



What Program Managers Need to Know about Product Registration

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AGENDA

- ❑ Expanding Effective Contraceptive Options (EECO)
- ❑ Registration Overview
- ❑ Pathways to Registration
- ❑ Real-World Examples
 - ❑ Progesterone Vaginal Ring - Nigeria
 - ❑ Levoplant WHO Prequalification
- ❑ After Registration...
- ❑ Learning about Expanded Access and Potential of the LNG-IUS (LEAP LNG-IUS) Initiative

Exploring Effective Contraceptive Options (EECO)



- USAID-funded
- Contraceptive product introduction in FP2020 countries
- EECO portfolio addresses method-related reasons for non-use



Exploring Effective Contraceptive Options (EECO)



STAGE 1

Regulatory Assessment & Product Registration

- Perform regulatory landscape assessment
- Engage stakeholders and meet with regulatory authorities
- Support identification of a suitable market authorization holder
- Prepare the registration package, submit and support its lifecycle upon approval



STAGE 2

Consumer & Market Research

- Plan and conduct market research
- Complete market segmentation analysis
- Determine pricing and branding strategies



STAGE 4

Marketing, Distribution & Service Delivery

- Launch product, with marketing and communications support
- Supply stock to commercial outlets and providers
- Deploy medical detailers to train and follow-up with providers



STAGE 3

Procurement & Quality Assurance

- Perform manufacturer audits
- Initiate pre-shipment inspection and testing of product
- Develop and initiate pharmacovigilance systems



STAGE 5

Monitoring & Learning

- Monitor and course-correct
- Conduct baseline and endline evaluations
- Disseminate lessons learned



Why does registration matter?



Regulatory authorities protect public health by ensuring the safety, efficacy, and quality of drugs, medical devices, and other regulated products.



Who regulates?

National Regulatory Authority (NRA)

- Responsible for reviewing and granting or rejecting registration applications in the countries where they have the legal authority to do so.
- ZAMRA, NAFDAC, DPM

Stringent Regulatory Authority (SRA)

- Provide expertise and resources for the proper evaluation of regulated products.
 - US FDA, Japan, Health Canada
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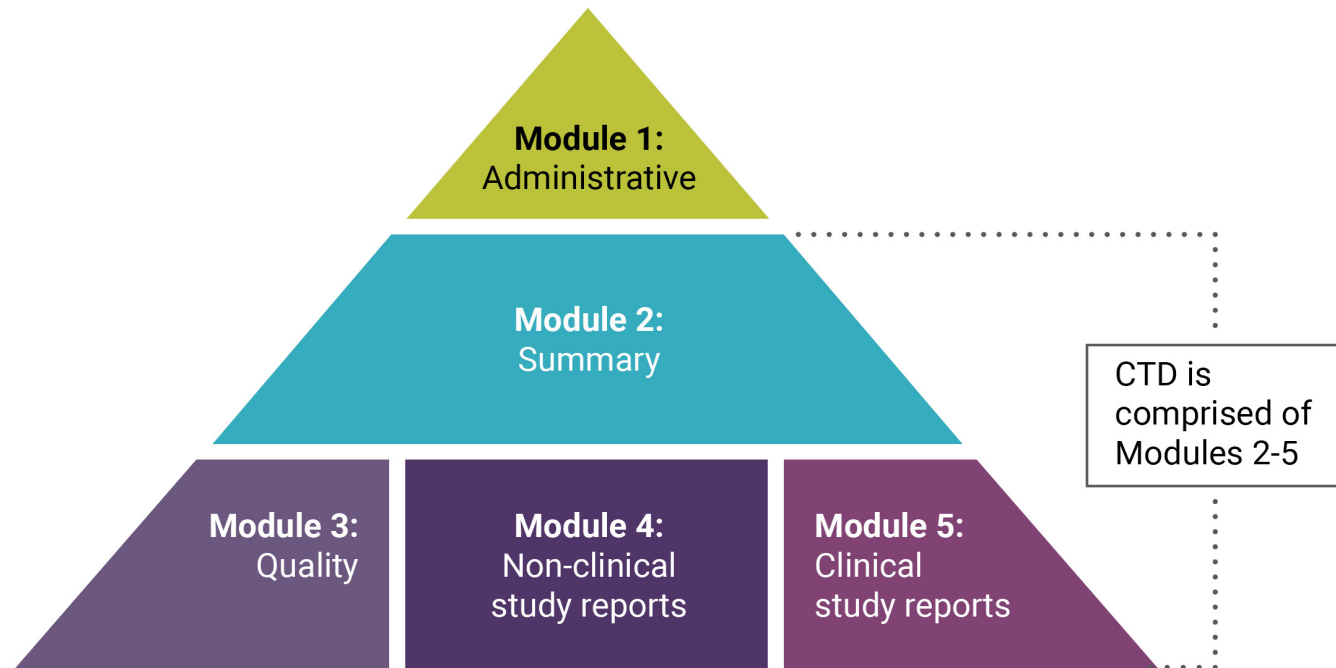


Role of the World Health Organization (WHO)



