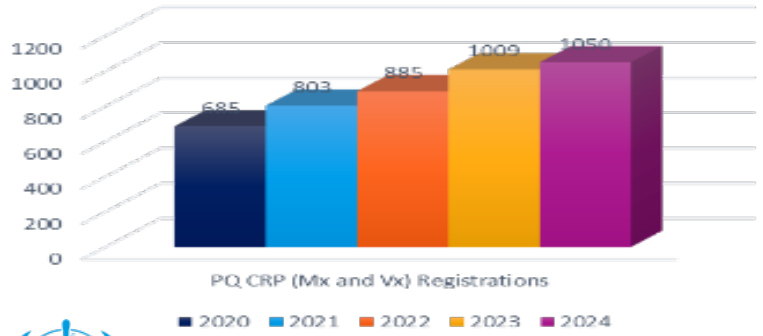
Accelerated assessment and registration of quality-assured products in countries

Faster access to priority quality-assured products by the population

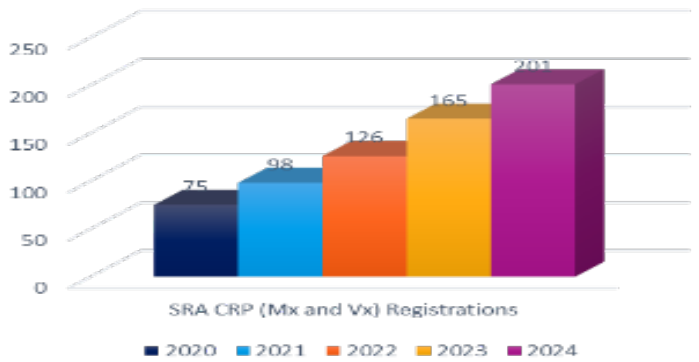
Median time for CRP Registrations (Working Days)



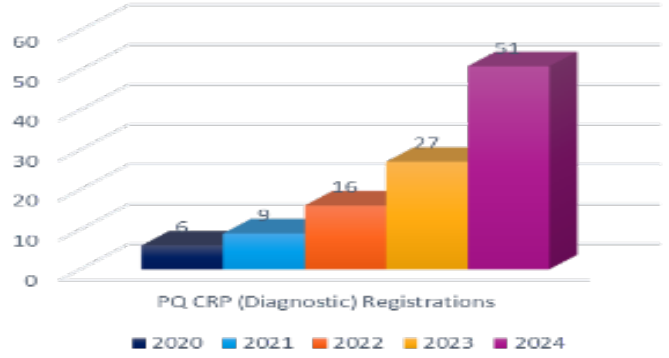
PQ CRP (Mx and Vx)



SRA CRP (Mx and Vx)



PQ CRP (IVDs)



World Health Organization

- Angola
- Armenia
- Azerbaijan
- Bangladesh
- Belarus
- Benin
- Bhutan
- Botswana
- Brunei Darrusalam
- 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
- Kyrgyzstan
- Lao People's Democratic Republic
- Lesotho
- Liberia
- Madagascar
- Malawi
- Malaysia
- Maldives
- Mali
- Mauritania
- Mozambique
- Namibia
- Nepal
- Niger
- Nigeria
- Pakistan
- Papua New Guinea
- Paraguay
- Philippines
- Qatar
- Republic of Congo
- Republic of Moldova
- Rwanda
- Sao Tome and Principe
- Senegal
- Sierra Leone
- South Africa
- Sri Lanka
- Sudan
- Tanzania (Mainland)
- Tanzania (Zanzibar)
- Thailand
- Timor-Leste
- Togo
- (Tunisia)
- Türkiye
- Uganda
- Ukraine
- Uzbekistan
- Yemen (Sana'a)
- Yemen (Aden)
- Zambia
- Zimbabwe

PQ CRP Mx,Vx: 67 NRAs + 1 REC (CARICOM)

SRA CRP: 64 NRAs + 1 REC (CARICOM))

