Vaccine assessment for prequalification

Briefing on Vaccine Prequalification for manufacturers
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Outline

- Vaccine regulation
- Overview on Prequalification
- Challenges PQ

WHO Goal for vaccines regulation

Ensure that "100%" of vaccines used in all national immunization programmes are of assured quality

Definition of "Vaccines of Assured quality"

- ✓ National Regulatory Authority (NRA) independent from vaccine manufacturer & procurement system
- ✓ NRA is functional (system + 6, 4 or 3 regulatory functions implemented)
- ✓ No unresolved reported problem with vaccine

WHO guidance by Experts Committee on Standardization of Biologicals (ECBS) recommendations on safety, efficacy and quality issued in WHO Technical Report Series (TRS)

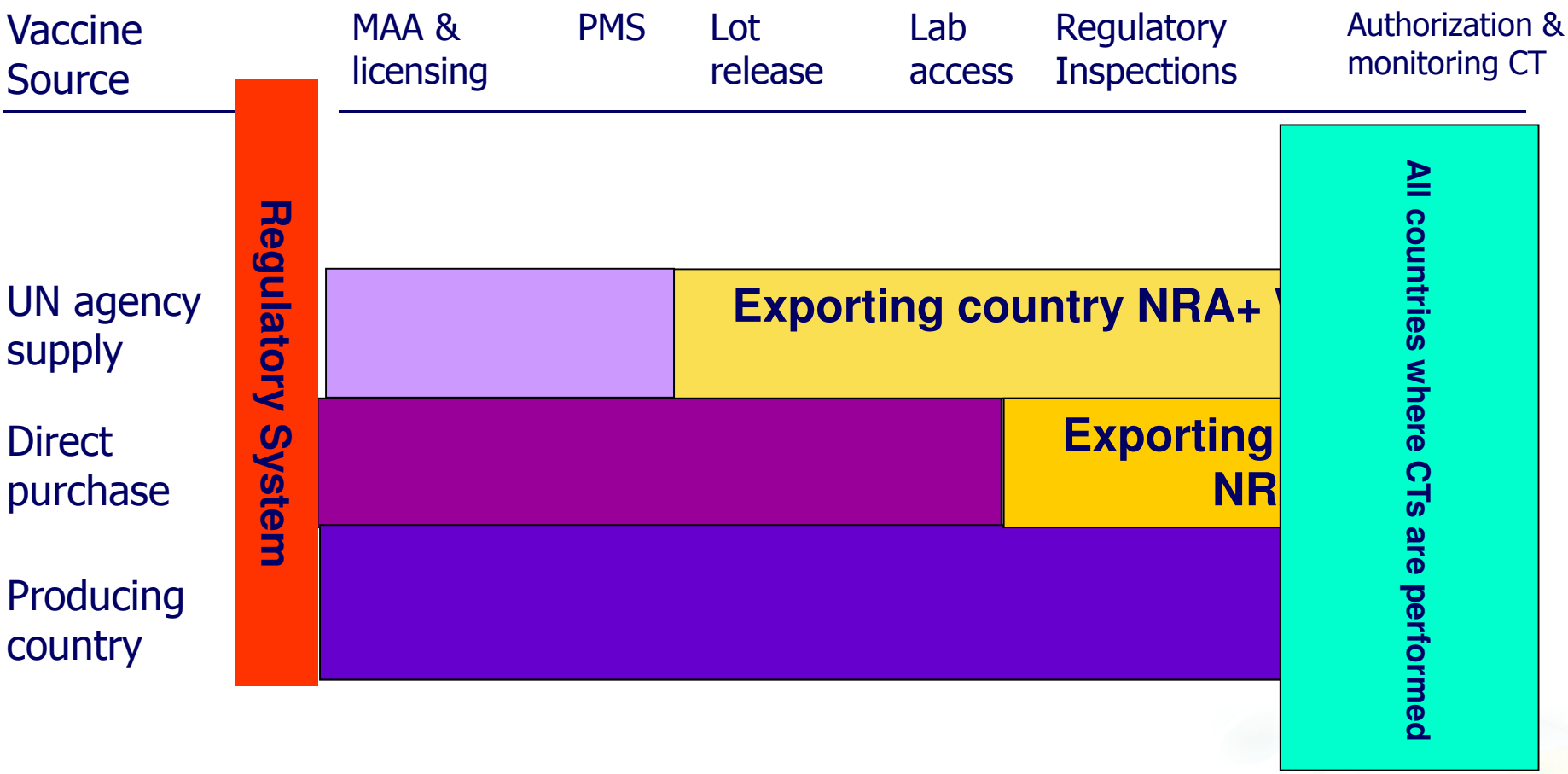
WHO concept of Vaccine Regulation

National Regulatory System : Governance

+ six regulatory functions

1. Marketing Authorization (MA) and Licensing Activities
2. Post-marketing activities including surveillance of Adverse Events Following Immunization (AEFI)
3. NRA Lot Release
4. Laboratory access
5. Regulatory Inspections
6. Authorization/Approval of Clinical Trials

Required functions according to vaccine source



Purpose of WHO vaccines prequalification programme

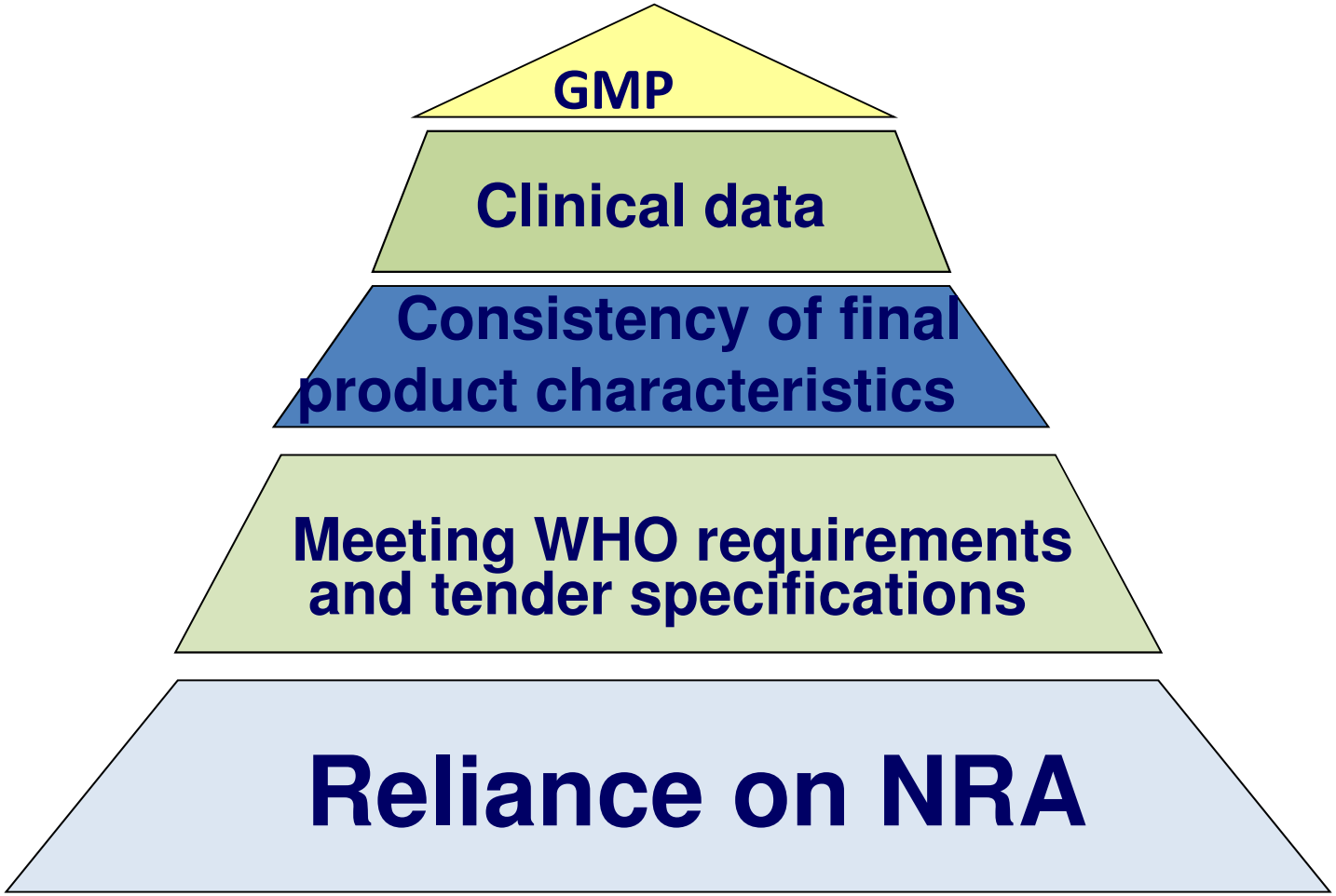
A service provided to UN purchasing agencies.

