

Programme update

Prequalification of Vaccines

UN Prequalification of Medicines, Diagnostics and Vaccines

6th Consultative Stakeholder Meeting

4 April 2011

David Wood, WHO/IVB/QSS

Outline

Good news

- A vaccine designed for Africa
- Approval, for regulation of vaccines, of China's State Food and Drug Administration
- Revision of the vaccines PQ process
- PQ statistics

Special challenges of vaccines

- discovery of a previously unidentified virus in a PQ'd vaccine
- identification of a serious adverse event associated with PQ'd vaccines

Bad news

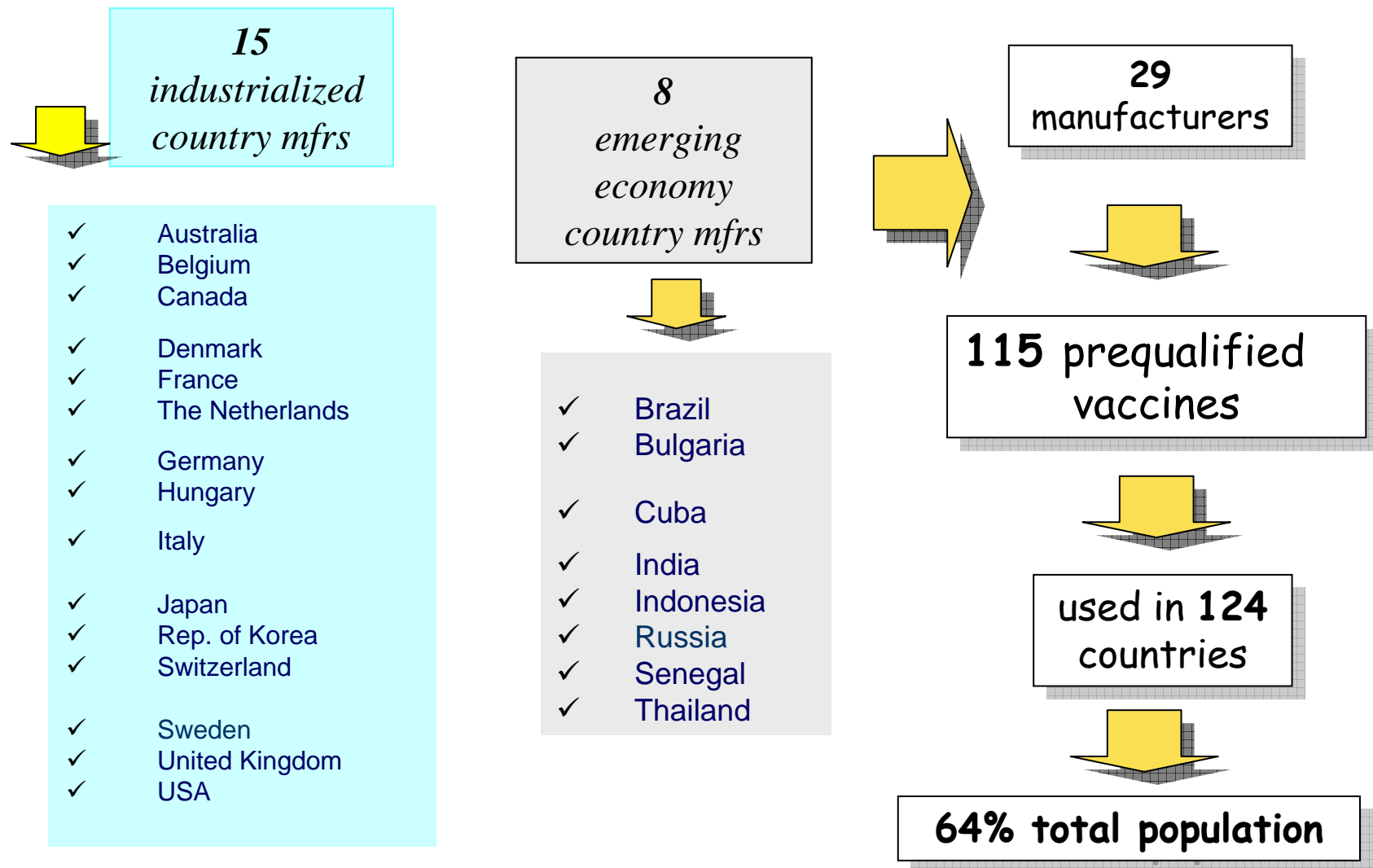
- delisting of a previously PQ'd vaccine
- increasing number of quality defects being reported from the field

Potential solutions

- intensified support to key NRAs?
- intensified risk mitigation evaluations of manufacturers?



