Clinical aspects during Prequalification of vaccines

Briefing on Vaccine Prequalification for manufacturers
DCVMN meeting, Kunming, China, 13 March 2016

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Chapter 8: Clinical experience

- Note 1 : Reference documents
  - TRS 978, Annex 6 (2012, PQ procedure) http://www.who.int/entity/immunization_standards/vaccine_quality/TRS_978_61st_report_Annex_6_PQ_vaccine_procedure.pdf
  - TRS 850 (1995, GCP); http://apps.who.int/prequal/info_general/documents/TRS850/WHO_TRS_850-Annex3.pdf
  - TRS 924 (2004; clinical evaluation of vaccines); http://who.int/entity/biologicals/vaccines/clinical_evaluation/en/index.htm
  - TRS 927 (2005; non-clinical evaluation of vaccines) http://who.int/biologicals/vaccines/nonclinial_evaluation_of_vaccines/en/
  - Points to consider for manufacturers of human vaccines: clinical considerations for evaluation of vaccines for prequalification http://www.who.int/immunization_standards/vaccine_quality/pq_vaccine_evaluation/en/
  - Any specific TRS
  - Related WHO position paper

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- Note 2
  - For vaccines originally licensed many years before application for prequalification, emphasis should be given to document history of safe and effective use.
- Note 3
  - Provision for request of raw data

8.1 Clinical development program

- Format: tabulated summary (1 or more tables)
- Objective: identification of critical parameters that may have changed during the clinical development of the product

8.2 Clinical trial information (1)

- 8.2.1 Applicant's sponsored clinical trial overview
  - List of all clinical trials conducted (in all countries relevant to the application for WHO PQ)
    - For each study sponsored by the applicant (before and after initial licensure)
      - Approved protocol (by NRA and Ethics Committee)
      - Evidence of registration in a CT registry (WHO ICTRP)
      - Compliance with GCP

8.2 Clinical trial information (2)

- 8.2.1 Applicant's sponsored clinical trial overview (cont'd)
  - For each study, to be provided (in a table or brief summary)
    - Type of study
    - Rationale
    - Study sites
    - Dates
    - Statement of final conclusions
    - Copies of publications and abstracts to be provided
  - List of ongoing trials
    - Details of the study plan
    - Expected date of results

8.2 Clinical trial information (3)

- 8.2.2 Other studies with the applicant's product
  - Not sponsored by the applicant
  - Vaccine as intervention of main interest or used as comparator
  - Also observational studies (e.g. case-control studies)
  - Identified by literature search

8.2 Clinical trial information (4)

- 8.2.3 Clinical summary – (similar to CTD 2.5)
  - Detailed summary and interpretation of the safety and efficacy data of all studies (pre- and post-licensure)
  - Relevance to support worldwide use
    - WHO recommended schedules
    - Co-administration with other vaccines
  - Expected to complement (not replace) the summary written by an independent clinical expert (8.2.5)

8.2 Clinical trial information (5)

- 8.2.4 Assessment reports
  - Whenever possible
    - Clinical section of the national regulatory authority (NRA) assessment report from the country of origin and/or country where initially licensed
    - Assessment reports for any subsequent variations to the license for changes relevant to clinical data
    - Assessment reports from other NRAs

8.2 Clinical trial information (6)

- 8.2.5 Clinical expert report
  - Independent clinical expert report
    - Evidence of expertise and independence to be provided
  - Particularly useful for products licensed long time before
    - Limitations put in the context of the requirements at the time of licensure
      - Ethical approval / GCP
      - Study design / sample size
    - Impact on disease control after introduction in vaccine programme
    - Post-marketing safety data

8.2 Clinical trial information (7)

- 8.2.6 Preclinical studies sponsored by the applicant
  - List of all preclinical studies sponsored by the applicant (TABULATED FORMAT)
  - For preclinical studies performed after initial licensure, indicate the reasons for these studies

8.3 Documentation of safety (1)

- 8.3.1 Pharmacovigilance plan
  - Introduced in the current PQ procedure (from 2012)
  - Important to determine whether evidence to support the use of the product in different populations (geographical areas, age groups, etc…) are planned
  - Some evidence will be expected as post-prequalification commitments

8.3 Documentation of safety (2)

- 8.3.2 Initial evaluation of vaccines that have been in the market for a long time (or reassessment of already prequalified vaccines)
  - Outline of the applicant's procedures for the collection, onward notification and assessment of adverse events
  - Listing of all reported AEFIs
  - Periodic Safety Update Reports (PSURs) may provide all the information needed
    - ICH format preferable

8.3 Documentation of safety (3)

- 8.3.3 Recently licensed vaccines
  - Ongoing phase IV studies
  - Ongoing active monitoring of the safety profile

8.3 Documentation of safety (4)

- 8.3.4 Documentation of serious advent events
  - Fullest possible description of each case, including any information there may be on investigations, actions, patient treatment and outcome
  - Periodic Safety Update Reports (PSURs) may provide all the information needed

Clinical Information in Package Insert

PSF Chapter 4.4

The information in the PI must be referenced to the clinical data.

Indications

- Dosage-regimen
- Side-effects
- Pregnancy
- Special precautions

THANK YOU