AUDA-NEPAD
AFRICAN UNION DEVELOPMENT AGENCY

Eligibility Criteria Guidance on

Priority Medicinal Products for Continental Assessment, 2023

Evaluation of Medicinal Products – Technical Committee (EMP – TC)

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1- Background

Priority medicinal products for continental assessment are medicines that will be assessed under the Evaluation of Medicinal Products Technical Committee (EMP-TC) and that require regulatory expertise not currently available in most countries or for which expertise is limited under Medicines Regulatory Harmonization (MRH) projects at Regional Economic Community (REC) level. Priority products may also be medicines needed across the continent but often in small volumes in each country to give enough incentives to manufacturers to apply for registration at country level or even to apply for joint assessments at regional level. They are also medicines needed under special circumstances, such as public health emergencies of continental, regional or national scope.

To assess priority medicines, EMP-TC will work with a pool of assessors from African NRAs but will also benefit at the start from support from international regulatory experts. The objective being to progressively build capacity of regulatory experts on the continent.

Product recommendations from the EMP-TC is envisaged to lead to a fast national registration by the 55 National Regulatory Authorities based on the assessment report produced by the EMP-TC using a reliance model. Therefore, the EMP-TC assessment process should be strong enough to guarantee the quality of the assessments done at continental level, to avoid duplication of efforts by NRAs and RECs and to attract manufacturers to apply using this pathway.

2- Eligibility Criteria

To identify criteria for eligibility of the priority products for continental assessments, the EMP-TC conducted a review of the lists of products jointly assessed so far by RECs, looked at products in the WHO PQ pipeline and at priority products under EMA centralized process.

This work was also guided by the Article 20 of the AMA Treaty, under the establishment of technical committees of the AMA which is stating that *"dossier assessments are considered for advanced therapies, biologicals (including biosimilars and vaccines), medicines for emergencies, orphan medical products and African traditional medicines".*

Based on the initial report discussed during the first meeting of the EMP-TC in Accra, Ghana on 6 and 7 Dec 2022[1], a first draft of priority products is proposed for consultation with all continental stakeholders.

Priority products will initially focus on essential medicines as defined in the WHO EML[2] (as no continental EML is currently available). The work done by the EMP-TC will then contribute to improve access to quality-assured essential medicines necessary for treatment and prevention of the priority diseases existing in Africa. In the future, the scope may progressively be expanded to non-essential medicines when the continental process is fully established and considering NRAs must register all products entering on their market.

a) Priority Diseases

In recent years, a lot has been done to improve the quality of medicines for communicable diseases and African NRAs have increased their capacity to assess medicines for

[1] See presentation attached.
[2] WHO EMLc 8th List (2021)

communicable diseases thanks to REC joint assessments and the collaborative registration process (CRP) allowing them to fast-track register products prequalified by WHO or SRA approved.

Noncommunicable diseases (NCDs) represent the leading cause of death globally. In 2015, NCDs were responsible for 40 million (70%) of the world's 56 million deaths, with 27% (15 million) dying prematurely (between the ages of 30 and 70); over 80% of these premature deaths occurred in low- and middle-income countries.[3]

WHO estimates that deaths from noncommunicable diseases (NCDs) are likely to increase globally by 17% over the next 10 years, and the African Region will experience a 27% increase, that is 28 million additional deaths from these conditions which are projected to exceed deaths due to communicable, maternal, perinatal, and nutritional diseases combined by 2030.

Therefore, the EMP-TC considers *noncommunicable diseases medicines* as a priority group for continental assessment as procurement volumes will increase significantly soon. The four main types of noncommunicable diseases are cardiovascular diseases (like heart attacks and stroke), cancers, chronic respiratory diseases (such as chronic obstructed pulmonary disease and asthma) and diabetes.

Among the medicines recommended by WHO to treat NCDs, capacity already exist at NRA or REC level to assess the quality, efficacy, and safety of small molecules in traditional dosage forms (oral products for hypertension, stroke or for diabetes, simple injectable products). However, among these medicines, some complex formulations exist that will be offered as originators or generics/biosimilars that require additional expertise such as:

- Human and analogue insulins (biological product)
- Biologic products for cancer treatment
- Inhaled medicines for asthma and COPD (combination of a formulation and a device)

Only few medicines are currently in the scope of the WHO PQ Programme (insulin[4] and biotherapeutic products[5]). The first biosimilar product was prequalified by WHO in December 2019[6]. This means that even at the level of WHO biotherapeutic products have only been recently considered in the prequalification scheme.

