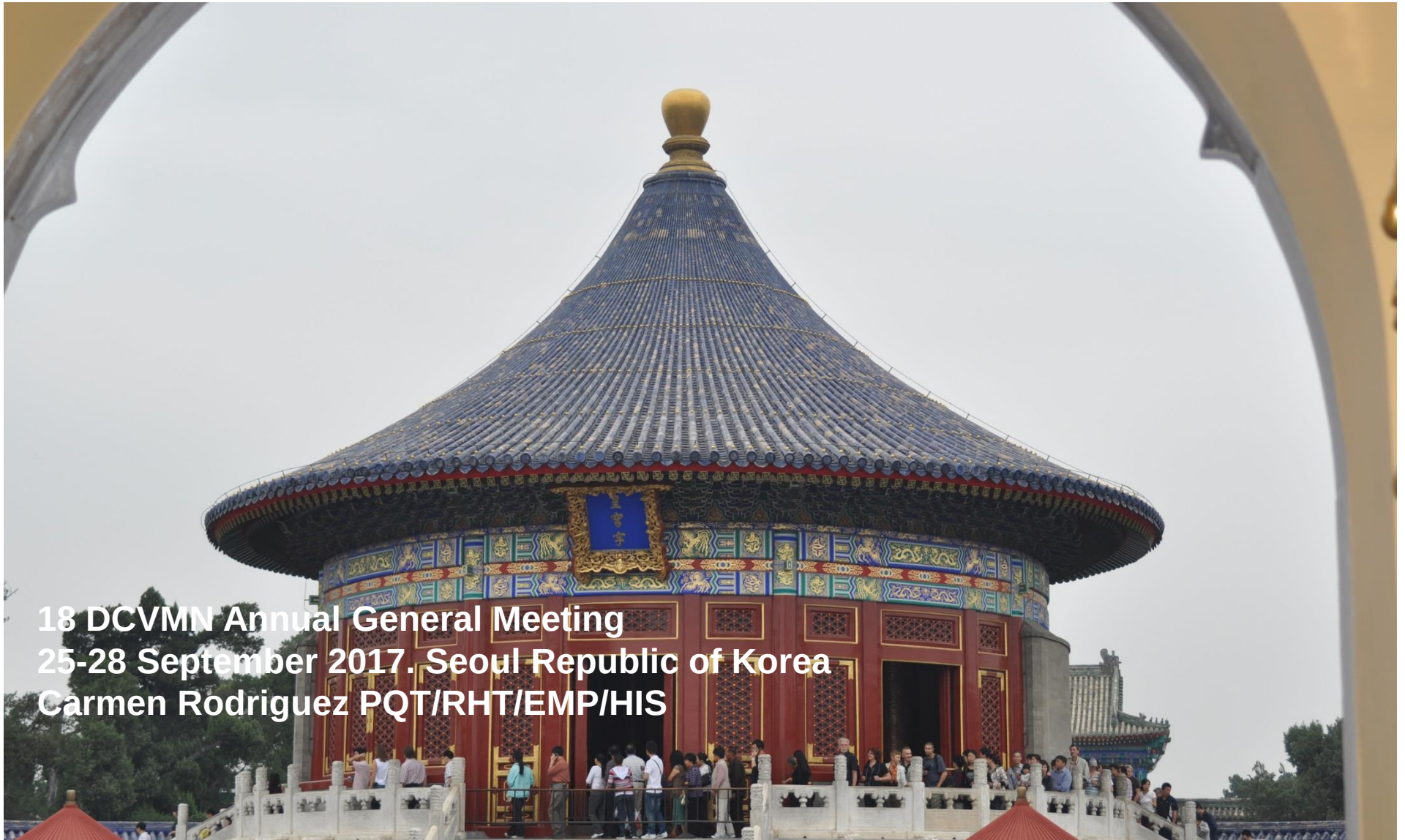
Prequalification overview.

