Stakeholders Workshop on Pilot of the Collaborative Registration Procedure (CRP) of Vector Control Products

Cotonou, Benin
28 -29 September 2023

Overview of the workshop objectives, agenda and approach

Marie Valentin
Team Lead
WHO
Objective of the meeting

Identify needs and challenges for facilitated product introductions of prequalified vector control products.
Specific objectives

To share experience and strategize on how to improve access to WHO-prequalified vector control products,

To discuss ways to facilitate registration of Vector Control products through reliance mechanisms;

To discuss and agree on criteria for participating in the pilot CRP for VCP (identify countries and products);

To agree on action points (short-term, midterm and long-term) towards implementation of the prospective CRP for VCP.
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<th>Session</th>
<th>Moderator/AFRO</th>
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<tr>
<td>08:30 – 09:00</td>
<td>Registration</td>
<td>All</td>
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<tr>
<td>09:00 – 09:20</td>
<td>Welcoming and opening remarks, Introductions</td>
<td>Angus Spiers, Director, IZI WHO AFRO or Marie Volirmot, WHO/REG/FP1</td>
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<tr>
<td>09:20 – 09:30</td>
<td>Overview of the workshop objectives, agenda and approach (10 minutes presentation)</td>
<td>Marie Volirmot, WHO/REG/FP1</td>
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<tr>
<td>09:30 – 10:00</td>
<td>Fighting vector-borne diseases by optimizing vector control tools</td>
<td>Angus Spiers, Director, IZI WHO AFRO</td>
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<td>10:00 – 10:30</td>
<td>Coffee break</td>
<td>All</td>
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<tr>
<td>10:30 – 11:15</td>
<td>Overview of Facilitated Product Introduction pathways (30 minutes presentation and 10 minutes of discussion)</td>
<td>Agnes Sithole, WHO/REG/FP1</td>
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<tr>
<td>11:15 – 12:00</td>
<td>Collaborative Registration Procedure: overview, mechanisms, tools, achievements (30 minutes presentation and 10 minutes of discussion)</td>
<td>Sunday Kyamw, WHO/REG/FP1</td>
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<tr>
<td>12:00 – 12:30</td>
<td>Reliance and collaborative approaches on in country registration of vector control products (20 minutes presentation and 10 minutes of discussion)</td>
<td>Angus Spiers, Director, IZI WHO AFRO</td>
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<tr>
<td>12:30 – 13:30</td>
<td>Lunch Break</td>
<td>All</td>
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<tr>
<td>13:30 – 14:30</td>
<td>Overview of WHO Prequalification and Vector Control Prequalification Stream: Product Assessment, Site Inspection, Prequalification output and life cycle maintenance (45 minutes presentation and 15 minutes of discussion)</td>
<td>Dominic Schuler, WHO/PQ/VCT</td>
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<td>14:30 – 15:00</td>
<td>Coffee break</td>
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<td>15:00 – 16:00</td>
<td>Panel Discussion: Country approaches and methods to vector-borne diseases control and status of VCP regulation. (60 minutes of Q&amp;A)</td>
<td>Panel discussion Moderator: Marie Volirmot, WHO/REG/FP1</td>
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<td>16:00</td>
<td>End of day one</td>
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### AGENDA - Day 2

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<tr>
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<tr>
<td>09:00 – 10:30</td>
<td>WHO Prequalification of vector control products: Manufacturer’s perspectives and envisaged support to CRP - VCP</td>
<td>Panel discussion Moderator: Dominic Schuler WHO/PQ/VCT Purpose: • Manufacturer of PQs, VCPs • Manufacturers of VCP under PQ • Vector Control Development Partner</td>
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(60 minutes presentations (20 minutes each) and 30 minutes of discussion)

| 10:30 – 11:00 | Coffee break | All |
| 11:00 – 13:00 | Collaborative registration procedure for WHO prequalified vector control products (CRP - VCP): Proposed pilot incl tools and sources of information to support CRP - VCP | Agnes Sika-Ako, WHO/REG/PPH Ana Rita Nogueira WHO/REG/PPH |

(60 minutes presentation) Reflections, Questions and Answers • reflections in line with existing registration framework • what could work • challenges foreseeable • solutions and what could be achieved • readiness for participating in the pilot; signing of CRP agreements for pilot phase (60 minutes discussion)

| 13:00 – 14:00 | Lunch break | All |
| 14:00 – 14:30 | Summary of discussions and next steps | Marie Valentinis, WHO/REG/PPH Ana Rita Nogueira WHO/REG/PPH |
| 14:30 – 15:00 | Coffee /discussion | All |
| 15:30 – 16:00 | Closing | Angus Spiers, Director, I2I |
| 16:00       | End of day two and adjourn | |

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[Logo of World Health Organization]
Thank you for your attention!