PQ CRP IVD : 35 NRAs

In green: PQ CRP Mx, Vx, IVD and SRA

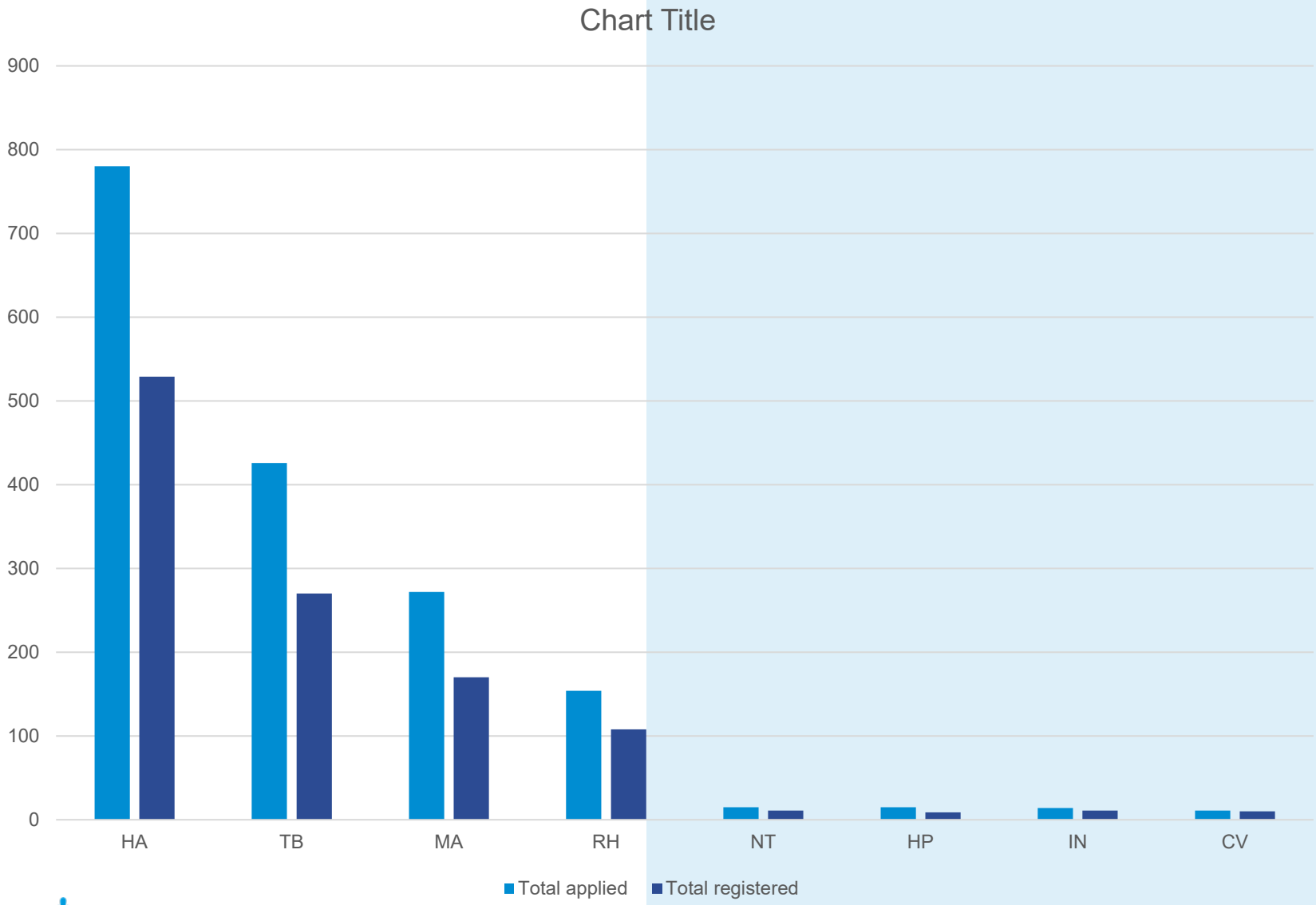
In blue: PQ CRP Mx, Vx and SRA

In orange: SRA CRP only

In black: PQ CRP Mx, Vx only

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

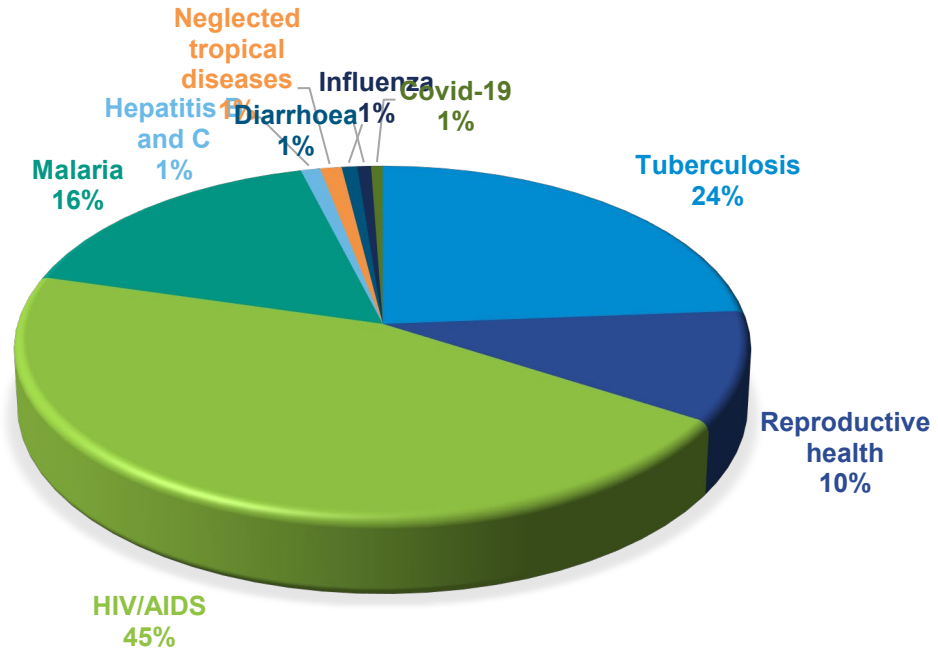
WHO PQ CRP Product scope and trends

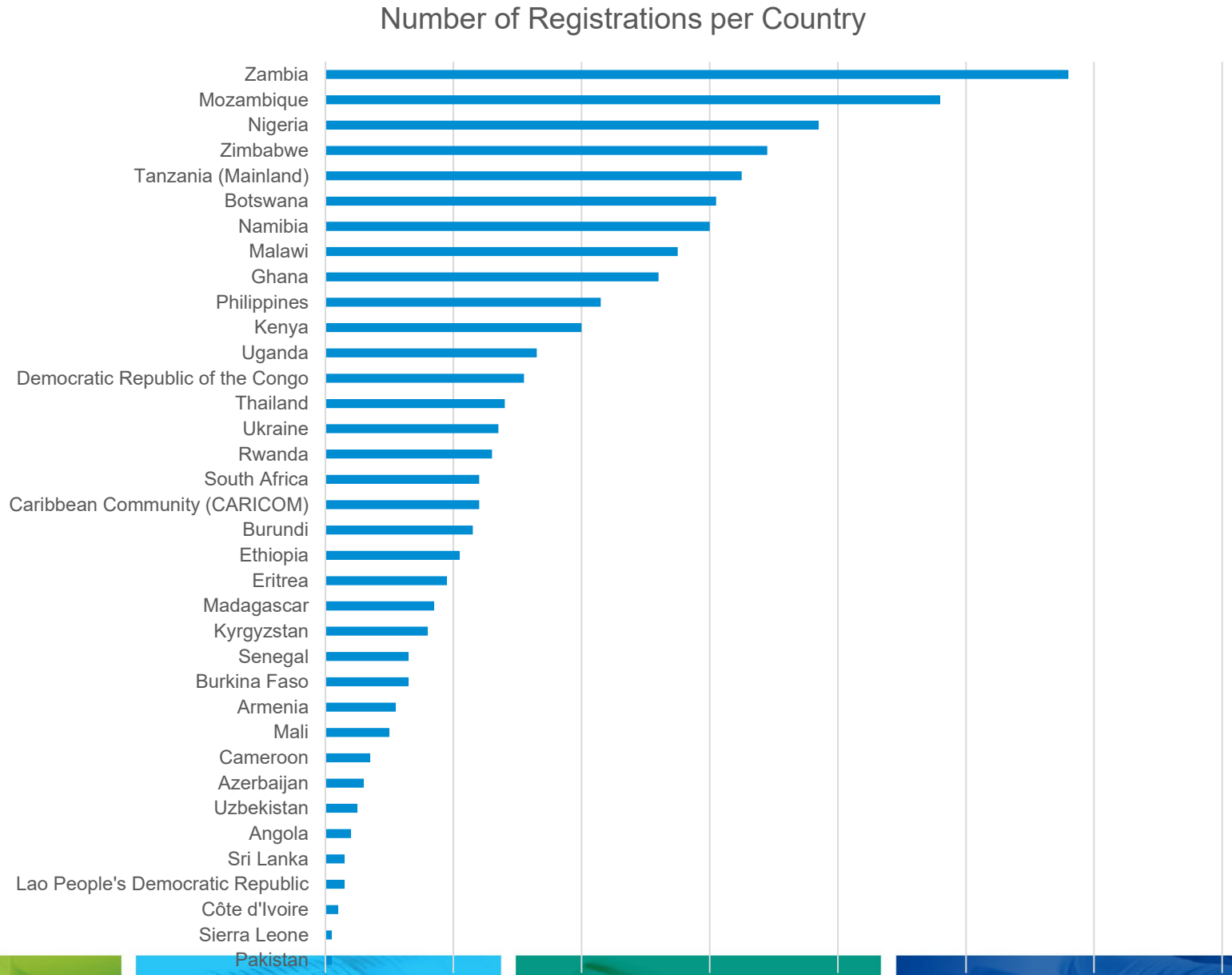


- Apnea in preterm infants
- COVID-19
- Diarrhoeal disease
- Ebola virus disease
- Hepatitis B and C
- HIV/AIDS
- Infections in newborn and childhood pneumonia
- Influenza
- Malaria
- Multi drug resistant bacterial infections
- Neglected tropical diseases
- Reproduction health
- Tuberculosis
- Tobacco use

