

WHO-DCVMN Joint workshop on Collaborative Registration Procedure (CRP) for Vaccines

dcvmn
Developing Countries Vaccine
Manufacturers Network



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Content of Presentation

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DCVMN RAWG CRP Survey - Overview of Respondents

- ❑ DCVMN has conducted an extensive survey between 10th August to 2nd September 2022 to capture the sentiments, experiences and opinions on improving the WHO Collaborative Review Procedure (CRP).
- ❑ The objective of survey was:
 - To understand how many members have attempted to register a product using CRP.
 - To determine the success of the applications.
 - To determine bottlenecks in the process.
 - To understand challenges and identify improvement steps of the current process.
- ❑ This survey was completed by more than 36 organizations and the key positive points are summarized below:
 - Majority of the participants have used CRP, and have experienced benefits from the abbreviated process.
 - The participants who has not utilized CRP till date have shown their keen interest to utilize it in future and would like to know more about the same (training module/session).
 - Few participants faced challenges to utilize CRP process for major post-approval variation.
 - Participants got approval as per stipulated time-line of the CRP process i.e., *120 days* (in comparison with standard local registration timeline)
 - Few participants also confirmed that there was no GMP audit requested by the local NRAs targeted through CRP.
- ❑ The survey also outlined some challenges, bottlenecks, which are captured in next slides (*including the suggestions for CRP process improvement*)

Advantages of CRP (1)

❑ FOR NRA:

- To receive a PQ-approved data package, well organized in CTD format, in line with PQ requirements.
- Availability of WHO assessment and inspection outcomes to support national decisions.
- Opportunity to interact and learn from PQ assessors and inspectors.
- Demonstrating and strengthening the NRA efficiency.
- Having assurance about registration of 'the same' vaccine, as is prequalified rather than only relying on WHO PQ certificate.
- Quality control by same methods and specifications for product release by NRA.
- Easier post-registration maintenance/ lifecycle management.
- Having a model process for mutual co-operation in registrations.
- National legislation and sovereignty are not affected.

Advantages of CRP (2)

❑ FOR WHO:

- Expedited availability of a WHO-PQ'ed vaccine to the target population in the Impacted country.
- Feed-back on WHO prequalification outcomes from the NRAs.

❑ FOR MANUFACTURER:

- Harmonized data for WHO-PQ and all over registrations in respective NRAs
- Facilitated interaction with NRAs in assessment, inspections, performance evaluations
- Expedited/ accelerated and more predictable registration
- Comparatively easier post-registration/ lifecycle management
- Confidentiality of commercially sensitive information is respected

Experience, so far...

- ❑ Even though small numbers of vaccine manufacturers used CRP, they have experienced advantages and positive results of this process i.e., Timeline stated as per the CRP process was followed during the approval, NRAs informed promptly after approval by providing registration certificates.
- ❑ It helped to achieve an expedited registrations in many countries. As many NRAs were interested for registration and availability of the vaccines in their region.
- ❑ Few countries requested country specific documents like country specific Risk Management Plans (RMPs), mock-ups/ labelling components, SmPC, package inserts etc.
- ❑ Few countries refused to accept PAC variations thereafter informing that WHO does not have any mechanism to approve such variations.
- ❑ Few NRA require submission of additional information like, “process data/ batch records, raw data of stability studies, facility inspection reports”, etc.

What can be Improved in CRP

- ❑ Success rate of the process for vaccines is still indistinct; However, the process is quite successful and streamlined for Pharma (medicinal) products.
- ❑ Manufacturers to be given restricted access to the exchange of information between the WHO-PQT and NRA (*currently the access of web-portal for data exchange is between NRA and WHO only*). Furthermore, a procedure tracking table/tool should be considered and implemented, for clarity and transparency in the process between applicant/WHO/NRA.
- ❑ Clarification needed on how the queries should be; from NRA's to the applicant/PQ holder keeping WHO in the loop OR NRAs to WHO OR WHO to the applicant/PQ holder.
- ❑ Few countries are issuing certificate with validity. Rather, registration should be valid till product is on PQ list
- ❑ As mentioned under Step 3, Appendix 3, Part B (*Decision on acceptance by the NRA*) is currently not received by the applicant/PQ holder.
- ❑ List of vaccines registered through this process is not published on WHO webpage.
- ❑ Variations management is still as per country specific requirement & the CRP PAC process is not followed.