For more information, please contact:
Marie Valentin
valentinm@who.int
Overview of the Vector Control Landscape

Case for change in the adoption of new tools
To promote innovation, efficiency and quality in vector control product development by working together with all the stakeholders involved in developing and bringing new vector control tools to market, identifying shared obstacles & catalyzing solutions.

A product development environment conducive to innovation and investment which efficiently delivers a steady stream of new, quality vector control tools to those who need them most, then safeguards their continued effectiveness.
Vector-borne diseases are varied and disproportionately affect sub-Saharan Africa

**Risk**
80% of the world’s population is at risk of one or more vector-borne disease

**Mortality**
Over 700,000 deaths are caused by vector-borne diseases annually, 80% of which are in sub-Saharan Africa

Sources: WHO Global Health Observatory & Global Health Estimates; Global vector control response 2017–2030
Despite strong progress, vector-borne diseases & NTDs continue to impose a significant challenge on African development

Significant progress made against malaria pre-2016, but limited progress for other NTDs & stalling momentum...

Number of deaths in Sub-Saharan Africa

- Malaria
- Other vector-borne NTDs
- Non-vector-borne NTDs

...with continued, significant social & economic cost

Example impacts of disease prevalence

- Malaria continues to slow economic growth by 0.25-1.3% per year and strains public health systems, accounting for up to 40% of spending in high-transmission settings
- The daily economic burden for a dengue illness infection can be 0.7 – 5X an individual's average daily income
- 10% increase in malaria incidence correlates to 0.1 years of schooling missed and literacy reduction of 1-2 percentage points

Eliminating vector-borne and other Neglected Tropical Diseases is a global agenda

The WHO has developed an integrated strategy to reduce the burden of vector-borne diseases: **Global Vector Control Response 2017-2030**

- Effective locally adapted sustainable vector control
- Strengthen inter- & intra-sectoral action & collaboration
- Engage & mobilize communities
- Enhance vector surveillance & monitoring & evaluation of interventions
- Scale up & integrate tools & approaches
- Enabling factors:
  - Country leadership
  - Advocacy, resource mobilization & partner coordination
  - Regulatory, policy & normative support
- Enhance vector control capacity & capability
- Increase basic & applied research, & innovation

The African Union has also highlighted a focus on the prevention of malaria & Neglected Tropical Diseases (NTDs)

One of AU's key health objectives is the continent-wide elimination of malaria by 2030\(^1\)

The AU also created the Africa Center for Disease Control and Prevention in 2017; one strategic objective is to support health systems strengthening by addressing NTDs

Finally, AU launched the Zero Malaria Starts with Me campaign in 2018, with the goal of building country ownership, awareness and political commitment to malaria elimination

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\(^1\) Agenda 2063, Catalytic Framework to End AIDS, TB and Eliminate Malaria by 2030
Source: WHO Global vector control response 2017–2030 (GVCR)
Vector control products are key in the fight against vector-borne diseases through prevention of new cases

Sample vector control products and impacts on malaria

Insecticide treated bed nets (ITN)

Single most important contributor to decline of malaria cases between 2000 and 2015, responsible for 451 million averted cases

Half of people at risk in Africa are estimated to be sleeping under an ITN at a median cost as low as $2.20 per person per year

Indoor residual sprays (IRS)

Depending on location, malaria infections have been reduced from between 30% and 90% by deploying IRS products; between 2000 and 2015 IRS are responsible for 66 million averted cases

An estimated 3% of African population at risk is protected by IRS at a median cost of $6.70 per person per year

However, resistance to insecticides used in vector control products has been steadily increasing...leading to a risk for resurgence of disease.
Furthermore, existing VC products are insufficient to eliminate the deadliest vector-borne disease: Malaria

Despite high coverage of control interventions, residual malaria transmission can still be prominent...

Infection rates in The Gambia despite mass distribution of LLINs and annual IRS spraying with DDT

... meaning further tools are required to achieve elimination

Reasons for residual transmission
- Avoidance of treated indoor surfaces
- Feeding on unprotected humans outdoors

Some strategies for tackling residual transmission
- Provide indoor protection to individuals who are not sleeping under nets
- Provide outdoor protection to humans
- Modify mosquito population genome to affect fertility / ability to transmit

Sources:
A new generation of products is being developed...