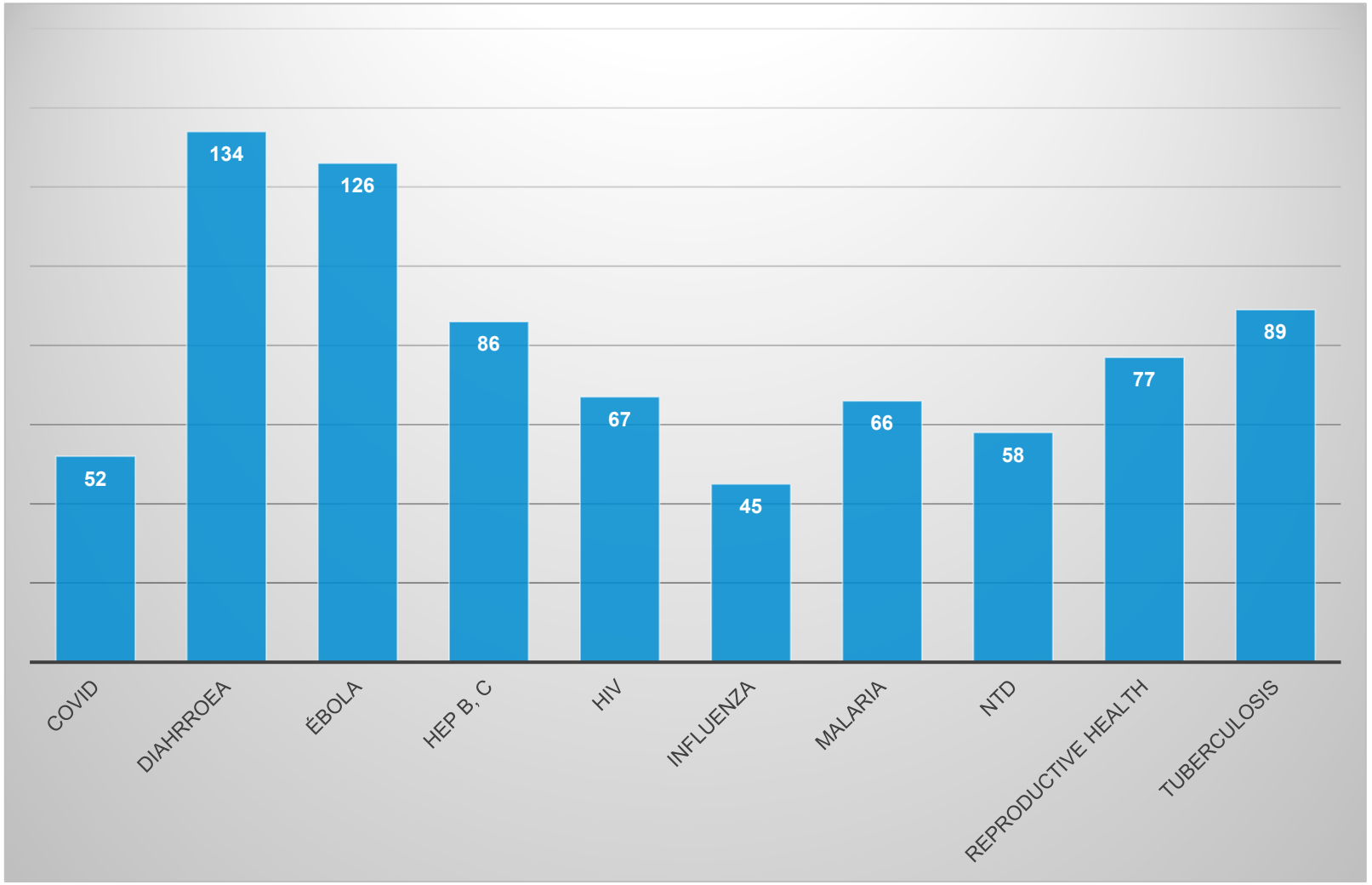
World Health Organization

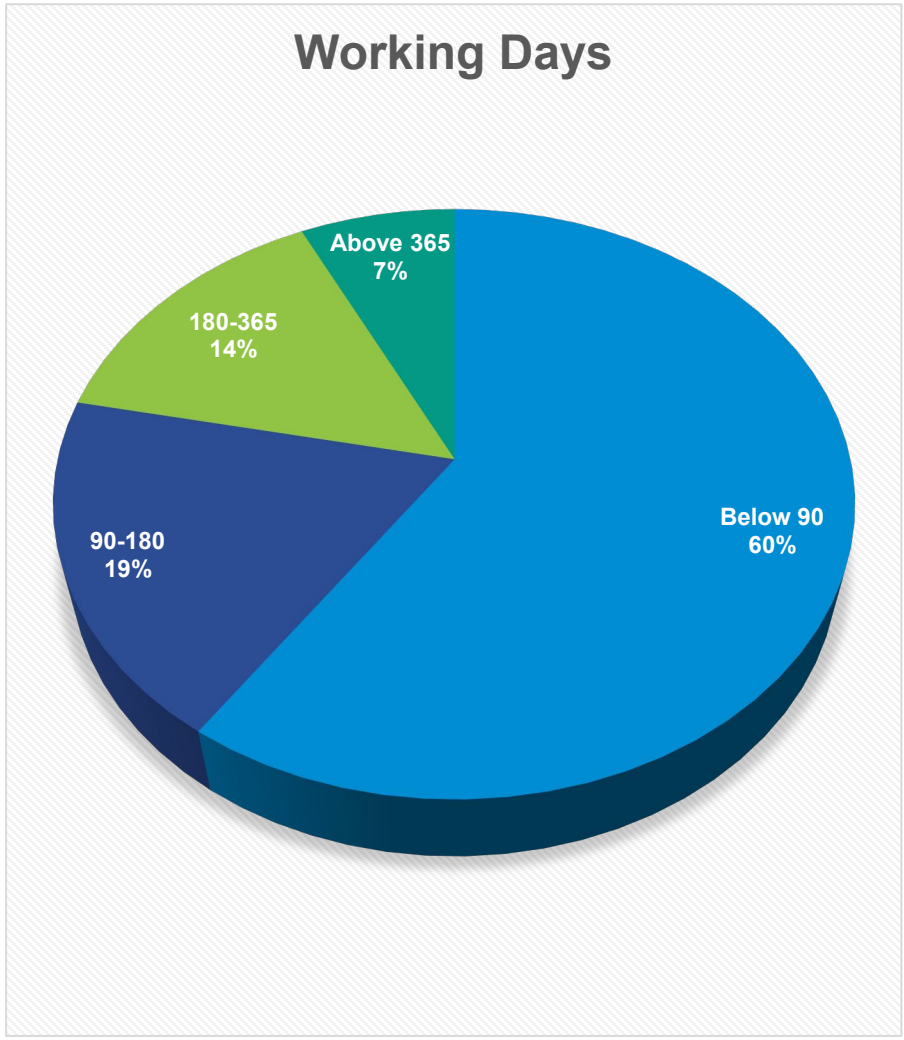
PQ CRP : Registrations and NRA trends





WHO PQ CRP registration times (days)





