Collaborative registration procedures: A brief introduction

Improving the Response of Global Public Health in a Fast-changing World
Joint UNICEF, UNFPA and WHO meeting with manufacturers and suppliers of in-vitro diagnostic products, vaccines & immunization devices, finished pharmaceutical products, active pharmaceutical ingredients, contraceptive devices and vector control products
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WHA Resolutions: WHA 67.20 (2014); WHA 67.21 (2014); WHA63.12 (2010)

• All pharmaceutical products, including multisource products, should be used in a country only after approval by the national or regional regulatory authority.

• Regulatory authorities should require the documentation of a multisource pharmaceutical product to meet the following requirements:
  • GMP;
  • Quality requirements; and
  • Pharmaceutical product interchangeability.
Why focusing on national regulatory approval?

- To improve **public health** by increasing rapid access to safe and effective medicines of good quality for the treatment of priority diseases;
- Focus on in-country registration as one factor in the time it takes for beneficial therapies to reach patients in need.

**Medicines Registration Preparation and Approval Process:**

- **Lead-times to dossier submission**
  - Product R&D: 6-18 months
  - Manufacture demonstration batches: 1 month
  - B/E and stability studies: 3-6 months
  - Submissions to NMRA(s): 1-2 months

- **Actual registration time**
  - Approval: 6-24 months +

**Time to in-country availability**
How to “transfer/translate” the regulatory information to facilitate in-country approval?

• WHO Prequalification and approval by “SRAs” provide good basis for national registration;
• How do we get the prequalified and “SRA”-approved product to the patients faster, and more efficient?
• How do we ensure continued supply of quality assured products post-registration?
Facilitated pathways to “transfer” regulatory information & knowledge

**PRINCIPLES**

- **Sharing information / expertise** (assessment, inspection and testing results or expertise) that serve as basis for national decisions – avoiding duplication.
- **Voluntary participation** – reference authorities, participating authorities and manufacturers/sponsors

**WHO collaborative procedure**
- Vaccines: 2004
- Medicines: Started in 2012
- Diagnostics: Pilot 2019
- Vector control: Pilot 2020

**“SRA” collaborative procedure**
- Initiated in 2015
- European Medicines Agency (EMA)
- Medicines and Healthcare Products Regulatory Agency (MHRA)
- 20 African NRAs

**Regional networks**
- African Medicines Regulatory Harmonization Project (AMRH)
- ASEAN SIAHR Project

**CRP-lite**
Applicable guidelines for CRP

Annex 8

Collaborative procedure between the World Health Organization (WHO) Prequalification Team and national regulatory authorities in the assessment and accelerated national registration of WHO-prequalified pharmaceutical products and vaccines

1. Definitions
2. Background information
3. Principles of collaboration
4. Steps in the collaboration for national registration of a pharmaceutical product or a vaccine
5. Collaboration mechanisms for post-prequalification and/or post-registration variations
6. Withdrawals, suspensions or delistings of prequalified pharmaceutical products or vaccines and national deregistrations

References

Appendix 1 National regulatory authority participation agreement and undertaking for national regulatory authority focal point(s)
Appendix 2 Consent of WHO prequalification holder for WHO to share information with the national regulatory authority confidentially under the Procedure
Appendix 3 Expression of interest to national regulatory authority (NRA) in the assessment and accelerated national registration, acceptance by NRA and notification of Procedure outcomes
Appendix 4 Report on post-registration actions in respect of a product registered under the Procedure

http://apps.who.int/iris/bitstream/handle/10665/255338/9789241209960-eng.pdf?sequence=1
Concept of facilitated registration (based on reliance)

To support the national registrations, regulators can benefit from already conducted scientific assessments and inspections, if:

- Have access to regulatory expertise from trusted party (complete assessment and inspection reports);
- Have the same product;
- Have the same essential technical data;
- Understand validity of B/R for local environment;
- National legislation and sovereignty are not affected;
- Respect confidentiality of commercially sensitive information;
- Manage properly regulatory follow-up.
If we share information (assessments, inspections, testing) for WHO PQ-ed or “SRA”-approved products

THEN...

NRAs can rely on the shared information to facilitate national decisions

- avoid duplications
- reduce regulatory burden
- assess B/R in local context

THEN...

Timely access to quality-assured products with positive B/R

Re-allocate resources

Enhanced NRA’s oversight on other products & sites

Normal pathway
How does the collaborative procedures work?

WHO
PQ

SRA

NRA

Submission
NRA

Marketing authorisation
KEY Principles of Facilitated Registration Pathways

• Voluntary;

• Product and registration dossier in countries are “the same” as **prequalified by WHO or approved by “SRAs”**;

• Shared confidential information to support NRA decision making in **exchange for accelerated registration process**;

• “Harmonized product status” is monitored and maintained.
Win-win outcomes for all concerned stakeholders

NRAs

- Having data well organized in line with PQ requirements;
- Availability of unredacted WHO assessment, inspection and performance evaluation 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;

Manufacturers

- Harmonized data for PQ and national registration;
- Facilitated interaction with NRAs in assessment, inspections, performance evaluations;
- Accelerated and more predictable registration;
- Easier post-registration maintenance;

Procurers

- Time, assurance, availability.
Collaborative Registration Procedure: Medicines
39 Participating NRAs

Armenia
Azerbaijan
Belarus
Botswana
Burkina Faso
Burundi
Cameroon
*Caribbean Community (CARICOM)
Comoros
Cote d'Ivoire
Eritrea
Ethiopia
Georgia
Ghana
Kazakhstan
Kenya
Kyrgyzstan
Lao PDR
Madagascar
Malawi
Mali
Mozambique
Namibia
Nigeria
Pakistan
Philippines
Senegal
Sierra Leone
South Africa
Sri Lanka
Sudan
Tanzania
Thailand
Uganda
Ukraine
Uzbekistan
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

As at August 2019
Pipeline of applications in countries

As at August 2019

Country (when started):

- Registered
- Under review
- Dossier awaited

No products registered or under review yet: Georgia, Lao PDR, Sierra Leone, Zanzibar, Pakistan, South Africa, Eritrea, Sri Lanka.
Median time to registration

*Including regulatory time and applicant time

As at August 2019
CRP for Vaccines: some history

2004–2005
WHO/SEARO requested the support from PQ vaccine to facilitate the registration of vaccines. It consisted to share summary protocol and sample testing results. Called expedited license procedure

2011–2012
Principles of the CRP (sharing reports of the assessment process) firstly used for registration of MenAfriVac in 26 countries of the African belt.