Examples of novel VC product groups

**Novel pesticides**
New chemical combinations to which vectors are not yet resistant

**Attractive targeted sugar baits**
A sugary and scented substance that attracts mosquitoes, ticks and other vectors and poisons them

**Passive Emanators**
Products that emanate repellent insecticides to deter mosquitoes

**Endectocides**
Drugs, such as Ivermectin, that have the potential to kill mosquitoes when taken preventatively in humans

...but **timely access** will be crucial to address these issues

Questions regulators are asking

**Which bodies/ministries** should assess novel products?

**Which standards** should be used for these novel products?

How do we deal with **cross-border impact** of these novel products?
IVCC Development Portfolio

IVCC Product Development Portfolio

Enabling Innovation
- Capacity Building
  - IP1 - MathNet (Testing capacity - PNG)
  - GLP certification (Testing capacity - EEA)
- Innovation Pool
  - New insecticidal compounds screening
  - Bioavailability optimisation
  - Automated surveillance
  - Mosquito attractants
  - Application technologies
- Biocatalysts for ATSP®

Creating Solutions
- Optimisation
  - MEA / xa ITN EEE
  - ITN X Company A
- Pre-development
  - ITN Y Company A
  - Sherlock ITN IVCC ICERIAL
  - TENERNAL® ITN Mixed Chemicals Agro TENERNAL® Incorporated
- Development
  - ATSS® Waterman Deltaplex
  - Sylander® UGJF Chlorfenapyr
  - VECTRON® T506 Mixed Chemicals Agro TENERNAL®
- Regulatory review
  - Res
  - Res

In Market Evaluation
- Market uptake
  - Actellic® 500CS
  - Samsill® 56WG (Forest pack - GM)
  - PI® BITE (Urban deployment - Malaysia)
- Integrated Vector Management
  - Modus® Fusion Bio
  - Deltamethrin
  - K-Otamin® Polyzonic Enviromental
  - Interceptor® 62 BIA
  - Alphacy® Chlorfenapyr
A new generation of products is being developed...

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- **Which bodies/ministries** should assess novel products?
- **Which standards** should be used for these novel products?
- How do we deal with **cross-border impact** of these novel products?
We have heard interest from all types of stakeholders to see increased collaboration for Vector Control regulation.

**Regulators**

*We don’t know what's on the cutting edge for vector control. We need standard guidelines and want to learn from more experienced regulators and authorities.*

*I see great benefits in terms of time and quality with a regional system, where certain activities like inspections and safety evaluations are done jointly.*

**Industry**

*We could get products to market much quicker if countries across the continent had standardized requirements and procedures for vector control.*

*We spend a lot of time while regulators review findings already approved by the WHO PQ process. We could speed up the process greatly if they could collaborate.*

**Procurers**

*We rely on WHO PQT-VC to indicate what to buy, and it would be fantastic if country regulators could leverage those assessments.*

*There is a great opportunity for regional and global stakeholders to help grow vector control expertise and streamlined processes at the country level.*
The WHO Prequalification process is a rigorous VC product evaluation system, offering a significant opportunity for regulators

WHO prequalification team (PQT) was set up to evaluate VC products...

- PQT-VC replaced WHOPES as the WHO evaluation process for VC products
- PQT-VC assesses product dossiers, inspects manufacturing sites and supports quality-control

The WHO PQT-VC publishes a list of (a) prequalified VC products and (b) manufacturing sites for public health pesticidal active ingredients

... that could help increase both speed and quality of decision-making at country level

- Can lower burden on regulatory authorities through information and analysis sharing
- Can enable capacity building through exchanges between vector control experts
- Can work with stakeholders to set standards for a new generation of vector control products
Partnerships in other areas have already demonstrated high impact and addressed similar challenges

**WHO Collaborative Registration Procedure (CRP)**

Allows regulators to leverage WHO assessments, and has reduced median registration time for in-scope medicines from >1 year to <3 months for 25 African member states.

**Comité permanent inter-État de lutte contre la sécheresse au Sahel\(^1\) (CILSS/COAHP)**

Enables manufacturers to register pesticide products in 12 member states through a single, 2-3 month joint review process.

**EAC Medicines Regulatory Harmonization (MRH)**

Builds regulator capacity and reduces assessment duplication via joint review process, with a reduced lead time from application to decision from 2-4 years to 225 days.
This is a **critical moment** in the fight against vector-borne diseases

We need to **engage now** to seize this opportunity and access new, effective tools
Thank you
Stakeholders Workshop on Pilot of the Collaborative Registration Procedure (CRP) of Vector Control Products
Region/Countries: WHO AFRO region
Venue: Azalai Hotel, Cotonou, Benin
Dates: 28-29 September 2023

Introduction to Facilitated Registration Pathways and Collaborative Registration Procedure (CRP)

Agnes Sitta Kijo
Technical Officer, Facilitated Product Introduction Regulation and Prequalification Department
WHO
Facilitated Regulatory Pathways (FRP) as a solution to NRAs

When timely access to quality-assured products is compromised...

FRPs, as a solution for NRAs and public health

What are Facilitated Regulatory Pathways (FRPs)?

