WHO Update

UNICEF Vaccine Industry Consultation
17 September 2019, Copenhagen

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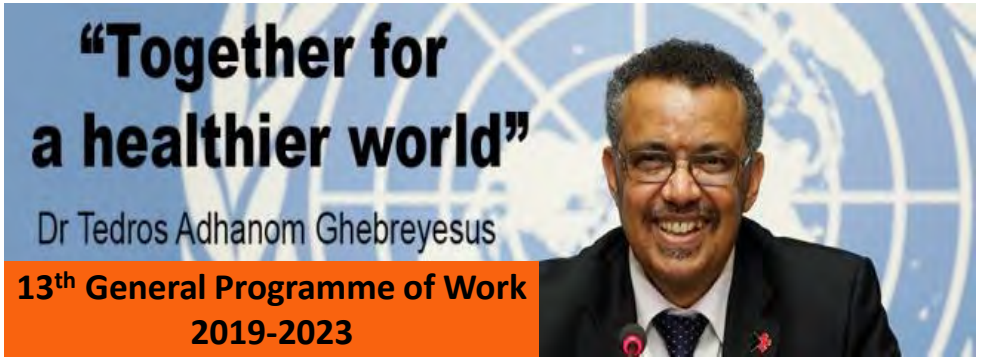
Overview

- WHO 5-year Action Plan to Help Build Effective and Efficient Regulatory Systems
  - Regulatory systems strengthening activities
  - Collaborative Registration Procedures
  - Accelerating convergence and harmonization of regulatory requirements
- Update on EUAL process: considerations for supply and procurement

WHO Transformation

Major reorganization of WHO to deliver the mission and strategic priorities of the 13th General Programme of Work



Mission

- **Promote Health**
- **Keep the World Safe**
- **Serve the Vulnerable**

Strategic Priorities

Division: Medicines & Health Products

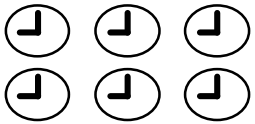
Health Products Policy and Standards	Regulatory and Prequalification
• Assistive technologies • Blood Products • Expert Committees • INN • Medical devices • Pricing policy	• Regulatory Systems Strengthening • Safety and vigilance related activities • Prequalification • Local production

Regulatory activities ensure normative and technical excellence to drive impact at country level

World Health Organization

Technologies, Standards and Norms	Regulatory Systems Strengthening	Prequalification Team	Safety & Vigilance
• Set global norms and standards (written & physical) and nomenclatures • Increase common understanding on regulatory requirements by authority & manufacturer • Standardize approach used by quality control labs	• Set effective and efficient regulatory systems in LMICs through collaborative & harmonized approaches with reliance principles • Increase confidence in medical products produced in LMICs	• Assure safety, quality, appropriateness & efficacy of medical products used in LMICs: medicines, vaccines, medical devices, cold chain equipment, vector control products & in vitro diagnostics • Increase competition to shape the market	• Increase knowledge and coordinate actions against adverse events following immunization (AEFI) • Mitigate risks and protect against substandard / falsified products • Contain antimicrobial resistance

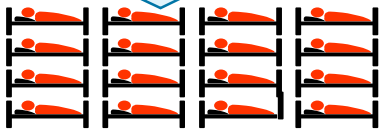
Decreased regulatory burden



Reduced time for regulation

Increased regulatory capacity in LMIC

Decreased cost of regulation



Reduced mortality and morbidity

WHO 5-year action plan to improve the quality and safety of health products

- Identifying the best ways to achieve a safe and quality-assured supply of medicines, vaccines and other health products for all
- Responding to the need for global health partners to work together towards a common goal
- Adopting a universal health coverage approach to reach the sustainable development goal
- Striving for better use of donor money and aid effectiveness by aligning milestones and activities among internal and external stakeholders

https://www.who.int/medicines/news/2019/strong-reg-systems-to-reach-UHC/en/

WHO 5-year action plan to improve the quality and safety of health products

Four strategic priorities aligned with 13th GPW

1) Strengthen country and regional systems in line with the drive toward UHC
2) Increase regulatory preparedness for public health emergencies
3) Strengthen and expand WHO prequalification and product risk assessment processes
4) Increase the impact of WHO's Regulatory Supportive activities - efficiency, advocacy, knowledge sharing, joint planning

https://www.who.int/medicines/news/2019/strong-reg-systems-to-reach-UHC/en/

Current Status of Regulatory Systems

WHO Global Benchmarking (for medicines and vaccines: as of February 2019)