World Health Organization



18 DCVMN Annual General Meeting
25-28 September 2017. Seoul Republic of Korea
Carmen Rodriguez PQT/RHT/EMP/HIS

Outline

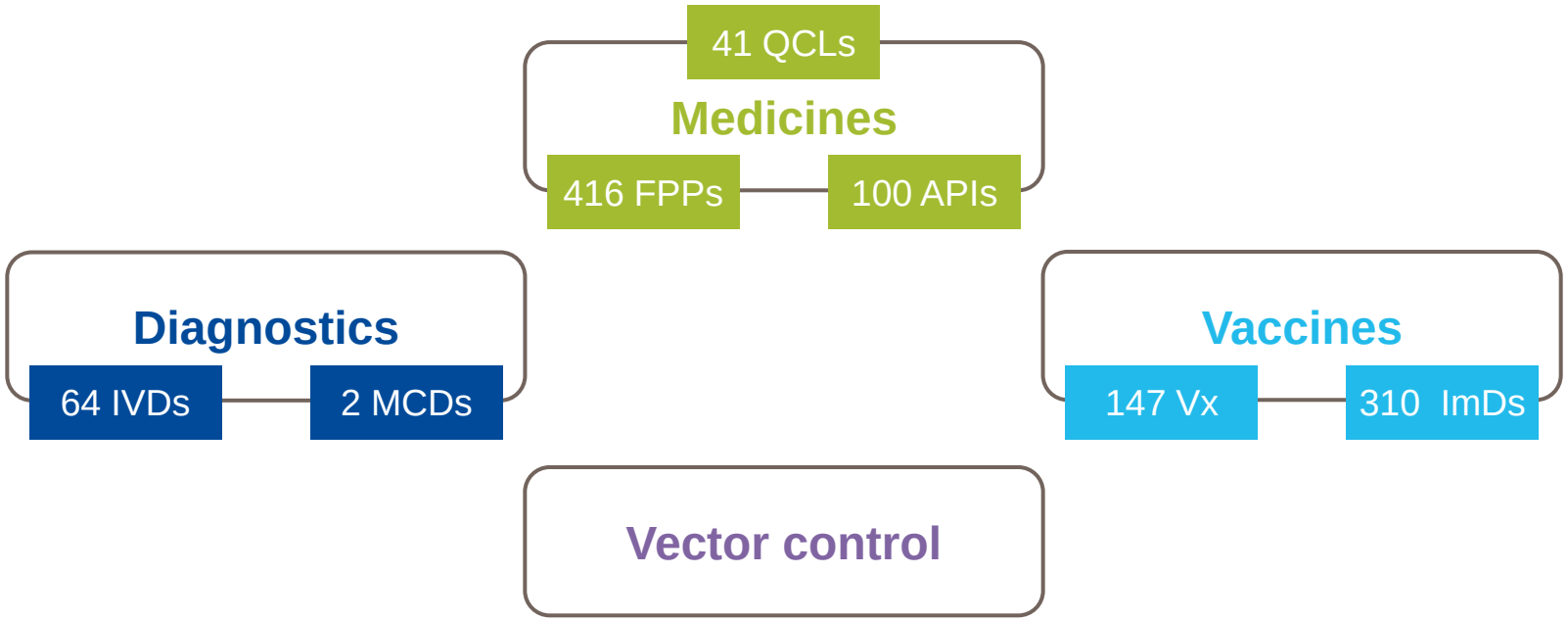
World Health Organization

- WHO PQ process
- PQ of vaccines:
  - Principles and conditions
- PQ process
- PSPQ
- Past and current challenges
- Post-PQ monitoring activities
- PQ of immunization devices and equipment

World Health Organization

→ *Through the prequalification process, WHO has made available numerous quality-assured products to WHO Member State markets*

At the close of 2016, PQT's list of prequalified products included:



Purpose of WHO vaccines prequalification programme

World Health Organization

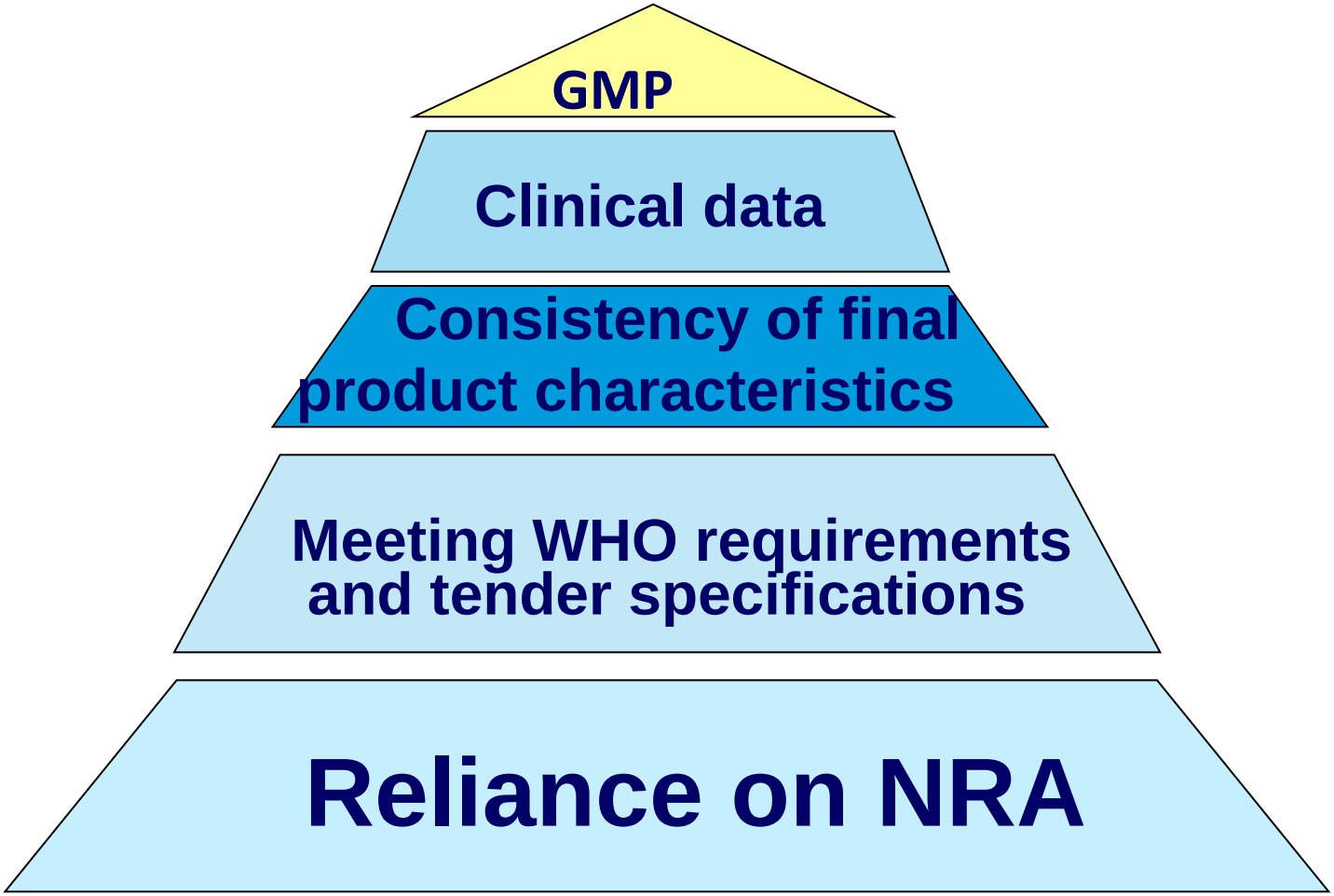
A service provided to UN purchasing agencies.

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 PQT-VXA evaluation

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

- NRA evaluated by WHO NRA Global Benchmarking Tool
- NRA's 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 PQT-VXA evaluation

- Vaccine is licensed/registered by the responsible NRA (or EMA article 58 scientific opinion)

- There are WHO guidelines/recommendations approved by the ECBS are available for the type of vaccine (published in the WHO Technical Report Series)

- Listed in the PQ vaccine priority list

Pre-submission and Dossier Review

- Pre-submission meetings with manufacturers interested in submission are available and encouraged

- Notification of intended submission

- Dossier Submission
  - Product Summary File
  - Common Technical Document

- Screening
- Acceptance decision

Prequalification process

World Health Organization

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

Prequalification process: timelines (excluding applicant response times)

