



# **WHO VACCINES PREQUALIFICATION UPDATE**

***14<sup>th</sup> DCVMN Annual Meeting***

***Hanoi, Vietnam***

***7-9 October 2013***



**World Health  
Organization**

# Outline of the presentation



**Updates on the following aspects:**

- **Strategic Priorities and related activities**
- **Main features of revised procedure**
- **Performance of the programme**

# 4 Strategic Priorities

**Secure the supply  
base for priority  
vaccines for  
developing  
countries**

**Facilitate access to  
quality products  
for developing  
countries**

**Improve efficiency  
of the  
prequalification  
procedure**

**Expand portfolio  
according to needs  
and options for  
introduction**

# Supply Security

**Monitor closely the performance of prequalified vaccines including FU audits and conducting production capacity assessments**

**Actively seek for additional sources for priority vaccines**

**Secure the supply base for priority vaccines for developing countries**

**Establish risk mitigation strategies in case of failure of NRA**

# PQ briefing workshops



**India, October 2012**

**16 participants:**

**8 Indian manufacturers**

**1 Bangladesh**

**1 Egypt**

**2 Iran**

**Indian NRA**

**23 Chinese participants**

**7 manufacturers,**

**PATH China**

**BMGF China**

**Chinese NRA (CFDA)**

**Targeted at manufacturers with potential for PQ of vaccines**



**China, May 2013**

# Notes for guidance for manufacturers

- **Guideline for the preparation of the Product Summary File for vaccine prequalification**
- **Clinical considerations for evaluation of vaccines for prequalification**
- **Assessing the Programmatic Suitability of Vaccine Candidates for WHO Prequalification WHO/IVB/12.10**
- **Guide to Master Formula**
- **Environmental Monitoring of clean rooms in vaccine manufacturing facilities**
- **Priority setting for WHO vaccines prequalification programme**
- **Guidance on variations to prequalified vaccines (under preparation)**
- **Validation of production process for vaccines and other Biologicals- Compliance expectations (under preparation)**
- **Deviations handling and Quality Risk Management (under preparation)**



# WHO guidance documents on changes

## **Guidelines for Procedures and data requirements for changes to approved vaccines : OBJECTIVE AND SCOPE**

- **These guidelines constitute guidance for national regulatory authorities (NRAs) and for marketing authorization (MA) holders of vaccines.**
- **These recommendations may be adopted as definitive national requirements.**

## **Guidance note on Variations to prequalified vaccines: OBJECTIVE AND SCOPE**

- **It provides guidance to marketing authorization holders (MA) of prequalified vaccines**
- **Informs which changes need to be submitted to WHO/PQ for review before implementation (after approval by the responsible NRA) and which can be notified on annual basis**
- **Advises on the information needed to support the changes**

# Access

**Facilitate access  
to quality  
products for  
developing  
countries**

**Single standard of quality  
(WHO recommended requirements)**

**Consolidated investigation, reporting  
and communication in response  
to quality or safety concerns**

**Implementation of an  
expedited/facilitated registration  
procedure for prequalified vaccines  
in receiving countries**



# **Expedited procedure for registration of WHO prequalified vaccines**

## **Objective**

**Assist countries to adopt a facilitated, expedited procedure for the national registration of prequalified vaccines.**

## **Who can benefit**

- **Countries procuring through UN agencies and/or**
- **Countries procuring directly but requiring WHO prequalification as a tender condition**

**where the national regulations include provisions to shorten the normal regulatory approval process.**

# Requirements for implementation

- **Political decision**
- **Integration into the national regulations**
- **Technical expertise to review the submission**

# Implementation of Procedure for expedited review of imported prequalified vaccines for use in national immunization programmes (WHO/IVB/07.08)

**Firstly used  
for registration  
of MenAfriVac in  
26 countries of  
the belt**





- **For meningitis vaccine two training workshops have been conducted and NRA personnel of 26 member states (43 participants) trained plus one to one follow up for implementation**
- **For other vaccines four workshops were conducted (50 participants trained in AFRO, EMRO and WPRO). 30 registration applications submitted for polio, pneumococcal conjugate and other vaccines have been already completed.**



- **In 2013, an internet based tool has been developed and hosted on WHO server for online submission, processing and monitoring of registration applications.**
- **Two applications were successfully processed online and additional 25 applications are currently underway.**

# New features of the prequalification procedure

- Guidance document and mechanism to assess the suitability of product characteristics for use in NIPs
- Implementation of a Streamlined Prequalification Procedure for products manufactured in countries with eligible authorities
- Increased reliance on NRAs (collaboration agreements)
- Strict monitoring of timelines for evaluation
- Improved communication and increased process transparency
- Establishment of annual reporting system (PQVARs) to monitor vaccine quality and performance