Vaccines prequalified by WHO: Status 2010 (assured quality)

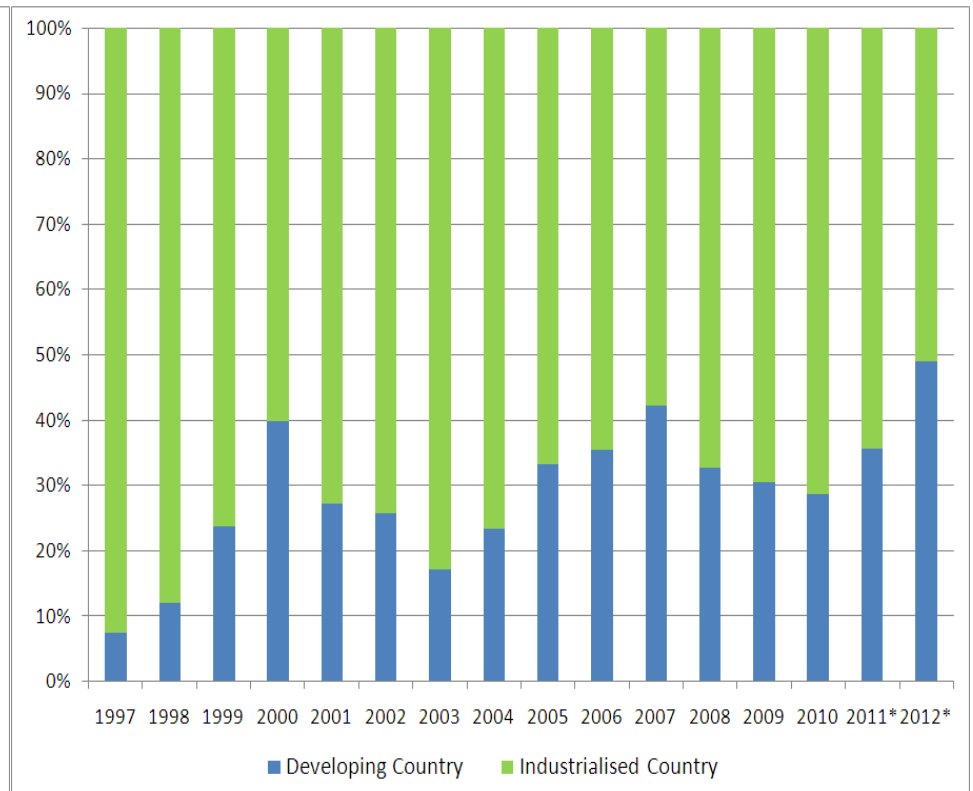
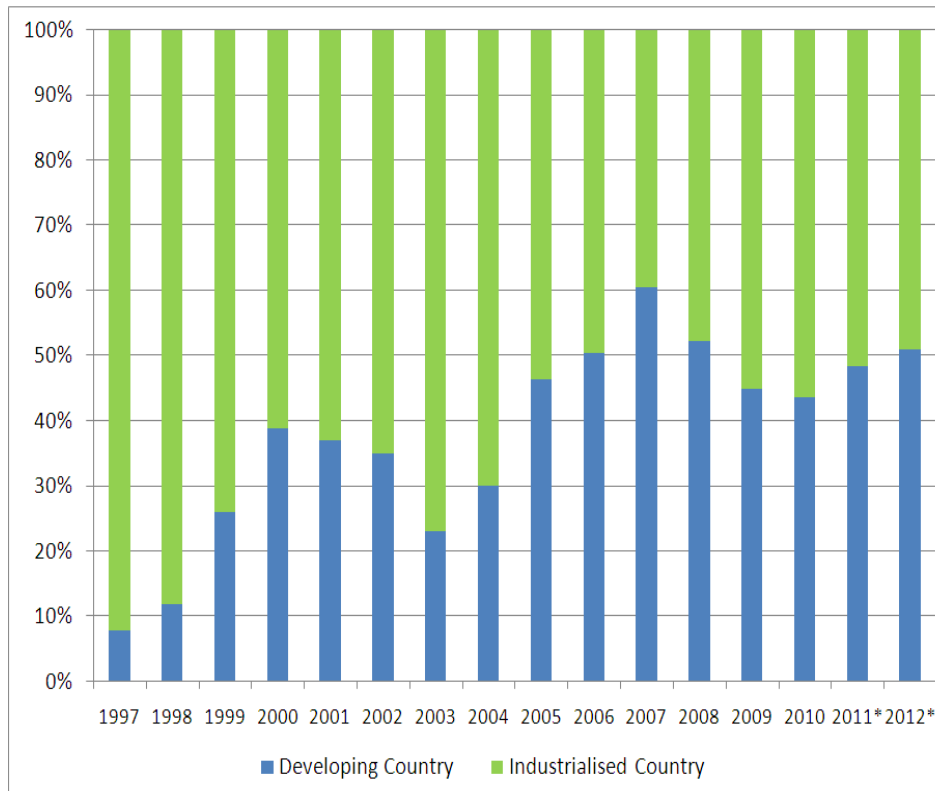


