Fast-tracking of PQ/Emergency use listing (EUL)

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At the Division of Access to Medicines and Health Products

DCVMN 22nd Annual General Meeting 2021
Vaccines: New challenges, New Paradigms, New Opportunities!
Session 2: Challenges and opportunities in Vaccine research and availability
# Features of PQ and EUL

## Prequalification (PQ) 1987
- Review of extensive quality, safety and efficacy and PSPQ for international supply
- Assessment performed by WHO independent experts
- Reliance on WHO Listed Authority (WLA) - abbreviated process under oversight of mature regulators (evaluation and oversight of programmatic aspects by WHO)
- Pre-submission meetings
- Post-PQ monitoring
- Reassessment/requalification

## Emergency Use Listing (EUL) 2015
- Risk benefit assessment of essential set of quality, safety and efficacy data for use during PHEs
- Rolling review of data
- Assessment performed by WHO independent experts in collaboration with National Regulatory Authorities (WLA)
- Reliance on WLA - abbreviated process under oversight of mature regulators (evaluation and oversight of programmatic aspects by WHO)
- Pre-submission meetings
- Post-deployment monitoring
- Time limited recommendation
- Development should continue for MA/PQ
WHO regulatory preparedness for COVID-19 vaccines

WHO released “Considerations for the assessment of COVID-19 vaccines” (2020)

WHO issued a call for Expressions of Interest for Emergency Use Listing of COVID-19 Vaccines (2020)

... aiming for timely regulatory process while maintaining high evaluation stds for EUL/PQ

Source: https://www.who.int/medicines/regulation/prequalification/prequal-vaccines/WHO_Evaluation_Covid_Vaccine.pdf?ua=1
WHO alignment activities for COVID-19 vaccines ongoing since Feb 2020

- Completed
- Ongoing
- Details on following slides

### Development criteria
- ✓ Target Product Profiles
- ✓ Expert Committee on Biological Standards guidance
- ✓ Regulatory guidelines

### Submission requirements
- ✓ EUL and PQ guidance and Questions & Answers
- ✓ EUL/PQ Expressions of Interest (conditions & evaluation criteria)
- • Labelling & packaging

### Assessment process
- • Evaluation of candidates for EUL/PQ (incl. inspection, lot release process & post-listing commitment)
- • Interactions & agreements with NRAs/SRAs*
- • Global assessment process* with region-designated national authority reps

### In-country approval for use & post approval monitoring
- • Country regulatory reliance on EUL/PQ*
- • Support for safety monitoring (based on safety preparedness manual)
- • Tools for risk communication and strengthening response capabilities

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- Roadmap* to enable product specific regulatory alignment (assessment process, in-country approval & post-listing monitoring)
- Alignment ongoing (Regulatory Advisory Group, ICMRA, regional regulatory networks, Vaccine cluster etc.)
- Regulatory updates and webinars
- Best practice principles for regulatory “agility”

* Elements of the Roadmap for WHO Assessment of vaccine x during the COVID-19 Public Health Emergency
In-country expedited approval for use & post-listing monitoring: the WHO regulatory alignment roadmap*

### 1. Preliminary activities
- Global regulatory cooperation
- Establishment of strategies for expedited approval in participants & post-listing monitoring

### 2. Launching of EOIs
- Manufacturers EOIs (Phase IIb/III & approval by NRA/SRA in charge of oversight within 6 months & compliance with criteria for assessment)
- Discussions on rolling submission procedure

### 3. Submissions & assessment
- Establishment of assessment pathway according to NRA/SRA in charge of oversight
- Establishment of Review Committee (NRA/SRA in charge of oversight & regulators /reviewers from potential user participants)

### 4. Recommendation for listing
- Approval granted by NRA/SRA in charge of oversight
- Advisory committee convened (post-listing commitment)
- WHO EUL/ PQ recommendation with conditions

### 5. Post-listing monitoring
- Implementation of strategies for safety, quality & effectiveness monitoring
- Validity of listing based on new data generated
- Possible conversion of EUL to PQ

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**Facilitated access to countries**

- Sharing of assessment/ inspection reports / lot release with regional-designated country reps
- WHO-facilitated national approval process

*Roadmap for WHO Assessment of vaccine x during the COVID-19 Public Health Emergency*
Support to regions & countries

Designate lead NRAs in the region: WHO EUL assessment
Facilitation expedited national approval

1. Sharing dossier and EUL reports > 400 reports > 100 countries LMIC and HIC
2. Discussion on outcome of review: Facilitated workshops
   One on one discussions with countries.
3. Additional guidance for decision making on expedited authorization
   Support to RO and agencies providing relevant docs for actual shipments
4. Post listing changes: > 152 changes clinical, CMC and labelling/packaging changes

Product Evaluation group (PEG):
Roster of experts, Regulatory experts all regions.