# New features of the prequalification procedure

- Risk based analysis conducted to prioritize products for reassessment
- Improved web list including summary document providing rationale for prequalification
- Meetings with manufacturers encouraged at early stages of vaccine development and prior to submission. Advice on product characteristics and clinical development provided
- Documentation system upgraded
- Documentation management system improved: links master PQ database (DB) to timeframe monitoring DB, risk analysis DB and expedited review procedure DB

Implemented since February 2012



# Programmatic Suitability of Product Characteristics (PSPQ)

## WHERE ARE WE

- PSPQ-Standing Committee has reviewed several products on pilot basis in 2011
- Three products deviating from critical characteristics were reviewed in 2012 (within one month)
- All currently PQd vaccines have been reviewed to identify those that deviate from critical characteristics.  
**Plans for correction will be discussed with manufacturers on a case by case basis**

[http://www.who.int/immunization/documents/WHO\\_IVB\\_12.10/en/index.html](http://www.who.int/immunization/documents/WHO_IVB_12.10/en/index.html)



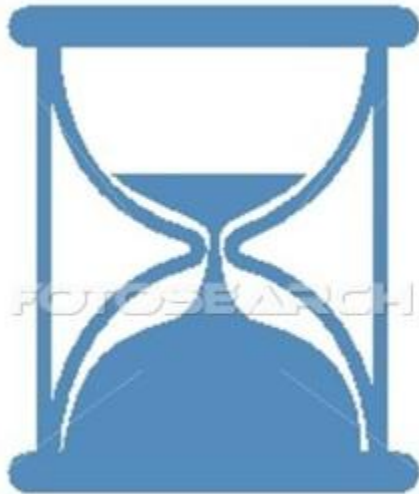
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# Streamlined prequalification procedure

- **Introduced option for increased collaboration with mature National Regulatory Authorities (NRAs) to streamline the PQ procedure**
  - Confidentiality and Collaboration agreements being signed with eligible NRAs: US, Canada, EMA, Australia, France, Belgium and Italy
  - Criteria to be defined to expand eligibility to other NRAs
- **Formalization of collaboration agreements with NRAs in countries with PQd vaccines for exchange of information in case of problems (quality, AEFIs, recalls, non-compliance with GMP, etc).**

Confidentiality and collaboration agreements are being signed with relevant NRAs

# Timelines for prequalification



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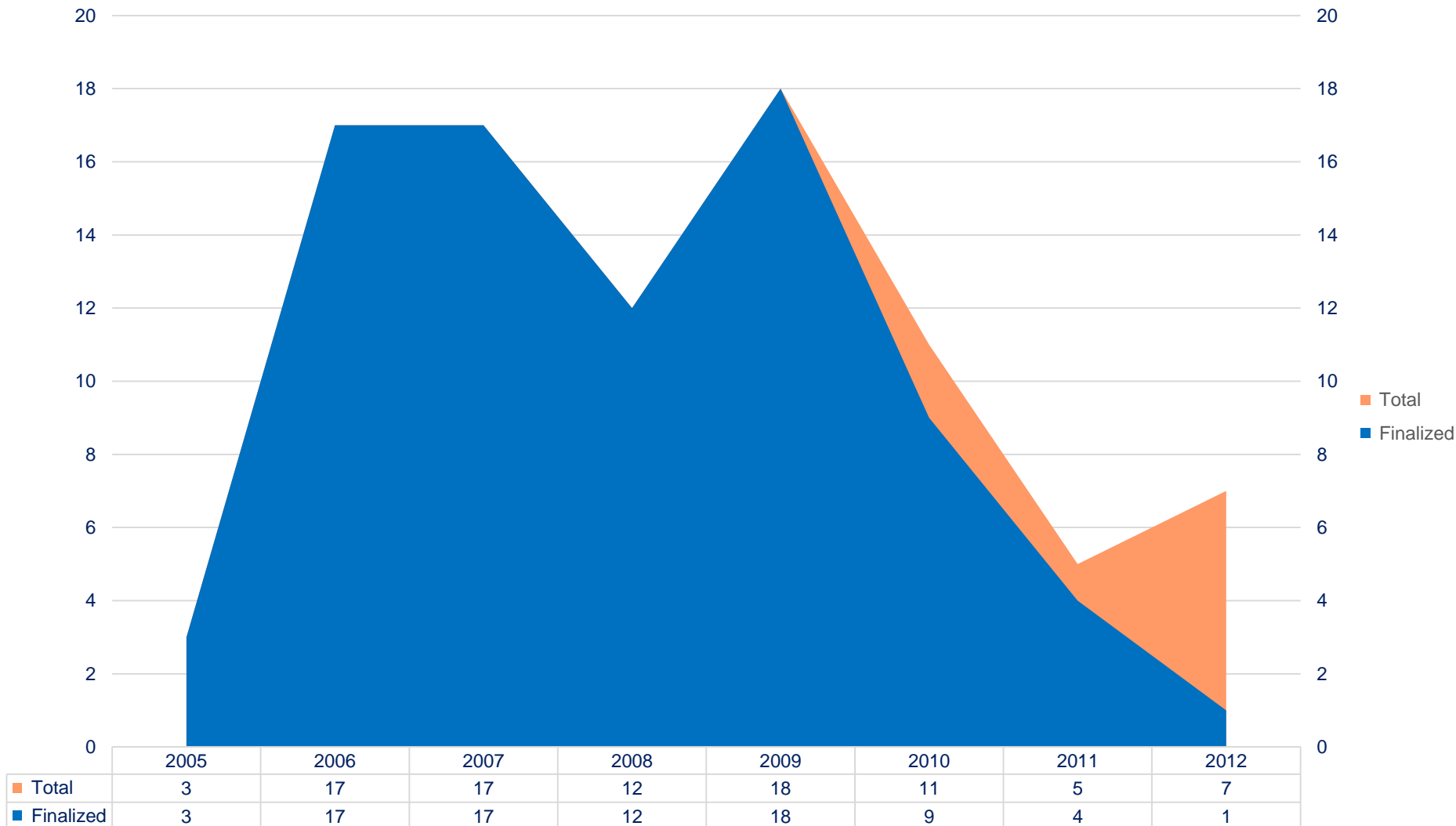
## **NORMAL PROCEDURE:**