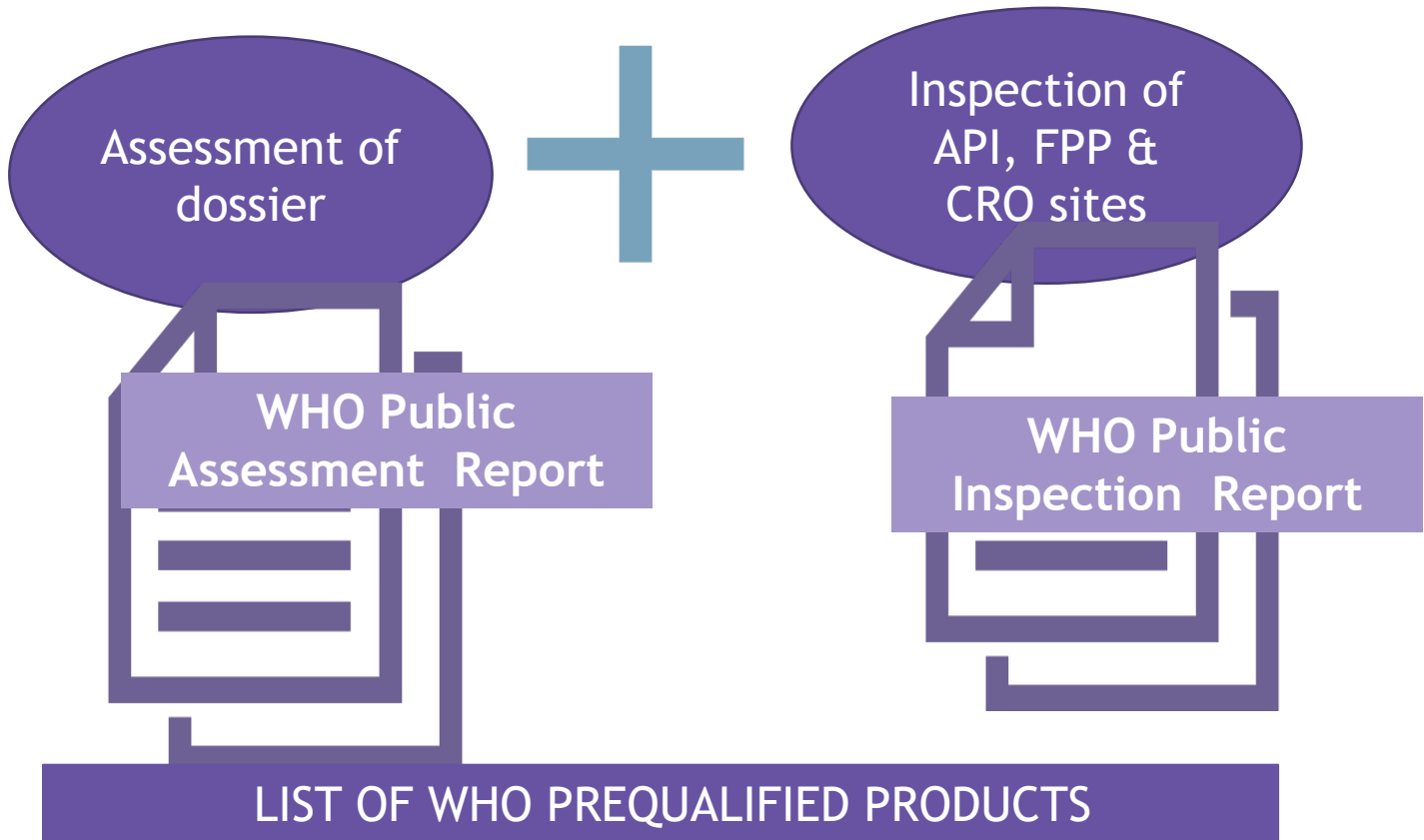
- Supports access to essential medicines
- Sets norms, standards, develops guidelines
- Advises on issues related to quality assurance
- Assists in building national regulatory capacity

Common Technical Document (CTD)



WHO Prequalification Programme

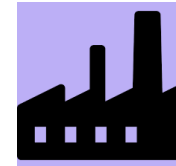
Expression of interest calls for interested manufacturers to submit dossier based on WHO Guidelines



WHO Collaborative Procedure - Full PQ



WHO shares assessments reports with NMRA

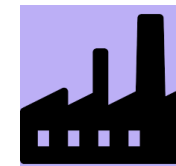


MAH submits dossiers and samples to NMRA) along with forms indicating that it wishes to follow the WHO CRP process