NRAs carry great responsibilities in ensuring timely access to quality assured products to their population

Internal factors: low maturity of many regulatory systems, lack of resources and expertise in-house, and lack of collaboration between countries

External factors: increasing complexity of supply chains and global challenges, such as health emergencies

➢ Overwhelm NRAs - lengthy regulatory approvals of much needed medical products
➢ Patients’ timely access to much-needed quality-assured medicines is compromised

FRP are a type of regulatory pathways available to NRAs, which are meant to facilitate and accelerate the regulatory decisions and the introduction of quality-assured products in countries, through the use of the concepts of reliance and collaboration. When well implemented:

- NRAs leverage on the work performed by others, improving efficiency of the regulatory systems by avoiding duplication of regulatory efforts and work
- NRAs optimize the use of human and financial resources and increase expertise and build capacities
- NRAs reduce the time needed to process a product application and reduce workload and backlog at NRAs
- NRAs perform science-based and transparent regulatory decision-making, while maintaining national independence on their decisions
- NRAs ensure timely access to priority quality-assured products in countries.
What are the FRPs available?
What is their relation with CRP?

Selection of FRP for a product based on the risk-based approach of each NRA

Level of effort, work, resources, expertise, time and duplication

Facilitated Regulatory Pathways

E.g. Product approval based on "SRA" or WHO PQ – CRP and EU mutual recognition

E.g. Secondary and abridged reviews of existing primary reports generated from “SRA” or WHO PQ – CRP and EU mutual recognition

E.g. Assessment conducted jointly by 2 or more NRAs (full review or with reliance) - EU centralised procedure, ASEAN JA or EAC JA

E.g. when it is agreed between 2 or more NRAs that only 1 NRA assesses (full review or with reliance) and the remaining ones grant MA based on that assessment. - EU decentralized procedure, ZAZIBONA

Assessment of full product dossier conducted by the NRA

Joint Assessment

Full/Accelerated assessment

New Assessment

Level of collaboration, reliance and efficiency

Recognition

Reliance

Work-sharing

Recognition
Regulatory Risk-based approach to implement pathways:
Key considerations for Good Regulatory decision-making processes for quality-assured products

1. Product type and complexity
   - Level of resources and expertise available
   - Maturity of Regulatory system
   - Public health needs and priorities
   - Possibility to use reliance or not, based on legal framework

2. Source of Product information
   - WHO Prequalified
   - Approved by reference NRA (or SRA/WLA)
   - Approved by non-reference NRA (or non-SRA/WLA)
   - Unlicensed

3. Other Factors
   - Full review
   - Joint Reviews
   - Work-sharing
   - Reliance
   - Recognition

Appropriate regulatory pathway to be used

Each NRA should define its own strategy for an appropriate risk-based approach for MA

define/select facilitated pathways available at the NRA based on its context

The availability of FRPs, their appropriate use (i.e. adequate selection and implementation)

Good Regulatory Decision Making at NRA
But how can NRAs apply FRPs in a confident manner?

1. Support to countries for the implementation of FRPs, as part of implementation of CRP and other Reliance approaches

   - Individual countries, through CRP and RJA
   - Regional systems, through CRP and RJA

2. WHO Mechanisms for collaboration/reliance between countries:

   Collaborative Registration Procedure (CRP)
   1. WHO Prequalified products
   2. SRA assessed and/or approved products
   3. Pilot on CRP-lite with FDA on HIV products

   Programmes aimed to facilitate and accelerate product registration and introduction in countries for specific public health needs and emergencies, e.g. COVAX (COVID-19 vaccines)

3. WHO supported activities for collaboration and Work-sharing:

   Technical support to Regional Joint Assessments and work-sharing arrangements among cooperating countries (ASEAN JA, African Regional JAs, CRS)
   - EU-M4All Procedure & Swissmedic MAGHP program, which aim to facilitate product introduction in countries based on reliance, following EMA opinion or Swissmedic approval
   - Reliance projects or programmes, such as Reliance for Post-Approval changes


Aligned with WHO GRP and WHO GRelP
Example of FRP- 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/PQ.

**WHAT it is and HOW does it work?**

- **Applicant**: Single product dossier + Prod. Assessment Reports from SRA/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
Implementation of FRP in countries

5 fundamental questions NRAs need to answer to properly implement FRPs, incl. CRP:

1. Do the national regulations of your country allow your NRA to apply reliance approaches towards MA activities? On the contrary, do they impede the use of reliance in your NRA for MA? If yes, is there an opportunity for your NRA to incorporate reliance provisions as part of upcoming revisions of the NRA legal framework?

2. Are there guidelines, policies or regulations at the NRA that define the reference authorities or institutions in which your NRA can rely upon?

3. Are there Guidelines to guide stakeholders on the existing facilitated pathways at the NRA, respective Admin and technical requirements (for initial approval and PAC)?

4. Are there internal procedures/SOPs to guide the NRA staff on the process of facilitated pathways applications, respective procedures to be followed and requirements to be met (for initial approval and PAC)?