A growing portion of vaccines procured by UNICEF come from emerging market country manufacturers

2010: 1.15 billion doses with a value of US\$ 240 million

● Share by volume

● Share by value



*2011 – 2012 Data based on awards already made



Good news



MenAfriVac – a long-awaited vaccine





Eliminating epidemic meningitis
as a public health problem
in sub-Saharan Africa



✓ **Advantages of the model of development of Menafrivac by MVP consortium**

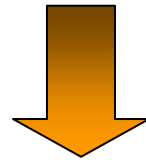
- Allows the production of a low-cost vaccine
- Includes a north-to-south transfer of technology and capacity
- Allows creation of a product custom-made for Africa

Example : Menafrivac has been formulated in 10-dose vials containing preservative, which is best suited for mass immunization campaigns but which would have limited use in industrialized countries.

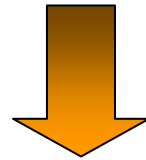


Vaccine prequalification- reliance on NRA

- The responsible National Regulatory Authority (usually that of the producing country) is independent and functional

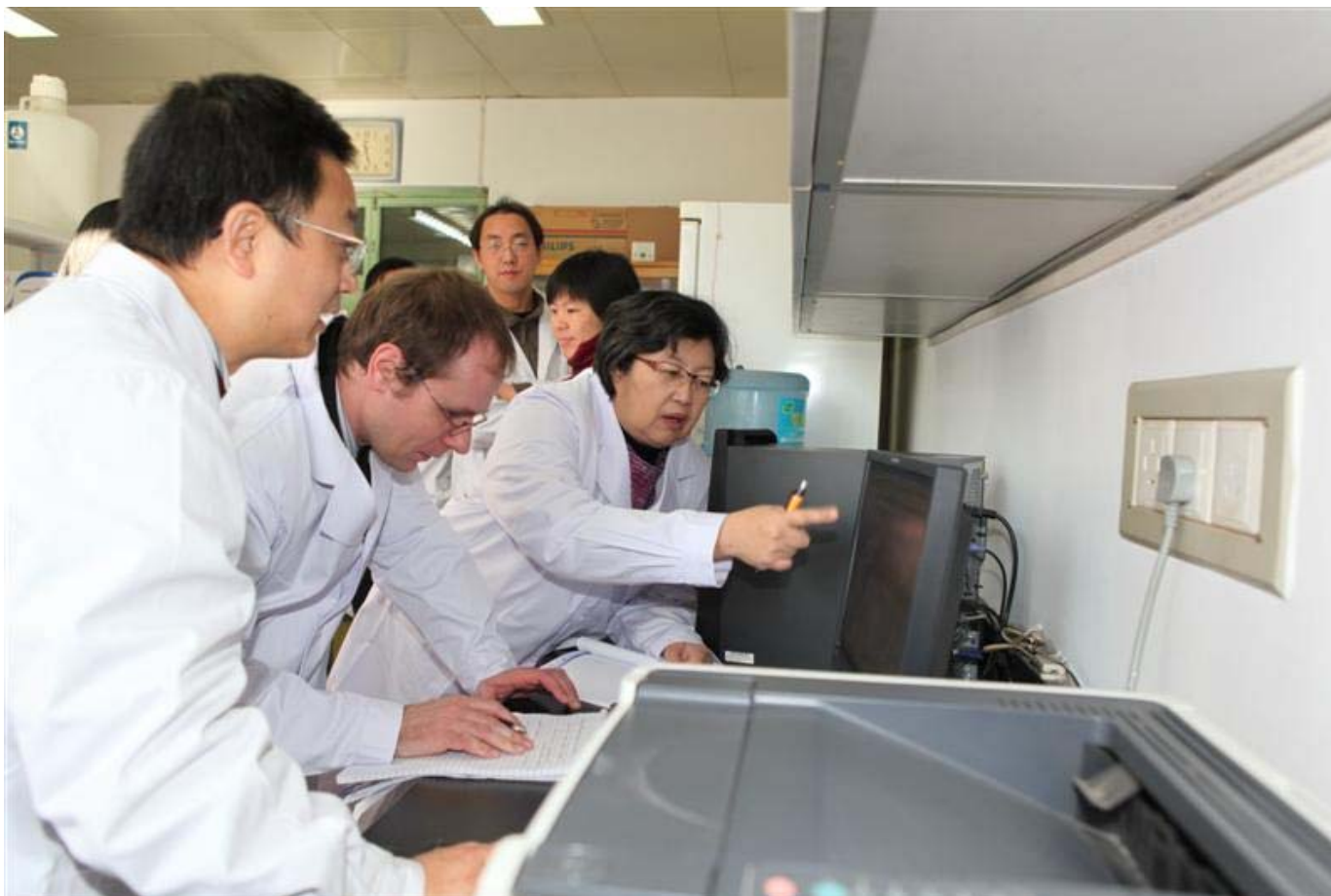


- Meets all the critical indicators required for prequalification purposes following a WHO independent assessment



- The status of the NRA is reassessed at regular intervals

Approval of the State Food and Drug Administration, China



Approval of the State Food and Drug Administration, China (2)

- *One of Lahouari's slides on the next steps in the roadmap to be added*



Approval of the State Food and Drug Administration, China (3)



- Meeting attended by more than 30 vaccine manufacturers from China
- Strong interest in supply to global market through WHO PQ and UN procurement
- Priorities being established for submissions from China

Prequalification process

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



Revised procedure in place from January 2012

Revised vaccines PQ procedure

- Introduced option for increased collaboration with mature National Regulatory Authorities (NRAs) following a risk-based approach
 - Collaborative agreements will be negotiated with eligible NRAs in the coming six months
 - WHO will retain responsibility for ensuring compliance with UN tender specifications and programme needs
 - WHO will also continue to be responsible for the continuous monitoring of the quality and safety of products, and also for a targeted testing programme



Revised vaccines PQ procedure (2)

- The revised procedure defines critical and desirable programmatic characteristics of vaccines and provides a clear review mechanism
 - clear message to manufacturers on what is required for prequalification.
 - reduced timeframe for PQ is expected
- Clear definition of desirable product characteristics expected to facilitate the development of vaccines better suited for the countries and circumstances in which they are expected to be introduced