NMRA

NMRA commits to a review in 90 days

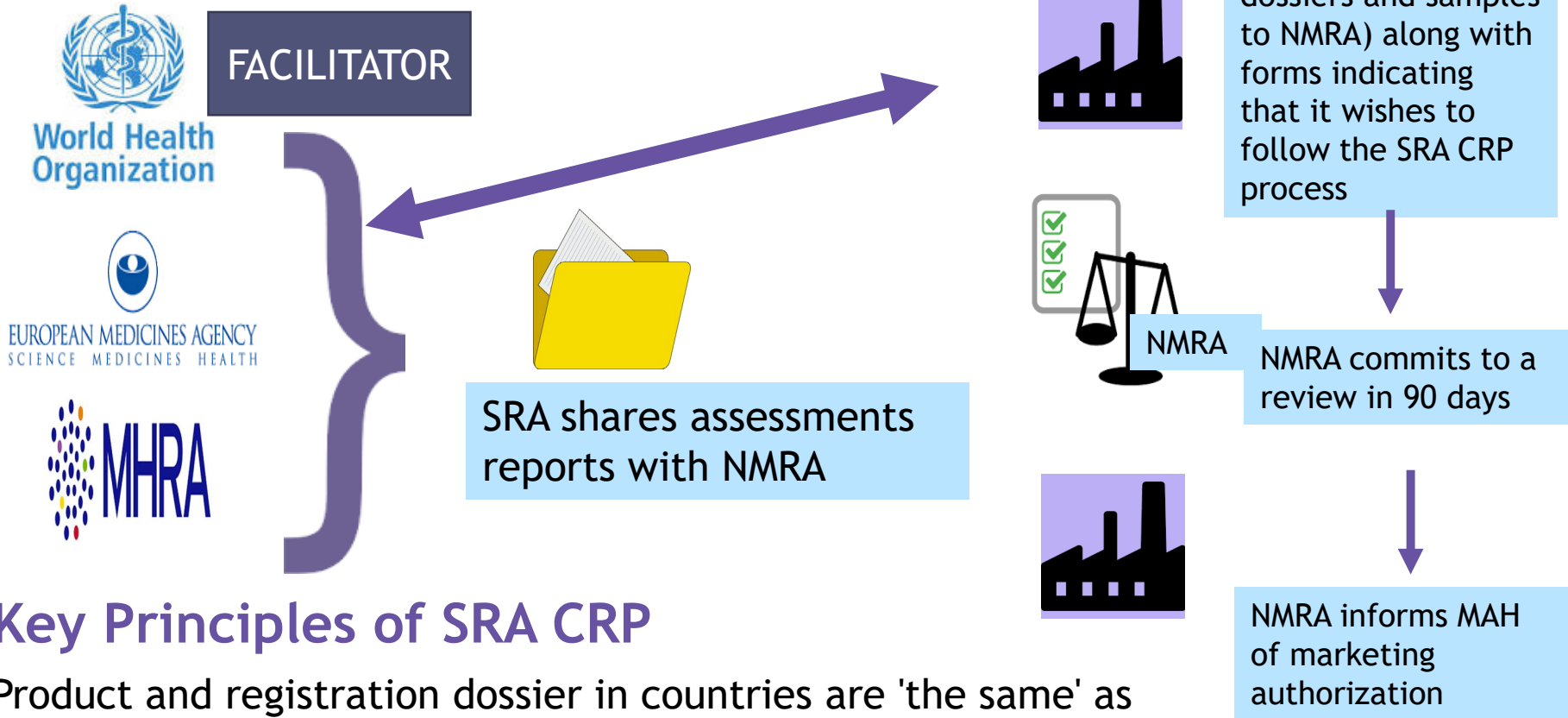


NMRA informs MAH of marketing authorization

Key Principles of WHO CRP

- Product and registration dossier in countries are 'the same' as approved by WHO.
- Shared confidential information to support NRA decision making in exchange for accelerated registration process
- Harmonized product status' is monitored and maintained

SRA Collaborative Procedure



Key Principles of SRA CRP

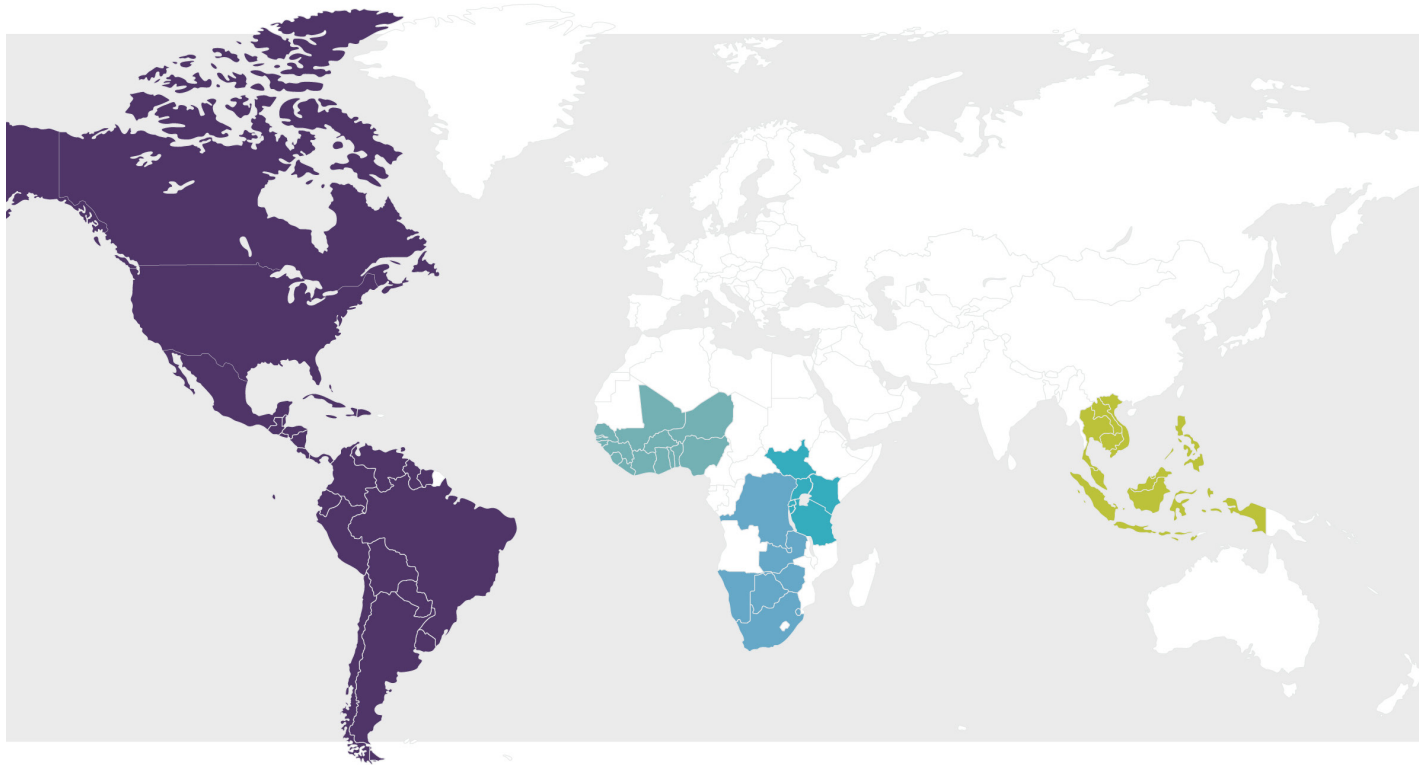
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Regional Harmonization Initiatives