5. Did the relevant NRA staff received adequate training on the procedures above to process FRPs, including technical trainings?
WHO support

1. WHO individual meetings/trainings: Applicants-WHO

2. WHO Advocacy meetings/Workshops on CRP to applicants

3. Annual Meeting on CRP – open sessions to applicants

4. Regular interactions with applicants through different channels to support the applications

5. The first 1-3 products/submissions, WHO to follow-up closer with applicants and NRAs to provide support.
- It is overwhelming for NRAs at all maturity levels to fulfil all regulatory work alone and independently from other regulators;

- **There are several tools nowadays available to NRAs and Industry to facilitate the regulatory decisions**, ensuring timely access to quality-assured products in countries and good regulatory-decision making. FRPs and mechanisms such as CRP and Joint assessments, are some of those tools available, using the concept of collaboration, reliance and work-sharing between NRAs, which is the future of medical products regulation.

- Applying those concepts, **NRAs and industry are able to make the best with their available resources and time**, reducing duplication of efforts and workload.
Questions and Answers

Agnes S. Kijo
Email: kijoa@who.int
Overview of Collaborative Registration Procedure

Sunday Kisoma,
Consultant, Facilitated Product Introduction,
WHO – MHP/RPQ/REG/FPI
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

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: US FDA tentative approval, EU M4-all (Article 58), Swissmedic Marketing Application for Global Health Products.
- Applies to any therapeutic area
CRP Process (PQ CRP or SRA CRP)

1. Source of Information to rely upon:
   - WHO PQ
   - Reference Authorities (SRAs)

2. Documentation to be shared:
   - a) Full Product Dossier (ICH CTD format)
   - b) Detailed Assessment reports (scientific evaluations, Inspections/audit reports, performance evaluation)
   - c) QIS validated by SRA or WHO

3. Actions for different stakeholders
   - Applicant and WHO
   - 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)
   - Lifecycle management

Reference: Authorities (SRAs)
Fundamental requirement: Sameness of product

1. Same product dossier;
2. Same qualitative and quantitative formulation,
3. Same manufacturing site(s) for drug substance and drug product,
4. Same manufacturing chain, processes, control of materials and finished product, and in the case of vaccines also by the same batch release scheme;
5. Same excipients, active ingredient and finished product specifications;
6. the same essential elements of product information for pharmaceutical products, in the case of vaccines by the same product information, packaging presentation and labelling.
7. Same provisions as for SRACP medicines, vaccines, and therapeutics
8. Add: Specific national requirements
   - application fees
   - product samples ..sometimes API samples
   - quality information summaries
   - site inspections
NRAs

- Providing a **convenient tool and procedure for NRAs wishing to apply reliance**, allowing them to **leverage the work performed by other authorities**, and **making their registration system more efficient and responsive** to the country population needs

- Having access to **data well organized in line with international and stringent requirements** - Availability of detailed SRA/WHO assessment and inspection outcomes

- **Opportunity for well-informed and quality decision-making** at NRAs, **saving efforts, resources** (human and financial) and **time**, maintaining their national independency

- **Capacity Building component** – NRAs can learn from SRA/WHO assessment reports

- **Introduction of quality-assured products** in the country in a **faster** manner.

**CRP win-win outcomes for all concerned stakeholders**
CRP win-win outcomes for all concerned stakeholders

• Providing a procedure to facilitate and accelerate national registration processes, with appealing registration timelines;

• Only one single dossier for multiple countries - harmonized data for national applications and registrations;

• Reduced burden of duplicated national GMP inspection to manufacturers and laboratory testing prior to registration;

• Enhanced and facilitated collaboration, interactions and information exchange with the NRAs, WHO and SRAs;

• Savings on time and resources;

• Allows more efficient post-registration maintenance.
WHO PQ Process

INPUTS
- Expression of Interest
- Dossier
- WHO Guidelines
- Assessors
- Inspectors
- Testing

PROCESS
- Assessment of Dossier
- Inspections (API, FPP, CRO)

OUTPUTS
- List of Prequalified products
- Assessment/Inspection/Lab Reports
- WHO Public Reports
Medicines/finished pharmaceutical products

This list contains finished pharmaceutical products used to treat HIV/AIDS, tuberculosis, malaria and other diseases, and for reproductive health, that have been assessed by WHO and found to be acceptable, in principle, for procurement by UN agencies.

Active pharmaceutical ingredients

This list contains sources of active pharmaceutical ingredients (APIs) that have been assessed by WHO and found to be acceptable, in principle, for use in finished pharmaceutical products procured by United Nations agencies.

Most of the APIs listed are those for which — at the time of assessment — submitted data and information submitted were evaluated and found by PQTM to meet WHO norms and standards and for which — at the time of inspection — the manufacturing site(s) were found to comply with WHO Good Manufacturing Practices. A small number of APIs have been listed on the basis of assessment and inspection carried out by stringent regulatory authorities who are willing to share information with WHO.

Disclaimer: Inclusion in the list of prequalified APIs does not constitute a WHO endorsement or warranty of fitness of purpose of the API for use in a particular finished pharmaceutical product (FPP), or of the safety or efficacy of the resultant FPP for treatment or health care. It remains the ultimate responsibility of the FPP manufacturer to ensure that the API, as accepted in principle, is suitable for the manufacture of the specific FPP.