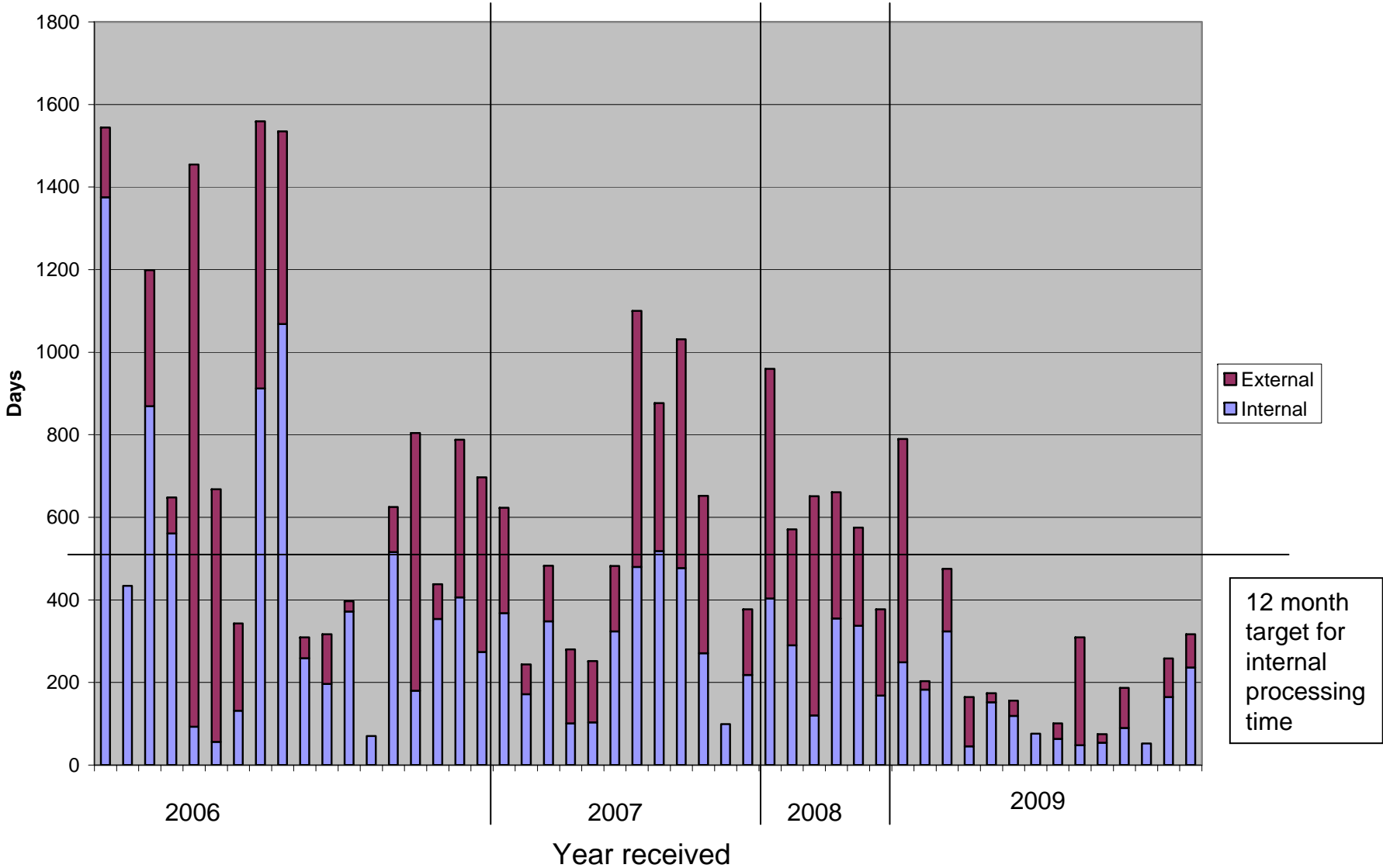
Technical resources to assist applicants

- Development of "**Points to Consider**" documents to guide manufacturers and reviewers on requirements for PQ:
 - "*Clinical considerations for evaluation of vaccines for prequalification*" (published on the web site)
 - "*Environmental monitoring of clean rooms in vaccine manufacturing facilities*" (new draft published for comment until 1 June 2011)
 - "*Variations in vaccine manufacturing*" (pending)
- Development of document on "**Programmatic suitability**"
 - "*Assessing the Programmatic Suitability of Vaccine Candidates for WHO prequalification*" (Final draft pending adoption by IPAC, April 2011)



PQ performance

Pre-Qualification Process Time
(completed applications)



More vaccine PQ statistics

Other PQ activities	2009	2010
Reassessments	11	12
Annual reviews and variations	6	21
Testing (lots)	124	NA
Complaints from the field	3	13
AEFI	7	7
Meetings w/manufacturers	62	80
Meetings w/NRAs	10	59
Other meetings	23	27