Provides independent opinion/advice on the quality, safety and efficacy of vaccines for purchase

Ensures that candidate vaccines are suitable for the target population and meet the needs of the programme

Ensures continuing compliance with specifications and established standards of quality

Principles


GMP
Clinical data
Consistency of final product characteristics
Meeting WHO requirements and tender specifications
Reliance on NRA

Pre-conditions for PQ evaluation

Reliance on the National Regulatory Authority (NRA) of the exporting country

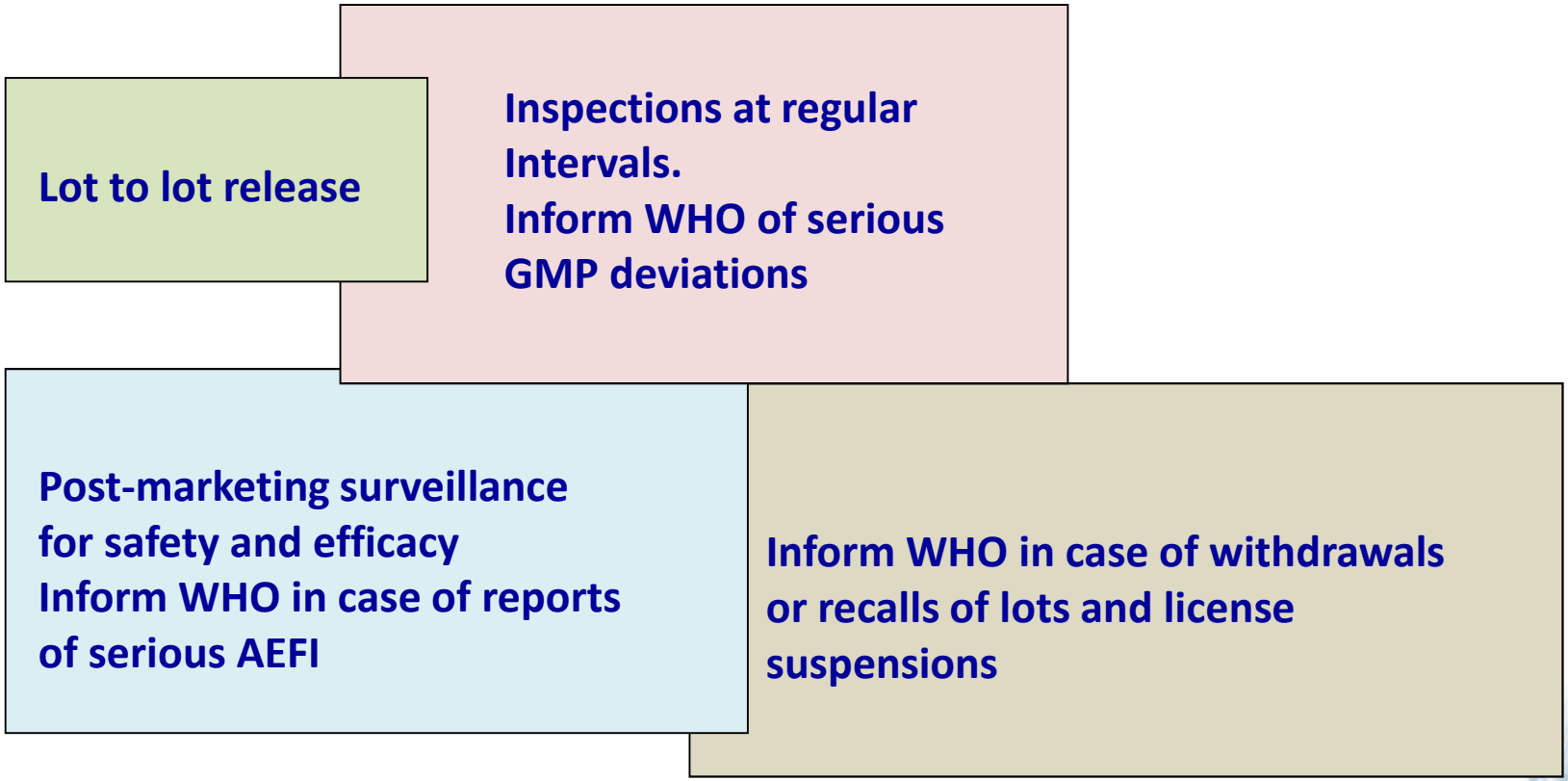
- NRA must be assessed as functional as a result of successful evaluation using the WHO NRA assessment tool
- NRA's functional status needs to be sustained over time
- Continued regulatory oversight by NRA is required as well as communication with WHO about potential problems with the vaccine
- Agreements are established with the NRAs for information exchange when a vaccine is about to be prequalified

