Collaborative evaluation of marketing authorization files of inactivated polio vaccines in countries of the Eastern Mediterranean Region

World Health Organization

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Outline

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- Strategy for the IPV registration
- Joint Evaluation Exercise of IPV vaccine
- Outcomes of the joint evaluation of IPV
- Advantages of the IPV joint evaluation
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- Conclusion

Context

Polio Eradication & Endgame Strategic Plan 2013-2018

Goal: complete the eradication, achieve containment & certification of all wild & vaccine-related polioviruses

- Sequential removal of Sabin strains
- Start with type 2, by replacing tOPV with bOPV in a synchronized manner globally
- ≥1 dose of IPV in all routine immunization programmes (at least 6 months before the introduction of bivalent OPV (bOPV) planned in April 2016)

Context

Polio Endgame Plan 2013-2018

1. Polio detection & interruption
2. **Systems strengthening, IPV registration and introduction and OPV withdrawal**
3. Containment & Certification
4. Legacy Planning

Regulatory challenges for OPV2 withdrawal

- At least one brand of IPV licensed (ideally 2) in all countries by end 2014
- bOPV licensed for routine immunization in all countries by end 2015
- At least 1-dose of IPV introduced in the NIPs in 2015
- bOPV replacing tOPV by April 2016

Context

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Objective2: Systems strengthening, IPV registration and introduction and OPV withdrawal

- **Limited global production capacity of IPV**

- **Classification Criteria of countries in tiers**
  - Wild polio virus endemic status
  - Existence of circulating vaccine derived poliovirus type 2 c(VDPV2)
  - Reporting of cVDPV1 or cVDPV3
  - DPT3 coverage rate since the last 3 years (≤ 80%)
  - Geographic localization of countries with the countries that are either endemic or having imported wild poliovirus or with cVDPV2 outbreak

- **3 main regulatory tracks**
  - Full evaluation process: Complete review of the manufacturer's dossier, Review of samples (testing), Inspection of manufacturing sites
  - Facilitated evaluation: Reliance on the review done by the WHO prequalification programme
  - Acceptance of prequalified vaccine without any additional review

Strategy for the IPV registration

- 2013: 1st correspondence signed by the heads of UNICEF, Gavi, the Vaccine Alliance, and WHO sent to the ministers of health of countries
- 16 April 2014: 2nd letter as Information note sent to the heads of the national regulatory agencies in target countries

Mapping of the EMR countries based on the tier, registration status of IPV and regulatory pathway

7 EMR countries with

- No IPV registered: Jordan and Morocco
- Only one brand of IPV registered: Egypt, Iran, Pakistan, Saudi Arabia, Tunisia

WHO Support: Joint evaluation of IPV marketing authorization dossier

Strategy for the IPV registration

3rd correspondence from WHO, signed by WHO/RSS/EMP sent to the heads of national regulatory agencies in the 7 EMR countries for participating in the joint IPV vaccines review that included:

- Background information on the polio endgame strategy,

- ToRs for participation in the joint evaluation meeting: principles, roles and responsibilities of
  - WHO: organizing the meeting for joint evaluation and follow-up until registration of IPV
  - Manufacturers: timely submission of MA files to NRA (1 month before the meeting)
  - NRA of participating countries: use the joint evaluation report as the basis for approval of the vaccines without further requirements

- Declaration of interests and confidentiality agreement signed by nominated participants valid for interactions during and after the review

Joint Evaluation Exercise of IPV vaccine

IPV joint evaluation meeting conducted in October 2014, Casablanca, Morocco
Objectives: Facilitate the review process of MA files for the registration of 2 IPV standalone from 2 Manufacturers A and B and expedite the overall timelines required for approval

- 5 day meeting (2,5 days dedicated for each IPV vaccine)
- Participation:
  - 2 regulators in charge of scientific evaluation of vaccine MA files from 6 countries:
    - Jordan and Morocco for IPV from both manufacturers A and B
    - Egypt, Iran, Saudi Arabia (representing all GCC countries), Tunisia for Manufacturer B
  - Regulators from NRA from IPV producing countries
  - Independent Expert on clinical evaluation from Medicine control council of South Africa
  - Representatives of the 2 manufacturing companies on the last day of the review
  - WHO secretariat (organizer and facilitator)

Joint Evaluation Exercise of IPV

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Principles of the joint evaluation:

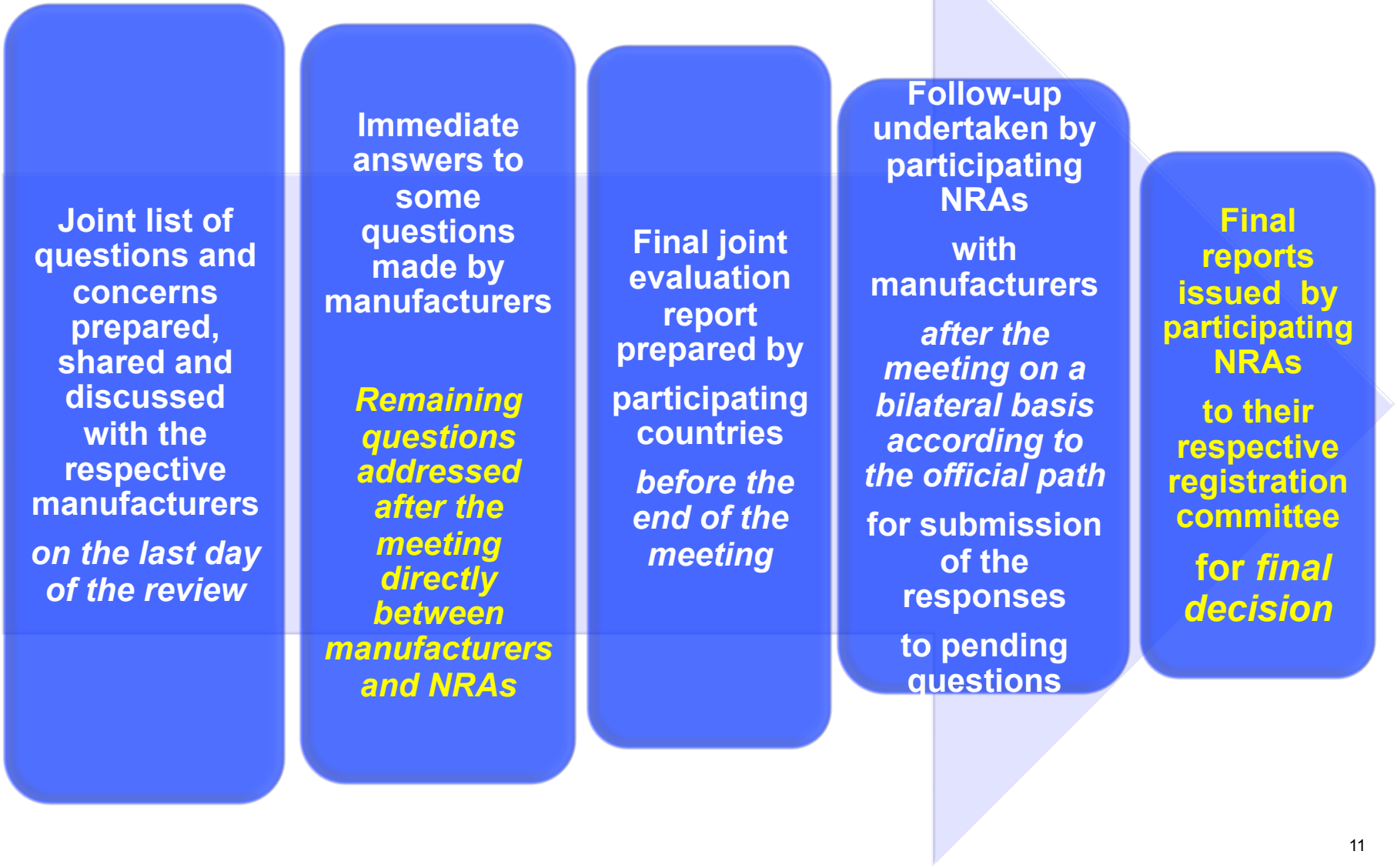
- Limited to MA applications of IPV vaccines submitted to the NRAs
- Joint evaluation process legally accepted by the countries for issuance of a marketing authorization
- IPV registration based on the information shared during the joint evaluation meeting
- Information provided in the assessment reports from the NRAs of the vaccine-producing country (MA file evaluation, GMP inspections and test results)
- No further testing or site inspections to be conducted by the countries before granting the MA
- Regulatory decision remained the prerogative and responsibility of each NRA