Neglected Tropical Diseases have also been identified as priority diseases, considering some of these diseases are specific to the African context which means it will be important for the continent to develop expertise to assess these products.[7]

Neglected tropical diseases (NTDs) encompass 17 bacterial, parasitic, and viral diseases that occur solely, or principally in tropical regions. They are often termed 'neglected' as the people who are most affected are the poorest populations living in rural areas, urban slums, and conflict zones. NTDs in Africa include Buruli Ulcer, Guinea Worm Disease, Helminthiasis, Leishmaniasis, Leprosy, Lymphatic filariasis, Onchocerciasis, Schistosomiasis, Trachoma, Trypanosomiasis African and Cysticercosis.

Considering procurement volumes for these medicines are often low in each country, it would make sense to consider assessing these products at continental level to give an incentive to

[3] Noncommunicable Diseases | WHO | Regional Office for Africa
[4] EOI_Insulin_V2_May2022.pdf (who.int)
[5] 04_EOI_PQ_BTPs_Feb2019.pdf (who.int)
[6] WHO prequalifies first biosimilar medicine to increase worldwide access to life-saving breast cancer treatment
[7] Neglected Tropical Diseases | WHO | Regional Office for Africa

manufacturers to register or obtain marketing authorization of their products in countries through a single assessment process at continental level. It could also encourage the establishment of pooled procurement initiatives at continental level.

Some of the medicines for NTDs are currently in the scope of the WHO PQ programme[8] so continental assessment could benefit from reliance on the work done by WHO PQ and for applications received at continental level to collaborate with WHO PQ team to progressively build capacities.

Rare and **orphan diseases** affect a small number of patients, and their management presents specific challenges, including the need for complex and specialized care. There are no treatments for many rare and orphan diseases. But when a treatment exists, its availability may depend on domestic legislation and regulations, including national orphan medicines policies, orphan medicines designations and marketing authorizations. Orphan medicines designations vary among jurisdictions[9,10]. So far, no definition exists on the African continent. Cell therapies, gene therapies and cell-based gene therapies have the potential to meet the medical needs of individuals with rare and orphan diseases. Cell therapies, gene therapies and cell-based gene therapies vary in nature, and the relevant regulatory framework and evaluations are not harmonized or even in place.[11] It should also be noted that volumes for orphan medicines are usually very small to provide an incentive to manufacturers to develop and register such products in countries.

For orphan medicines, the most member states in the continent are currently fully relying on assessment done by Stringent Regulatory Authorities but soon, it would be important for NRAs to build capacity to assess these products. Starting through a continental procedure will help to pool the expertise needed and to benefit from the experience from more advanced NRAs within the continent and outside the continent through technical partners collaborating with the EMP TC.

New Chemical Entities (NCE)/Novel products for noncommunicable diseases, NTDs and orphan diseases will be considered as part of the priority products on a case-by-case basis based on public health priorities as they will require assessors having pre-clinical and clinical competencies that may not always exist in NRAs or RECs.

In addition, **some new products for communicable diseases** such as malaria and TB may be considered as part of the priority products for continental assessment. Same for the HIV/AIDS medicines that are not in the scope of the WHO Prequalification program.

b) Medicines for emergencies

[8] EOI-NTD-v7_Jan2020_v2.pdf (who.int)

[9] **EMA:** A medicine for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating condition that is rare (affecting not more than five in 10,000 people in the European Union) or where the medicine is unlikely to generate sufficient profit to justify research and development costs.

[10] **US FDA:** an orphan drug is defined as one "intended for the treatment, prevention or diagnosis of a rare disease or condition, which is one that affects less than 200,000 persons in the US" (which equates to approximately 6 cases per 10,000 population) "or meets cost recovery provisions of the act.

[11] Expanding access to effective treatments for cancer and rare and orphan diseases, including medicines, vaccines, medical devices, diagnostics, assistive products, cell- and gene-based therapies and other health technologies; and improving the transparency of markets for medicines, vaccines, and other health products (who.int)

According to a recent report published by WHO AFRO[12], main emergencies are Ebola, Monkey pox, yellow fever, cholera, lassa fever, rift valley fever, Chikungunya… As recently seen with the COVID-19 pandemic or the Ebola outbreak, responding to public Health Emergencies as declared by the WHO, Africa CDC or Ministries of Health require the fast availability of medicines including vaccines with sometime the need for quick assessments and decisions on new medicines being developed by manufacturers.