 PANDRH

 ECOWAS/UEMOA

 ZAZIBONA

 EAC

 ASEAN

Country-by-Country Registrations



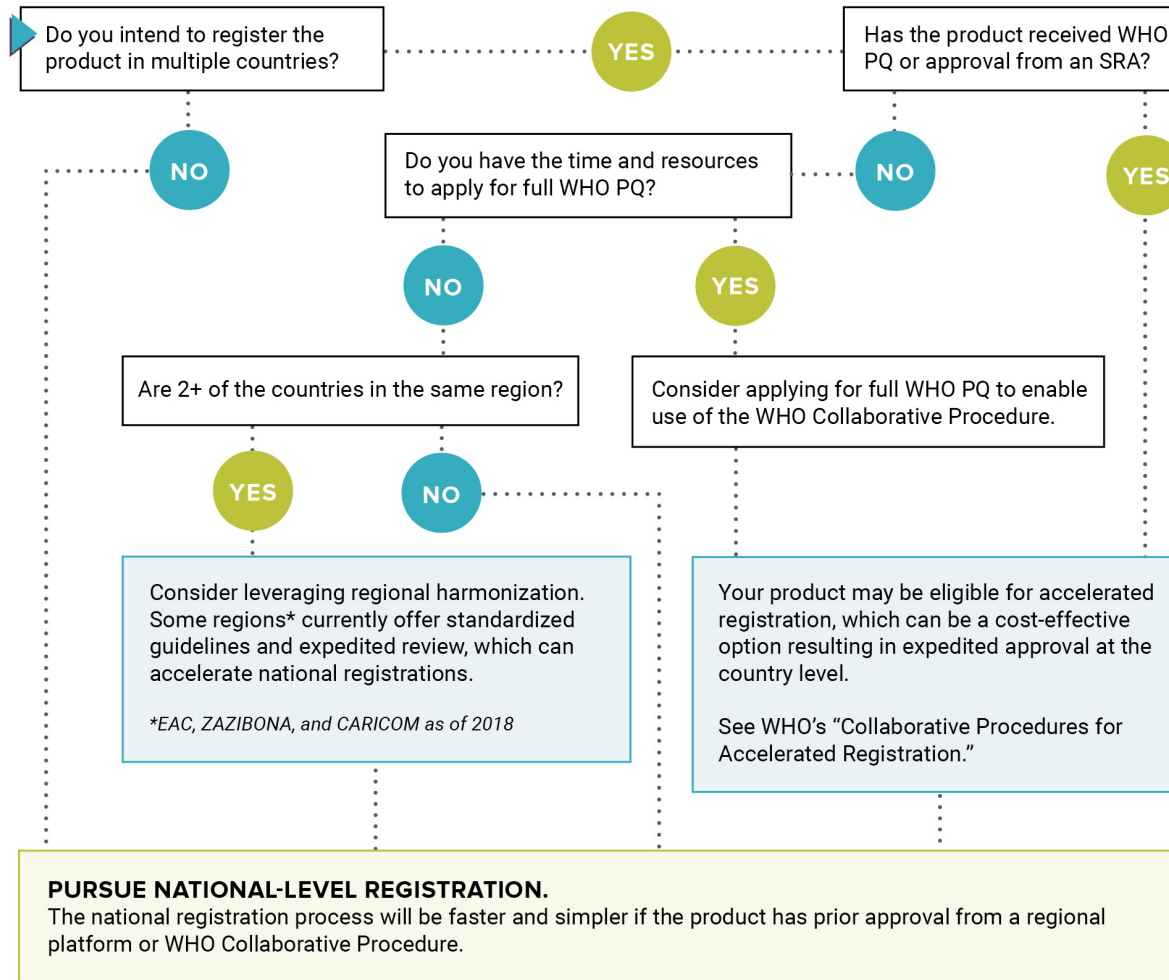


Special Import Permits

- Short-term use
 - Research
 - Emergencies
- Application guidelines, and willingness to approve special import permits, are country-specific



So, which pathway to choose?