Include manufacturers timelines

Stringent Regulatory Authorities - CRP

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

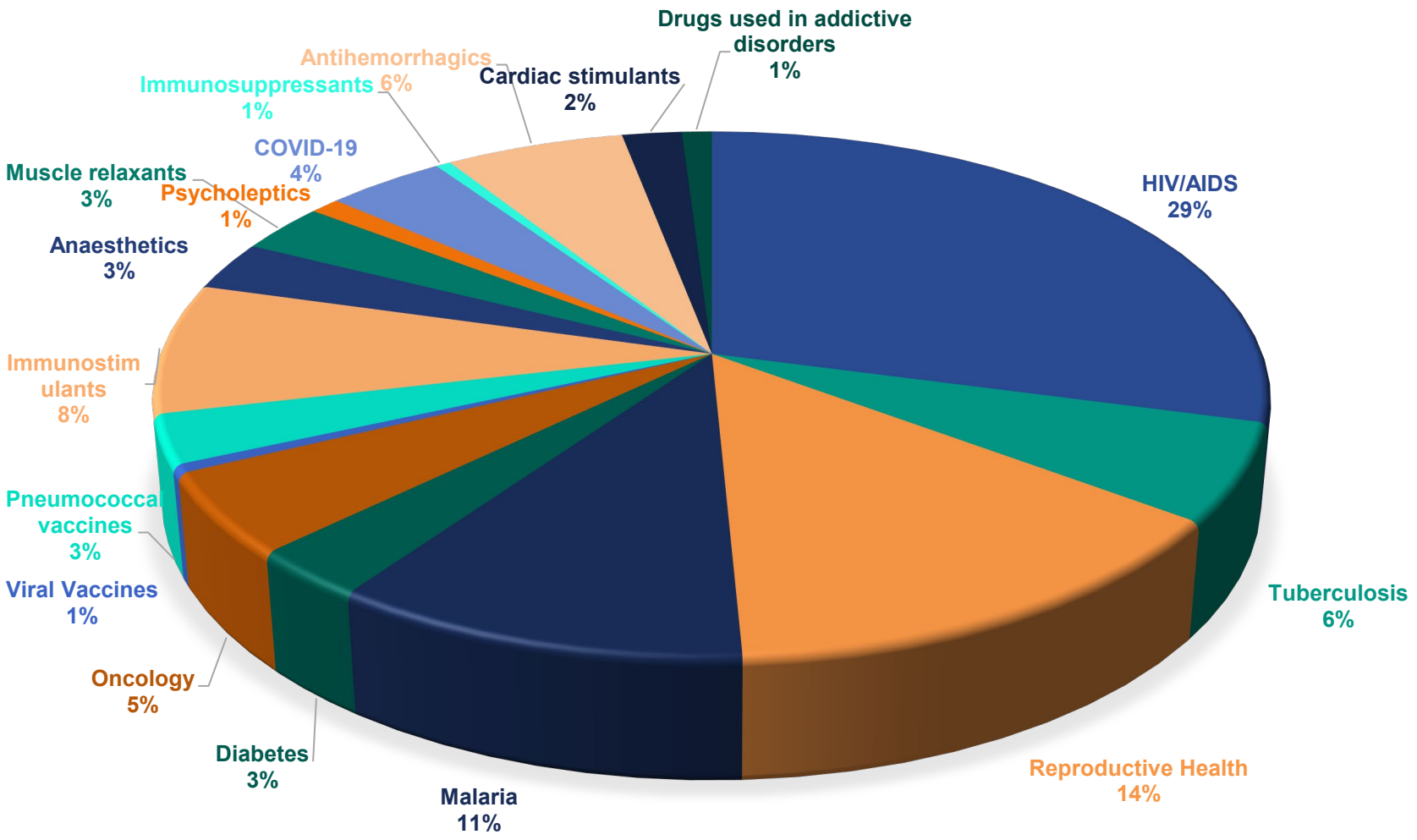
Plus

European Medicines Agency (EMA)

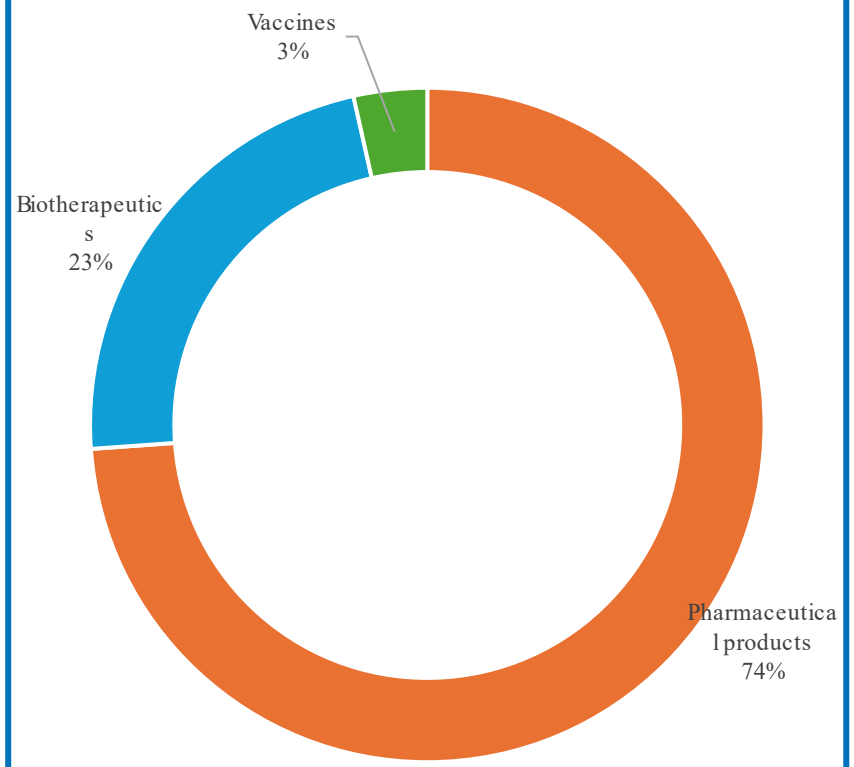
- As defined in WHO Technical Report Series 1003
- “SRAs" that have participated so far:
  - EMA
  - FIMEA (Finland)
  - MEB (The Netherlands)
  - MHRA (UK)
  - MPA (Sweden)
  - Swissmedic (Switzerland)
  - TGA (Australia)
- No restrictions to participation - any SRA that can share reports can participate
- Procedure will be updated to incorporate WHO-Listed Authorities (WLAs) - ECSPP decision expected in spring 2025