Medicines quality control laboratories

https://extranet.who.int/pqweb/medicines
PQ CRP for medicines, vaccines & IVD.: 59 Participating NRAs, plus 1 Regional Economic Community

As of Aug 2023

*CARICOM Member States: Antigua and Barbuda, Bahamas, Belize, Dominica, Grenada, Haiti, Jamaica, Montserrat, Saint Lucia, St. Kitts and Nevis, St Vincent and the Grenadines, Suriname and Trinidad and Tobago

*CARICOM Associate Member States: Anguilla, Bermuda, British Virgin Islands, Cayman Islands and Turks and Caicos Islands

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

https://extranet.who.int/pqweb/medicines/collaborative-registration-faster-registration
PQ CRP: Country submissions and registrations of medicines

- Median = 69 days
- 903 registrations
- More than 1500 product submissions (321 medicines)
- 63 countries plus CARICOM

WHO

NRA

manufacturer
Prequalified In Vitro Diagnostics

The List of WHO-prequalified In Vitro Diagnostic products contains diagnostics used to diagnose a number of conditions and diseases, and that have been assessed by WHO and found to be acceptable, in principle, for procurement by UN agencies.

- List of prequalified in vitro diagnostic products (pdf version)
- List of prequalified in vitro diagnostic products (xls version)

General information – WHO List of Prequalified In Vitro Diagnostic Products

The WHO List of Prequalified In Vitro Diagnostic Products is updated regularly, generally with the inclusion of newly-prequalified products.

Diagnostic products are added to the list (following the voluntary participation of relevant applicants) as and when the data on such products has been assessed and evaluated, and relevant sites inspected by WHO, and considered (the time of the assessment, evaluation and inspection) to meet WHO prequalification requirements, as described elsewhere on this web site. WHO cannot represent that the listed products and manufacturing sites will continue to meet the aforesaid standards. WHO may suspend or remove products from the list based on information that may subsequently become available to it.

https://extranet.who.int/pqweb/vitro-diagnostics/vitro-diagnostics-lists
Particularities of the CRP for IVDs

- **Type of reports shared with NRAs**
  - Three reports: Dossier assessment report, Site audit assessment report and performance evaluation report

- **Verification of sameness of the WHO-prequalified product vs submitted dossier**
  - the same product name
  - the same regulatory version
  - the same product code(s)
  - the same site of manufacture and quality management system;
  - the same data on quality, safety and performance;
  - the same design, with the same components from the same suppliers;
  - the same information, labelling and packaging, including instructions for use and intended use.
List of SRAs as per current WHO Guidelines

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

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<tr>
<th>Country</th>
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<td>Australia</td>
<td>Germany</td>
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<td>France</td>
<td>Malta</td>
<td>Norway</td>
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</tbody>
</table>
SRA CRP : 7 participating SRAs

1. European Medicines Agency (EMA)
2. UK Medicines and Healthcare products Regulatory Agency (MHRA)
3. Dutch MEB
4. Swiss Agency for Therapeutic Products, (Swissmedic)
5. Therapeutic Goods Administration Australia (TGA)
6. Finish Medicines Agency (FIMEA)
7. Medical Products Agency of Sweden (MPA) (upcoming submissions)

As of 1 December 2022:
SRA CRP: Submissions and Countries Registrations

- **Median = 120 days** (regulatory time + applicant time)

- **230 product submissions** (approximately 80 from 2018 to July 2021)

- **115 registrations** (approximately 50 from 2018 to July 2021)

- **50 medical products** (16 products from 2018 to July 2021)

- **47 countries + CARICOM** (24 from 2018 to July 2021)
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

Annex 11

Good regulatory practices in the regulation of medical products

Background
A fundamental role of government is to protect and promote the health and safety of the public, including by delivering health care. A well-functioning health care system requires available, affordable medical products that are safe, effective and of assured quality. As medical products are essential in the prevention, diagnosis and treatment of disease, the consequences of substandard and falsified medical products can be life threatening. This is a concern, as users of medical products
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 E.g. VIA, a wh. ref. to national regulatory authority (NRA) in the a.v. sm. in. and acc. rated national registration, acceptance by NRA and notification of Procedure outcomes
Appendix 4 Report on post-registration actions in respect of a product registered under the Procedure

https://extranet.who.int/pqweb/medicines/collaborative-registration-faster-registration
Annex 4

Collaborative procedure between the World Health Organization and national regulatory authorities in the assessment and accelerated national registration of WHO-prequalified in vitro diagnostics