QUIZ: Who can be a Marketing Authorization Holder?



- Local NGO
- Foreign Supplier
- Foreign Manufacturer



Real-World Example:

Registering the Progesterone Vaginal Ring in Nigeria



- A contraceptive developed by the Population Council for use by breastfeeding women for up to one year postpartum
- Manufactured by Grünenthal Chilena Ltda. as Progering®
- Registered in 10 countries in Latin America
- USAID-funded Delivering Contraceptive Vaginal Rings (DCVR) project

Photo Credit: Population Council



Real-World Example: PVR Registration in Nigeria

STEPS IN THE PVR REGULATORY PROCESS IN NIGERIA

1. Complete desktop and in-country Regulatory Landscape Assessment
2. Identify, evaluate and select MAH
3. Prepare and submit registration application to NAFDAC
4. Request from NAFDAC an import permit for samples
5. Send samples to NAFDAC for evaluation/analysis
6. Respond to queries, as necessary, during NAFDAC's review of the registration application
7. Receive Marketing Authorization from NAFDAC



Real-World Example:

Levoplant WHO Prequalification

Levoplant: DKT WomanCare's Core Business

- DKT WC is responsible for regulatory, marketing, distribution and sales
- Leveraging DKT country offices and DKT WomanCare distribution network (100+ countries)
- Regulatory footprint for Levoplant in 20 Countries (approved) - additional 17 pending





Levoplant Prequalification

- Under BMGF grant FHI 360 provided technical and operational support to Shanghai Dahua Pharmaceutical Co, Ltd. on all international regulatory matters until 15 November 2018 including WHO Prequalification of Levoplant and regulatory submission in over 28 countries
- DKT WomanCare who became exclusive distributor of Levoplant in February 2018 has continued to expand Levoplant regulatory footprint including leveraging WHO CRP



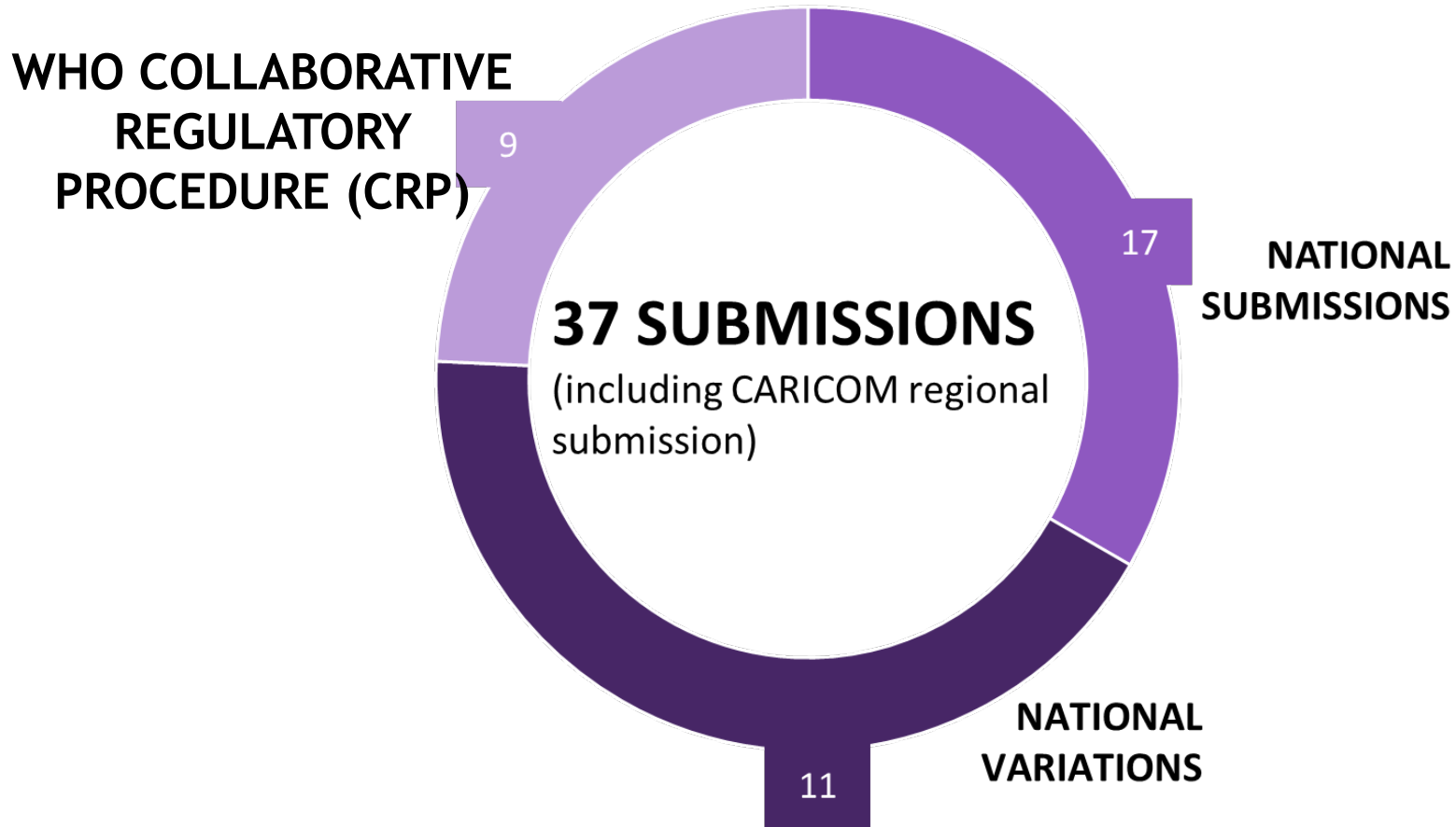
Levoplant (RH028) Regulatory strategy post WHO PQ