Few Suggestions from DCVMN for CRP Process Improvement

- ❑ List of vaccines approved through CRP procedure to be listed on WHO website along with the approving NRAs.
- ❑ The validity of the vaccine registration certificate licensed via CRP, should be harmonized with the WHO-PQ validity of the vaccine as the CRP relies on the WHO-PQ assessment.
- ❑ Furthermore, a procedure tracking table/tool should be considered and implemented
- ❑ NRA's are requesting applicants to submit country specific dossier (*through CRP process*) that delays the registration process; Therefore, in order to avoid delay, WHO shall emphasize on the acceptance of the agreed format (as per the WHO CTD guidance) to the NRAs.
- ❑ NRA's should accept the WHO's granted GMP status to avoid duplication.
- ❑ There is no clear guidance regarding variation process through CRP. DCVMN suggest that the variation to such NRA's should be simplified and in harmonization with the WHO's guidance for reporting of variations to PQ'ed vaccines July 2015.
- ❑ As the local registration is based on the WHO-PQ under CRP, the mock-ups, SmPC/ package insert, labelling component should be identical with the ones as approved during grant of prequalification by the WHO-PQ.

Expectation of DCVMN (1)

❑ **Reliance on the functional (semi-stringent) NRA** may expedite review and approval of new vaccines & PAC (Post Approval Changes)

- ❑ PQD* - Submission to WHO submission in Parallel to NRA
- ❑ PAC - Submission to WHO submission in Parallel to NRA
- ❑ Inspection - Relay on NRA on-site inspection report

**Pre-Qualified Dossier*

❖ **Action:**

- There's a strong need for a harmonised regulatory guidelines for evaluation of vaccine candidates on high priority.
- Once a harmonised set of guidelines has been established, to extract sections that are most important to be included for standard guidelines for Emergency Use Listing (EUL)/ Licensure of vaccines.

❖ **Condition:**

- Complete data set submission to both (NRA & WHO) and WHO to grant PQ/Approval after the NRA approval.

Expectation of DCVMN (2)

❑ **Lifting the Functional NRAs to Stringent NRA.**

❖ **Action:**

- Roadmap to be designed between WHO and such NRAs
- Action plan and timeline to be published and tracked.

❑ **WHO-PQ/ EUL team may consider to increase the numbers of vaccine reviewer's/experts to incase the availability of PQ/EUL submission slot with overall strengthening of WHO assessment**

❑ **For Novel Vaccine Technologies like mRNA technology, it may be a good idea to set a procedure aimed at 'Platform' rather than Product**

Expectation of DCVMN (3)

Several cost intensive guidelines having been issued by WHO which will have huge impact on both, the overall capacity as also the cost e.g.,

❑ **Batch Specific Sterilization of Lyophilizers**

❖ **Impact**

- It will reduce production capacity of the product by 25%. It will also impact on the over all working life of current Lyophilizers after batch specific sterilization.
- The practice of manual loading to Lyophilizers also criticized, which indirectly put pressure on manufacturers to shift to auto loader which is costly.

