Tools to accelerate vaccine registration in developing countries

World Health Organization

18th DCVMN Annual General Meeting

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Emer Cooke, Head, Regulation of Medicines and other Health Technologies

Photo by Jeon Han, www.korea.net

Outline of presentation

- Overview of WHO's role in the regulation of medicines and other health technologies
- Tools to accelerate vaccine registration in developing countries

Director General’s 5 priorities

1. Health for all
2. Health emergencies
3. Women, children and adolescents
4. The health impacts of climate and environmental change
5. A transformed WHO

Programme of Essential Medicines and Health Products

VISION: A world where every child, man and woman has access to the quality essential medicines, vaccines and other health products they need to lead a healthy and productive life.

MISSION: To support the WHO Member States to **improve and sustain access to quality medicines and health products** to achieve Access 2030 goals and universal health coverage:

- Provide leadership and technical expertise,
- Define norms and standards,
- Shape the research agenda according to public health needs,
- Generate relevant evidence, articulate policy and monitor progress towards equitable access.

WHO Cluster of HEALTH SYSTEMS AND INNOVATION (HIS)

Department of Essential Medicines and Health Products (EMP)

Innovation, Access and Use (IAU)

- Innovation/research & Development
- Intellectual property,
- Evidence-based selection of Model List of Essential Medicines
- Pricing, Health technology assessment (HTA)
- Procurement and supply chain management
- Improved use of medicines and health products

Regulation of Medicines and other Health Technologies (RHT)

Head: Emer Cooke

- **Technologies Standards and Norms (TSN)**
- **Regulatory Systems Strengthening (RSS)**
- **Prequalification Programme (PQT)**
- **Safety and Vigilance (SAV)**

Regulation of Medicines and other Health Technologies (RHT)

Head: Emer Cooke

Technologies Standards and Norms (TSN)
Coordinator: Francois-Xavier Lery*

Establish/maintain international standards
Promote unified standards, as well as a global nomenclature

****from 1st November 2017***

Regulatory Systems Strengthening (RSS)
Coordinator: Mike Ward

Strengthen NRAs for capacity building and promote harmonization, reliance, best practices & integrate framework for new products

Prequalification Team (PQT)
Coordinator: Deus Mubangizi

Assure quality, safety & efficacy/performance of health products
(vaccines, diagnostics, medicines, medical devices, vector control products)

Safety and Vigilance (SAV)
Coordinator: Clive Ondari

Respond to and minimize health risks from medical products through proactive, end-to-end, actionable, smart safety surveillance

Cross Cutting Activities

- Antimicrobial resistance
- Benchmarking tools
- **Data integrity**
- **Emergency preparedness**
- Environmental issues
- Local production
- Non-communicable diseases
- Paediatric medicines
- **Shortages**
- Substandard & falsified

WHO written standards: ECBS 2016-2019

Written standards (eg, Guidelines, Recommendations) - Vaccines

- Influenza vaccines for non-producing countries – new (ECBS 2016)
- Maternal immunization – labelling of flu vaccines – new (ECBS 2016)
- Ebola vaccines – new (ECBS 2016)
- Clinical evaluation of vaccines – revision (ECBS 2016)
- Human Challenge Trials – new (ECBS 2016)
- Safe production of IPV – revision of TRS 926 (ECBS 2018)
- Biosafety of flu vaccines – revision (ECBS 2018)
- RSV vaccines –new guidelines (ECBS 2019)

Written standards – Biotherapeutic products (BTP) /Similar biotherapeutic products (SBP)

- Guidelines on Mabs developed as biosimilars - (ECBS 2016)
- BTP post-approval changes - new (ECBS 2017)

WHO written standards – projects in the pipeline and implementation of standards

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Vaccines

- Hepatitis E vaccine – new, important for Prequalification
- Nucleic acid based vaccines for public health emergencies
- Meningitis B – new, Guidelines or Points to consider
- Enterovirus 71 –TBD

Implementation workshops

- clinical evaluation of vaccines
- Post-approval changes for vaccines
- Post-approval changes for BTP
- GMP for biologicals