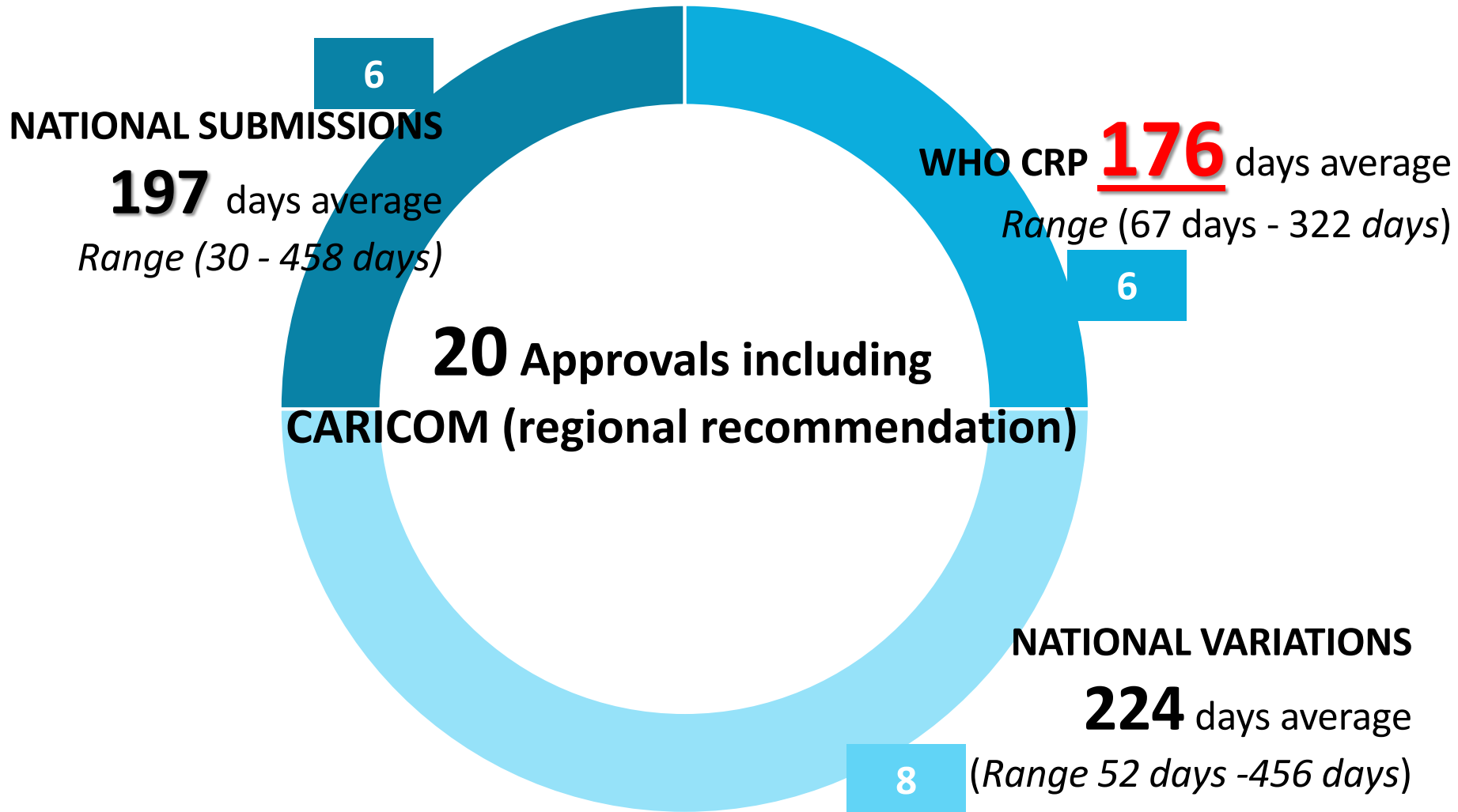
3 pathways for Levoplant submissions to NMRAs for marketing authorization

- National Variation where the earlier version of the product was already registered (new API manufacturer, brand name change, improvements, duration of use from 4 years to 3 years)
- National Submissions
- National Submissions through the WHO Collaborative Regulatory Procedure

Levoplant submission June 2017-March 2019



Levoplant Regulatory Approval June 2017 - March 2019



RHO28 (Levoplant) WHO CRP experience to date

- ❑ Excellent follow up and updates from WHO CRP Team.
- ❑ Easy to follow process with minimal paperwork
- ❑ Excellent experience with agencies that are committed to and familiar with process (Zimbabwe, Namibia, Tanzania, *CARICOM)
- ❑ Advantage of having a point person within NMRA
- ❑ Guidance from CARICOM and PAHO team on procurement options and engaging with local MOHs/Procurement agencies
- ❑ CARICOM approval is a gateway to a number of markets where there is limited information on national registrations.
- ❑ Acceptance of harmonized module 2 - 5 and less queries from NMRA
- ❑ Often quicker than national variations which sometimes ‘fall through the cracks’; and get parked or don’t have a dedicated review

