Collaborative Registration Procedure for Advancing Vaccines’ Registration in Emerging Countries

19th Annual General Meeting
DCVMN
31 October 2018
Kunming, China

Emer Cooke
Director
Regulation of Medicines and other Health Technologies
"Together for a healthier world"
Dr Tedros Adhanom Ghebreyesus

Key Themes of WHO’s 13th General Programme of Work 2019-2023

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

Strategic Priorities
Health Coverage: 1 billion more people with health coverage
Health Emergencies: 1 billion more people made safer
Health Priorities: 1 billion lives improved

NEW Cluster
Access to Medicines, Vaccines and Pharmaceuticals (MVP)
Dr. Mariângela SIMÃO, Assistant Director General

at EB 2019
Roadmap on access to medicines and vaccines
http://www.who.int/medicines/access_use/road-map-medicines-vaccines/en/
**WHO Regulatory Activities: Focus on Access and Outcomes**

Ensuring normative and technical excellence drives impact at country level

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

Decreased regulatory burden | Reduced time for regulation | Increased regulatory capacity in LMIC | Decreased cost of regulation | Reduced mortality and morbidity
WHO ACTIVITIES in REGULATION of MEDICINES and other HEALTH TECHNOLOGIES

- Harmonization of pharmacopeia & good pharmacopeia practices
- Collaborative registration procedure for accelerated registration
- Prequalification
  - diagnostics
  - vaccines
  - medicines
  - vector control
- Coalition of Interested Partners
- Regulatory System Strengthening
- Global Benchmarking Tool (GBT) and SRAs
- Safety & Vigilance
  - post-marketing surveillance and vigilance
  - Emergency use assessment and listing
- CAPACITY in LMICs
- TECHNICAL STANDARDS & NORMS
- technologies standards and norms
- ↓ REG BURDEN
- ↓ REG for REG
- ↓ TIME for REG
- ↓ COST for REG
- Common Core

Emer Cooke 10/2
From Prequalification to Access:
How do we get quality vaccines to every child, man and woman faster and more efficiently?
Collaboration, Reliance, Harmonization, Information Sharing

- Collaborative registration procedure (CRP)
- Facilitate sharing of SCARCE RESOURCES
- Build regulatory capacity and trust
- Platforms for info exchange, Pic/s
- Eliminate duplication
- Requires political will and support
- Starts with CONVERGENCE... gradually align and become similar

Faster and increased access to medicines

Regulatory System Strengthening through NETWORKING, COOPERATION, and HARMONIZATION

October 4 - WHO TBS

Confidence building, Harmonization/convergence, Information Sharing

RECOGNITION
- EAC
- IGAD
- ECOWAS
- Common Technical Documents (CTD)

Reliance/work Sharing

AMRH, ASEAN SIAHR

Human financial structural

~85 days
Accelerated registration through Collaborative Registration Procedures (CRP)

**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
CRP Participating NRAs

<table>
<thead>
<tr>
<th>Armenia</th>
<th>Georgia</th>
<th>Philippines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Botswana</td>
<td>Ghana</td>
<td>Senegal</td>
</tr>
<tr>
<td>Burkina Faso</td>
<td>Kenya</td>
<td>Sierra Leone</td>
</tr>
<tr>
<td>Burundi</td>
<td>Kyrgyzstan</td>
<td>South Africa</td>
</tr>
<tr>
<td>Cameroon</td>
<td>Lao PDR</td>
<td>Sri Lanka</td>
</tr>
<tr>
<td>*Caribbean Community</td>
<td>Madagascar</td>
<td>Tanzania</td>
</tr>
<tr>
<td>(CARICOM)</td>
<td>Malawi</td>
<td>Thailand</td>
</tr>
<tr>
<td>Cote d'Ivoire</td>
<td>Mali</td>
<td>Uganda</td>
</tr>
<tr>
<td>Eritrea</td>
<td>Namibia</td>
<td>Zambia</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>Nigeria</td>
<td>Zanzibar</td>
</tr>
<tr>
<td></td>
<td>Pakistan</td>
<td>Zimbabwe</td>
</tr>
</tbody>
</table>

*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

As at 30 June 2018
CRP: Median time to registration
(> 350 registrations for PQ Medicines)

*Including regulatory time and applicant time
But what about access to vaccines? some examples of collaboration

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)
## Polio end-game strategy

<table>
<thead>
<tr>
<th>SAGE (2012) recommendation to withdraw type 2 component of OPV in all countries, facilitated by the introduction of at least one dose of IPV</th>
<th>Mapping regulatory status in all countries:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Already licensed</td>
<td></td>
</tr>
<tr>
<td>2) Accept PQed vaccine (waive)</td>
<td></td>
</tr>
<tr>
<td>3) Facilitated registration</td>
<td></td>
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</tbody>
</table>

<table>
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<tr>
<th>Facilitated registration:</th>
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<tbody>
<tr>
<td>&quot;Joint review&quot;</td>
</tr>
<tr>
<td>1) Standard:</td>
</tr>
<tr>
<td>EMRO (8 countries)</td>
</tr>
<tr>
<td>2) PQ approach:</td>
</tr>
<tr>
<td>AFRO (19 countries)</td>
</tr>
<tr>
<td>SEARO (3 countries)</td>
</tr>
</tbody>
</table>

Facilitated registration of two vaccines, IPV and bOPV, in all countries
<table>
<thead>
<tr>
<th>Country</th>
<th>Year</th>
<th>Vaccine Description</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ukraine</td>
<td>2016</td>
<td>6 vaccines applied</td>
<td>5 registered in &lt; 12 months</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>2017</td>
<td>1 vaccine BCG (India)</td>
<td>Registration still pending</td>
</tr>
<tr>
<td>DRC</td>
<td>2017</td>
<td>1 vaccine DTwP-HepB-Hib (Korea)</td>
<td>Registration still pending</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>2017</td>
<td>1 Vaccine DTwP-HepB-Hib (Korea)</td>
<td>Registered About 6 months</td>
</tr>
</tbody>
</table>
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:
  
  * 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

  Nigeria in June 2018 - < 3 months

  CARICOM* in April 2018 - < 5 months
Experiences of CRP for Vaccines: 2018

<table>
<thead>
<tr>
<th>Country</th>
<th>Year</th>
<th>Vaccines</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thailand</td>
<td>2018</td>
<td>4 Pqed vaccines successfully registered</td>
<td>Reduced registration times by more than 6 months, “excellent reports”</td>
</tr>
<tr>
<td>Ukraine</td>
<td>2018</td>
<td>Tetanus (Indonesia)</td>
<td>Documentation ready to be shared</td>
</tr>
<tr>
<td>Belarus</td>
<td>2018</td>
<td>DTwP-HepB-Hib (Korea)</td>
<td>Documentation ready to be shared</td>
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</table>

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

Work on Ebola vaccine ongoing with AVAREF members
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?
Focussing resources

• Need to define priority vaccines and countries: for example,
  o priority vaccines representing major public health benefits or vaccines to contain an outbreak or vaccines under shortages
  o 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
  o Interest from countries that will benefit from the review - future “champions”
  o Adjustments may be needed depending on knowledge base of countries
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.
  o Good Regulatory Practices
  o Collaborative Registration Procedures
  o 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
  o the power of the patient and stakeholder voice
  o the role of regulatory champions
• Opportunities to streamline in other areas, e.g., post approval changes/variations and inspections
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.

CRP is a key enabler

Thank you for your attention

Emer Cooke
Director, Regulation of Medicines and other Health Technologies