NA: Not available



Equipment prequalification (PQS): progress overview

PQS Categories	Description	# Products PQ 2009	# Products PQ 2010
E001	Cold rooms and related equipment	0	2
E003	Refrigerators and freezers.	7	16
E004	Cold boxes and vaccine carriers.	1	32
E005	Coolant packs - water-packs	0	16
E006	Temperature monitoring devices.	9	10
E008	AD syringes	30	28
E010	Waste management: Safety boxes	9	10
E013	Therapeutic injection devices	37	48
		93	162

- 57% PQ increase in 2010
- Stabilization of # Temperature monitoring devices, syringes, safety boxes
- One model of jet injector under PQ process
- Additional anti-freeze cold boxes and solar powered equipment in the pipeline



Equipment categories: innovations

Collaborative efforts with partners for innovations

- E003: Refrigerators/freezers**

Develop specifications for a maxi-fridge 300 to 800 liters for an increased storage volume at district level

- E004: Cold boxes and vaccine carriers**

CDC and SEEDRL3C on their concept of cold box with an anti-freeze property although using icepacks

Progressive introduction of non-water phase change material (cooling performance with no freezing)



Equipment categories: innovations (2)

Collaborative efforts with partners for innovations

- **E007: Accessories**

Revision of specifications for auto-voltage regulators

- **E008/E013: Injection devices**

ISO revision

- **E010: Waste management**

Specifications for autoclave (decontamination of waste)



Special challenges of vaccines



Rotavirus vaccines

Two rotavirus vaccines have been PQ'd and are being supplied through UN procurement

- April 2010 – use of novel technology shows porcine circovirus (PCV) in one product and PCV DNA in the other product
- August 2010 – reports of a small excess of cases of intussusception with one product

Benefit/risk re-evaluated for each product after each event

- Excellent cooperation from NRAs of record (EMA and US FDA)
- Excellent cooperation from manufacturers (GSK and Merck)
- Risk assessment done by WHO Global Advisory Committee on Vaccine Safety
- Risk mitigation done by WHO Strategic Advisory Group of Experts on Immunization

Conclusion in both cases was that benefit/risk continued to be very favourable



Bad news



Delisting of a PQ'd vaccine



WHO Statement
28 July 2010

SHAN5 VACCINE DELISTED FROM WHO PREQUALIFICATION

As of 28 July 2010 the World Health Organization (WHO) has removed the Shantha Biotechnics (India) produced pentavalent Shan5 (DTwP-hepatitis B-Hib) vaccine from the list of prequalified vaccines.

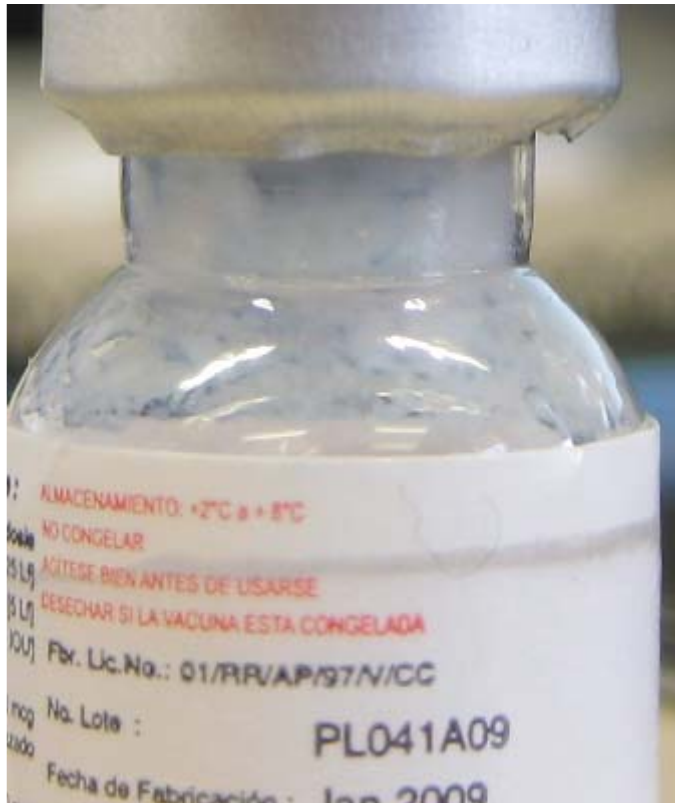
This action is based on the advice of an ad hoc committee of experts, following incidents of white sediment sticking to Shan 5 vaccine vials that was difficult or impossible to resuspend (flocculation). There have been no reports of any side effects from the use of Shan5.

