An Urgent and Strong Need for Harmonized Regulation of Biologics Including Vaccines in the East African Community and Africa at large

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A Decade of regulatory harmonization in Africa: Where are we? Where do we go from here?

Outline

1. Define Biologics.
2. How are biologics different from chemically synthesized medicines?
3. Why the need to harmonize the regulation of biologics in Africa?
4. Status on harmonization of regulation of medicines in Africa
5. Way forward.
Biologics are products that are produced from living organisms or contain components of living organisms.

Biologic drugs include:

- Vaccines
- Blood and blood components
- Advanced Therapy Medicinal Products (Somatic cells, tissue therapy and gene therapy)
- Allergenics
- Recombinant proteins.

Biologics are used to treat life-threatening, life-altering diseases such as cancer, rheumatoid arthritis, multiple sclerosis, and other rare diseases for which there were no previous treatment options.

There is an increasing trend in investment in the manufacture of biologics. Biologics are projected to contribute 52% of the top 100 product sales by 2022.
### Biologics Vs Conventional chemical molecules

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Chemically synthesised medicine</th>
<th>Biological medicine (protein-based)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Example</td>
<td>Acetylsalicylic acid /Aspirin (Anti-inflammatory and analgesic)</td>
<td>Monoclonal antibody e.g Bevacizumab (treats cancer and autoimmune diseases)</td>
</tr>
<tr>
<td>Molecular weight</td>
<td>180 Daltons</td>
<td>~ 149,000 Daltons</td>
</tr>
<tr>
<td>Size</td>
<td>Small</td>
<td>Large</td>
</tr>
<tr>
<td>Structure</td>
<td>Simple and defined</td>
<td>Complex</td>
</tr>
<tr>
<td>Manufacturing</td>
<td>Predictable chemical process, identical copies can be made</td>
<td>Each manufactured in a unique living cell line, similar but not identical copies can be made</td>
</tr>
<tr>
<td>Characterization</td>
<td>Easy to characterize</td>
<td>Difficult to characterize</td>
</tr>
<tr>
<td>Stability</td>
<td>Usually stable</td>
<td>More sensitive than chemical molecules to handling and storage conditions</td>
</tr>
<tr>
<td>Immunogenicity</td>
<td>Usually</td>
<td>Higher potential; always need to be tested during development</td>
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</tbody>
</table>
Comparison of structure of small chemicals molecules and biologics

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Why the need and the urgency for harmonization?

- Biologics assessment require a multidisciplinary approach which is hard to be satisfied with in a single NMRA.
- Limited capacity (personnel and facilities) for effective assessment of the quality, safety and efficacy of highly complex and variable biological products.
- Increasing need for access to quality assured biologics especially for life threatening and rare diseases for which there were no treatment options.
- Less interest of applicants in small markets. Harmonization will attract biologics manufacturers to the big African market (1.3 billion) and hence improve access.
- Weak or non-existent regulatory systems in most NMRAs. For example USFDA licensed its first biosimilar in 2015 yet some African NRAs (non-stringent) had approved some biosimilars by 2015.
Why the need and the urgency for harmonization?

- Unlike chemical pharmaceutical products, biologics rarely have pharmacopeial monographs.
- The WHO guidelines for biologics usually leave acceptance criteria for certain tests to the discretion of the NRAs that have no standards for such.
- Some biologics (e.g. Ebola vaccine) are developed majorly for Africa. Africa must be prepared to ensure quality, safety and efficacy of such products.
- Manufacturing processes for biologics are sensitive to minor changes and hence they must be robust and highly controlled.
- Even stringent regulatory agencies such as EMA have centralized the registration of most biologics.
- EAC launched its medicines harmonization process in 2012
- Harmonised technical documents have been developed for registration of pharmaceuticals
- Joint dossier assessments and GMP inspections have been conducted
- By May 2019,
  - 04 Immunological Veterinary Product applications assessed
  - 13 Human pharmaceutical (chemical) products evaluated.
  - Some biosimilars (e.g. Mabthera®) registered under the EAC joint assessment under the same framework as for chemical pharmaceuticals
  - Other biologics currently not under the EAC centralised procedure
- Other RECs such as SADC and ECOWAS are at different levels of harmonization
Gaps in the EAC harmonization process

- The EAC not mandated to grant marketing authorization. Each NRA grants its own marketing authorization which may lead to delays.
- Variations handled individually by each NRA for products jointly assessed.
- Post marketing surveillance and pharmacovigilance not centrally coordinated.
- Differences in the legal framework for the regulation of medicines in the individual NRAs.
Way forward

- Establish the current regulatory systems for biologics in Africa (what is regulated, legal framework, available guidelines and expertise)
- Build on the harmonization experience gained with other medicines in different RECs to accelerate the harmonization of registration and variation for biologics
- Develop a system for centralized post authorization monitoring of biologics
- Establish a control laboratory for testing of biologicals especially vaccines for lot release
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