1. Introduction
2. Purpose and scope of the Procedure
3. Terminology
4. Principles and general considerations
   4.1 Participating parties
   4.2 Parameters of the WHO prequalified and nationally registered IVD
   4.3 Submission format and content of product dossiers for NRAs
   4.4 Information shared under the Procedure
   4.5 Applicable national registration fees
   4.6 Participating authority commitments
   4.7 Regulatory decision(s) on a WHO-prequalified IVD
   4.8 Manufacturer commitments
5. Steps in the Procedure for market authorization of a WHO-prequalified IVD
6. Collaboration mechanisms for post-prequalification and/or post-registration changes
7. Withdrawals, suspensions or delisting of WHO-prequalified IVDs and national deregistration
8. References

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

https://www.who.int/publications/i/item/9789240024373
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
Annex 6

Good practices of national regulatory authorities in implementing the collaborative registration procedures for medical products

1. Background
2. Alims and objectives
3. Scope
4. Glossary
5. Key principles
6. Essential elements of a registration system (in the context of collaborative registration procedures)

References
Appendix 1 An example of information to applicants for registration via the WHO collaborative registration procedure
Appendix 2 Verification for product submitted under the WHO collaborative procedure
Appendix 3 Abridged abbreviated review for product submitted under the WHO collaborative procedure
Appendix 4 Additional information to be included in the screening checklist
Appendix 5 Example of a national regulatory authority reliance model approach; information, documentary evidence and assessment activity
Appendix 6 Model acknowledgement or approval letter for variations of products registered through the WHO collaborative procedure

http://apps.who.int/iris/bitstream/handle/10665/272452/9789241210195-eng.pdf?ua=1
Annex 9

Guidance on good practices for desk assessment of compliance with good manufacturing practices, good laboratory practices and good clinical practices for medical products regulatory decisions

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1. Introduction 273
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4. Glossary 277
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   5.3 Convergent standards of good practices 280
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   5.5 Management tools to support consistent and objective assessment 281
   5.6 Risk-based assessment of available information 281
   5.7 Mutual trust and confidence among inspectorates 282
   5.8 Quality assurance of the desk assessment process 282
   5.9 Communication of assessment outcomes 282

http://apps.who.int/iris/bitstream/handle/10665/272452/9789241210195-eng.pdf?ua=1
Questions and Answers

Sunday Kisoma
Thank you

Sunday Kisoma,
Consultant, Facilitated Product Introduction,
WHO – MHP/RPQ/REG/FPI
Regulatory Landscape for Vector Control Products
Project objectives

Build a comprehensive fact base around registering VC products in sub-Saharan Africa

Deepen the understanding of existing challenges through selected country reach out

Co-create opportunities to optimize access to VC tools through engagement with broader African stakeholders

Involved stakeholders
We have created an extensive fact-base using stakeholder interviews and in-depth country research

Over 130 stakeholders interviewed regarding registration across the continent...

- 24 African & global partners
- 9 RECs & pan-African leadership
- 37 Industry players & country reps
- 26 Regulatory authorities
- 36 National Malaria Control Programs, other relevant Ministries & research institutes

...and 13 countries selected for in-depth research, including field visits for 10

Selection criteria include:

- 2017 malaria burden
- Regional distribution (East, West, Central, Southern)
- Potential regional influence

Note: Interviews conducted between Dec 2018-July 2019
For each focus country, the fact-base includes:

- Summary of vector control tool registration
- Key authorities and legislation
- Overview of registration process
- Descriptions of process variations and exceptions
- Dossier overview
- Detail on enabling environment

Today, we're only sharing our general findings across the continent...

...but please visit our website to find the full materials!
Across the continent, significant variation in registration authority

Registration authority most commonly the Ministry of Health, but high degree of fragmentation across the continent

<table>
<thead>
<tr>
<th>Registration ministry</th>
<th>% of countries*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ministry of Health</td>
<td>48%</td>
</tr>
<tr>
<td>Ministry of Agriculture</td>
<td>23%</td>
</tr>
<tr>
<td>Ministry of Environment</td>
<td>6%</td>
</tr>
<tr>
<td>More than one</td>
<td>23%</td>
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</tbody>
</table>

* of the 48 African countries for which data on the registering authority was available

1. Most commonly, but not always, split authorities register different products (e.g. IRS under MoA/MoE and nets under MoH);
Note: FDA is classified as MoH. Source: 2017 ALMA; Interviews Dec 2018-July 2019; BCG analysis
Registration requirements also differ considerably

There is no universal set of dossier requirements specifically for vector control

The largest requirement that varies is the length of in-country field trials, which can have major ramifications for registration speed

---

2. Country regulators were not interviewed; understanding based on interviews with int’l orgs, manufacturers, etc. 3. e.g. WHO, US FDA, etc. 4. Documentation varies, but can include additional safety certificates, environmental dossiers, labels and others requiring a significant investment from the applicant. 5. Trials are required only for new AI. 6. Trials are technically required for new AI, but no historical instance of this occurring for VC products: unclear if enforced.