SRA CRP Submissions

SRA CRP Registrations by therapeutic areas

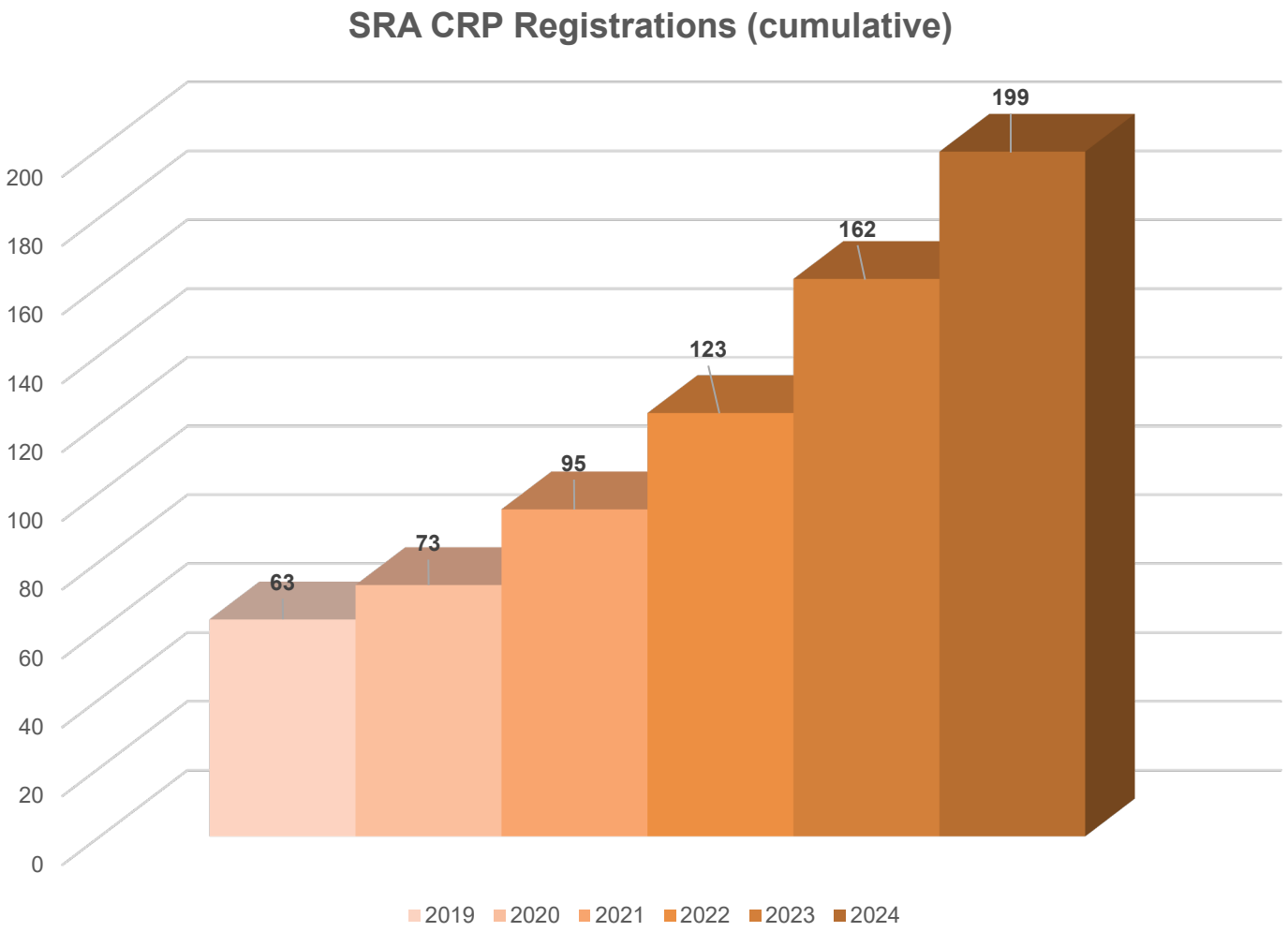


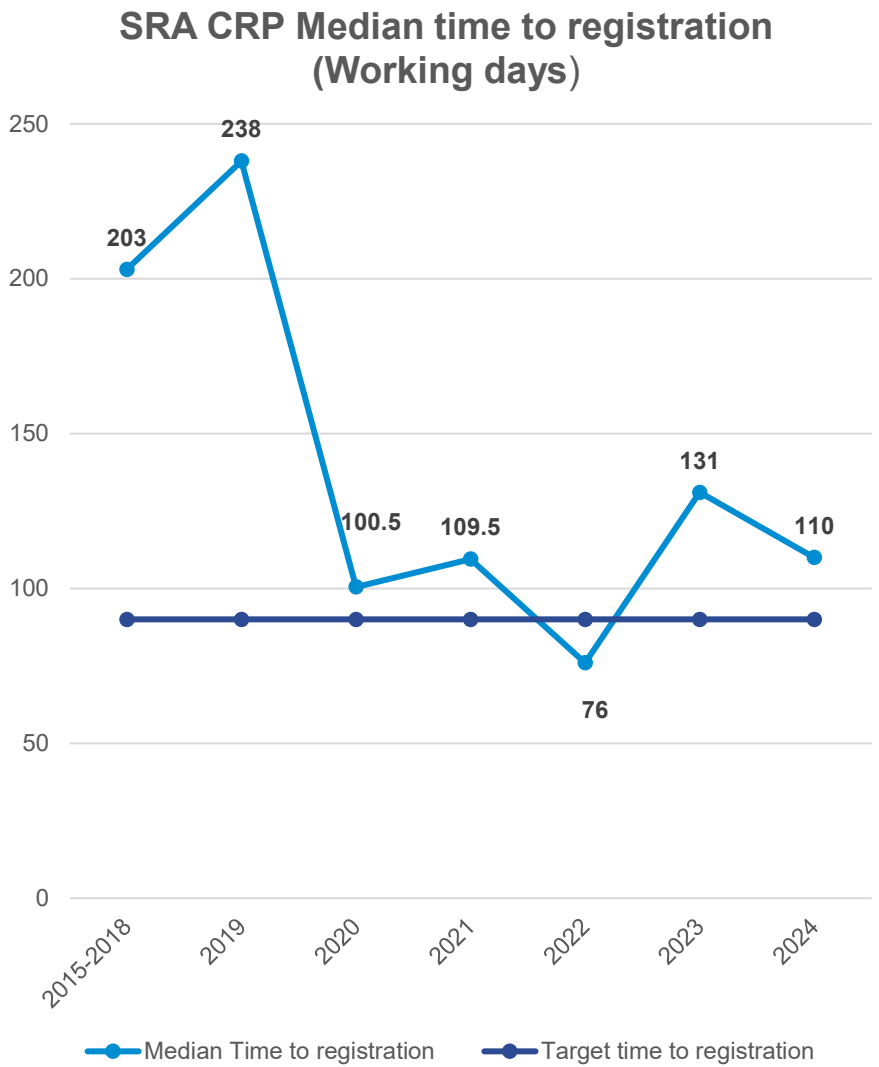
SRACRP Registrations by product type



Data as at 31 October 2024

SRA CRP Registrations





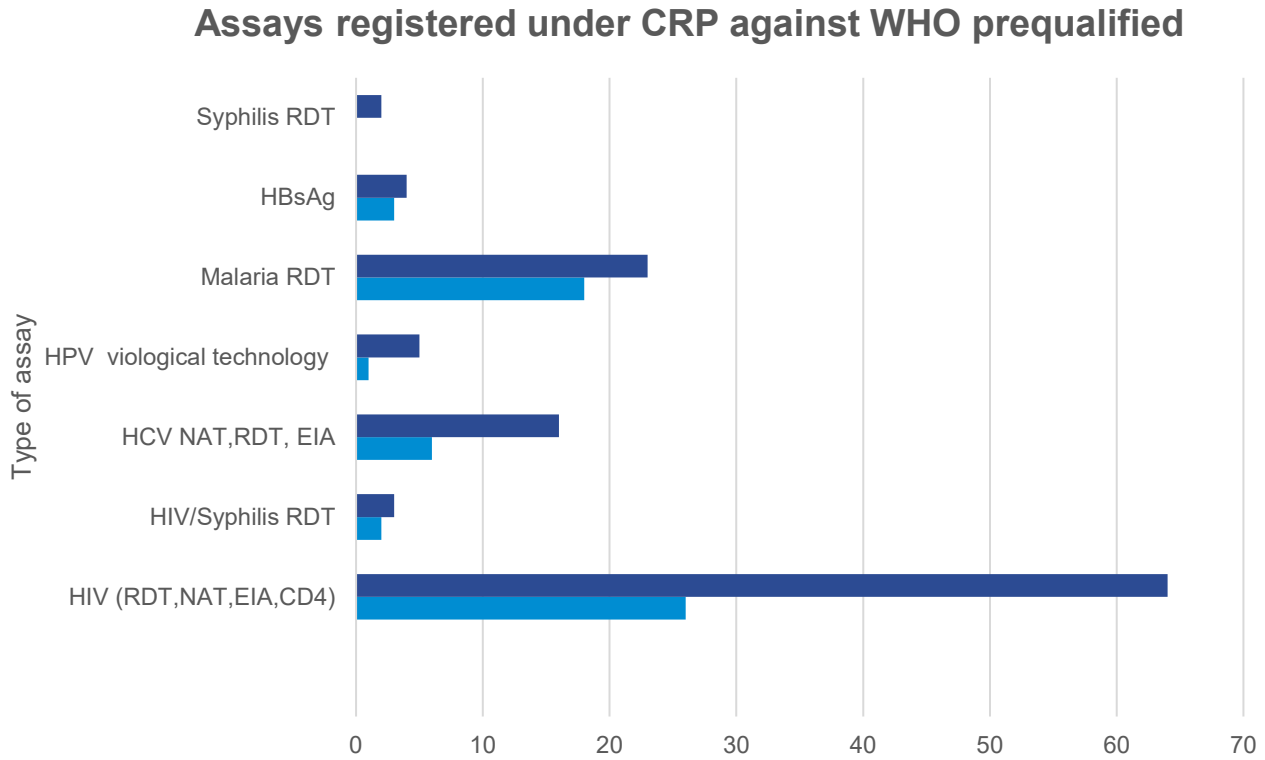
Data as at 31 October 2024

WHO collaborative registration procedure for IVDs: product scope

CRP IVDs: Product scope

- ✓ Focus on IVDs that address major public health concern and needed in member states
- ✓ IVD products eligible for CRP: WHO prequalified IVDs [List of Prequalified In Vitro Diagnostics]
- The list is regularly updated as new IVDs are added to the prequalification scope.