Joint Evaluation Exercise of IPV

World Health Organization

NRA of producing country	• Summary of the production process and quality control testing • Assessment report of the quality part of the CTD • Lot release and test results reports of the previous 3 years • GMP inspection reports discussed via TC by GMP inspectors from NRAs of the IPV manufacturing country
Independent expert from South Africa	• Review of: Clinical and PMS data
Regulator from participating country	• Review of the MA file performed ahead of the meeting, Main findings, observations and points for further clarification

Joint Evaluation Exercise of IPV



Joint Evaluation Exercise of IPV

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Information shared

- Full IPV standalone CTD: 10-dose presentation (A); 1- & 5-dose presentations (B)
  Additional information required for approving the variation for the 5-dose presentation (B)
- Information contained in the MA applications and variations received by any participant
- Test results shared by the NRAs of the producing countries
  Outcomes of GMP inspections conducted by the NRAs of the 2 manufacturing countries
- Assessment reports made by the participants
  Presentations made during the meeting
  Final list of questions resulting from the review by all participants
- PMS data of significant public health interest to other participants
- Manufacturers' immediate responses to questions

Outcomes of the joint evaluation of IPV

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	IPV Standalone (A)	IPV Standalone (B)
Egypt:		Registered in 2015
Jordan	Registered in the first quarter of 2015	Approval delayed until full compliance with the information required in module 1
Iran		Registered in the first quarter of 2015
Morocco	Registered in the first quarter of 2015	Approval delayed until full compliance with the information required in module 1
Saudi Arabia		No registration
Tunisia		Special approval in 2014 based on emergency provisions

Advantages of the IPV joint evaluation

- Benefit from the information and guidance received from the NRAs of the producing country
- Rich and fruitful discussion from observations and questions raised by the 6 participating countries and inputs from regulators from the NRAs of the producing countries
- F2F meeting, sharing assessment reports, test results and GMP inspection reports provided by NRA from producing country helped to address questions that takes long time in regular circumstances
- Participation of manufacturers in the meeting accelerated the process of addressing the questions and concerns expressed by participating NRAs
- Joint evaluation process was different from the regular full review pathway that avoided duplication of inspections and unnecessary testing at the time of registration of the vaccine

Constraints of the IPV joint evaluation

- Delayed reply from countries with the agreement and acceptance of the ToRs by NRAs
- Participants not appropriately briefed neither on the objectives and expected outcomes of the exercise nor on the commitments taken by their heads of agencies
- No submission of the MA files by the manufacturers ***at least 1 month*** before the meeting to participating countries: 3 countries received advanced copies of the IPV CTD file (B) through WHO with permission from manufacturers
- Diversity of country-specific requirements in terms of content, language and format of the CTD particularly of module 1
- Lack of responsiveness from some of the agents representing the manufacturers and difficulties in complying with the specific country requirements expressed by the NRA

Conclusion

- Great benefits from joint evaluation of product. IPVs were registered prior to its introduction
- However this requires more coordination between all stakeholders to achieve the objectives
- WHO will continue to support Member States in organizing joint review meetings to facilitate registration of vaccines when requested