Technical Advisory group EUL (TAG-EUL):
Risk benefit assessment
https://extranet.who.int/pqweb/vaccines/TAG-EUL

Collaboration agreement with NRAs of references and others on regulatory oversight

>100 countries granted EUAs within 15 days post EUL
Over 500 regulatory approvals of AZ donations based on reliance
## WHO listed Covid-19 vaccines

<table>
<thead>
<tr>
<th>Platform</th>
<th>Manufacturer / EUL holder / name</th>
<th>NRA of Record</th>
<th>Post-EUL commitments</th>
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</thead>
<tbody>
<tr>
<td>mNRA-based vaccine encapsulated in lipid nanoparticle (LNP)</td>
<td>BioNTech Manufacturing GmbH BNT162b2 / COMIRNATY: Tozinameran (INN)</td>
<td>EMA, US FDA</td>
<td>• CMC updates</td>
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<td>Moderna Biotech, mRNA-1273: elasomeran (INN)</td>
<td>EMA, US FDA</td>
<td>• Clinical</td>
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<td>• Updated data on the efficacy/effectiveness</td>
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<td>• Updated RMP</td>
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<td>• Monthly safety reports, and Periodic Benefit Risk Evaluation Reports (PBRER) every 6 months</td>
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<td>• Updated labelling, shipping validation (if applicable) and data for VVM</td>
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<td>• Others:</td>
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<td>Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2</td>
<td>AstraZeneca, AB: AZD1222 Vaxzevria</td>
<td>EMA, Health Canada, MFDS, MHLW-PMDA, TGA</td>
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<td>Serum Institute of India Pvt. Ltd: Covishield (ChAdOx1_nCoV-19)</td>
<td>DCGI</td>
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<tr>
<td>Recombinant, replication-incompetent adenovirus type 26 (Ad26) vectored vaccine encoding the SARS-CoV-2 Spike (S) protein</td>
<td>Janssen–Cilag International NV: Ad26.COV2.S</td>
<td>EMA</td>
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<tr>
<td>Inactivated, produced in Vero cells</td>
<td>Sinopharm / Beijing Institute of Biological Products Co., Ltd. (BIBP)</td>
<td>NMPA</td>
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<tr>
<td></td>
<td>Sinovac Life Sciences Co., Ltd.: Coronavac™</td>
<td>NMPA</td>
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Post-EUL commitments (details)

- CMC updates: stability, trends and others
- Clinical: ongoing efficacy/effectiveness data in different target population/comorbidities
- Updated data on the efficacy/effectiveness of the vaccine against disease caused by emerging SARS-CoV-2 variants of concern (such as B.1.1.7, B.1.351, P.1, B.1.617.2 and others).
- Updated RMP based on assessment vaccine safety profile
- Monthly safety reports, and Periodic Benefit Risk Evaluation Reports (PBRER) every 6 months
- Updated labelling, shipping validation (if applicable) and data for VVM
Post-EUL commitments (details)

- Others:
  a) report serious adverse events following immunization (within 15 days of receipt of the report);
  b) report quality complaints from the field for batches supplied;
  c) report any change that may have an impact on the quality, safety and/or efficacy of the vaccine or change the basis of the regulatory approval by the NRA of reference (NMPA);
    - Expansion capacity: New sites
    - New storage conditions
    - New indications
    - New presentations
    - Shelf life updates
  d) report any problems/constraints in production or quality control which might affect the emergency use condition granted to this product.
Additional information EUL:

Covid 19 vaccines: Guidance documents and EUL submissions

https://extranet.who.int/pqweb/vaccines/covid-19-vaccines

Target product profile


Evaluation criteria and EOI. https://www.who.int/medicines/regulation/prequalification/prequal-vaccines/resouces/1_EOI-Covid-19_Vaccines.pdf?ua=1

Roadmap https://www.who.int/publications/m/item/roadmap-for-evaluation-of-astrazeneca-azd1222-vaccine-against-covid-19

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