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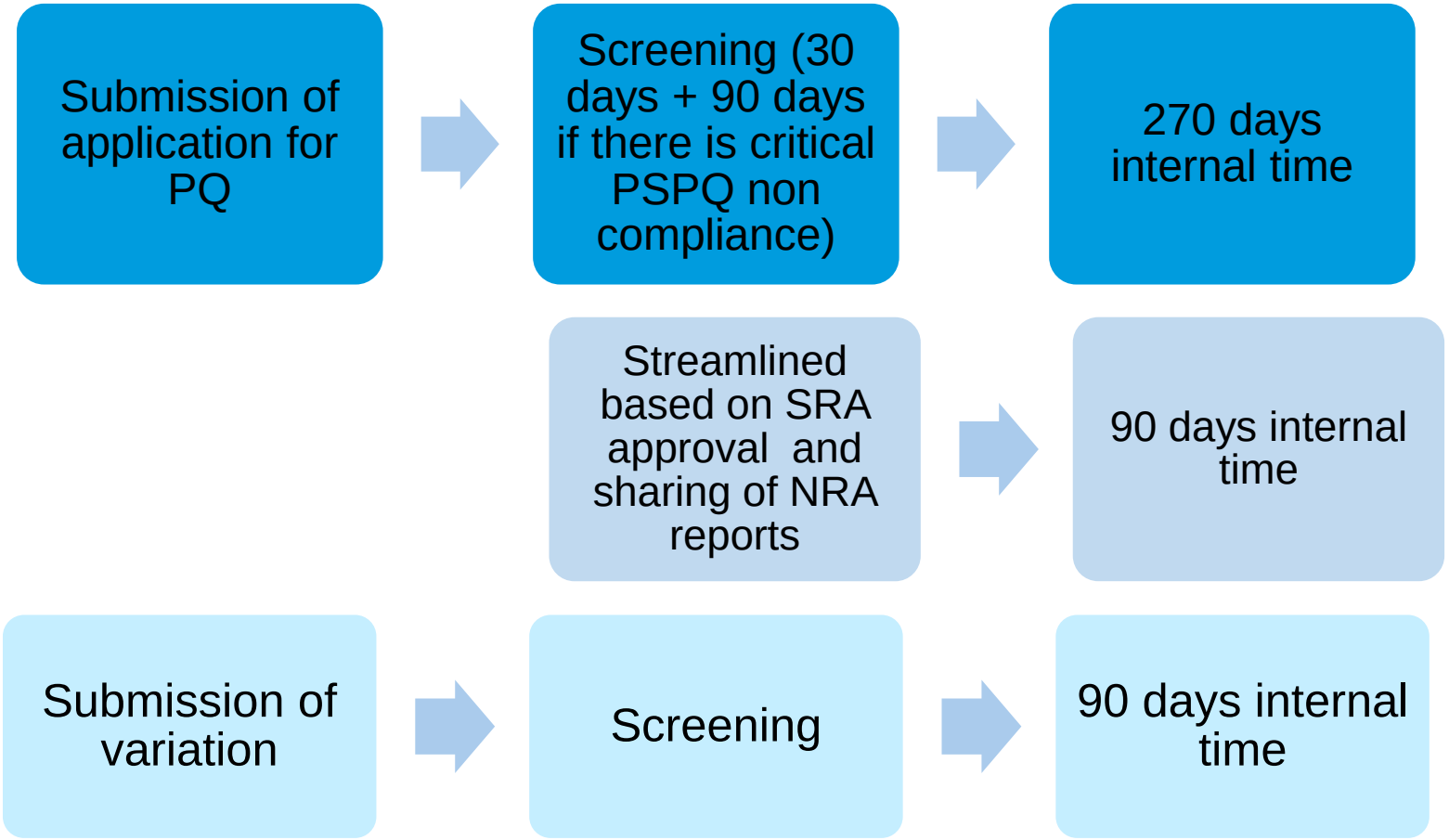
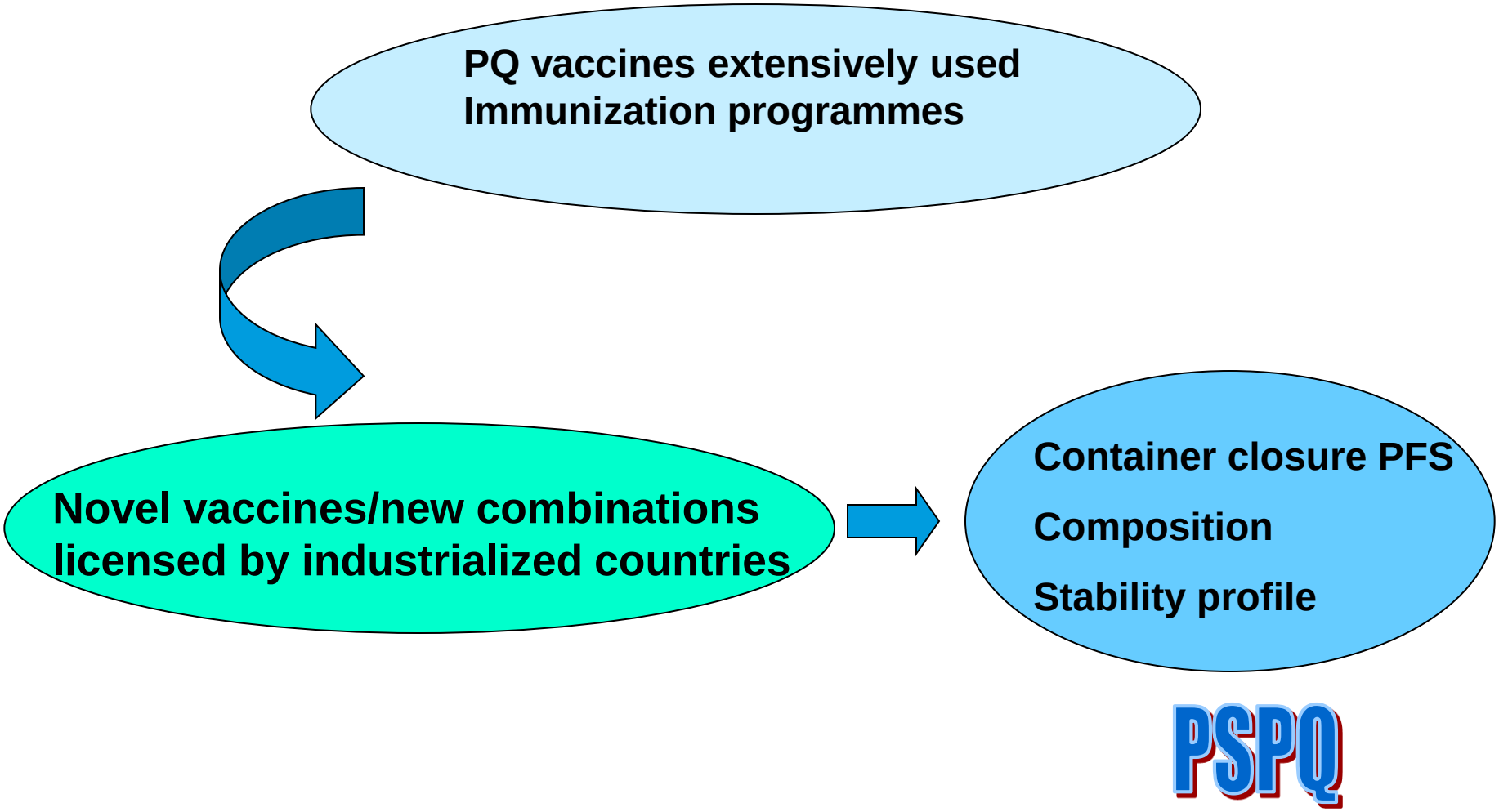