Therefore it is proposed to assess **new medicines/vaccines for emergencies** at continental level to be able to mobilize quickly the expertise existing on the continent but also to use existing collaborations with WHO or more advanced NRAs, when needed.

The example of what has been done for COVID-19 vaccines, COVID-19 medicines[13] or Ebola vaccines and what is currently being done for Malaria with the support of AVAREF should now be transferred to the EMP-TC committee.

c) Complex products (complexity being understood as complex products to assess)

For the EMP-TC, complex products include biologicals among which vaccines but also products with complex formulations such as products containing nano particles or liposomes, combined products (composed of a formulation and a medical device), advanced technologies or products with new "advanced delivery innovations". It is proposed that complex formulations should be eligible for continental assessment under the EMP TC regardless of the diseases conditions they are meant for.

Advanced expertise might be needed to effectively assess these products. This may sometime include a combination of expertise in medicines and medical devices assessments which can easily be pooled by the EMP TC through collaboration with the continental African Medical Devices Forum (AMDF) TC or its technical partners.

I. Biologicals

According to WHO terminology[14], biologicals are products for which the API is a biological substance. Biologicals include[15]:

a) Products of genetically modified organisms (such as insulins)
b) Conventional/traditional Vaccines (bacterial, viral or combinations)
c) Immunotherapeutic products (cell-based tumor vaccines, human cellular vaccines)
d) Peptides and Polypeptides based medicinal products.
e) Monoclonal antibodies and for prophylaxis
f) Other human cell-based products (such as fibroblast, epithelial cells, chondrocytes)

Based on an analysis of the WHO EML 2021, a list of biological essential medicines has been identified that could be considered for the selection of priority products for continental assessment to support the public health agenda of Africa:

[12] WHO AFRO EPR Cluster_Q2_2022 report_-1.pdf
[13] EOI_EbolaVirusDisease_V1_Oct2021.pdf (who.int)
[14] Terminology Listing by category (who.int)
[15] GUIDELINES FOR REGISTERATION OF BIOLOGICAL PRODUCTS.pdf (fdaghana.gov.gh)

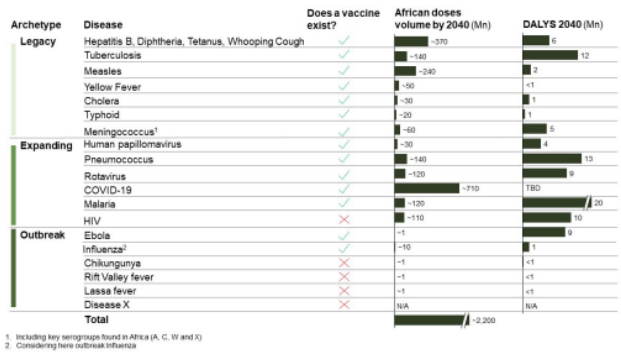
Biological medicines in WHO EML 2021	
	Included as part of the complementary list in WHO EML
	In the scope of WHO PQ Programme
Medicine name	**EML section**
Adalimumab	Immunomodulators for non-malignant disease
Anti-D immunoglobulin	Human immunoglobulins
Anti-rabies immunoglobulin	Human immunoglobulins
Anti-rabies virus monoclonal antibodies	Immunologicals > Sera, immunoglobulins and monoclonal antibodies
Anti-tetanus immunoglobulin	Human immunoglobulins
Antivenom immunoglobulin	Immunologicals > Sera, immunoglobulins and monoclonal antibodies
Asparaginase	Cytotoxic medicines
Bevacizumab	Ophthalmological preparations > Anti-vascular endothelial growth factor (VEGF) preparations
Certolizumab pegol	Immunomodulators for non-malignant disease
Coagulation factor VIII	Blood Coagulation factors
Coagulation factor IX	Blood Coagulation factors
Dalteparin	Medicines affecting coagulation
Darbepoetin alfa	Antianaemia medicines
Diphteria antitoxin	Immunologicals > Sera, immunoglobulins and monoclonal antibodies
Enoxaparin	Medicines affecting coagulation
Epoetin alfa	Antianaemia medicines
Epoetin beta	Antianaemia medicines
Epoetin theta	Antianaemia medicines
Equine rabies immunoglobulin	Immunologicals > Sera, immunoglobulins and monoclonal antibodies
Erythropoiesis-stimulating agents	Antianaemia medicines
Etanercept	Immunomodulators for non-malignant disease
Filgrastim	Immunomodulators
Golimumab	Immunomodulators for non-malignant disease
Heparin sodium	Medicines affecting coagulation
Infliximab	Immunomodulators for non-malignant disease
Insulin	Insulins
Insulin degludec	Insulins
Insulin detemir	Insulins
Insulin glargine	Insulins
Intermediate-acting insulin	Insulins
Long-acting insulin analogues	Insulins
Methoxy polyethylene glycol-epoetin beta	Antianaemia medicines