Pre-conditions for PQ evaluation

- Vaccine is licensed/registered by the responsible NRA (Scientific opinion by EMA accepted)
- WHO guidelines/recommendations approved by the ECBS are available (published in the WHO Technical Report Series)
- Listed in the vaccine priority list (low priority vaccines may be postponed depending on workload and no priority vaccines will not be reviewed)

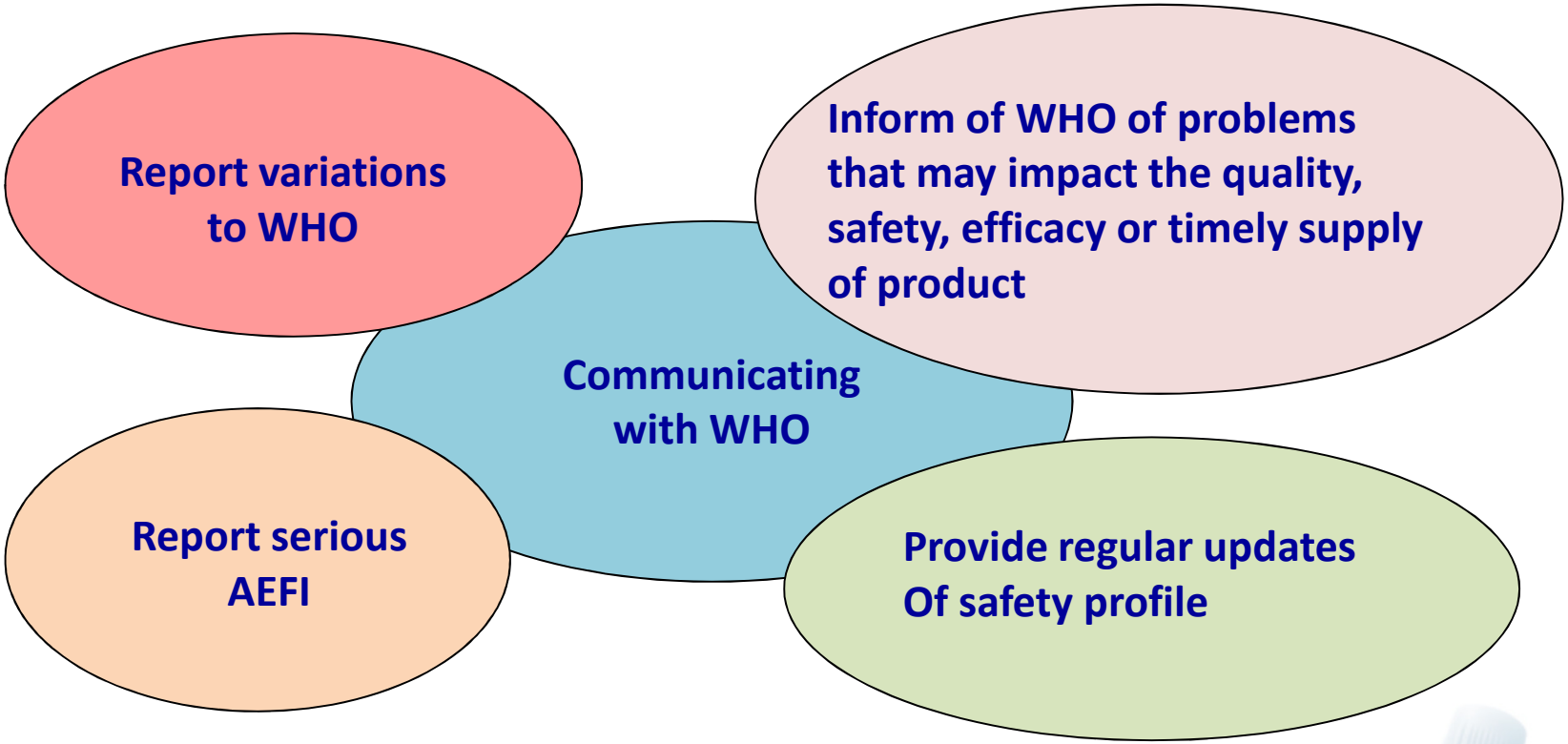
Conditions for prequalification

Ongoing oversight and commitments by the NRA



Conditions for PQ evaluation

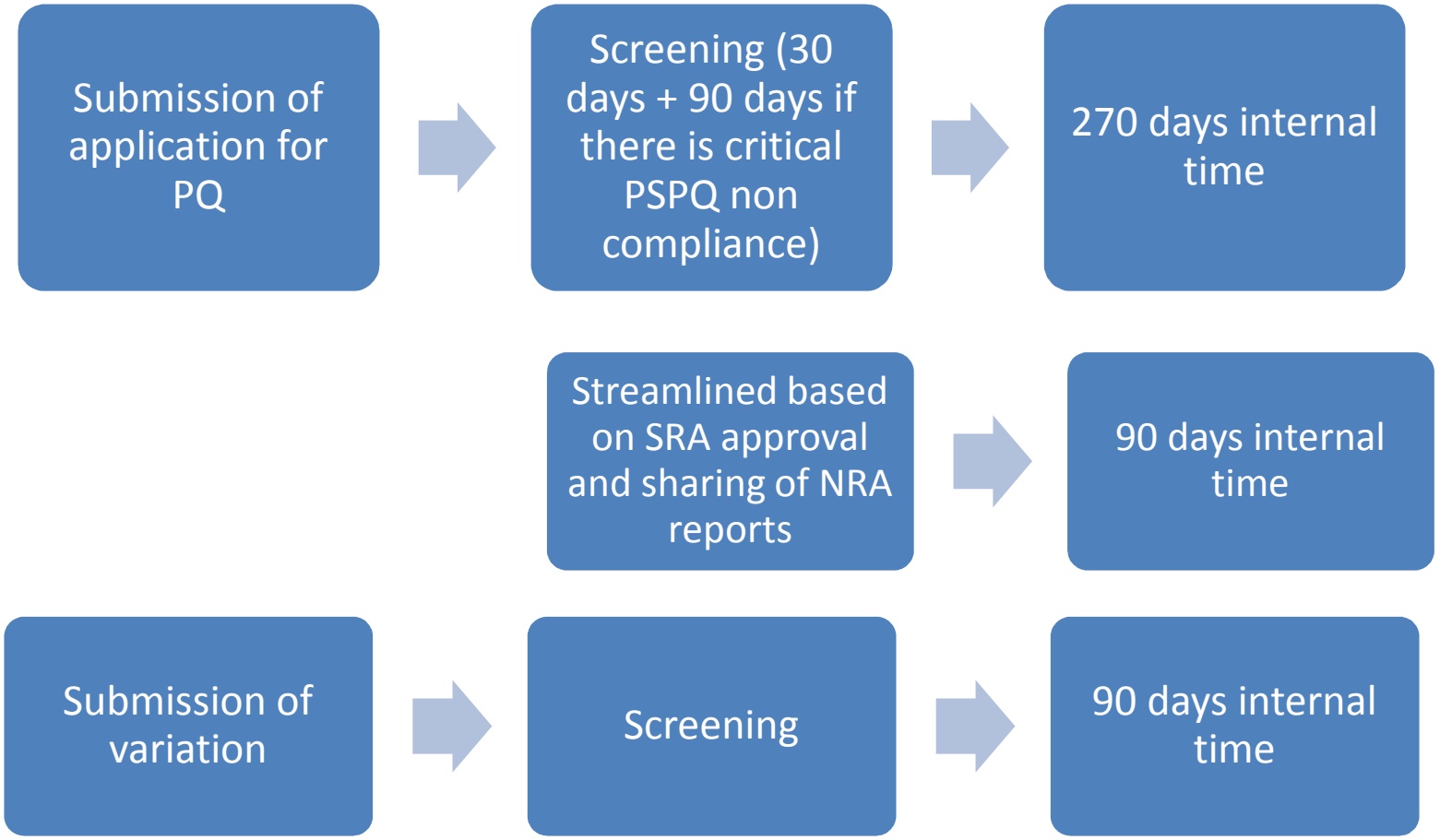
Commitments from the manufacturer



Prequalification process

- Scientific review of quality dossier
- Scientific review of clinical data
- Testing of samples
- Consultation with responsible NRA
- Site audit to manufacturing facilities

Prequalification process: timelines (excluding applicant response times)



Role of NRA during PQ process