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THANK YOU

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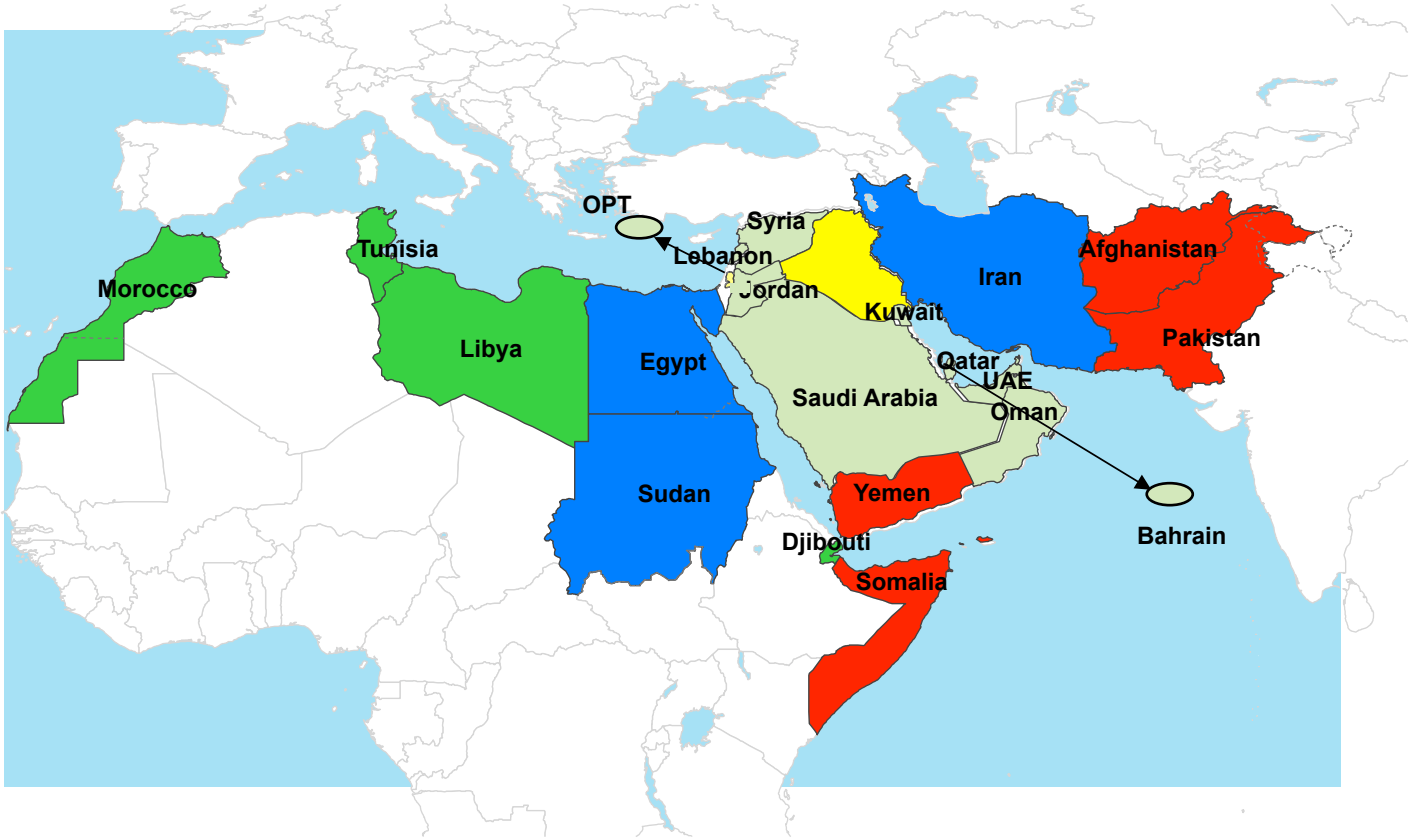
Eastern Mediterranean Region

21 Member States and Occupational Palestinian Territory (West Bank and Gaza Strip)
Population: 664.336 million



Tier 1: Wild polio virus endemic countries or countries with cVDPV2 since 2000

Tier 2: Countries reported a cVDPV1/cVDPV3 since 2000 or large/medium sized countries with 3 doses of DTP3 coverage ≤ 80% in 2011, 2012 and 2013

Tier 3: Large/Medium countries adjacent to Tier 1 countries with wild polio virus since 2003, or bordering countries with a current persistent cVDPV2 outbreak or countries with a wild polio virus importation since 2011

Tier 4: All other OPV-only using countries

No tier

Source of IPV vaccines in EMR countries

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	UN Agencies (UNICEF)	Self-procurement directly from the manufacturers
Public sector (EPI)	• **GAVI eligible countries:** Afghanistan, Djibouti, Pakistan, Somalia, Sudan, Yemen • **Non Gavi eligible countries:** OPT, Egypt, Lebanon, Morocco and some LMIC countries with humanitarian crisis, IDP/Refugees	• GCC countries: Bahrain, Kuwait, Oman, Qatar, Saudi Arabia an UAE • Jordan, Iran, Iraq, Libya, Syria, Tunisia
Private sector		All EMR countries

No IPV production in EMR

IPV Registration Status in EMR countries

- GAVI eligible countries except Pakistan, Sudan: IPV accepted based on WHO prequalification status
  - Pakistan: Registration based on full evaluation of MA file
  - Sudan: registration using WHO expedited review procedure

- IPV self-procuring countries: at least one IPV stand alone or IPV containing vaccines is registered either through
  - Full evaluation of the registration dossier
  - Acceptance of WHO prequalification vaccines
  - Special approval for emergency situations
  - Reliance on USFDA and EU registration