Development of measurement standards for Vaccines: 2013 – 2016

working with networks of laboratories (collaborating centres)

1) Trivalent inactivated polio vaccine (TIPV) for D antigen assay (3rd IS)

1) Tetanus toxoid for flocculation assay (3rd IS)
2) Anti-Toxoplasma Serum, Human (2nd IS)
3) Typhoid Vi Polysaccharide (1st IS)

1) Human serum anti-malaria Plasmodium falciparum (1st RR)
2) Haemophilus influenzae b polyribosylribitol phosphate polysaccharide (2nd IS)
3) Human anti-Vi polysaccharide IgG (1st IS)

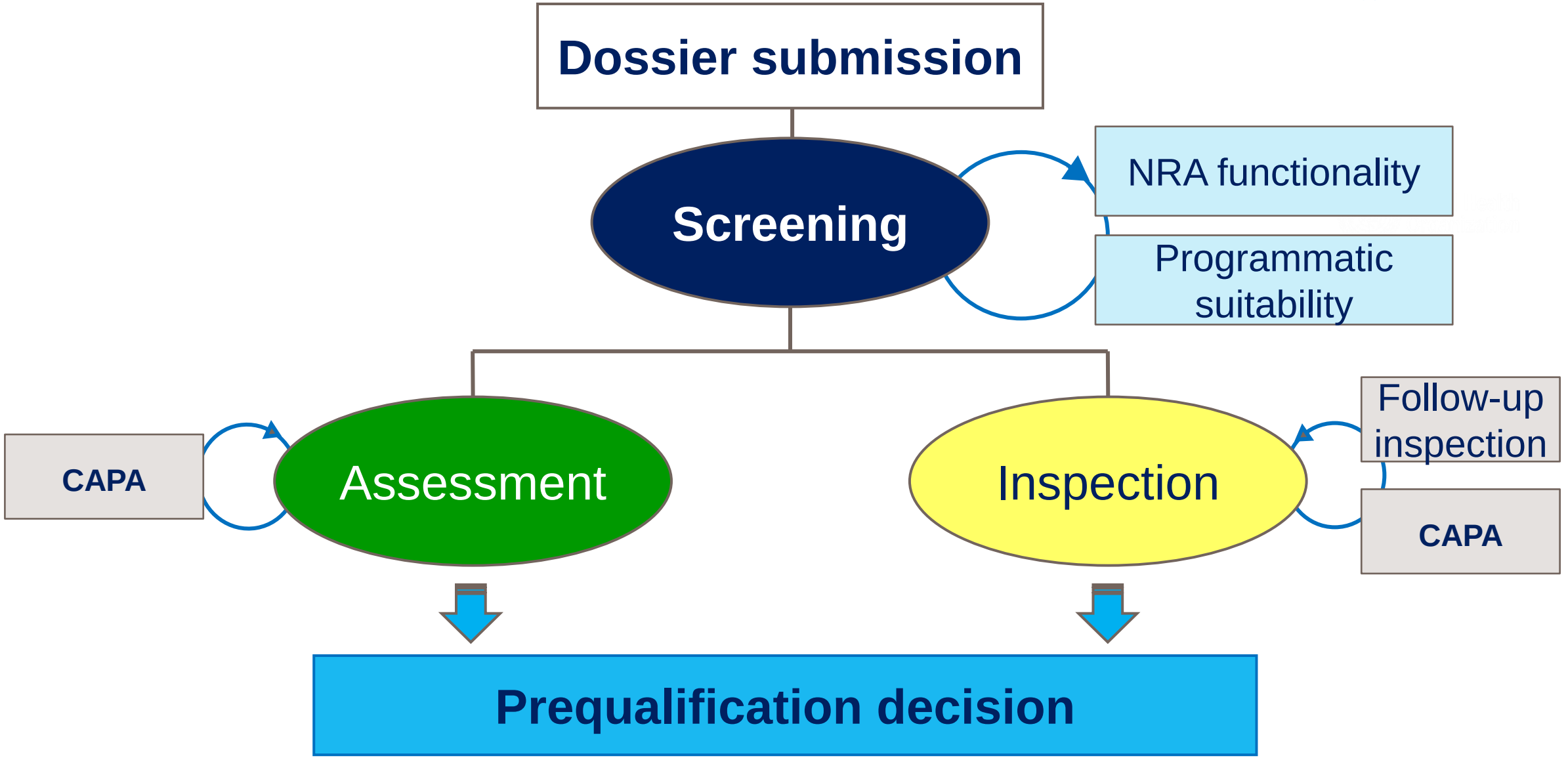
1) Antibodies, human, to enterovirus type 71 (1st IS)
2) Meningococcal serogroup A polysaccharide (1st IS)
3) Meningococcal serogroup X polysaccharide (1st IS)
4) Diphtheria toxoid (3rd IS)