- ✓ Product scope:
  - HIV
  - Hepatitis B virus
  - Hepatitis C virus
  - Malaria parasites
  - HPV
  - Glucose-6-phosphate dehydrogenase (G6PD) enzyme
  - Toxigenic Vibrio cholerae
  - Syphilis
  - MTBC and resistance to first and/or second line anti-tuberculosis drugs
  - SARS-CoV-2
  - Blood Glucose
  - HbA1c

WHO Number of Product Submissions: registered assays under CRP against WHO - Listed assays

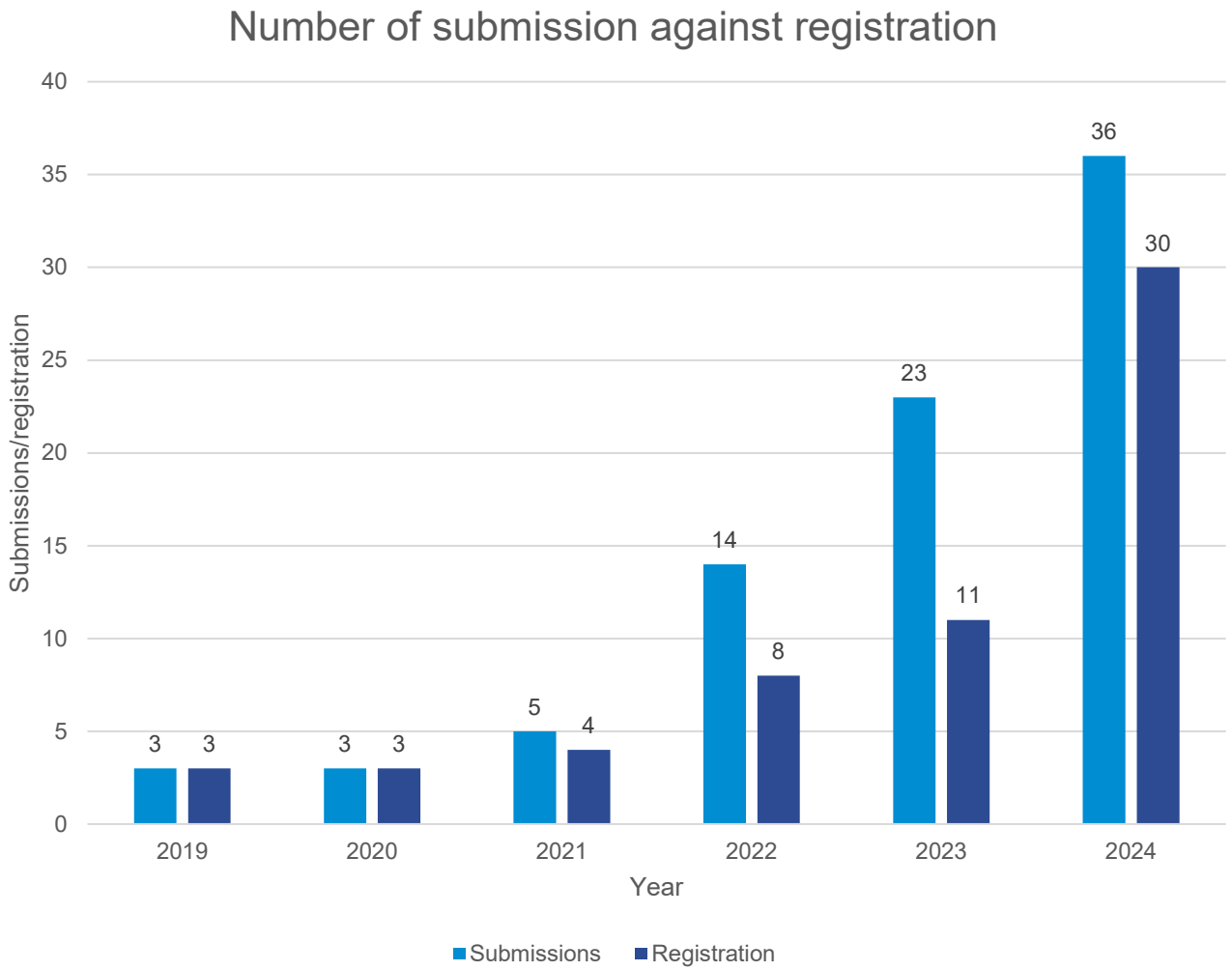


	HIV (RDT,NAT,EIA ,CD4)	HIV/Syphilis RDT	HCV NAT,RDT, EIA	HPV viological technology	Malaria RDT	HBsAg	Syphilis RDT
PQ	64	3	16	5	23	4	2
CRP	26	2	6	1	18	3	