2015
CRP Procedure (under revision) used as a pilot to facilitate registration of IPV vaccine. Joint review option

2016–2019
CRP procedure used on ad hoc basis to facilitate registration of other vaccines.

CRP for vaccines endorsed by ECBS
# Confirmation and submission of updated CRP Agreements, inclusive of vaccines, is still pending.
## Vaccine registrations

<table>
<thead>
<tr>
<th>PQ number</th>
<th>Product</th>
<th>Prequalification holder</th>
<th>Country</th>
<th>Registration date</th>
</tr>
</thead>
<tbody>
<tr>
<td>87.40</td>
<td>Easyfive-TT 10 Vials</td>
<td>Panacea Biotec Ltd</td>
<td>Botswana</td>
<td>3/Jul/18</td>
</tr>
<tr>
<td>304.10</td>
<td>Eupenta Carton of 1 dose</td>
<td>LG Chem Ltd</td>
<td>Ethiopia</td>
<td>20/Dec/17</td>
</tr>
<tr>
<td>304.10</td>
<td>Eupenta Carton of 1 dose</td>
<td>LG Chem Ltd</td>
<td>DRC</td>
<td>23/Mar/18</td>
</tr>
<tr>
<td>305.10</td>
<td>Eupenta carton of 10 vials (100 doses)</td>
<td>LG Chem Ltd</td>
<td>Ethiopia</td>
<td>20/Dec/17</td>
</tr>
<tr>
<td>305.10</td>
<td>Eupenta carton of 10 vials (100 doses)</td>
<td>LG Chem Ltd</td>
<td>DRC</td>
<td>23/Mar/18</td>
</tr>
<tr>
<td>336.10</td>
<td>Euvichol-Plus (Cholera) 50 dose</td>
<td>EuBiologics Co., Ltd.</td>
<td>CARICOM</td>
<td>12/Apr/18</td>
</tr>
<tr>
<td>336.10</td>
<td>Euvichol-Plus (Cholera) 50 dose</td>
<td>EuBiologics Co., Ltd.</td>
<td>Nigeria</td>
<td>6/Jun/18</td>
</tr>
</tbody>
</table>
Path forward for vaccines CRP

• Selection of vaccines;
  - Vaccines PQ-ed in the last 5 years:
  - Availability of shareable clinical, CMC, inspection and testing reports;

• Identification of priority countries based on:
  - WHO priorities - benchmarking/assessment and status of IDP implementation;
  - willingness of the manufacturers.

• Initiation of CRP in selected countries in several implementation waves;

• Follow-up, evaluation of the impact and expansion to other countries.
This Collaborative Procedure has been developed to enhance timely access to WHO-prequalified products in countries, to ensure that the product in countries is the same as the one which is WHO-prequalified and to provide a model for regulatory information exchange between countries.
Steps and timelines of the IVD CRP Pilot

- **Q3/Q4 2018**: Workshop in Nairobi: 15 NRAs, survey of status of regulation in selected countries.
- **Q4 2018**: Confirmation of countries to be included in the pilot.
- **Q2 2019**: Identification of potential products and preliminary discussions with applicants.
- **Q3 2019**: Workshop to explain requirements, process and content of reports and demonstrate how to verify sameness.
- **Q3 2019**: NRA verification of application against the PQ reports for sameness. Feedback to applicant and WHO.
## Steps and Timelines

### Preparation
- Identification of countries – **Cameroon, Ivory Coast, Ethiopia, Nigeria, United Republic of Tanzania**
- Identification of products - **m-PIMA VL (Abbott)**

### Initiation
- Interest and consent from companies - **Abbott**
- Confidential agreements by NRAs and nomination of focal persons (All except signed Cameroon)

### Application
- Application – submission of dossiers, samples and fees to NRA(s) (**July-Aug 2019**)
- Sharing of reports via access controlled database (**Aug 2019**)

### Workshop
- Workshop to explain content of reports and how to verify sameness – **April 2019, Dar Es Salaam, Tanzania**

### Registration
- Verification of sameness and decision making (**Aug-Nov 2019**)

### Feedback
- Notification to the applicant
- Feedback to WHO
- Summative evaluation workshop
Instead of conclusions:
Timely access to medical products – never-ending challenge

1) Patients/consumers – wherever they are – deserve access to quality assured medical products with positive benefit-risk characteristics - UHC;

2) Not a single regulator anymore can fulfil all regulatory work alone;

3) Today’s reality and demand: to generate quality national decisions regulators globally **MUST** collaborate and **MUST** take into consideration the information available from other regulatory authorities;

4) Not using the outputs and outcomes from other regulatory authorities means lost opportunity, duplication of efforts, increased regulatory burden and waste of scarce resources.
Questions to answer:

1. What worked well and what does not work well with CRP – regulators’ and industry’s perspective?

2. How to increase awareness of the CRP and its benefits among various stakeholders?

3. How to improve the procedure and its use for all products groups?
Thank you!

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