Clinical aspects during Prequalification of vaccines

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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/

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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 searc

Points to consider

b) a completed clinical trial model summary protocol (according to TRS No. 924, p. 95) for pivotal (often phase III) trials;

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
  - For preclinical studies performed after initial licensure, indicate the reasons for these studies
- TABULATED FORMAT

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