World Health Organization

	1	2	3	4
ISO 9004	***No formal approach***	***Reactive approach***	***Stable formal system approach***	***Continual improvement emphasized***
WHO GBT	Some elements of regulatory system exist	Evolving national regulatory system that partially performs essential regulatory functions	Stable, well-functioning and integrated regulatory system	Regulatory system operating at advanced level of performance and continuous improvement
	Can ensure the quality of products if rely on ML3 / ML4 regulatory systems		Target of WHA Resolution 67.2	Advanced/reference Regulatory Authorities
	100 COUNTRIES	**44** COUNTRIES	**50** COUNTRIES	

Strategic priority 1: focus on actions with vaccine implications

Strengthen country and regional systems in line with the drive toward UHC

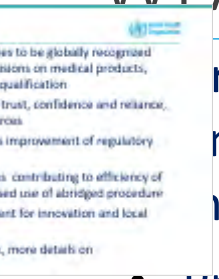
- Global Benchmarking Tool version VI published December 2018
- WHO Listed Authorities concept nearing finalization – consultation meeting this week
- Local production joint statement- 5 UN (including UNICEF) and Global Fund partners
- Consultation towards Policy on traceability of health products
- Support for countries transitioning out of GAVI and Global Fund
- WHO's network of laboratories avoiding duplicative lot testing

A new proposal aimed at promoting reliance:

WHO Listed Authority (WLA):

- Term ‘Stringent Regulatory Authority (SRA)’:
  - defined as original ICH member/observer,
  - developed to guide procurement decisions
- Widely used and recognized
- However growing concerns with term SRA:
  - with the fact that ICH doesn’t have remit or competence to assess regulatory capacity; coupled with expanding membership
- WHO expert committee asked WHO to develop new proposal in October 2017 – based on Global Benchmarking Tool assessments
- Extensive discussions and consultations, concept note published May 2019, stakeholder meeting 23 September

WLA – Why and when?



- rovides pathway for regulatory authorities to be globally recognized nd thereby help guide procurement decisions on medical products, ncluding for products not eligible for prequalification
- Provides a robust framework to promote trust, confidence and reliance, enabling efficient use of regulatory resources
- Encourages investment in and continuous improvement of regulatory systems
- Expands the pool of regulatory authorities contributing to efficiency of Prequalification program through increased use of abridged procedure
- Creates an enabling regulatory environment for innovation and local production
- Policy document to be finalized this week, more details on operationalization under development

Accelerated registration through Collaborative Registration Procedures (CRP)

World Health Organization

Objectives:

- to facilitate the assessment and accelerate national registration of Prequalified products
- to accelerate registration of health products that have already received approval from a “stringent regulatory authority”

Principles:

