AUDA-NEPAD
AFRICAN UNION DEVELOPMENT AGENCY

World Health Organization

Guidance on Eligibility Criteria for Priority Medicinal Products Through Continental Assessments

Evaluation of Medicinal Products – Technical Committee (EMP – TC)
African Medicines Regulatory Harmonisation (AMRH) Initiative

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 incentivise manufacturers to apply for registration at country level or even for joint assessments at regional level. They are also medicines needed under special circumstances, such as continental, regional or national public health emergencies.

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 is to build the capacity of regulatory experts on the continent progressively.

Product recommendations from the EMP-TC are envisaged to lead to rapid national registration by the 55 National Regulatory Authorities based on the assessment report produced by the EMP-TC using a reliance model in alignment with continental reliance frameworks. 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.

Guidance on Assessing Eligibility Criteria of Medicinal Products through the EMP TC

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

This work was also guided by Article 20 of the AMA Treaty, under the establishment of technical committees of the AMA, which states 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 , a first version of the Guidance on Eligibility Criteria for priority products is published for use. The criteria of medicinal products which are considered eligible through the continental assessment route under AMRH and eventually AMA once operational will be classified into four (4) categories as follows:

Category 1: Medicinal Products for which there is limited expertise at Regional and National Level

Category 1 is comprised of four sub-categories of medicinal products which are considered eligible through the EMP TC based on the current situation in terms of expertise and resources existing in regional initiatives and national regulatory agencies in Africa as follows:

- New Chemical Entities or New Biological Entities (NCEs/NBEs) (First-time global introduction, i.e., no evidence available to the EMP TC of approvals elsewhere in the world)
- NCEs/NBEs [with MAs in what is considered well-regulated markets* (i.e., current SRAs countries) but not in any African NRAs]
- Complex generic products (i.e., Products that have complex active ingredients, formulations, dosage forms, or routes of administration or are complex drug-device combination products) and other complex medicinal products.
- Vaccines and other biological products include other Biotherapeutic and Similar Biotherapeutic Products (Biosimilar), including gene and advanced gene therapies.

* Countries whose regulatory authority is:

- a member of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), the European Commission, the US Food and Drug Administration and the Ministry of Health, Labour and Welfare of Japan, also represented by the Pharmaceuticals and Medical Devices Agency (before 23 October 2015); or
- an ICH observer, being the European Free Trade Association, as represented by Swissmedic and Health Canada (as before 23 October 2015); or a regulatory authority associated with an ICH member through a legally binding, mutual recognition agreement, including Australia, Iceland, Liechtenstein and Norway (as before 23 October 2015).

Rationale

NCEs/NBEs are included because there is limited expertise in Africa for assessing pre-clinical and clinical data to ensure any new NCE, even with US FDA or EMA approval, has a positive benefit-risk profile in African populations and to address African-specific risk management after approvals, including safety profiles monitoring.

Complex products (complexity being understood as complex products to assess). These products include products containing complex active ingredients, formulations, dosage forms, or routes of administration, or are complex drug-device combination products) and other complex formulations such as products containing nanoparticles or liposomes, advanced technologies or products with new "advanced delivery innovations". These kinds of products will be eligible for continental assessment under the EMP TC regardless of the disease conditions they are meant for.

It is understood that advanced expertise might be needed to assess these products effectively. This may sometimes include a combination of expertise in medicines and medical device assessments, which the EMP TC can easily pool through collaboration with the continental African Medical Devices Forum AMDF-TC or its technical partners.

The list in **Annex 1** is an example of medicinal products considered complex formulations and combined products adopted from the current WHO EML, which will be eligible for continental assessment. The EMP TC will recognise the list as it is updated from time to time by the WHO without needing to revise this Guidance document, provided that they still meet the criteria prescribed under this document.

Biological products, as adopted in WHO terminology[1], are the types of medicinal products for which the API is a biological or immunogenic substance. Biologicals include[2]:

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

Based on an analysis of the current WHO EML, a list of biological essential medicines has been identified to serve as an example for this category that could be considered eligible as priority products for continental assessment to support the public health agenda of Africa. The list is provided in this document as **Annex 2**. This is, therefore, **not an exhaustive list** for the EMP-TC but rather an example under this category of medicinal products, as highlighted previously.

An example of **vaccines** eligible for continental assessment is extracted from the PAVM Framework for Action (PAVM FFA)[3]. In contrast, a list of 22 diseases is prioritised and addressed through the 18 vaccine products detailed in **Annex 3**. Considering the continent is now investing and building capacity

1 Terminology Listing by category (who.int)
2 Guidelines for Registeration of Biological Products.pdf (fdaghana.gov.gh)
3 PAVM-Framework-for-Action (2).pdf

for vaccines production, it is critical to reinforce the capacity of NRAs to register and properly release vaccines produced on the continent.

Limited expertise exists currently in NRAs and RECs to assess vaccines. Only the NRAs of Egypt and South Africa have attained a WHO Maturity Level 3 for vaccine-producing countries. At the same time, the WHO recognises Tanzania and Ghana as vaccines non-producing ML3 countries. Through the AMRH or AMA, once operational, it is vital to pool expertise at continental level to assess vaccines. This process will be driven by the established sub-committee for biologicals and vaccines under EMP-TC, which will also collaborate closely with the WHO PQ Programme for vaccines. This subcommittee is expected to take the lead in focusing on new vaccines being developed, targeting priority vaccines produced on the continent and 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 the WHO PQ Programme to progressively build the capacity of African inspectors and assessors and complement the efforts for collaborative registration procedures.