WHO recommends that countries continue vaccination using pentavalent vaccine from an alternative manufacturer or an alternative DTP-containing vaccine. Countries should contact WHO or UNICEF country offices (or the in-country entity facilitating the shipments or procurement of these vaccines) for assistance with ensuring sufficient supply of vaccine for continuation of immunization programmes.

http://www.who.int/immunization_standards/vaccine_quality/quality_issues/en/



Quality defects being reported increasing



White sediment sticking to vaccine vials of Shan5 vaccine

**Sample received from Shantha Biotechnics (India)
Lot: PL041A09 February 2010**

Potential solutions



Options being explored

- Intensified support to key NRAs
- Intensified risk mitigation evaluations of manufacturers
 - quality management systems
 - post-marketing surveillance capacity



Further information

- www.who.int/immunization
- http://www.who.int/immunization_standards/
 - www.who.int/biologicals
 - www.who.int/vaccine_safety



Back-up slides



2011/12 PQ Priorities (High)

- Bivalent oral polio (bOPV1+3)
- DTwP based pentavalent combination (fully liquid DTwP-Hep B-Hib)
- Inactivated polio (IPV)
- Meningococcal A-containing conjugate
- Meningococcal AC-containing polysaccharide
- Meningococcal W-containing polysaccharide
- Meningococcal W-containing conjugate
- Pneumococcal conjugate
- Rotavirus
- Trivalent oral polio (tOPV)
- Yellow fever



2011/12 PQ Priorities (Medium)

- DTwP-based combination containing IPV (DTwP-Hep B-Hib-IPV)
- Human papillomavirus
- Influenza H5N1 for stockpile
- Influenza seasonal
- Japanese encephalitis
- Measles and measles-containing combination
- Monovalent oral polio (1, 2 and 3)
- Oral cholera



2011-2012 PQ Priorities (Low)

- BCG
- Diphtheria-tetanus-pertussis (DTwP)
- DTwP-based pentavalent combination (lyophilized-liquid DTwP-Hep B+Hib)
- DTaP and DTaP combination (aP = acellular pertussis)
- DTwP-based tetravalent or pentavalent combination containing IPV (DTwP-Hib-IPV or DTwP-IPV)
- Hepatitis A
- mOPV2 for stockpile
- Rabies
- Rubella monovalent
- Tetanus toxoid (TT)
- Typhoid
- Varicella



Vaccines with no priority (and will not be accepted for PQ evaluation)

- DTwP-based tetravalent combination (DTwP-Hep B, DTwP-Hib or DTwP+Hib)
- Diphtheria-tetanus vaccine for children (DT)
- *Haemophilus influenzae type b* monovalent
- Hepatitis B monovalent
- Polysaccharide pneumococcal
- Tetanus-diphtheria for adults (Td)
- Influenza H1N1
- Any other vaccine not in the PQ priority categories





Regulatory functions depending on vaccine source

Regulatory functions	Vaccine source		
	UN agency	Direct Procurement	Production
Regulation System	✓	✓	✓
Licensing	✓	✓	✓
AEFI monitoring	✓	✓	✓
Lot release	Functions assured by NRA of producing country and WHO PQ system	✓	✓
Access to laboratory		✓	✓
Regulatory inspections	Functions assured by NRA of producing country		✓
Authorization of clinical trials			✓



Communication resources

- Database of prequalified vaccines (providing more details on Pq'd product) **Implemented**
- Publication of short document providing rationale for acceptance of a specific vaccine (Vaccine Product Assessment Report: VPAR) **Pending**
- Publication of list of contracted laboratories **Pending**
- Publication of list of products accepted for evaluation and charts of progress for each product **Pending**
- Publication of updated priority list for 2011-2012 **Implemented**



Vaccine prequalification

Partnership with NRA of producing country