Prequalification (PQ) of Vaccines by WHO

- Response to the need of procurement agencies and Member States for quality-assured health products, by creating and applying quality-assurance mechanisms
- PQ of Vaccines
  - started 1987, originally request by UNICEF and PAHO to evaluate quality, safety and efficacy of vaccines in the context of national immunization programmes,
  - 148 vaccines prequalified to-date
- Facilitates registration in developing countries
- Countries can rely on PQ assessment, inspection, lot testing, etc.

www.who.int/immunization_standards/vaccine_quality/progress_report_who_pqp_june2013.pdf?ua=1

Vaccine Prequalification workflow



Emergency Use and Assessment Listing (EUAL) for candidate vaccines – not prequalification

- A time-limited special procedure for assessment of candidate products under special public health emergencies
- Used for UN procurement decision-making
- Intended to support highly impacted countries in their regulatory decision-making

Consultation meeting held in May 2017

- Revision of the procedure based on the experience gathered
- Idea of a Pre-EUAL process
  - Could use PIP and Smallpox experiences as input on vaccine side
- Mapping of regulatory requirements for emergency use

http://www.who.int/medicines/news/public_consult_med_prods/en/

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Collaborative procedures and joint assessments:

Facilitating and accelerating registration of vaccines

Collaborative procedures and joint assessments – facilitating and accelerating registration of vaccines

- R&D Blueprint : preparing the ground
- African Vaccine Regulatory Forum (AVAREF) - successful model for joint reviews of clinical trials
- Regional Harmonisation Networks (e.g. AMRH, SEARO, GCC, CRS) facilitate registration
- Joint assessments : experience to-date
- **Collaborative Registration Procedure**

Facilitating registration: Implementation of Procedure for expedited review of imported prequalified vaccines for use in national immunization programmes

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First used for registration of MenAfriVac in 26 countries

MenAfrivac experience – forerunner of Collaborative Registration Procedure?

- MenAfrivac developed through Meningitis Vaccine Project consortium
- Regulatory support from Health Canada (HC) to Indian DCGI
- PQ using a fast track approach with reliance on HC/DCGI reviews
- Workshop in AFRO : sharing of reports that were the basis for PQ
- Successful registration in 26 countries

POLIO Eradication and Endgame STRATEGIC PLAN 2013-2018

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The Strategic Advisory Group of Experts on Immunization (SAGE), recommended in 2012 the withdrawal of the type 2 component of oral polio vaccine (OPV) from routine immunization programmes in all countries, facilitated by the introduction of at least one dose of IPV

Weekly epidemiological record WER 8901

The last case of wild poliovirus type 2 (WPV2) was seen in 1999

88% of the total of the circulating vaccine derived poliovirus (cVDPV) cases in recent years were caused by the vaccine derived type 2 strain

Introduction of IPV by 2015 and bOPV by 2016 in all countries

www.who.int/immunization/diseases/poliomyelitis/inactivated_polio_vaccine/en/
www.polioeradication.org

Facilitating Registration of IPV

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Joint review

AFRO countries
20-24 October 2014
Turkey

SEARO countries
10-14 November 2014
Thailand

Francophone countries:

Benin, Burkina Faso, Cameroon, Cote d'Ivoire, Mali, Senegal, Togo

Anglophone countries:

Botswana, Ethiopia, Ghana, Sierra Leone, Tanzania, Uganda, Zambia, Zimbabwe

Bhutan, Myanmar and Sri Lanka

Objective and Principles of WHO PQ Collaborative Registration Procedure

- **Objective:** Accelerate access to prequalified products by reducing duplication of efforts, optimizing use of resources, promoting collaboration and reliance concepts
- **Principles:** Voluntary
- Product and registration dossier in countries are 'the same' as **prequalified by WHO.**
- Shared confidential information to support NRA decision making in **exchange for accelerated registration process (90 day commitment)**
- 'Harmonized product status' is monitored and maintained

Experience with the procedure for pharmaceuticals: participating NRAs

As at 18 Sept 2017

Armenia
Botswana
Burkina Faso
Burundi
Cameroon
Caribbean Community (CARICOM*)
Cote d'Ivoire
Dem. Rep. Congo
Eritrea
Ethiopia
Georgia
Ghana
Kenya
Kyrgyzstan
Lao PDR
Madagascar
Malawi
Mali
Mozambique
Namibia
Nigeria
Philippines
Senegal
Sierra Leone
South Africa
Tanzania
Uganda
Ukraine
Zambia
Zanzibar
Zimbabwe

* CARICOM
Member States: Antigua and Barbuda, Bahamas, Belize, Dominica, Grenada, Haiti, Jamaica, Montserrat, Saint Lucia, St. Kitts and Nevis, St Vincent and the Grenadines, Suriname and Trinidad and Tobago
Associate Member States: Anguilla, Bermuda, British Virgin Islands, Cayman Islands and Turks and Caicos Islands

Win-win outcomes for all stakeholders (1)

Manufacturers

- Harmonized data for PQ and national registration
- Facilitated interaction with national regulatory authorities on assessment, inspections & testing
- Accelerated and more predictable registration
- Easier post-registration maintenance

Procurers

- Faster start of procurement and wider availability of PQ products
- Assurance about 'the same' product as is prequalified (website)

Win-win outcomes for all stakeholders (2)

National Regulatory authorities

- Having data well organized in line with PQ requirements
- Availability of WHO assessment, inspection & testing outcomes to support national decisions and save internal capacities
- Having assurance about registration of 'the same' product as is prequalified

