Comparison of Regulatory Performance of WHO Maturity Level 3 National Medicines Regulatory Authorities in Africa: Identifying Best Practices

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Background

The World Health Organization (WHO) has developed the WHO Global Benchmarking Tool (GBT) to assess the drug regulatory systems and practices in the National Medicines Regulatory Authorities (NMRAs). The NMRAs have been encouraged to benchmark themselves as this is a way of satisfying various stakeholders' and public interests that these institutions are being efficient, effective and transparent in executing their mandate of assuring safety, quality and efficacy of medical products.

AIMS

1. Compare the Regulatory Process in the African countries that have attained WHO Maturity Level 3 (ML3)

2. Identify best practices and opportunities for improvement by comparing the regulatory performance across all five WHO Level 3 NMRAs to enhance patients' access to medicines.

Methods

Study Participants
- » Egypt – Egyptian Drug Authority
- » Ghana – Ghana Food and Drugs Authority
- » Nigeria – National Agency for Food and Drug Administration and Control of Nigeria
- » South Africa – South African Health Products Regulatory Authority
- » Tanzania – Tanzania Medicines and Medical Devices Authority

CIRS Centre for Innovation in Regulatory Science

Data Collection
- » The Optimising Efficiencies in Regulatory Agencies (OpERA) tool was completed by all 5 NMRAs

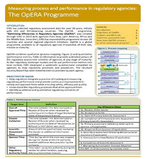
Data Analysis
- » Data were analysed for regulatory process milestones as well as the metrics for both generics and new chemical entities (NCEs) using descriptive statistics.

Method - OpERA Questionnaire

Divided into 6 Modules

- » **Module 1:** Organisation of the agency
- » **Module 2:** Types of review models
- » **Module 3:** Key milestones in the review process
- » **Module 4:** Good Review Practices
- » **Module 5:** Quality decision-making processes
- » **Module 6:** Concluding observations

OpERA Optimising Efficiencies in Regulatory Agencies



Results - Organisation of the agencies

Structure of NMRAs
- » Organized as autonomous agencies (except FDA Ghana) while all agencies regulate medical products for human and veterinary use and medical devices.

Scope of regulatory activities
- » Marketing authorizations
- » Product licences,
- » Clinical authorization,
- » Post-marketing surveillance,
- » Regulation of advertising,
- » Laboratory analysis of samples and regulatory site inspections.

Results - Types of Review Models

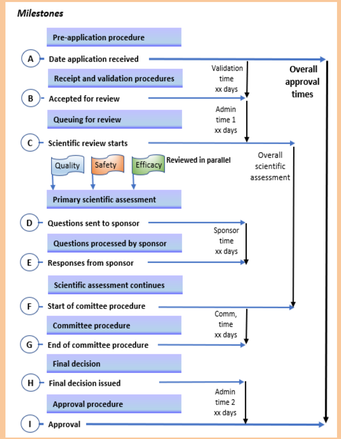
Three types of review models
- » Type 1 - Verification
  - Used for WHO- Prequalified products and Marketing Authorisation for Global Health Products (MAGHP) procedure by Swiss medic.
- » Type 2 – Abridged
  - Used for products previously approved by a Stringent Regulatory Authority (SRA)
- » Type 3 – Full
  - Used for all major applications.

Priority/fast-track procedure for applications by all agencies
- » Used for diseases with unmet medical need when a rapid assessment is required to obtain additional pharmacological, marketing/commercialization, pharmacovigilance and clinical trials information.

Results - Types of Review Models

Review model	Egypt	Ghana	Nigeria	South Africa (Backlog Clearance programme)	South Africa (BAU)	Tanzania
Type 1 - Verification	√	√	√	√	√	×
Type 2 - Abridged	√	√	×	√	√	√
Type 3A - Full	√	√	√	√	√	×
Type 3B - Full	√	×	×	√	√	√

Map of a typical NMRA Maturity Level 3 review process and key Milestones:



» **Map of the review process and authorization of a product that is approved on the first cycle**
- It does not include a second or more cycles for products approved.
- It correlates with the 'key milestones' of the review process.

Comparison of target times in the regulatory review process

Key milestones	Egypt (working days)	Ghana (Calendar days)	Nigeria (Working days)	South Africa (Backlog Clearance programme) (Calendar days) [a]	South Africa (BAU) (Calendar days)	Tanzania (working days)
Receipt and Validation	18	28	5	35	15	14
Scientific assessment	60	112	56	150	N/A	14
Applicant response time	3 months	12 months[b]	90	30	N/A	180
Expert Committee (s)	N/A	1	30	N/A	N/A	1
Authorization procedure	10	30	30	35	N/A	30
Overall approval time	N/A	266	120	250	275	240

a Based on the review process of generic applications (Assessment of NAS is longer, but these targets are currently based on limited data)
b Not later than 12, 6 and 3months from the date of 1st, 2nd and 3rd deferrals

Comparison of transparency and communication parameters implemented by the agencies