Source: 2017 ALMA; Interviews Dec 2018-July 2019; BCG analysis
In summary, African VC registration is a complex landscape.

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2. Country regulators were not interviewed; understanding based on interviews with int’l orgs, manufacturers, etc. e.g. WHO, US FDA, etc. 4. Documentation varies, but can include additional safety certificates, environmental dossiers, labels and others requiring a significant investment from the applicant.
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Note: FDA is classified as MoH. Source: 2017 ALMA; Interviews Dec 2018-July 2019; BCG analysis.
Due to the complex nature of VC, national regulators and industry are facing multiple challenges

1. Unclear/overlapping mandates between national authorities
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4. Delayed communication between authorities
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1. Unclear/overlapping mandates between national authorities

2. Lack of funds to ensure adequate evaluation or quality control

3. Requirements aren't tailored for Vector Control products

4. Delayed communication between authorities

5. Insufficient transparency on registration process/requirements
Selected quotes from stakeholder interviews

1. Unclear/overlapping mandates

"VC products are either chemicals managed by us or as medical products managed by the Ministry of Health, but we know the MoH has granted authorization for IRS, which are our jurisdiction"
~ Ministry of Agriculture regulator

2. Lack of funds for adequate evaluation

"We do a review and a chemical composition test, but don't have the appropriate capabilities to conduct efficacy trials or other lab tests"
~ Ministry of Health regulator

3. Requirements aren't tailored

"There is always a long back and forth with [country] because they require residue studies, which are simply irrelevant for a bed net"
~ Global manufacturer

4. Insufficient transparency

"If we knew exactly what to submit it wouldn’t be a problem – but registration for VC often involves lengthy discussions about which documents are required"
~ Global manufacturer

Source: Interviews Dec 2018-July 2019
We researched four on-going collaborative efforts for pesticide or medicines registration

<table>
<thead>
<tr>
<th>Member states</th>
<th>WHO Collaborative Registration Procedure</th>
<th>EAC Medicines Regulatory Harmonization</th>
<th>CILSS/CSP¹ &amp; resulting ECOWAS efforts</th>
<th>SEARCH² &amp; resulting EAC &amp; SADC efforts</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Product focus</strong></td>
<td>WHO Prequalified finished pharmaceutical products</td>
<td>Non-WHO Prequalified medicines</td>
<td>Pesticides, including VC products (regardless of WHO Prequalification)</td>
<td>Agricultural pesticides (regardless of WHO Prequalification)</td>
</tr>
<tr>
<td><strong>Scope of harmonization</strong></td>
<td>Guidelines, process and assessment</td>
<td>Guidelines, process, assessment and recommendation</td>
<td>Guidelines, process, assessment and recommendation</td>
<td>Guidelines</td>
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<tr>
<td><strong>Years active</strong></td>
<td>2012-Present</td>
<td>2012-Present</td>
<td>1992-Present</td>
<td>1996-Present</td>
</tr>
</tbody>
</table>

1. CILSS = Comité permanent inter-État de lutte contre la sécheresse au Sahel, CSP = Comité Sahélien des Pesticides 2. SEARCH = South East African Regulatory Committee on Harmonization; Source: WHO; AUDA-NEPAD; interviews; BCG Analysis
There are two common impacts across the efforts studied

**Helps regulators make quality registration decisions**

- **WHO CRP**: 5 of 6 NMRAs reported to the WHO that dossier quality was higher for PQ products, making it easier for them to assess. "We rely on WHO assessments, which allows us to focus our time on dossier sections we find most relevant for a particular application."

- **EAC MRH**: Drug companies reported that queries received from joint procedure were more stringent than for national registration.

**Increases speed of country registration**

- **WHO CRP**: Median registration for products in scope reduced from >1 year to <3 months

- **EAC MRH**: Application to decision lead time reduced from 2-4 years to ~225 days

- **CILSS/CSP**: Products registered in 9 member states with only one set of required efficacy trials and a single 1-2 month assessment.

There are several **key takeaways** for the impact of collaborative efforts in regulation

Bring a diverse set of stakeholders together when developing potential models
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- Bring a diverse set of stakeholders together when developing potential models.
- Respect country sovereignty in decision-making, and minimize the legislative changes required.
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- **Leverage existing expertise and capabilities** in African countries/international bodies and provide **effective capacity building support**.
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- Bring a diverse set of stakeholders together when developing potential models.
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- Iteratively incorporate learnings throughout implementation.
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1. **Bring a diverse set of stakeholders together** when developing potential models.
2. **Respect country sovereignty** in decision-making, and minimize the legislative changes required.
3. **Leverage existing expertise and capabilities** in African countries/international bodies and provide effective capacity building support.
4. **Leverage existing forums with political buy-in** of relevant stakeholders as platforms for discussion.
5. **Iteratively incorporate learnings** throughout implementation.
6. **Plan for financial sustainability** from the start.
Thank you