❑ **0.2 µm filter implementation**

❖ **Impact**

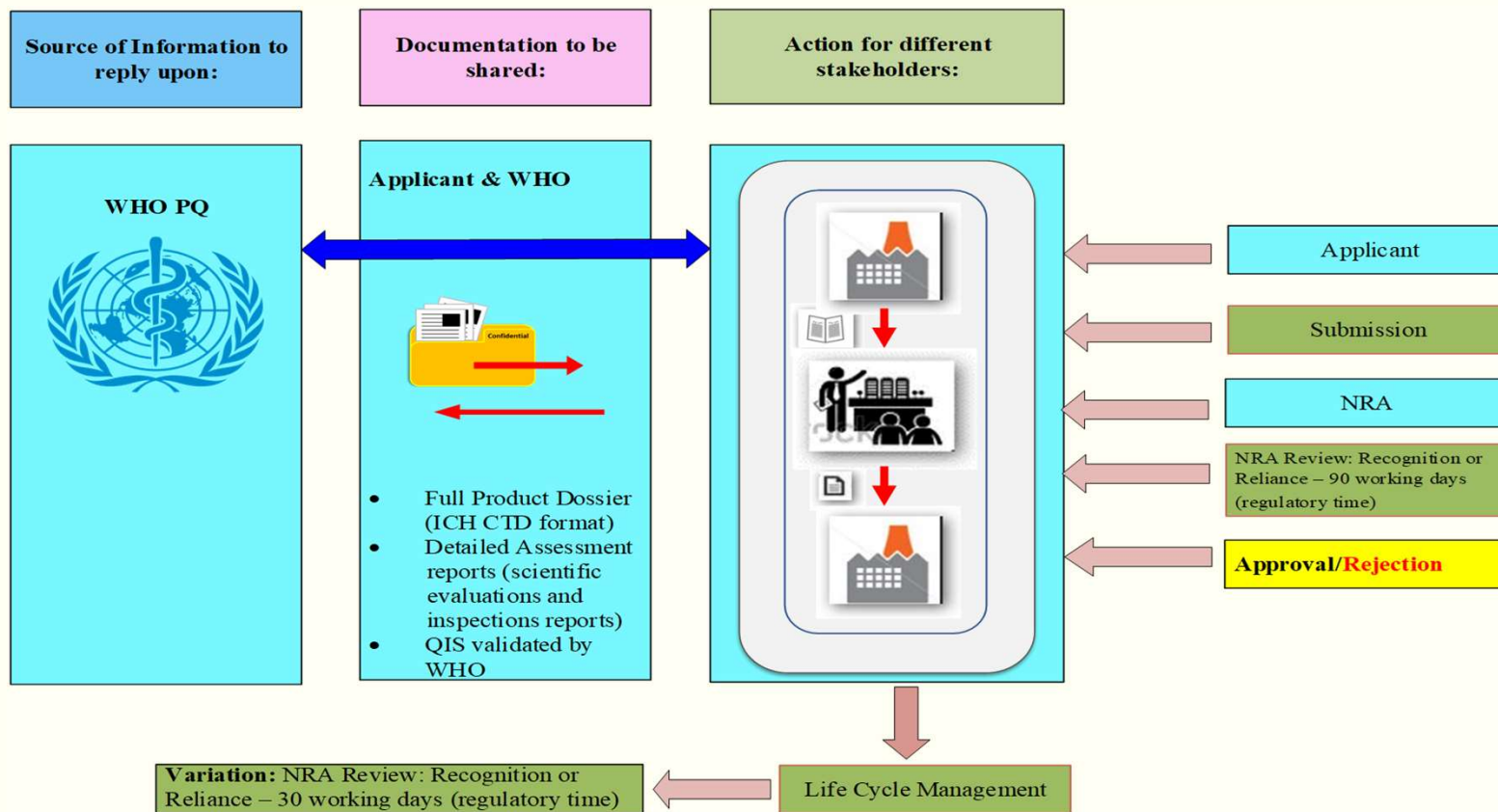
- The viral vaccines i.e. Measles, Rubella, Rabies, Rota will have impact on the yield and indirectly to meet the demand; manufacturer's need to increase the capacities to compensate the losses during 0.2 micron filtration

❑ **Installation of RABS on filling line will call for temporary shutdown of facilities**

❑ **Practice of manual loading being criticised that can indirectly put pressure on manufacturers to switch to auto loader which are very costly.**

BACK-UP

Overview of Collaborative Registration Procedure (CRP) (1)



Confidential & Proprietary Information

Overview of Collaborative Registration Procedure (CRP) (2)

- ❑ In many countries with limited regulatory resources, registration of medicinal products can take considerable time. In the worst cases, this time can extend to two or three years or even more, meaning that the medicinal products may not be received well in time to save lives or improve the state of health.
- ❑ WHO has responded to this situation mainly by creating a [collaborative procedure to facilitate the assessment and accelerated national registration of WHO-prequalified products](#)
- ❑ As the process involves reliance mechanism between WHO and the participating NRA for WHO prequalified products, it is referred as collaborative process. Actually, process involves participation of three different stakeholders viz., WHO-PQT, participating National Regulatory Authorities (NRA) and Prequalification holder (manufacturer/applicant).
- ❑ It accelerates registration through improved information sharing between WHO-PQT and NRAs. By leveraging assessment and inspection outputs already produced by WHO-PQT, and thereby eliminating duplicative regulatory work, it speeds up *in-country* registration of quality-assured products and contributes to their wider availability.