Parameter	Egypt	Ghana	Nigeria	South Africa (Backlog Clearance programme)	South Africa (BAU)	Tanzania
Feedback to industry on submitted dossiers	√	√	×	√	√	√
Details of technical staff to contact	√	√ (informally)	×	√	√	×
Pre-submission scientific advice to industry	√	√ (informally)	√	√ (informally)	√ (informally)	√
Official guidelines to assist industry	√	√	√	√	√	√
Industry can track progress of applications	N/A	√	√	√ (informally)	√ (informally)	√
Summary of grounds on which approval was granted	√	√	×	√	√	×
Approval times	√	√	√	√	√	√
Advisory committee meeting	√	√	√	√	√	√
Approval of products	√	√	√	√	√	√

Conclusions – Best Practices

The Best Practices identified from this study for effective and efficient review procedures and decision-making processes include:
- » Continuous professional training,
- » Continuous internal audit,
- » Development of published timelines,
- » Integrated quality management systems,
- » Competency of the assessors,
- » Implementation of good review practices

Moving Forward – AMA & NMRAs

The African Medicines Agency (AMA) is dedicated to improving access to quality, safe and efficacious medicines in Africa

The AMA should engage with WHO maturity level-3 NMRAs in order to explore ways that the AMA could benefit from the experience and resources of these NMRAs.

This will ensure that the AMA is effective and efficient in achieving its overall goal.

Recommendations – WHO ML3 African NMRAs

Collaboration:
- » NMRAs should improve the expertise of the assessors from these NMRAs so that they can apply their relatively stringent standards in the contribution to the African Medicines Agency (AMA) .

Mutual Recognition:
- » A mutual recognition procedure by the ML 3 agencies should be established such that the duplication in assessments is significantly reduced whilst resources are implemented more efficiently.
- » This could enhance patients' access to much-needed medicines in Africa.

Regulatory review process:
- » The NMRAs should review the timing of their product labelling so that it is conducted at the end of the review process but prior to the authorization of the application as this would facilitate the preparation of public assessment reports.

Quality Decision-Making Practices:
- » These should be formally implemented in order to improve the quality of their decision-making processes.

Implementation of Quality Decision-Making Practices

Practice	Egypt		Ghana		Nigeria		South Africa (Backlog Clearance programme)		South Africa (BAU)		Tanzania	
	Implemented in framework	Adhered to in practice	Implemented in framework	Adhered to in practice	Implemented in framework	Adhered to in practice	Implemented in framework	Adhered to in practice	Implemented in framework	Adhered to in practice	Implemented in framework	Adhered to in practice
Have a systematic, structured approach	N/A	N/A	√	√	√	√	√	√	√	√	√	√
Assign clear roles and responsibilities (decision makers, providers, information providers)	N/A	N/A	√	√	√	√	√	√	√	√	√	√
Assign values and relative importance to decision criteria	N/A	N/A	√	√	√	√	√	√	√	√	√	√
Evaluate both internal and external influences/biases	N/A	N/A	√	√	√ (partially)	√ (partially)	√	√	√	√	√	√
Examine alternative solutions	N/A	N/A	√	√	√ (partially)	√ (partially)	√	√	√	√	√	√
Consider uncertainty	N/A	N/A	√	√	√ (partially)	√ (partially)	√	√	√	√	√	√
Re-evaluate as new information becomes available	N/A	N/A	√	√	√	√	√	√	√	√	√	√
Perform impact analysis of the decision	N/A	N/A	√ (In progress)	√ (In progress)	√ (partially)	√ (partially)	Not specified	Not specified	Not specified	Not specified	√	√
Ensure transparency and provide a record trail	N/A	N/A	√	√	√	√	√	√	√	√	√	√
Effectively communicate the basis of the decision	N/A	N/A	√	√	√	√	√	√	√	√	√	√

Comparison of continuous improvement initiatives implemented by the agencies

Initiative	Egypt	Ghana	Nigeria	South Africa (Backlog Clearance programme)	South Africa (BAU)	Tanzania
External peer review	N/A	×	×	×	×	×
Internal peer review	N/A	×	√	×	×	×
Internal tracking systems	N/A	×	√	√ (informally)	√ (informally)	√
Review of assessors' feedback	N/A	√	√	√	√	√
Review of stakeholders' feedback	N/A	√	√	√ (indirectly through Industry Task Group)	√ (indirectly through Industry Task Group)	√

Comparison of quality measures implemented by the agencies

Quality measures	Egypt	Ghana	Nigeria	South Africa (Backlog Clearance programme)	South Africa (BAU)	Tanzania
Internal quality policy	√	√	√	√	√	√
Good review practice system	√	√	√	√	√	√ (informally implemented)
Standard operating procedures for guidance of assessors	√	√	√	√	√	√
Standard operating procedures for the product registration committee consulted during the review process	√	√	√	√	√	√
Assessment templates	√	√	√	√	√	√
Assessment report	√	√	√	√	√	√
SOP for completing the assessment report	√	√	√	√	√	√
SOP for any other procedures in the regulatory review process (e.g. validation)	√	√	√	Not specified	Not specified	√
Dedicated quality department	√	√	√	√	√	×
Scientific committee	√	√	√	√	√	√
Shared and joint reviews	Not specified	√	√	√	√	√