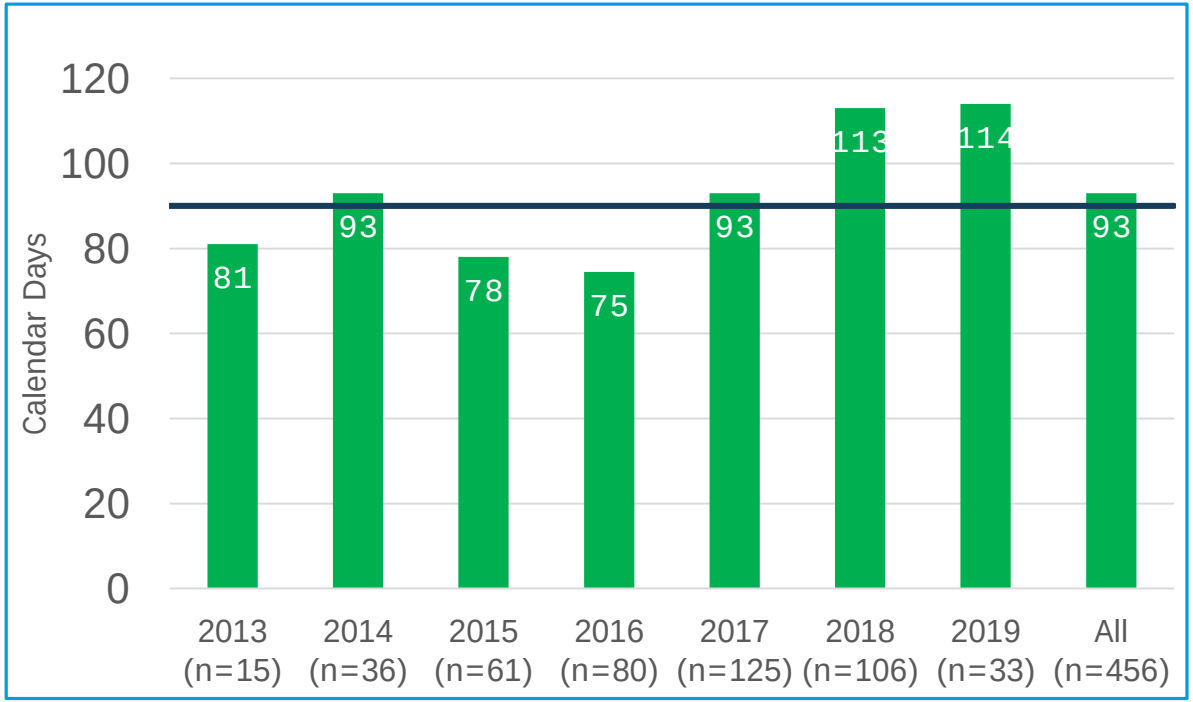
- ✓ Voluntary
- ✓ Sovereignty
- ✓ Identicality
- ✓ Co-operation
- ✓ Reliance
- ✓ Monitoring and maintenance

Sovereignty: Participating NRAs agree to respect principles, but national requirements still apply, decision remains national decision

Reliance: WHO PQT share the assessment reports, inspection reports and laboratory results with participating NRAs

Median time to registration for medicines

*Including regulatory time and applicant time



As at 26 Aug 2019

Collaborative Registration Procedure (CRP)

Countries participating to vaccines CRP

World Health Organization

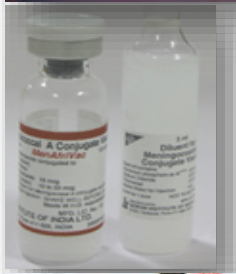
As at 26 Aug 2019

Armenia
Azerbaijan
Belarus
Botswana
Burkina Faso
Burundi
*Caribbean Community (CARICOM)
Comoros
Eritrea
Georgia
Ghana
Kazakhstan
Kyrgyzstan
Madagascar
Malawi
Mali
Namibia
Nigeria
Pakistan
Philippines
Sierra Leone
South Africa
Sri Lanka
Sudan
Tanzania
Thailand
Uganda
Uzbekistan
Zambia
Zanzibar
Zimbabwe

Red: newly joined

* 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

accelerating access to vaccines?
an examples of collaboration predating CRP



MenAfriVac (2010) - How it worked:

- Regulatory support from Health Canada (HC) and Indian DCGI
- Fast track, expedited procedure, prequalification approach, using HC/DGCI assessment (PQed in 5 months)
- Workshop in AFRO for sharing of reports that were the basis for PQ

Benefits:

- Assessment resources saved and targeted to other activities, for example, strengthening post-marketing surveillance

Successful registration of MenAfriVac in 26 countries of the meningitis belt (2011)

Experiences of CRP for Vaccines 2016/2017:
Ukraine, Zimbabwe, DRC, Ethiopia

World Health Organization

 Ukraine	2016 6 vaccines applied	5 registered in < 12 months
 Zimbabwe	2017 1 vaccine BCG (India)	Registration still pending
 DRC	2017 1 vaccine DTwP-HepB-Hib (Korea)	Registration still pending
 Ethiopia	2017 1 Vaccine DTwP-HepB-Hib (Korea)	Registered About 6 months

Experiences of CRP for Vaccines:
2017: workshop in Accra on oral cholera vaccine

- CRP workshop on registration of PQed oral cholera vaccine manufactured in Korea
- Participating NRAs:
  Ghana, Nigeria, Tanzania, Uganda and representatives from CARICOM
- Oral Cholera vaccine registered in:

Nigeria in June 2018 - < 3 months

CARICOM* in April 2018 - < 5 months

* 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

2018 Experiences of CRP for Vaccines:

 Thailand	2018 4 PQed vaccines successfully registered	Reduced registration times by more than 6 months, “excellent reports”
 Ukraine	2018 Tetanus (Indonesia)	Documentation shared Registration to be completed
 Belarus	2018 DTwP-HepB-Hib (Korea)	Documentation shared Registration to be completed

- Other “mature” authorities requesting reports, particularly for emergency products

Optimizing CRP for vaccines (1):

- Mapping of current regulatory pathways in countries critical to ensure efficient use of resources
  - Countries accepting PQed vaccines supplied through UN
  - Countries ready to accept CRP
  - CRP Agreements extended to vaccines if necessary and focal points designated

- Identification of possible constraints for implementation of the procedure in countries
  - Need for local agent in countries?
  - understanding of inspection and testing requirements,
  - interest from manufacturers to submit an application?

Optimizing CRP for vaccines (2):

Focussing resources

- Need to define priority vaccines and countries: for example,
  - priority vaccines representing major public health benefits or vaccines to contain an outbreak or vaccines under shortages
  - countries with long timelines, specific national requirements
- PQ to improve preparedness for sharing reports
- Joint review option may also facilitate registration (not CRP)

But

- Dossiers need to be first submitted in countries
  - Interest from countries that will benefit from the review - future "champions"
  - Adjustments may be needed depending on knowledge base of countries

Focus on adapting CRP from medicines to vaccines world

- Medicines based on voluntary system
- For vaccines – a need to prioritize countries and products has been identified
- Also to build on successful experiences for MenAfriVac and Polio end-game strategy
- DCVMN and IFPMA working with WHO on exploring how best to take it forward
- Some notable successes, but more work to do!

Strategic priority 2:

Increase regulatory preparedness for public health emergencies

- Roadmap for revision of emergency use procedures (EU(A)L) nearing finalisation
- Ebola Crisis DRC - accelerating access to vaccines
- Roadmaps for specific products (Merck and J&J vaccines, discussions with other vaccine developers ongoing)
- Facilitating additional evidence through additional clinical trials and expanded access
- Use of EUL for novel Polio vaccines
- Recommendation for release into the global polio stockpile of mOPV2 vaccines
- Vigilance preparedness



World Health Organization

Update on EUAL vaccine related activities


WHO Regulatory work to prepare for Public Health Emergencies

- Support for WHO's R & D Blueprint
- Technical guidelines and standards
- Regulatory Systems Strengthening (mapping of provisions and competences, table top exercise, support for guidelines and SOPs)
- Regulatory platforms to facilitate registration of drugs/vaccines through joint reviews
- Emergency Use (Assessment) and Listing (EU(A)L)
- Safety monitoring
- Communication and coordination

Assessment of Ebola vaccines

Emergency Use and Assessment Listing (EUAL):

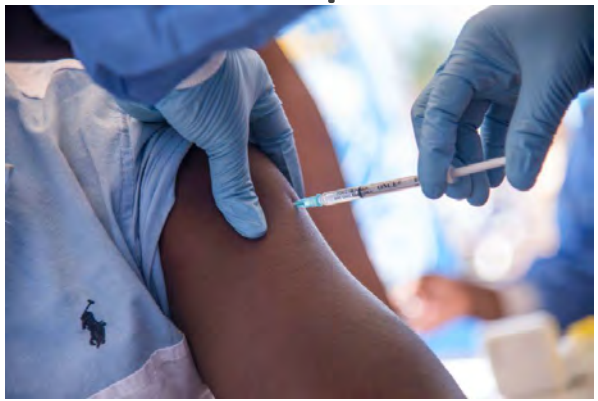
risk-based evaluations on quality, safety and efficacy data of investigational products under PHEIC

1. Merck vaccine: EUAL – positive scientific assessment
   - SAGE recommendation for use under Expanded access protocol (EAP)
2. J&J and Cansino:
   - Scientific assessments concluded
   - Additional efficacy data needed

Additional issues:

- Complexity DRC crisis and
- limited supply: Clinical trials

Accelerating access to Ebola vaccines: Roadmap and licensing



- Roadmap published on licensing of Merck's Ebola vaccine (VSV-ZEBOV) in countries at risk

https://www.who.int/medicines/news/2019/roadmap_for_intro_roll_out_licensed_ebola_vaccine/en/