Aspects considered during evaluation of vaccines for WHO Prequalification

- Production
- Quality Control
- Clinical development, including data relevant to target population for supply through UN agencies
- Compliance with WHO recommendations and UN tender specifications including labels and inserts
- Compliance with GMP
- Programmatic suitability

Prequalification process: the Past



Programmatic Suitability for PQ (PSPQ)

Ensure that vaccines used in low and middle income countries can be used safely and effectively, given the constraints and conditions of their immunization systems

Nicaragua, rotavirus delivery, Photo: Gates Foundation

Mali, polio campaign, Photos: WHO/Olivier Ronveaux

Programmatic Suitability for Prequalification

- Objectives of PSPQ
  - Judge the programmatic suitability against defined mandatory, critical and preferred characteristics
- Benefits of PSPQ
  - Give clear directions to vaccine industry before submission
  - Reduce decision making time

Vaccine characteristics that will affect pre-qualification

World Health Organization

Mandatory

- Compliance with PSPQ criteria is compulsory
- Failure to meet this characteristic will prevent the vaccine to be further considered for pre-qualification

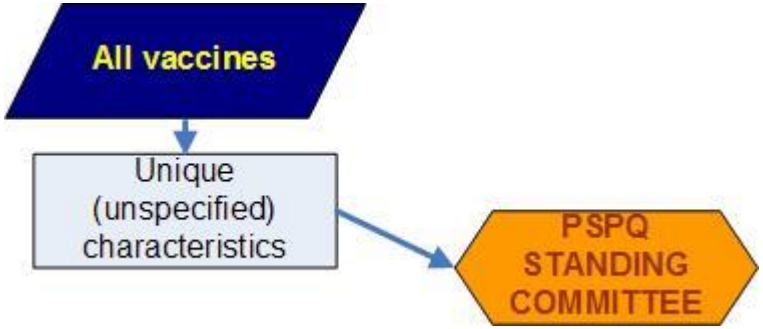
Critical

- Compliance with PSPQ criteria is also compulsory
- However, deviations in vaccine characteristics will be reviewed by the Programmatic Suitability for WHO Prequalification (PSPQ) Standing Committee
- Under special circumstances exceptions can be granted to vaccines that deviate from the critical characteristics.
- Decision can only be taken by the PQ Secretariat and will include consideration of recommendations from the PSPQ Standing Committee and consideration of topics such as public health need and access to vaccines.

