

Post- prequalification Monitoring: focus on variations to a PQd vaccine

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Presentation Outline

- ✓ Revised PQ procedure & post PQ monitoring activities.
- ✓ Reporting to WHO/HIS/EMP/QSS-VQR-PQ of changes to PQed vaccines.
- ✓ PQ position & proposals.



Background information on the PQ procedure

The latest revision of the PQ procedure took place in 2010

Adopted by ECBS in October 2010. Published on Technical Report Series 978 Annex 6

Features of the revised procedure with regards to post-PQ monitoring include:

- ✓ Annual reporting by manufacturers (PQVAR) (Section 8)
- ✓ Reassessments (Section 9)
- ✓ Testing programme (Section 10)
- ✓ Investigation and resolution of complaints and reports of AEFI from the field (Section 11)



Contents of PQVAR

- The manufacturer should provide a summary of changes/updates to the product(s) that have been implemented since the previous annual report
- The manufacturer should provide testing results from the ongoing stability programme since the previous annual report
- Production and distribution data, (Different presentations to be listed separately).
- The manufacturer should provide details of GMP inspections (in which the prequalified product was within the scope of inspection) performed since the previous annual report
- A summary update on the implementation of post-prequalification commitments should be provided by the manufacturer if these are indicated in the approval letter or commitment report.
- The Public Safety Update Report should be provided

PQVAR CAN BE SUBMITTED ONLINE



Reporting changes to PQd vaccines

PQ Secretariat is frequently asked on how & what to report, what information has to be provided to support:

- A change in the production process
- A change in testing methods
- A change due to production scaling up
- Change of facilities (new / refurbished building).



Reporting changes to PQd vaccines

TRS 978 Annex 6 Section 8: Annual Reporting. PQVAR.

Part A refers to changes / variations.

In view that WHO is not a NRA and that the PQ Programme relies on the oversight of NRAs.

We need to define:

What changes should be part of the Annual reporting (PQVAR)?

What changes should be immediately notified to WHO?

What changes require review and approval by PQ before implementation



Reporting changes to PQd vaccines

In principle:

- “Every” change should be part of the annual reporting (PQVAR).
- Minor changes that may impact on the administrative information of the PQd product/company should be of immediate notification to WHO PQ Secretariat. (i.e. name of the company, contact person, etc)



Reporting changes to PQed vaccines

A note for guidance is under preparation: "Guidance on variations to a prequalified vaccine" in which the WHO PQ Secretariat is proposing 3 levels of reporting:

R: Annual reporting (PQVAR).

N: Immediate notification to WHO PQ Secretariat.

A: Approval by WHO PQ Secretariat before implementation.



Reporting changes to PQd vaccines

“GUIDANCE ON VARIATIONS TO A PREQUALIFIED VACCINE” .

- Defines the three levels of reporting (R, N, A).
- Describes the conditions that have to be fulfilled in every category or level of reporting.
- Defines clearly what information or supporting data has to be reported.
- Defines time frame to assess the changes.



Reporting changes to PQed vaccines

“GUIDANCE ON VARIATIONS TO A PREQUALIFIED VACCINE”.

1. Introduction.
2. Objectives.
3. Scope and application.
4. National and WHO reporting requirements.
5. Reporting categories.
6. Appendix 1: Administrative changes.



N: Immediate notification to WHO PQ Secretariat.

Description of the change	Conditions to be fulfilled	Supporting data	Reporting category
A.1 Change in the name and/or address of the marketing authorization holder that was granted the prequalification of the vaccine.	1	1, 2	N
Conditions			
1. The marketing authorization holder shall remain the same legal entity.			
Documentation 1. Approval for change of name as per statutory requirements. 2. Notification of new name if the manufacturer is sold or merged with another company. Note that if address changes due to site change then PSF needs to be resubmitted with fresh quality; safety and efficacy data.			
A.2 Company sale, purchase, merger.	1	1, 2, 3	N
Conditions			
1. The marketing authorization holder shall remain the same legal entity.			
Documentation 1. Approval for sale/purchase as per statutory requirements. 2. Notification of new name if the manufacturer is sold or merged with another company. 3. Revised labeling.			



A / R: Notifications to WHO PQ Secretariat.

Description of the change	Conditions to be fulfilled	Supporting data	Reporting category
J2. Effect on the existing finished products in a finished product manufacturing facility involving introduction of a new product or change in concurrence:			
a) Conversion of a finished product manufacturing facility from single-product to multi-product).	None	1 - 3	A
b) Conversion of formulation and filling area(s) from campaign to concurrent for multiple product mfg areas.	1	1 - 2	R
c) Introduction of new product into an approved multi-product formulation/filling suite.	2 - 4	1 - 3	R
Conditions			
<ol style="list-style-type: none"> 1. The manufacturing process is a closed process for shared areas. 2. The newly introduced product does not introduce significantly different risk issues. 3. The newly introduced product is not of significantly different strength (i.e., mg .vs. µg). 4. The maximum allowable carry-over is not affected by the introduction of the new product. 			
Documentation			
<ol style="list-style-type: none"> 1. Cleaning procedures (...validation report; cleaning protocol); demonstrating lack of cross-contamination. 2. Change-over procedures for shared product-contact equipment, segregation procedures, as appropriate. If no revisions, a signed attestation that no changes were made to the change-over procedures. 3. Information on the product(s) which share the same equipment (e.g., therapeutic classification). <p>Mfr could make reference to relevant documents (SOPs, validation protocols / reports, change-over and segregation procedures, etc. WHO Prequalification Secretariat may request documented evidence.</p>			

Reporting changes to PQd vaccines

Type A: Safety & Efficacy

Clinical data required as evidence of safety and efficacy in populations where vaccines are supplied through UN agencies, thus subject to the prequalification by WHO, may differ from the set of clinical data that an NRA considers sufficient to issue a Marketing Authorization.

Variations Type A are defined as those changes to the labeling of a prequalified vaccine that has the potential to increase the exposure levels of the product, either by expanding the population that is exposed, or by increasing individual exposure. In principle, these are changes to the existing text of the labeling of a PQd vaccine.

Supported by:



This may include but is not limited to: clinical trials (whether focused on efficacy or safety), epidemiological data/study results, pharmacovigilance studies, PSURS, review reports/analysis of specific safety concerns, pharmacovigilance plans.

Reporting changes to PQd vaccines

Type R: Safety & Efficacy.

This is defined as any change to the label that is not expected to impact the safety, efficacy, and/or effective use of the PQed vaccine. Implementation without prior review by WHO PQ Secretariat. Changes are reported as part of the PQVAR.

It may include results of confirmatory clinical trials (either intermediate or final) that were part of a commitment by the manufacturer at the time of PQ, that does not imply any change in the labeling of the prequalified vaccine.



2 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



Risk based approach to reassessments

- Database developed that saves information from PQVAR
- Risk analysis conducted based on the following criteria:
 - Status of NRA (functionality, information sharing, warning letters, etc)
 - Number and type of variations made
 - Stability data
 - Distribution data
 - Testing programme results (OOS)
 - Complaints, reports of AEFI
- Products are prioritized based on outcome of the risk analysis (RPN) for reassessment the following year



Post prequalification activities

Other PQ activities	2009	2010	2011	2012
Reassessments	11	12	10	12
Annual reviews and variations	6	21	74	53 (448)*
Testing (lots)	124	159	183	105
Complaints/other issues of concern	3	13	16	15
AEFI	7	7	7	14
Meetings with manufacturers	62	80	71	119
Meetings with NRAs and others	33	86	64	109

* changes



Thank you