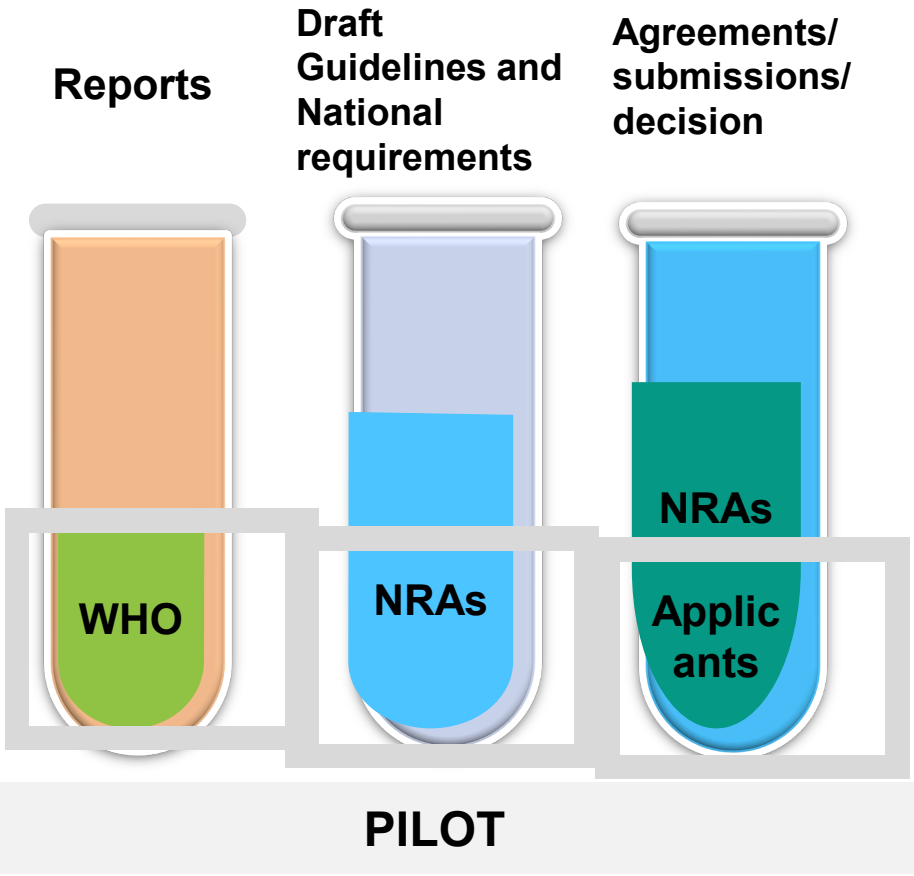
- ✓ Only 26% of the total number of WHO –listed assays are registered under CRP.
- ✓ HIV assays have high percentage among WHO listed – assays.
- ✓ There is improvement in the types of assays registered including HBsAg HCV and HPV.
- ✓ No application for Syphilis RDT.

WHO CRP IVDs progress and achievements : Number of Product submissions and registrations per year

- ✓ More than 90% of submissions resulted in successful registrations over years.
- ✓ Almost 50% of submission in 2023 resulted in registration.
- ✓ Significant increase in number of submissions and registrations in 2024
- ✓ Median registration time : 52 working days



CRP VCP Pilot project January to December



Objective

- Use the WHO –prequalification assessment outcome obtained for a long-acting insecticide-treated mosquito net as a basis for country registration
- Assess feasibility of new WHO collaborative Procedure for VCP including impact on registration timelines and requirements for additional country specific requirements.

Countries

Democratic Republic of Congo, Ghana, Kenya, Nigeria, Rwanda and Tanzania.

Products

Two Insecticide-treated nets (ITN)

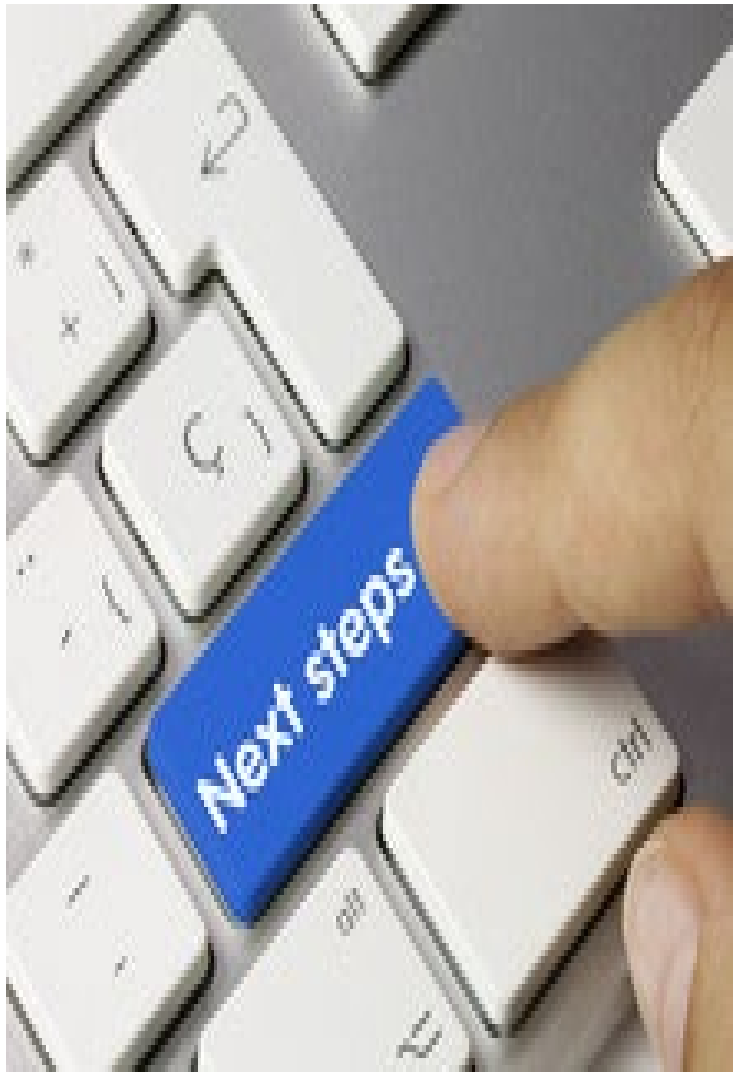
Update

- *One country (Ghana) has registered the product within 90 days (28 working days).*
- *CRP for VCP has proved to be great innovative mechanism that can accelerate registration of VCPs and facilitate timely availability.*
- ***CRP VCP Guideline adopted by ECSPP in October 2024***
- *Pilot ongoing : 2nd product*

