Attendees: Adriansjah Azhari (AA), Apoorv Kumar (AK), Caroline Kitakami (CK), Chuxiafei (Ch), Clark Huang (CH), Cynthia (Xianmen Wantai) (CX), Elenita (Bionet) (E), Han (H), Jeni Tresnabudi (JT), Jooyoung Park (JP), Laura Viviani (LV), Lingjiang Yang (LY), Marcos Freire (MF), Martin Reers (MR), Parag Nagarkar (PN), Rajinder Suri (RS), Rangsita Yooyen (RY), Sandra Cho (SCh), Sunil Gairola (SG), Sonia Pagliusi (SP), Sonia Villasenor (SV), Tamires Lacerda (TL), Yuting Qi (YQ), Zhanghan (Z). **Started** at 12:01 CET and **finished** at 13:00CET

AA welcomed the participants and introduced PN. PN presented SII's experience and knowledge on EUL procedure as SII got 2 EUL last year for 2 different COVID-19 vaccines. PN explained that an Emergency Use Authorization (EUA) is given when in a declared medical emergency, like a pandemic, it may not be possible to have all the evidence that one would usually have before approving a drug or a vaccine. Judgement is made without all evidence, but minimum requirements are that the known potential benefits outweigh the known potential risks.

Once the full data package is available, the manufacturer shall move to full authorization. Different agencies have different procedures to handle the (EUA). WHO has the Emergency Use Listing (EUL). WHO EUL procedure it is mainly to enable vaccines for early access and targeted use in response to a Public Health Emergency of International Concern (PHEIC). This mechanism was previously used for Ebola and Zika diagnostic products in 2014-2016; and then in 2020 for COVID-19 vaccines. Its goal is to define steps that WHO follows to establish eligibility of unlicensed products to assess and determine whether an unlicensed product can be listed on time limited basis, while further data is being gathered and evaluated.

The difference between PQ and EUL is that in EUL is based on a risk benefit assessment of essential set of quality, safety and efficacy data for use during PHEs. Rolling review data is acceptable. The assessment is performed by WHO independent experts in collaboration with National Regulatory Authorities (WLA) in an abbreviated process under oversight of mature regulators. It includes post-deployment monitoring; it is a time limited recommendation and the manufacturer commits to continue for MA/PQ.

WHO EUL procedure helps address the potential imbalance of vaccines supply for LMICs by accelerating the global market access following Stringent Regulatory Authority (SRA) or NRA approval, particularly those aiming to supply to Low Income Country markets within short timeframe compared to WHO PQ.

The WHO eligibility criteria include 4 points:

1. The disease for which the product is intended is serious or immediately life threatening, has the potential of causing an outbreak, epidemic or pandemic.
2. Existing products have not been successful in eradicating or preventing the disease outbreaks.
3. The product is manufactured in compliance with current GMP
4. The applicant undertakes to complete the development of the product and apply for WHO PQ.

WHO has published a separate guideline as "WHO Target Product profiles (TPP) for COVID-19 vaccine Version 3.0 dated 29th April 2020. https://www.who.int/publications/m/item/who-target-product-profiles-for-covid-19-vaccines

It includes some critical/minimal profile and some preferred (but not mandatory). e.g. All ages are preferred, but the minimal requirement is adults, including elderly. VVM on the primary container is preferred, but not mandatory for an EUL. However, the company has to provide the assurance that the studies are ongoing and will be completed.

The EUL procedure has 3 phases: Pre-Emergency/Preparedness, Emergency and Post-listing. The first one includes the establishment of an assessment platform for collaboration with WHO, external experts, and the NRA; it also needs an agreement on the essential requirements that the product shall meet under quality, safety and efficacy, and determine if the product is eligible. Then the filing, review and evaluation from the Product Evaluation Group (PEG). A report is issued by the Chair of the PQ team to the Technical Advisory Group (TAG) who does a rigorous assessment of all the data submitted and additional information and they give a recommendation to WHO. Based on it, EUL is granted or not.

The 7 EUL steps are: Submission of the Expression of Interest (EOI), Pre-submission meeting, submission of CTD dossier, signature of Letter of agreement (LoA), assignment of assessment category and allocation of accessors, Q&A, WHO decision on EUL.