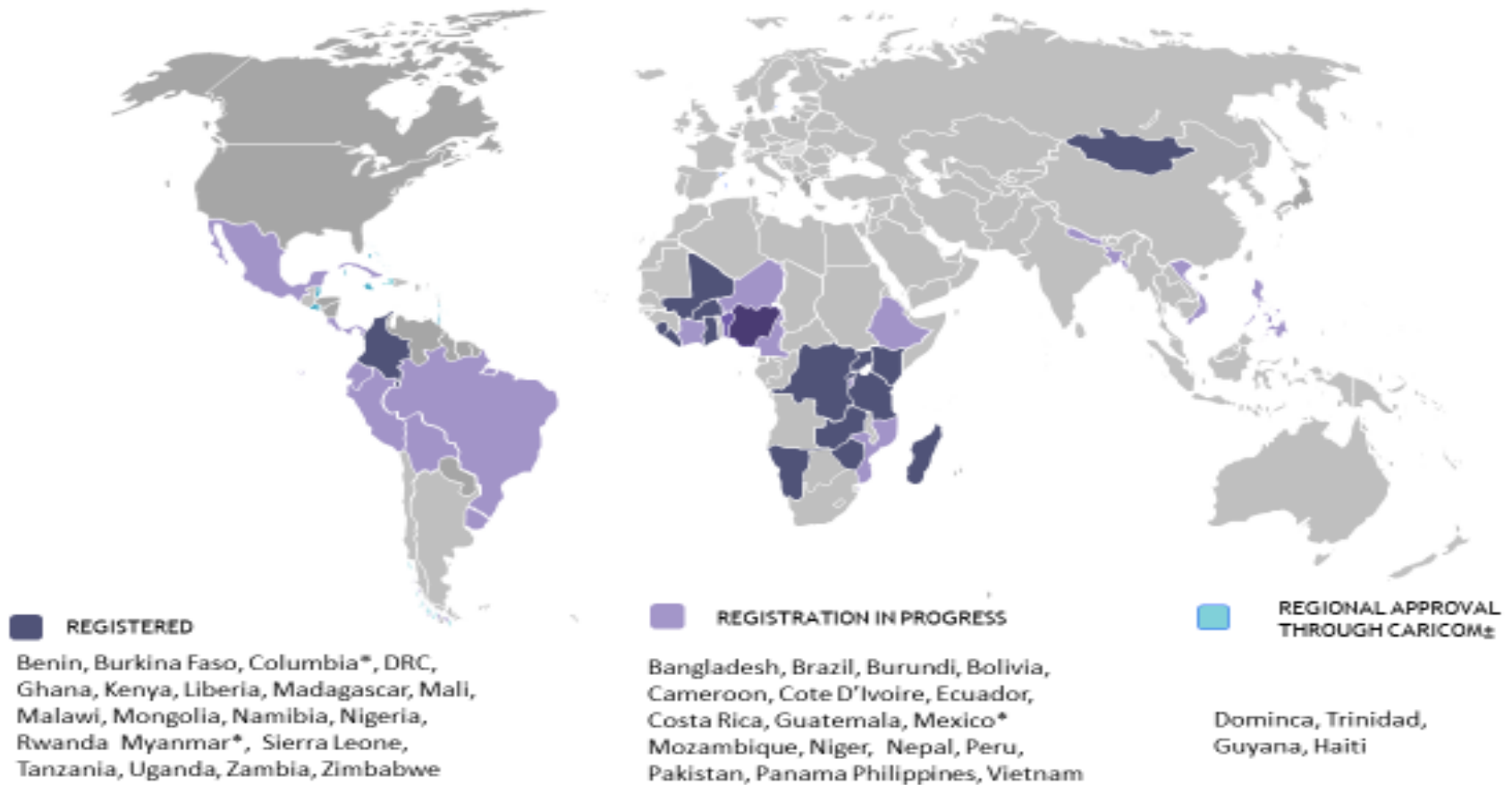


RHO28 (Levoplant) WHO CRP experience to date :