Vaccine characteristics that are unique

Unique (characteristics not otherwise specified)

- Are reviewed by the PSPQ Standing Committee
- May be pre-qualified if considered suitable by the PQ Secretariat on the advice of the PSPQ Standing Committee



Submission Screening and Standing Committee Assessment

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•Upon receipt, dossiers are screened for completeness and compliance with the required format and contents by the PQ secretariat

•Dossiers are also screened for compliance with programmatic suitability criteria

- If mandatory characteristics are not met, the dossier is rejected
- If there is a deviation from a “critical” criterion or if a unique characteristic is identified, the vaccine will be referred to the PSPQ standing committee for independent review.

http://www.who.int/immunization_standards/vaccine_quality/pspq2_v140512.pdf

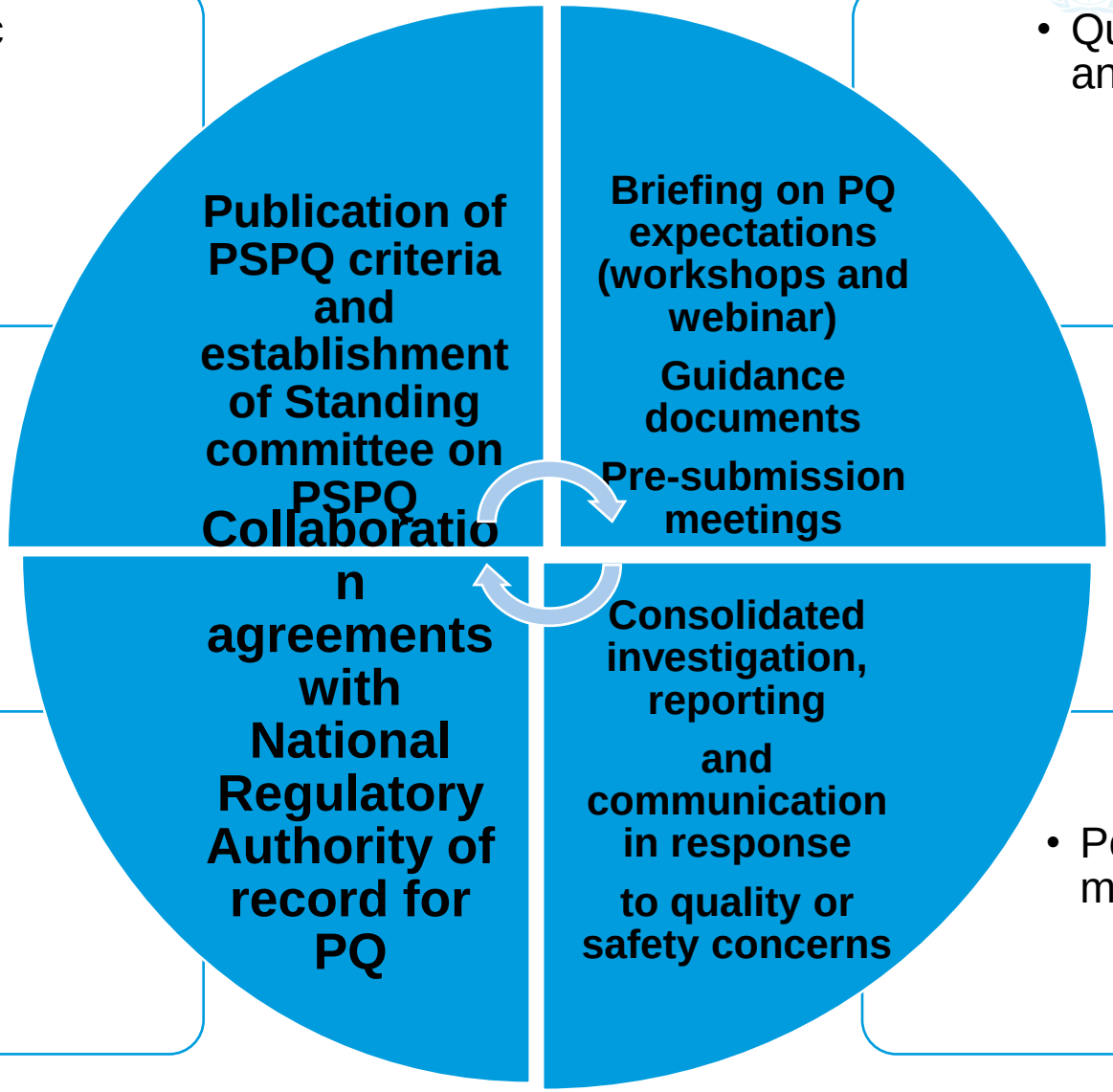
Past and current challenges

Quality	Clinical	Programmatic	GMP
Incomplete dossier Lack of data at commercial scale No history of characterization Master and Working cell banks Novel devices: eg, 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

Post Prequalification WHO Activities

- Variations
- Annual Report evaluation
- Reassessment
- Targeted testing program
- Monitoring/Investigation of vaccine quality and cold chain complaints
- Monitoring/investigation of Adverse Events following immunization (AEFI)
- Collaborative National Registration
- Technical Review of tenders for UNICEF

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: AVAREF