- **365 days target without counting clock stops**

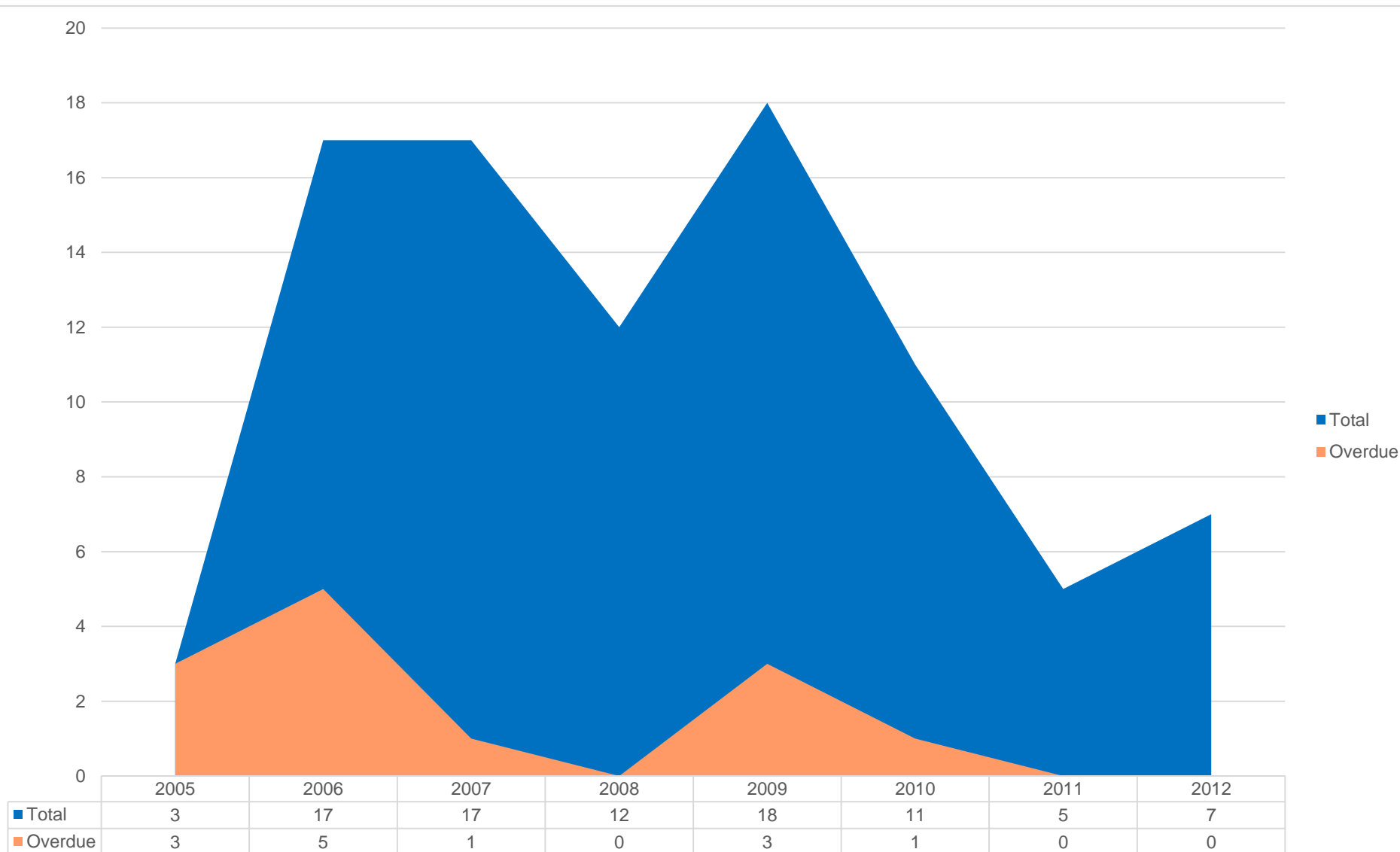
## **STREAMLINED PROCEDURE:**

- **180 days months target without counting clock stops**

# Number of submissions (2005-2012)



# Overdue submissions (2005-2012)



# Vaccines processed using streamlined procedure

submit	start	vaccine	Auth	total	internal	external
27/01/2012	17/04/2012	II	USA	400	141	259
26/09/2012	24/01/2013	III	Europe	176	73	103
01/10/2012	20/02/2013	IV	USA	142	25	117
29/01/2013	27/02/2013	V	Europe	32	32	0

# Communication and Transparency

- **Shared point for Prequalification for confidential and non-confidential information**
- **Web based communication statements in case of quality or safety concerns with prequalified vaccines. Communication to all affected stakeholders**
- **Upgraded list of UN prequalified vaccines providing detailed information on the products**
- **Publication on website of list of WHO contracted labs for testing**
- **Vaccines priority list published on Web and updated every two years. New list published in February 2013**



# **PERFORMANCE OF THE PROGRAMME**



# Customers' survey 2012

**Commissioned by WHO to an independent specialized company**

**Objective: To look at quality of service design (process) and service delivery (people)**

**Context: Focused on file review and site audits**

**Framework: Manufacturers with one or more prequalified vaccines**

**Staff consulted: Regulatory Affairs and Quality Assurance**

**23 manufacturers approached, 23 complete responses received, 79 responses**

**Methodology: Service performance measured on a 7-point scale**

# Main findings

- **Vaccine manufacturers consider that the service provided by the WHO vaccines prequalification programme is within the range of an acceptable level of performance compared to agencies that review and approve vaccine products.**
- **In no area in the study is the PQ programme performing significantly below manufacturers' minimum expectations.**