Nadroparin	Medicines affecting coagulation
Normal immunoglobulin	Human immunoglobulins
Nivolumab	Immunomodulators
Pegaspargase	Cytotoxic medicines
Pegylated interferon alfa (2a or 2b)	Antivirals for hepatitis C
Pembrolizumab	Immunomodulators
Rituximab	Targeted therapies
Trastuzumab	Targeted therapies
Vaccines	

II. Vaccines

For **vaccines** and based on the PAVM Framework for Action (PAVM FFA)[16], a list of 22 diseases were prioritized addressed by 18 vaccine products which currently exist or are under development. We can add to this list the Monkey Pox vaccine and. This will include vaccines using different technologies including mRNA vaccines.

Exhibit 11: 22 diseases prioritized for the FFA



Considering the continent is now investing and building capacity for vaccines production, it is critical to reinforce capacity of NRAs to register and properly release vaccines produced on the continent. Limited expertise exists currently in NRAs and RECs to assess vaccines. To date only the NRAs of Egypt and South-Africa have attained a WHO Maturity Level 3 for vaccines. With the support of AMRH and PAVM Regulatory bold program, it will be critical to pool expertise at continental level to assess vaccines. This will be done through the establishment of a sub-committee for biologicals and vaccines under EMP-TC that will also collaborate closely with the WHO PQ Programme for vaccines. This committee will focus on new vaccines being developed, targeting priority vaccines produced on the continent as well as other vaccines necessary for the continent. Considering most of these vaccines are in the scope of WHO PQ, reliance and collaboration will be put in place with WHO PQ Programme to progressively build capacity of African inspectors and assessors.

III. Complex products

In addition to biologicals and vaccines, complex products that require specific regulatory expertise that is not always available at country or REC level have been identified among the essential medicines listed on WHO EML 2021. The list below includes complex formulations

[16] PAVM-Framework-for-Action (2).pdf

and combined products from the WHO EML 2021 and shall also be eligible for continental assessment.

- Amphotericin B **liposomal** complex 50mg inj
- Copper containing device
- Levonorgestrel-**releasing intrauterine system** (WHO PQ scope RH[17])
- Etonorgestrel **releasing implant** (WHO PQ scope RH)
- Levonorgestrel releasing implant (WHO PQ scope RH)
- Ethinylestradiol + etonogestrel **vaginal ring**
- Progesterone vaginal ring (WHO PQ scope RH)
- Nicotine **transdermal patch**
- Budesonide **inhaler**
- Budesonide + Formoterol inhaler
- Ipratropium inhaler
- Salbutamol inhaler
- Tiotropium inhaler
- Products in **pre-filled syringes**

As stated, earlier products with new delivery innovations will also be considered eligible and will include Vaccine Microarray Patches (VMAPs), thermostable vaccines, multiple dose pouches and any other human medicinal products meeting this criterion.

3- Note

It should be noted that, this document proposes ELIGIBILITY CRITERIA that assigns priority to human medicinal products that will qualify to use the EMP TC assessment pathway. The list has taken into consideration all factors existing at country and RECs levels to establish a pathway that will build a foundation for reliance and recognition of EMP TC recommendations.

This list has been defined at the start of the EMP-TC and could be amended/updated based on new priorities. A provision should allow manufacturers to approach the EMP TC to check if a product could be eligible for continental assessment by the committee. This should appear in the Expression of Interest that will be published.

[17] EOI_ReproductiveHealth-V9.pdf (who.int)