Prequalification of immunization devices and equipment

World Health Organization

Scope Prequalification immunization devices and equipment

Three steps cycle

Standards and Innovation	• Identify requirements • Develop and maintain performance specifications and verification protocols
Prequalification	• Immunization devices • Cold chain equipment
Post- PQ monitoring	• Monitor products and inform new requirements

Innovation 3 + 2

- **Product performance validation protocol (field monitoring and field testing**
- **Target product profile**

STANDARDS, GUIDELINES & INNOVATION

Develop product Specifications that suit the environmental, infrastructural and socio-economic context of countries (LMICs) for procurement by UN Agencies

Develop verification protocols to test the candidate products against the specifications

Develop guidelines for manufacturers on how to apply for prequalification for each category of product

Develop guidelines for countries in the PQS catalogue on how to go about the selection of the various equipment available

Shipping guidelines revision  Consultation process

PRE-QUALIFICATION

Expression of interest from the manufacturer – a letter explaining the manufacturers intentions and any specific questions from the manufacturers

Invitation to apply for PQ

List of documents, samples and/or laboratory tests to be submitted for the pre-qualification

Dossier examination

Prequalification

PRE-QUALIFICATION

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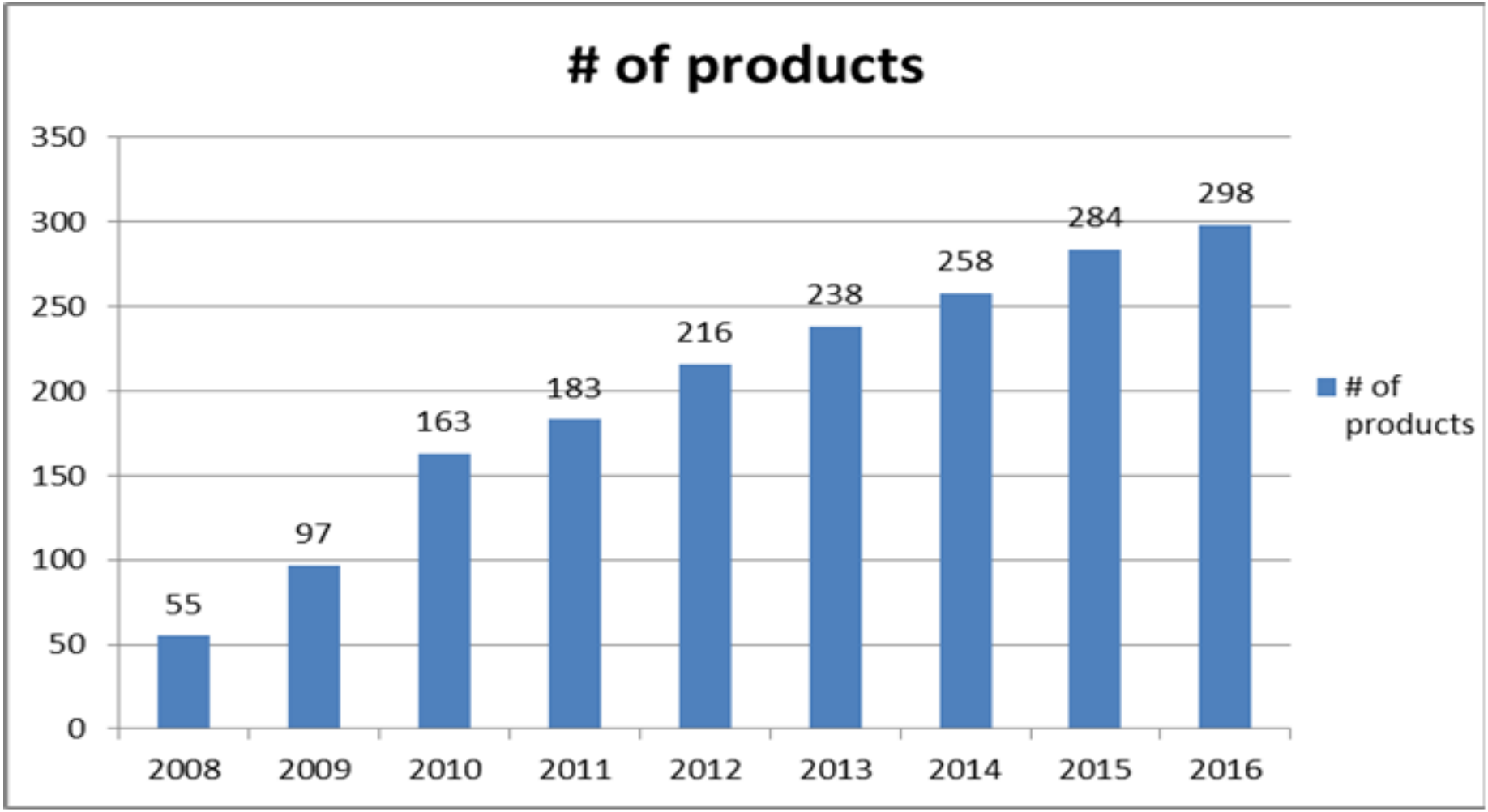
Categories of Devices