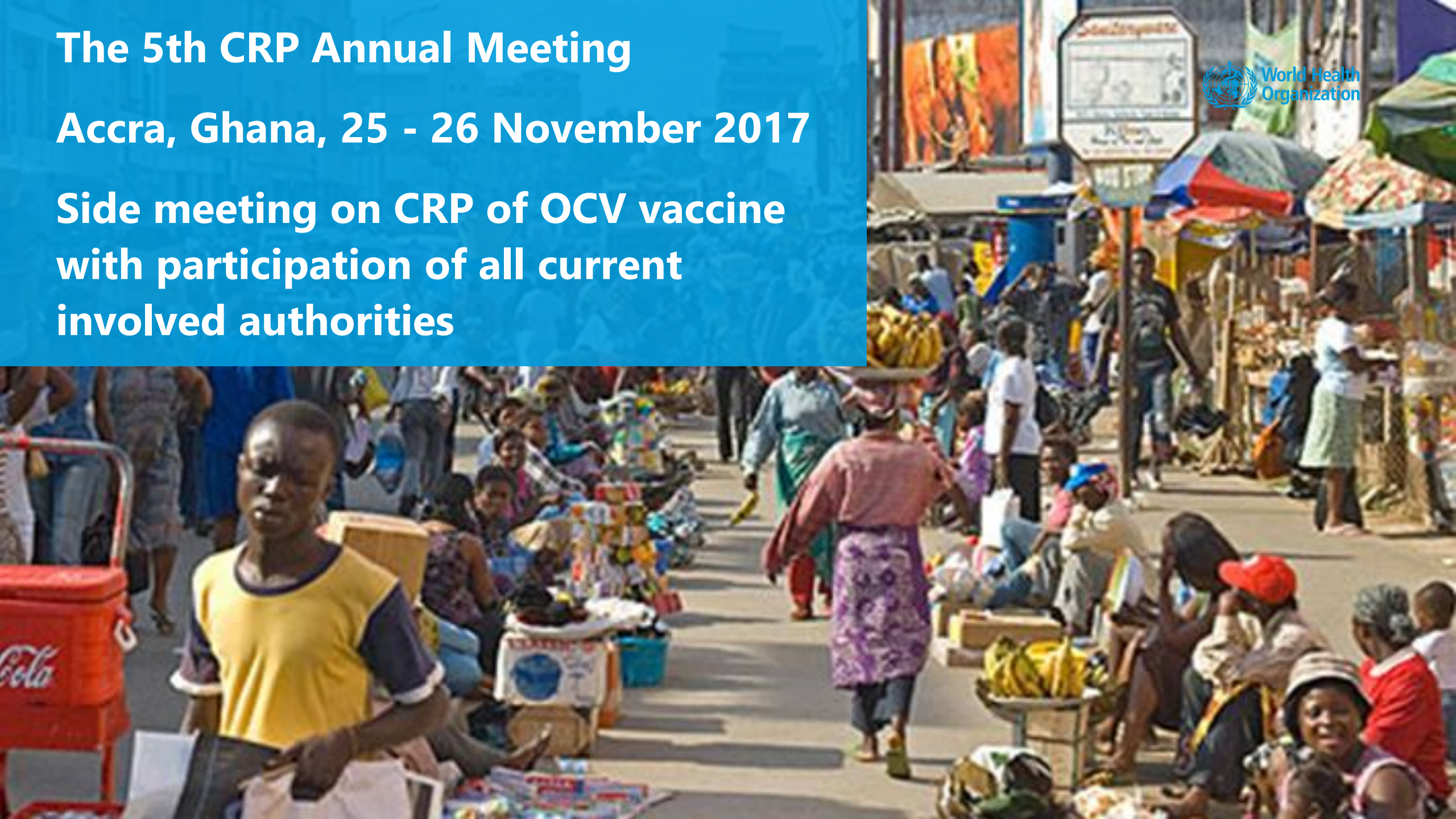
WHO

- Prequalified products are faster available to patients
- Feed-back on WHO prequalification outcomes

The 5th CRP Annual Meeting

Accra, Ghana, 25 - 26 November 2017

Side meeting on CRP of OCV vaccine with participation of all current involved authorities



Registration needs to be followed by post-marketing surveillance:

Development of mechanisms for safety surveillance

- AEFI surveillance documents prepared for different settings
  - Surveillance system in place – functioning
  - Surveillance system in place – weak
  - No surveillance system in place
- Adapted for EVD and also for smallpox
- Vaccine Rate sheets available for different diseases

http://wwww.who.int/vaccine_safety/initiative/tools/vaccininforsheets/en/

Contributing to Coalitions

- Coalition of Epidemic Preparedness Innovations (CEPI)
  - Regulatory group, Standards group
  - Supporting Tabletop exercise on emergency access to products (Ghana, November 2017)
- Coalition of Interested Partners (CIP)
  - WHO led initiative to coordinate and collaborate across donors and other stakeholders
- International Coalition of Medicines Regulatory Authorities (ICMRA)
  - Contribution to Crisis management, Vigilance work and Track and Trace

Conclusion

- ✓ Enabling Access to Vaccines and other medical products a priority for WHO
- ✓ Multiple initiatives underway to facilitate registration of vaccines
- ✓ Evolving principles of joint assessments and reliance concepts
- ✓ Success of Collaborative Registration Procedure for medicines needs to be extended to Vaccines
- ✓ Importance of creating synergies and avoiding duplication
- ✓ Collaboration and Communication across stakeholders essential