SERUM INSTITUTE OF INDIA PVT LTD

Vaccine Prequalification Dossier – Module I Requirements and Challenges.

DCVMN WORKSHOP ON CTD 27TH MARCH 2019 SINGAPORE.

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Formats of PQ application

- **Existing format** - Product summary file (PSF) having 10 chapters.
- **Alternate Format** - CTD linked PSF wherein manufacturing and QC information from PSF can be referred to respective CTD sections
- **Proposed format –** CTD format consisting of ICH M2 to M5 with additional WHO specific Module 1.

Ref: Procedure for Prequalification of Vaccines (WHO Technical Report Series 978/WHO TRS 978.

Transition from PSF to CTD format

- In September 2016, WHO advised us to submit WHO PQ application in CTD format as submitted to the NRA of country of origin along with “Supplement to CTD submissions for prequalification of vaccines”.
- in March 2017 a draft guideline on PQ submission format was published for comments from industry wherein WHO proposed to submit PQ dossier in CTD format (M2-M5) + WHO specific Module 1. Several comments were provided by many manufacturers.
- In December 2017, WHO again published a revised procedure wherein Module 1 requirements were amended.
- Till the grace period for complete switch from PSF to CTD is announced by the WHO, manufacturer can still submit WHO PQ application in PSF format.

Amendments in Module 1 requirements

Module 1 as on March 2017		Module 1 as on December 2017	
Section	**Description**	**Section**	**Description**
1.4.3	Copy of marketing authorizations for all formulations and presentations of the vaccine submitted for prequalification.	1.4.3	1.4.3. Copy of marketing authorizations for all formulations and presentations in the Country of Manufacture and/or the Country of Reference of the vaccine submitted for prequalification, or the EMA scientific opinion for article 58 products
1.4.5	If the vaccine is a Genetically Modified Organism, supply a copy of the Environmental Risk Assessment.	1.4.5	If the vaccine contains or consists of genetically modified organisms (GMOs), supply a copy of the Environmental Risk Assessment (GMO means an organism in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination)
1.5.8	Not available	1.5.8	1.5.8 self-assessment against programmatic suitability for prequalification (PSPQ) criteria. http://apps.who.int/iris/bitstream/10665/148168/1/WHO_IVB_14.10_eng.pdf

Amendments in Module 1 requirements

Module 1 as per the March 2017		Module 1 December 2017	
Section	**Description**	**Section**	**Description**
1.6	Supplemental pre-clinical and clinical Information (Pre and post marketing). It was not clear that do we need to provide same pre-clinical and clinical information as provided in Module 2 and Module 5.	1.6	A note has been introduced as "**Where data is not already included in the NRA submission or modules 2-5 submitted for Prequalification"**
1.6.9.2	Under post marketing safety documentation: Initial evaluation of vaccines that have been in the market for a **long time** or reassessment of already prequalified vaccines .	1.6.9.2	Initial evaluation of vaccines that have been in the market for **more than five years** or reassessment of already prequalified vaccines (**The latest PSUR may be provided**)
1.7.5	**Under Regulatory Actions:** Dosage or schedule changes since the initial marketing authorization	1.7.5	Dosage or schedule changes since the initial marketing authorization in the country of manufacture and/or the country of reference
--	Grace period till 31 December 2017 was mentioned to accept PQ application in PSF format	--	Grace period is still to be announced.

Structure of Current WHO Module 1

1.1 Table of contents

1.2 Correspondence (New)

1.2.1 Copy of the letter from the manufacturer indicating the intention to submit an application for prequalification of the vaccine and of the acknowledgement from WHO of the acceptability for submission.

1.2.2 Agreed minutes of any pre-submission meetings between WHO/PQT and the applicant

1.3 Site master file (Chapters 1, 2 and 3)

1.4. Compliance information (Chapter 10, 10.1)

1.4.1 – 1.4.5 contains establishments certificate, GMP certificate, manufacturing licence and environmental risk assessment and policy for assigning manufacturing date **(Chapter 7, 7.4)**.

Structure of Current WHO Module 1

1.5. Vaccine composition, presentations and scheduling information

1.5.1. Description of presentations available to UN agencies, including diluent (if applicable), combination products, forms, dose sizes and type of containers and indicate Vaccine Vial Monitor (VVM) type and location. **(Chapter 4, 4.2)**

1.5.2 Vaccine temperature stability profile. **(Chapter 7, 7.2)**

1.5.3 Description of immunization /administration devices to be delivered with the vaccine **(Chapter 4, 4.2)**

1.5.4 Recommended schedule and route of administration **(Chapter 4, 4.3)**

1.5.5 Artworks or mockups of labels of primary containers and secondary packaging for the product **(Chapter 4, 4.4)**

Structure of Current WHO Module 1

1.5.6. Samples of package inserts (in English) to be used for supply through UN agencies. **(Chapter 4, 4.4)**

1.5.7. Template of lot summary protocol to be provided to UN agencies.

(Chapter 4, 4.5)

1.5.8 self-assessment against programmatic suitability for prequalification (PSPQ) **(New)**

Structure of Current WHO Module 1

1.6. Supplemental pre-clinical and clinical Information (Pre and post marketing)

1.6.1. List of pre-clinical studies sponsored by applicant – not included in M 2.6 and M 4. **(Chapter 8, 8.2.6)**

1.6.2 List of all clinical trials sponsored by the applicant relevant for the application not part of M-5.2. **(Chapter 8, 8.2.1)**