- **Overall, the programme is especially strong in those aspects of service that build applicant's confidence and increase their comfort level with the overall process.**

# Major strengths identified

- **Providing the same reviewers throughout the file evaluation**
- **Clarity of questions asked during the site audits**
- **Auditors who handle confidential data/information in a way that makes applicants feel safe**
- **Providing direct access to team leader to address technical questions or deficiencies**
- **Providing timely announcement of audits**
- **Agency rationale for the list of priority vaccines**

# Major areas for improvement

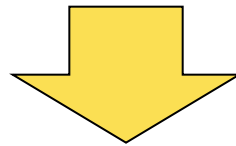
- **Concern about overall time required for prequalification and process time inefficiencies (overall elapsed time, knowing when to expect a response).**
- **Sample testing is an area in which the programme is performing at minimum level of expectations.**

# Recommendations from manufacturers

- **Implementing fixed timelines for review and response.**
- **More up-front collaboration between applicants and the WHO-PQ to develop a shared understanding of requirements and deliverables.**
- **Sample testing performed in parallel with the Product Summary File (PSF) review.**

# **Additional Informal feedback on procedure**

- **Need for harmonization of expectations between different GMP auditors, categorization of deviations and GMP code applied**



- **Retrospective independent review of 20 audit reports commissioned in 2012. The 33 recommendations received triggered a CAPA which is currently being implemented**





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[http://www.who.int/immunization\\_standards/vaccine\\_quality/PQ\\_vaccine\\_list\\_en/en/](http://www.who.int/immunization_standards/vaccine_quality/PQ_vaccine_list_en/en/)

[http://www.who.int/immunization\\_standards/vaccine\\_quality/vq\\_index/en/index.html](http://www.who.int/immunization_standards/vaccine_quality/vq_index/en/index.html)