As part of the evaluation procedure, consultation with NRA

- To discuss regulatory status of the concerned vaccine/s
- Clinical performance in country of manufacture if used
- Quality evaluation, outcome of recent GMP inspections
- Compliance with specifications (trends from lot release data)
- Regulatory actions
- Informal agreement for information sharing with WHO recorded in Consultation report

Programmatic suitability and its assessment

- Vaccines produced in developed countries may not have taken into account programmatic challenges in developing countries.
- Examples:
  - Non auto-disable prefilled syringe presentations
  - Stability of components in the event of cold chain breakdown

- WHO PQT has always considered programmatic suitability but it was in 2012 that a written guidance (PSPQ) was developed and put in place

Monitoring performance of PQd vaccines

- **Targeted testing by WHO contracted labs: Once a year testing of samples of lots shipped to countries to ensure continuing compliance with specifications**
- **Monitoring and resolution of complaints and reports of AEFIs (with collaboration of the responsible NRA)**
- **Reassessments frequency defined on risk analysis basis**

Why is Vaccines PQ important for user countries and its NRAs?

- It represents a source of vaccines of "assured quality"
- In addition the evaluation is focused on programmatic needs
- WHO follows up on complaints and reports of AEFIs and publishes the outcome of investigations
- WHO monitors the quality of prequalified vaccines on a continuing basis, through testing of samples, reassessment of the products, targeted audits, and delists vaccines if they do not meet the established specifications and/or standard
- Opportunity for NRAs in user countries to save resources to focus on other priorities, since registration can be granted through a facilitated and shortened procedure

