Vaccine Assessment for Prequalification and Programmatic Suitability for Prequalification

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Pharmaceuticals Vs Vaccines

- **Pharmaceuticals**
  - Produced and controlled using physicochemical methodologies

- **Vaccines**
  - Production and testing using biological systems
    - Raw materials
    - Manufacturing processes
    - Quality control methodologies
  - Each vaccine is a unique product
Complex release process

- QC
- lab. tests
- certificate of analysis
- vaccine lot
- Manufacturer’s release
- Mfr. Country Reg Authority
  - lab tests
  - doc. review
- NRA release
- specific to vaccines
- UN supply
- PQ vaccines

- QA
- GMP compliance
- batch records

- vaccine distribution on the market
- specific to vaccines
Quality Relationships

Quality Control
- Sampling
- Specifications
- Testing

GMP

Quality Assurance

Quality Management
- Quality Objective
- Quality Manual
- Quality System
- Quality Policy
- Management
- Aspect
- Self inspection
Quality aspects considered

- Production process of Drug Substance and Drug Product
  - Control of Materials
  - In process controls
  - Process validation
  - Consistency of Production at commercial scale
  - Capacity of Production
Quality aspects considered

- Compliance with GMP

- Compliance with WHO recommendations and UN tender specifications including labels and inserts

- Programmatically suitable presentation
Dossier Review – Clinical aspects

- Clinical development program
- Applicant’s sponsored clinical trial overview
- Clinical summary
- Independent Clinical expert report
- Pharmacovigilance plan
### Common deficiencies as per categories

**Safety**
- Unclear definition of AE
- Insufficient safety follow up time
- Insufficient safety information
  - (limited safety database, incomplete SAE details, Absence of list of AE)
- No data on specific at risk population

**Immunogenicity**
- Lack of evidence for surrogate of protection
- Discrepancies in numbers
- Unclear statistical analysis
- Unsatisfactory immunogenicity results
- No info on assays or assay validation
- Lack of information on co-adm vaccines
- No data on specific at risk population

**Clinical development/Protocol**
- Missing info on status and results of listed studies
- Lack of evidence of CT registration
- Lack of info on sample size and stat analysis
- Missing info on ethical oversight
- Unacceptable comparators
- Lack of info on protocol, DSMB and study procedures

**Post licensure**
- Missing or incomplete PSUR
- Missing or incomplete PV plan
Outcome of the review of Dossier

- **Scenario 1:** Dossier review does not raise any outstanding issues
- **Scenario 2:** Dossier review raises outstanding issues for clarification/additional information (no major)
- **Scenario 3:** Dossier review raises major technical and programmatic issues
- Consistency testing and inspection are scheduled
- Outstanding issues may be followed up at site inspection &/or request for additional information
- Consistency testing and inspection are scheduled
- Ad Hoc committee is convened
  - Request for additional information to give final recommendation
  - Stopping the PQ
Programmatic Suitability for Prequalification

- Objectives of PSPQ
  - Judge the programmatic suitability against defined mandatory, critical and preferred characteristics

- Benefits of PSPQ
  - Give clear directions to vaccine industry before submission
  - Reduce decision making time
Submission screening and SC assessment

- Upon receipt, product summary files (PSFs) are screened for completeness and compliance with the required format and contents by the PQ secretariat.

- PSFs are also screened by the PQ Secretariat for compliance with programmatic suitability criteria,
  - if mandatory characteristics are not met the PSF is rejected.
  - if the PQ Secretariat identifies a deviation from the critical characteristics or finds a unique characteristic, the product will be referred to the PSPQ Standing Committee for independent review of the characteristic.
Can a review by the standing committee happen before submission?

- Yes

- Vaccine development an extended process

- Manufacturers can discuss with PQ Secretariat pre-submission

- A briefing package can be prepared with company input for the SC to consider.
Who makes the final decision?

- The PSPQ SC makes a recommendation to the Director of the Essential Medicines and Health Products Department (EMP) considering programmatic risk from non compliance with a criterion and public health needs for a vaccine as to whether the product should be accepted for review for prequalification.

- Decision-making rests with EMP.
Mandatory characteristics

- Antimicrobial preservative is required in ready to use injectable vaccines containing more than two-doses.

- Thermostability: The vaccine or any component presented for prequalification should not require storage at less than -20°C.

- Dose volume for injectable vaccines for children 5 years and under should be not more than 1 ml.

- Vaccine presented for prequalification should not require an intravenous route of administration.
Unique or innovative characteristic

- No guidance documents developed
- Examples: Nano-patches, nasal aerosols, micro-needle application
- Based on programme knowledge SC will judge the suitability of such vaccines for the developing market
Critical characteristics (1)

- The vaccine should fit into currently commonly used schedules of vaccination visits.
- Oral vaccines should be ready to use.
- Thermostability: If the vaccine requires storage below +2°C during its shelf-life period, it should be stable at +2°C and +8°C for a minimum of 6 months.
- Vaccine Vial Monitor (VVM): Proof of feasibility and intent to apply appropriate VVM if a tender requirement.
Critical characteristics (2)

- Antimicrobial preservative is required in ready to use injectable vaccines containing two-doses or in vaccines requiring reconstitution that are not live-attenuated

- Dose volume of injectable vaccines can be delivered using available PQed auto-disable syringes

- Vaccines in pre-filled injection devices should have an auto-disable feature

- Packaging material can be disposed of appropriately in the field using standard procedures
Preferred characteristics

- A vaccine not complying to preferred characteristics are not reviewed by PSPQ SC before evaluation for pre-qualification.

- They indicate what WHO and national immunization programmes would want in a best case scenario.

- They provide a guide vaccine manufacturers during the development of the new vaccine formulations.

- In time, a preferred characteristic may be reclassified as critical.
Preferred characteristics (1)

- Antigenic stability following reconstitution
- Small packed volume
- Small, standardised dose volumes for oral vaccines
- Minimize number of doses that cannot be reused in subsequent sessions once the container is open
- \( \leq 10 \) doses per vial in routine setting; \( \geq 10 \) doses per vial in campaign setting
Preferred characteristics (2)

- Doses per secondary container reflect logistical needs
- Small, standardised dose volumes for oral vaccines
- Ready to use vaccines
- Multicomponent vaccine formats reduce potential for error
  - If components are packed in separate secondary containers, they should contain the same number of doses
Preferred characteristics (3)

- Increased thermostability
- No freeze sensitivity
- Packaging designed to minimise environmental impact
- Novel delivery devices that reduce risk of contamination
- Compact prefilled auto-disable injection system (eg. UniJect®)
- Labelling (TRS revision in preparation)
- Barcoding
http://www.who.int/immunization_standards/vaccine_quality/pspq2_v140512.pdf
Thank you