Background and Development

1) Initial discussions November 2018
2) Draft prepared January 2019
3) Consultation with FDA, EMA, AVAREF
4) Discussed at AVAREF TCC and SC February 2019
5) Revised version published May 2019

Purpose of the Roadmap:

- to facilitate the introduction and roll-out of a licensed Merck Ebola Vaccine in concerned African countries
- to describe the roles and responsibilities of different stakeholders
- to clarify the potential role of AVAREF as a platform

Challenges and Options

→ PHEIC declared 17 July 2019

Constraints:

- Security situation in DRC limiting effectiveness of ring vaccination
- Limited supply of Merck Vaccine

- Contract manufacture being explored
- Limited data and/or supplies on other vaccines
- How to get additional data on other candidate vaccines?
- Licensed vaccines a priority
- Post-deployment monitoring of AEFIs critically important

PHEIC: Public Health Emergency of International Concern

SUPPLY

ICG approach?

Allocation of vaccines based on epidemiological information

Liaison with UN agencies and manufacturers

Prequalification (PQ) Achievements

World Health Organization

At the close of 2018, WHO had prequalified over 1770 products*

Diagnostics

- ✓ 88 IVDs
- ✓ 2 male circumcision devices

Medicines

- ✓ 663 FPPs
- ✓ 140 APIs
- ✓ 53 quality control labs

Vaccines

- ✓ 333 vaccines
- ✓ 413 immuni-zation device & cold chain equipment

Vector Control

- ✓ 76 vector control products (FPPs & APIs)

Through PQ, WHO has made available numerous quality-assured products to Member State markets

*: cumulative numbers of products since inception

Strategic priority 3:

Strengthen and expand WHO prequalification and product risk assessment processes

- PQ pilot for Biosimilars launched – exploring Human insulin
- First antivenom listed following risk assessment – May 2019for
  - Workshop
- IVDs – Syphilis and HBV viral load assays – new eligibility criteria for In-Vitro Diagnostics
- Reproductive health? Other Cancer medical products? Antibiotics?
- Ongoing collaboration with IVB on vaccines at all stages of development
- Use of information from WHO Listed Authorities (WLA) to facilitate prequalification

Strategic priority 4:

Increase the impact of WHO's Regulatory Supportive activities - efficiency, advocacy, knowledge sharing, joint planning

- Improve our business processes – Quality Management System
- Increase impact and efficiency – IT system, KPIs
- Step-up cross functional collaboration and communication and increase our cooperation across WHO
- Increase awareness of WHO support during product development
- Streamline policy and PQ processes, particularly for innovative products
- Increase regulatory support and focus on transitioning countries

Highlights 2019-2023 – what we promise

- Roll out of WLA process
- 60 countries with improved regulatory systems by 2023 – 2024 to reach at least ML3
- 30 countries with risk-based approach for medical devices and IVDs
- Launch of Coalition of Interested Partners
- Countries in transition – focus on regulatory and supply chain aspects
- 10 countries better prepared for emergencies, including adapted pharmacovigilance system
- Expanded scope of PQ and new routes to prequalification (WLA)

Key messages

- Strong and efficient Regulatory systems use concepts such as reliance, work-sharing and international collaboration
- Rich portfolio of concepts, tools, networks and enablers now exist – e.g.
  - Good Regulatory Practices
  - Collaborative Registration Procedures
  - Joint reviews, Regional networks…
- More work needed to translate into practical realities for vaccines
- "Political will" and understanding as well as "regulatory will" are crucial
  - the power of the patient and stakeholder voice
  - the role of regulatory champions
- Opportunities to streamline in other areas, e.g., post approval changes/variations and inspections


Regulatory Action Plan 2019-2023
Vision
Collaboration
KPIs
Strategic
Efficiency
Public Health
Emergency
Priority
Training
Global Standards
Regulation
Actions
Norms
Effective
Vigilance
Prequalification
Health
Access
Impact
Quality
Quality Assurance
Safety
Regulatory Systems
Partnership
Innovative
GBT
Reach the people
Goals
Universal Health Coverage
Reliance
Quality-Assured Medical Products

World Health Organization

thank you for your attention

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.

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Director, Regulation and Prequalification