Some post-EUL commitments include: CMC updates, clinical updates, shipping updates and other updates (post approval changes & Quality Complaints).

The experience of SII was that EULs were granted in a timeframe of around 2 months. Some of the challenges are streamlining of the process, communication, mutual recognition agreement with various NRA, pre-submission, storage conditions and shelf-life, product labelling, continuous monitoring / assessment of new data, cold chain and supply strategies, post-listing (WHO accredited testing labs and harmonize assay).

PN suggested that this mechanism should be used for vaccines for other deadly diseases, not necessarily for pandemics, e.g. Malaria. In Nov 2020, WHO issued an EUL recommendation for type 2 novel OPV.

MR asked if WHO is only giving EUL based on efficacy data. PN confirmed this, since for COVID-19 there is no correlation of protection establish yet. MR said that at present it is very difficult to perform efficacy trials because of the seroprevalence, so vaccines without efficacy data will have a very hard time in getting EUL as it is only based on efficacy; so there needs to be a policy change within WHO. ICMRA is working on this, to find a correlate of protection, and for the future vaccines to have some kind of non-inferiority studies based on immunogenicity. The intention is there but not yet the pathway.

AK mentioned that for vaccines that are WHO PQ there is an option for countries to go through Collaborative Registration Procedure (CRP) to expedite registration. He mentioned that during the EUL process there was an option for NRAs to contact WHO to exchange information, however in his experience, it seems that WHO is not timely responding to NRAs requesting for information. PN mentioned that CRP is a very good process, which unfortunately has not worked that good enough for vaccines in contrast to drugs. PN saw that many countries did their own assessment and it was quicker than WHO. RS congratulated PN and said that the reliance mechanism has been used very effectively in the last 18 months by most NRAs based on information provided by SRAs. RS asked what is the next step after EUL to get PQ. RS also mentioned that in an internal discussion it was expressed that probably CRP is not getting as much importance from WHO as it needs to, so he advised manufacturers who have concerns respect to CRP to write clearly the concern and the mitigation requested, so that DCVMN can address them to WHO with the right information to get the right kind of solution.

AA asked if for EUL there is a mandatory site inspection. PN said that WHO assess differently if the manufacturer has any other PQ vaccine than if they don't. WHO also looks at inspection reports from SRAs to the site and assess based on them. The site inspection is decided upon case by case based on previous WHO experience with the manufacturer. AA asked what is the timeframe to go from EUL to PQ. PN said the agencies require 1.5 to 2 years follow-up for phase 3 studies. So, this is what extend the timeline for the final CSR, so till that moment, the agencies are not giving a final authorization; then a new application to WHO has to be made requesting the WHO PQ. SCh asked if maybe the PQ procedure after EUL could take less time. PN said that we could assume that the PQ review process could be faster than a regular application. SG said that now in US Pfizer and Moderna have a full license, and they should be going for a full PQ.

LV then gave an update on the discussion held last week on the UNICEF COVID-19 Supply Division, dedicated to industry consultation. CEPI, GAVI and WHO also participated. There will be another industry consultation on 28-29 September where they will be reporting more information on the potential forecasting for COVID-19 doses and the supply mechanism to be used. It was mentioned that the availability of doses is higher than the demand; therefore, UNICEF made clear that there will not be any new agreements in 2022. The global market assessment group and also the Vaccine Delivery Partnership are soon issuing respective reports; whenever available, they will be shared with DCVMN members. Basically, they are all confirming the same trend: there is less interest, mostly in African countries,

in having their vaccination coverage increased. There is a huge variability in terms of what countries consider what is a successful vaccination coverage.

LV said there was a request from all those parties to industry to try to extend the shelf life of the vaccines so to ensure that all the available vaccines will be used. Another request to industry was that for any kind of future vaccines, to stay within 0.5 ml doses, as they reported the complexity of having 0.3 ml doses for mRNA vaccines. All materials of this meeting will soon be shared in UNICEF's website. DCVMN reported on the importance of collaboration.

AA said that many of our members are developing COVID-19 vaccines, so these reports will be of great importance. AA closed the meeting. Next meeting will be on July 14th.

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Notes taken by SV

Adriansjah Azhari
Chair DCVMN COVID-19 Committee,
June 8th, 2022