Activities and Strategies in 2024

- Consolidation : Pending applications
- Advocacy : Workshops, Annual meeting, Webinars
- Training and orientation: NRAs, RECs, manufacturers
- Expansion : Volume of applications, number of manufacturers, new SRAs, new NRAs, CRP VCP
- Automation : electornic prequalification information management system (ePQS)
- Collaboration : NRAs, SRAs, manufacturers, partners
- Optimization : Good CRP practices guideline : reviewed and updated
- Simplification and transparency : Internal Quality Management System, FPI Web page
- Response to Public Health Emergencies : EUL FP procedure for Mpox Vx and Dx

Plans for 2025



- Guidelines and guidance : dissemination, training, revision
- Post Approval Changes : to further define, collaborate, revise
- ePQS – the game changer
- Expansion and optimization : regions, NRAs, SRAs, product stream (SRA MD/IVD?), PQ CRP (Vx)
- Bridging the EOI/PQ Listing **gap?**
- Efficiency - % registrations, timelines
- Collaboration and engagement
- Country/Regional specific requirements

World Health Organization

Thank you !

valentinm@who.int
kisomas@who.int
prequalreg@who.int

SAHPRA
South African
Health Products
Regulatory Authority

WHO CR Procedure Update

05 December 2024

Update on our current status

SAHPRA joined WHO PQ CRP in 2016, and SRA approved CRP in 2019

Since joining, SAHPRA has registered 26 new medicine dossiers using the PQ(24) and SRA (2) CRP procedures.

What was required for SAHPRA to implement WHO CRP process?

- Change to legislation to allow for the implementation of reliance.
- Drafting of internal policy and processes for the use of reliance.
- Drafting of guidelines, assessors guides and templates.
- Training of assessors.

Accessing reports

The completed documents are sent to PQ requesting access to the shared reports.

Usually received timeously unless appendix 3B has not been completed by the API manufacturer.

We have not had any issues relating to downloading or access to the reports once received.

Benefits

Reports received directly from WHO – do not have to rely on the applicant for the reports.

Full scientific inspection reports and assessment reports are provided.

The reports assist in training of medicines evaluators and improvement of the standard of assessment.

Reliance is facilitated thereby decreasing time spent in review.

Challenges

- Local clinical epidemiology
- Inspection reports unavailability – full data for reliance
- Applicants requiring variations to be processed outside of the CRP approval
- Internal challenges is aligning with SAHPRA's current internal review pathway
- Applicants understanding that CRP reliance must be maintained through product lifecycle.
- Majority of Reliance authorities reports are easily obtainable. Some authorities e.g. USFDA reports are not easy to obtain.

Closing

Approximately 40% of applications have challenges, but progressively we have improved where there have been no challenges experienced this year.

- Internal process improvements
- Communication improvement with stakeholders

THANK YOU

Thailand's experience in WHO CRP participation

Ms. Worasuda Yoongthong
Director of Medicines Regulation
Thailand Food and Drug Administration

CRP Experiences - Thailand

Registration Status	Number of products			
	New Drugs	Generics	Biologics	Vaccines
Cohort 1: WHO PQ CRP (2017 - 2022)				
Submission	-	4	-	-
Approval	-	4**	-	-
Cohort 2: WHO PQ CRP + SRA CRP year 1 (2023)				
Submission	2	7	2	-
Approval	2**	7 (2* + 5**)	2**	-
Cohort 3: WHO PQ CRP + SRA CRP year 2 (2024)				
Submission	12	4	2	1
Approval	6*	4*	-	1*
Ongoing	6	-	2	-

*Approval time is within CRP working time

**Approval time is more than CRP working time

CRP Journey Towards Regulatory Efficiency and Public Health Benefits

Cohort 1: WHO PQ CRP (2017 – 2022)

- Unestablished Post-Approval Changes (PAC) process.
- Insufficient information from abbreviated assessment report.

Cohort 2: WHO PQ CRP + SRA CRP year 1 (2023)

- CRP is an efficient tool for clearing previous backlogs and streamline the review process.
- Industries need a year to create internal process for SRA CRP.
- Need to prepare internal process and understanding of reviewer team as well as mechanism to rely on the reference country.
- Need to understand and learn about the system requirement and guideline of WHO PQ and reference SRAs.

CRP Journey Towards Regulatory Efficiency and Public Health Benefits

Cohort 3:
WHO PQ CRP + SRA CRP year 2 (2024)

- Effective communication and collaboration among NRAs, industries, and WHO.
- The corrective action to timely access to the WHO Shared Platform.
- Expanding the scope of CRP to include **SRA CRP.**
- Build trust and understanding of WHO PQ and reference SRA's regulatory framework.
- The expectation of the comprehensive assessment report of Generics particularly for quality aspects.
- Leveraging QIS endorsed by SRA can facilitate a better understanding of quality part.
- Digital process can create transparency and efficiency for product licensing.




THANK YOU

Prequalification of VCPs and CRP

5 December 2024

Vector Control Product Assessment Team
World Health Organization

Types of products

- Includes the evolution of traditional VCPs and exciting new innovations for all categories of VCPs

- VCP categories
  - Chemical products (e.g., IRS, Space Sprays)
  - Biological products (e.g., Larvicides, Wolbachia infected mosquitoes)
  - Chemical + delivery device (e.g., ITNs, spatial repellents)
  - Biological + deliver device (e.g., larvicide in novel delivery system, auto-dissemenation mosquito traps)

WHOPAR - Structure

- New structure for the WHO public assessment reports
  - Part 1 - Letter of Prequalification
  - Part 2 - Executive summary
  - Part 3 - Quality Assessment (Module 3)
  - Part 4 - Safety Assessment (Module 4)
  - Part 5 - Efficacy Assessment (Module 5)

- All WHOPARS for all modules published simultaneously with prequalification decision

- Supporting data evaluation records and confidential assessments available for sharing under CRP

Regional rotation of ASVCP meetings

- Engage with regional offices to plan ASVCP meetings
  - 2024 – AFRO, AMRO/PAHO
  - 2025 – WPRO, EMRO
  - 2026 – SEARO, EURO
- Generate opportunities for engagement with regional/country offices and local authorities

Regional rotation of ASVCP meetings

- 2024.2 ASVCP in Brasilia – Engagement day
  - Eighteen participants - Representation from PAHO Washington DC, OPAS Brazil country office, ANVISA, Brazilian Ministry of Health
  - Outcomes:
    - Increased awareness of
    - PQT/VCP purpose, processes, and requirements
    - ANVISA supporting legislation, processes, and requirements
    - MoH VC programs, implementation strategies/challenges, pursuit to deploy novel strategies (e.g. modified mosquitoes) all within the social/environmental contexts and disease pressures/burden in Brazil
    - PAHO/OPAS role in procurement and support to MoH in supply of VCPs and QA mechanisms

THANK YOU