1. E001 – Cold Rooms and Freezer Rooms
2. E002 – Transport
3. E003 – Refrigerators and Freezers
4. E004 – Cold boxes and vaccine carriers
5. E005 – Coolant packs
6. E006 - Temperature monitoring devices
7. E007 - Cold chain accessories
8. E008 - Injection devices for immunization
9. E010 - Waste management equipment
10. E013 - Injection devices for therapeutic purposes

Prequalification of Immunization equipment

World Health Organization



PRE-QUALIFICATION FIELD PERFORMANCE EVALUATION

Introduced in 2016

Generic field evaluation protocol published

Applies to new technology

Purpose is to have a minimum of field performance data before prequalification

POST-QUALIFICATION MONITORING

- Systematic feedback from the field on equipment performance and failures
- Serves as an important information source for the development of future product TPPs
- Currently there is no active system in place

Reference documents

World Health Organization

- PQT/VXA procedure [TRS 978, Annex 6 (2013]
  http://www.who.int/entity/immunization_standards/vaccine_quality/TRS_978_61st_report_Annex_6_PQ_vaccine_procedure.pdf

PQ vaccines: Priority setting and Review

- http://www.who.int/immunization_standards/vaccine_quality/pq_priorities/en/

Programmatic Suitability for Prequalification

http://www.who.int/immunization_standards/vaccine_quality/pspq2_v140512.pdf

Clinical

- http://apps.who.int/prequal/info_general/documents/TRS850/WHO_TRS_850-Annex3.pdf
- http://who.int/entity/biologicals/vaccines/clinical_evaluation/en/index.htm
- http://who.int/biologicals/vaccines/nonclinial_evaluation_of_vaccines/en/
- http://www.who.int/immunization_standards/vaccine_quality/pq_vaccine_evaluation/en/

Variations to prequalified vaccines

- **http://who.int/immunization_standards/vaccine_quality/variations_pq_vaccine/en/**

HO contracted testing laboratories

- **http://www.who.int/immunization_standards/vaccine_quality/contracted_labs_vaccines/en/**

Reference documents

World Health Organization

Good Manufacturing Practice

WHO GMP for biological products, Annex 2, WHO TRS 999, 2016, http://who.int/biologicals/areas/vaccines/Annex_2_WHO_Good_manufacturing_practices_for_biological_products.pdf

WHO GMP for pharmaceutical products: main principles, Annex 2, WHO TRS 986, 2014

WHO GMP for sterile pharmaceutical products, Annex 6, WHO TRS 961, 2011

World Health Organization