1.6.3 Cross reference to the final approved protocol by ERC and NRA **(Chapter 8, 8.2.1)**

1.6.4 List of any clinical trials that are known to be currently ongoing with the vaccine candidate, not relevant to the current PQ application **(Chapter 8, 8.2.2)**

1.6.5 List of other studies with applicant product – not included in Module 5 - for which the applicant is not the sponsor **(Chapter 8, 8.2.2)**

Structure of Current WHO Module 1

1.6. Supplemental pre-clinical and clinical Information (Pre and post marketing)

1.6.6 Complementary Clinical summary supporting the use of the product worldwide by UN agencies. **(Chapter 8, 8.2.3)**

1.6.7 Assessment Report from the NRA(s) **(Chapter 8, 8.2.4)**

1.6.8. Clinical Independent expert report **(Chapter 8, 8.2.5)**

1.6.9 Post marketing Safety documentation **(Chapter 8, 8.3)**

Structure of Current WHO Module 1

1.7. Regulatory actions

1.7.1 Information on refusals, withdrawals, suspensions, including those initiated by the manufacturer. **(Chapter 10, 10.1)**

1.7.2. List of lots rejected by an NRA, if applicable **(Chapter 10, 10.2)**

1.7.3. Restrictions on distributions and recalls of lots, including those initiated by the manufacturer **(Chapter 10, 10.3)**

1.7.4. Clinical trial suspensions **(Chapter 10, 10.4)**

1.7.5. Dosage or schedule changes since the initial marketing authorization in the country of manufacture and/or the country of reference **(Chapter 10, 10.5)**

1.7.6. Changes in target populations since the initial marketing authorization in the country of manufacture and/or the country of reference **(Chapter 10, 10.6)**

Structure of Current WHO Module 1

1.8. Distribution information

1.8.1. Quantity of finished product distributed in the domestic market of the country of manufacture and/or the country of reference and exported in the last three years, by presentation. Clearly indicate if numbers refer to vials or doses. **(Chapter 9, 9.1)**

1.8.2. List of countries where the product has received a Marketing Authorization, indicating if product has been supplied in those countries. **(Chapter 9, 9.2)**

1.8.3. Description of the release process by the NRA/NCL and recording system for distribution **(Chapter 9, 9.3)**

1.8.4 Summarize the packaging procedures for international shipments for UN agencies and the validation (according to relevant, current WHO guidelines) of this packaging. **(Chapter 9, 9.4)**

Comparison between WHO M1 and M1 proposed by DCVMN

M 1 proposed by DCVMN		WHO M1	
Section	**Description**	**Section**	**Description**
1.0	Cover letter	1.2	Correspondence
1.1	Comprehensive table of content	1.1	Table of Contents
1.2	Application Form (Administrative data)		
1.3	Product Information	1.5.1	Description of presentations available to UN agencies, including diluent (if applicable),
		1.5.3	Description of immunization /administration devices to be delivered with the vaccine
		1.5.4	Recommended schedule and route of administration
		1.5.4	Recommended schedule and route of administration
		1.5.5	Artworks or mockups of labels of primary containers and secondary packaging *(Continue.... on next slide)*

Comparison between WHO M1 and M1 proposed by DCVMN

M 1 proposed by DCVMN		WHO M1	
Section	**Description**	**Section**	**Description**
1.3	Product Information	1.5.6.	Samples of package inserts (in English)
		1.4.4.	Policy for assignment of date of manufacture of each component as well as the final product
1.4	Information about experts	1.6.8.	Clinical Independent expert report
1.5	Specific Requirements for Procedures - Applications	1.5.8	self-assessment against programmatic suitability for prequalification (PSPQ)
1.6	Environmental Risk Assessment	1.4.5	Environmental Risk Assessment (If GMO)
1.7	Information relating to Pharmacovigilance	1.6.9	Post marketing Safety documentation
1.8	Correspondence	1.2.2	Minutes of pre-submission meetings
1.9	Clinical/ Bioequivalence	1.6	(1.6.1 to 1.6.8) Supplemental pre-clinical and clinical information

Comparison between WHO M1 and M1 proposed by DCVMN

M 1 proposed by DCVMN		WHO M1	
Section	**Description**	**Section**	**Description**
1.10	Regulatory Certification	1.4.1.	Certificate of Establishment Licensing.
		1.4.2.	Copy of GMP certificate
		1.4.3.	Marketing authorizations
		1.7	1.7.1 to 1.7.6 Regulatory actions
1.11	Manufacturer declarations and Certificates	1.5.2	VVM Type and location - Vaccine temperature stability profile
1.12	Shipping & Distribution Details	1.8	1.8.1 to 1.8.3 - Distribution information
		1.8.4	Packing for international shipment
1.13	Lot / Batch information	1.5.7.	Sample of lot summary protocol
1.14	Country additional data	1.3	Site master file (SMF)

Challenges in adoption of CTD format

- The revised PQ application format will not be helpful for countries not using CTD (Like Guyana, Liberia, Sierra Leon, Madagascar,....) and having differences in CTD format (Viz. Asian countries using ACTD format, which is different from ICH CTD.).
- WHO module 1 requirements varies from country specific requirements and from the manufacturers proposed module 1. It would be very helpful if WHO also could align to the proposed manufacturers proposed format

THANK YOU FOR YOUR TIME AND ATTENTION