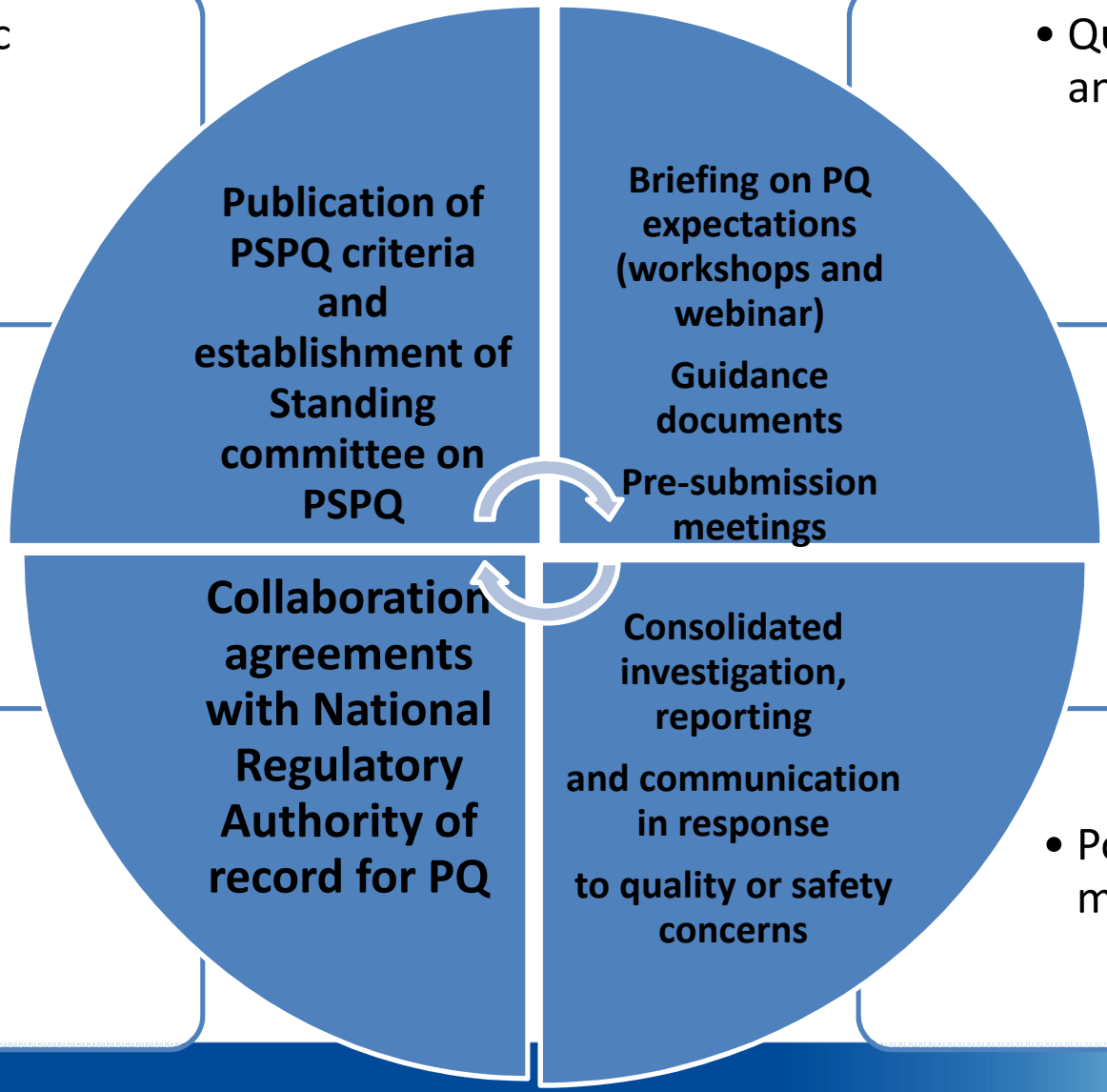
Past and current challenges

Quality	Clinical	Programmatic	GMP
Incomplete dossier Lack of data at commercial scale No history of characterization Master and Working cell banks Inappropriate devices: nasal administration	Lack of clinical consistency data, unclear ethical oversight Clinical trial comparator product not acceptable Lack of access to data and/or old data not meeting current GCP Lack of registration of CTs	Deviation Programmatic suitability criteria (PSPQ): eg, non autodisable prefilled syringes, stability profile and VVM	Quality systems Manufacturing process
Regulatory	National Vs WHO requirements: Test methodologies and GMP Schedules and target population Monodose Vs multidose presentation (preferred)		

Past/current Challenges and solutions

- Programmatic suitability criteria

- Quality, safety and efficacy



- Regulatory

- Post-PQ monitoring

Technical assistance and capacity building

- Meetings with manufacturers at early stages of vaccine development. Advice on product characteristics and clinical development.
- PQ briefing workshops
- Support to IFPMA and DCVMN
- Support to regulatory networks: DCVRN, AVAREF