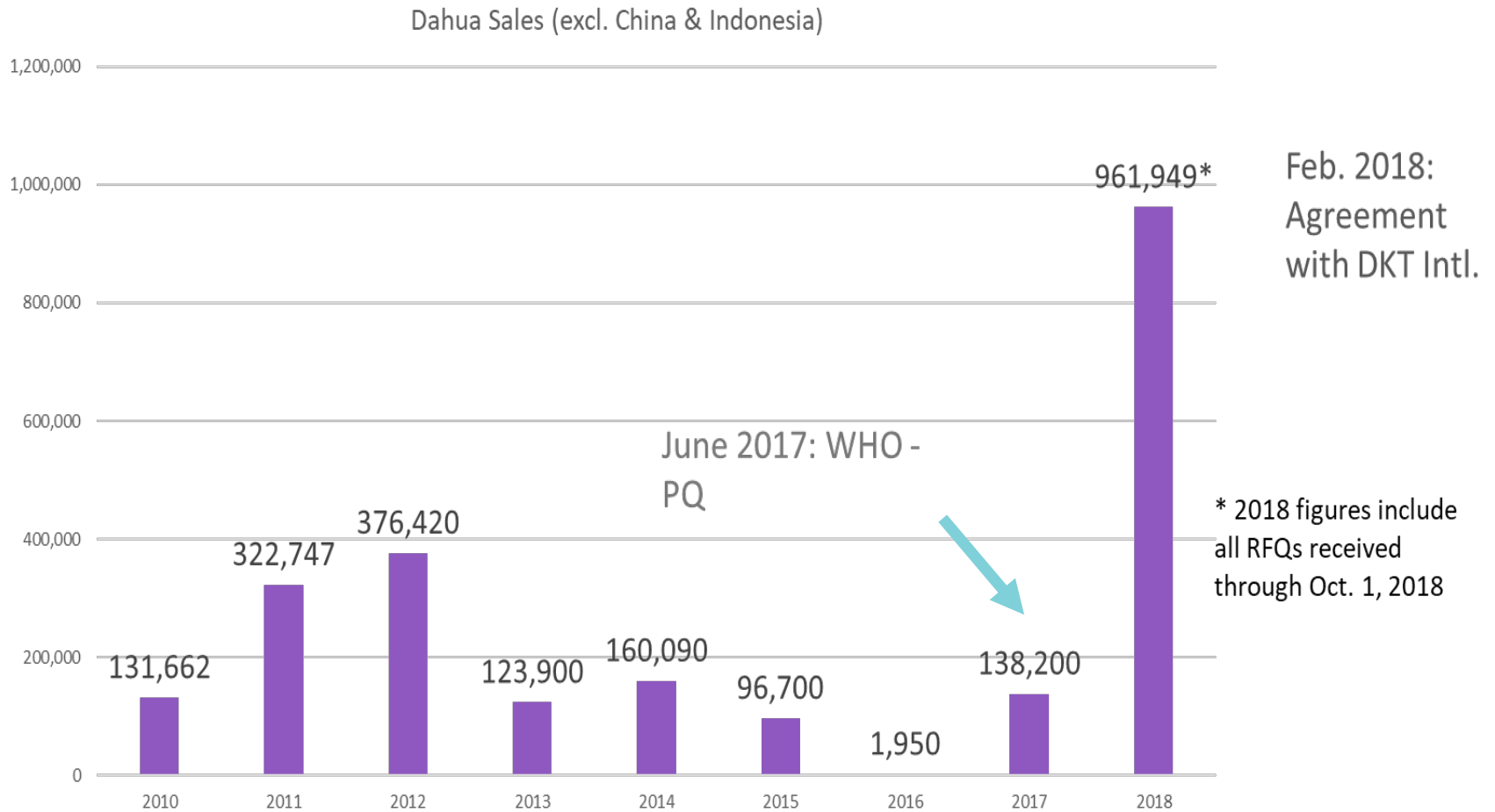
HOWEVER SOME CHALLENGES:

- Non responsive NMRA's or NMRA's not sufficiently engaged
- NMRA not accepting dossiers due to internal issues
- NMRA only applying WHO CRP to certain therapeutic areas (i.e. not Reproductive Health)
- NMRA WHO CRP liaison person has left
- In some instances NMRAs don't recognize inspections conducted by WHO (require own inspection)
- Time-lapse from submission to acknowledgement of submission and acceptance of WHO CRP
- Translations, legalization of documentation and requirement for a LTR are unfortunately not solved by WHO CRP

Levoplant regulatory footprint: March 2019



How 2018 Compares: Post WHO prequalification and aggressive regulatory strategy





Recommendation from Levoplant experience on WHO CRP

- ✓ ENGAGE early on with WHO CRP Team to discuss regulatory strategy and schedule annual/bi-annual meetings to discuss pending and in progress submissions.
- ✓ Ensure LOCAL TECHNICAL REPRESENTATIVE is aware of the procedure and highlights this during submission.
- ✓ MODULE 1 is still country specific and might required translations, notarization/legalization, local agents/local MAH and country specific samples. Be prepared for this!
- ✓ In most cases for countries familiar with the WHO CRP using the WHO CRP is a faster and more efficient pathway to marketing authorization.



After Registration...

- Marketing Authorization Approval
 - Renewals
- Post-Approval Changes or Variations
- Post-Approval Surveillance or Pharmacovigilance
 - Adverse Event Reporting



Photo Credit: Lucian Coman/Shutterstock.com



Learning about Expanded Access and Potential of the LNG-IUS (LEAP LNG-IUS) Initiative

- Funded by the Bill & Melinda Gates Foundation, and lead by FHI 360, in partnership with WCG Cares and PSI.
- Intended to help determine if and how expanded access to the LNG-IUS could increase contraceptive use and continuation rates in sub-Saharan Africa.
- Research among women and providers in Nigeria and Zambia as well as demand forecasting in Kenya, Nigeria and Zambia.
- A regulatory assessment was conducted in 2018 to identify potential strategies to expedite national registrations of LNG-IUS product(s) in FP2020 countries.
- An assessment of the national regulatory requirements in three countries which may be viewed as priorities for LNG-IUS registration and introduction: **Ghana, Ethiopia, and Vietnam.**



THANK YOU!

Questions?