Category 2: Medicinal Products Addressing Africa's Public Health Priorities

The work done by the continental EMP TC is expected to contribute to access to quality-assured essential medicines necessary for the treatment and prevention of the priority diseases in Africa and to consider medicinal products meant for the treatment of rare and neglected diseases in Africa as well as to support AU member states in assessing medicinal products needed during public health emergencies.

Category 2 will comprise of the following three sub-categories of medicinal products:

- Medicinal Products for addressing priority diseases identified in African populations, e.g., Noncommunicable Diseases (NCDs), Neglected Tropical Diseases (NTDs) and priority Communicable Diseases.

- Medicinal Products intended for use in rare or life-threatening, seriously debilitating, or chronic disease that affects very few people in Africa for which no satisfactory method of diagnosis, prevention or treatment has been authorised or, if such method exists, the medicinal product would be of significant benefit to those affected by the disease such as Orphan Medicines.

- Medicinal Products for Emergency Use.

Rationale

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[4].

WHO estimates that deaths from Noncommunicable Diseases (NCDs) are likely to increase globally by 17% over the next ten 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 exists at the NRA or REC level to assess the quality, efficacy, and safety of small molecules in traditional dosage forms (oral products for hypertension, stroke or 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:

4 Noncommunicable Diseases | WHO | Regional Office for Africa

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

Only a few medicines are currently in the scope of the WHO PQ Programme (insulin[5] and biotherapeutic products[6]). WHO prequalified the first biosimilar product in December 2019[7]. This means that even at the level of WHO, biotherapeutic products have only been recently considered in the prequalification scheme.

In addition, some new products for communicable diseases, such as Malaria HIV/AIDS and TB, may be considered part of the priority products for continental assessment when not covered by the scope of the WHO Prequalification Programme, or they meet other criteria under other categories.

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 necessary for the continent to develop expertise to assess these products[8]. 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.

Since procurement volumes for these medicines are often low in each country, it would make sense to consider assessing these products at continental level to incentivise manufacturers to register or obtain marketing authorisation 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[9], so continental assessment will benefit from reliance on the work done by WHO PQ and for applications received at the continental level to collaborate with the WHO PQ team to progressively build capacities and consider the data for Africa's specific markets and to assist in advocacy for adoption of recommendations.

Rare diseases affect a small number of patients, and their management presents specific challenges, including the need for complex and specialised care. There are no treatments for many rare diseases. But when a treatment exists, its availability may depend on domestic legislation and regulations, including national orphan medicines policies, designations, and marketing authorisations. Orphan medicines designations vary among jurisdictions[10][11]. 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 harmonised or even in place[12]. 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, most member states in the continent currently rely entirely on assessments done by Stringent Regulatory Authorities. Still, soon, it would be necessary for NRAs to build capacity to assess these products. Starting through a continental procedure will help pool the expertise needed and benefit from the experience of more advanced NRAs within and outside the continent through technical partners collaborating with the AMRH EMP TC.

5 EOI_Insulin_V2_May2022.pdf (who.int)
6 04_EOI_PQ_BTPs_Feb2019.pdf (who.int)
7 WHO prequalifies first biosimilar medicine to increase worldwide access to life-saving breast cancer treatment
8 Neglected Tropical Diseases | WHO | Regional Office for Africa
9 EOI-NTD-v7_Jan2020_v2.pdf (who.int) L
10 **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.
11 **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.
12 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 the current report published by WHO AFRO, medicines for emergencies are meant for emergency diseases. The main emergencies are Ebola, Monkeypox, Yellow Fever, Cholera, Lassa Fever, Rift Valley fever and 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 requires the fast availability of medicines, including vaccines, sometimes with the need for quick assessments and decisions on new medicines being developed by manufacturers.

Therefore, these new medicines/vaccines for emergencies at the continental level will be eligible for continental assessment to quickly mobilise the expertise on the continent and use existing collaborations with WHO or more advanced NRAs when needed through the AMRH PP.

The example of what was done for COVID-19 vaccines, COVID-19 medicines or Ebola vaccines and what is currently being done for Malaria with the support of AVAREF. These types of medicinal products will be considered with this proper technical group on the continent.

Category 3: Locally Manufactured Medicinal Products

To support and create an enabling environment for local production in Africa in alignment with the AU Pharmaceutical Manufacturing Plan for Africa (PMPA) and Partnership for African Vaccines Manufacturing (PAVM), products manufactured in Africa regardless of formulation complexity, nature or therapeutic class will be considered eligible for continental assessment route through the EMP TC.

Generics manufactured outside Africa will not be considered for continental assessment unless they meet other criteria in this guidance under Category 1 and 2, such as complex formulation, medicines for priority diseases as defined by the African Union and Africa CDC, etc. The EMP-TC will assess eligibility criteria before a product is accepted for continental assessment in alignment with this guidance and other EMP-TC-established procedures.

The definition of a "Local Manufacturer" may differ from one jurisdiction to another. Therefore, this will be based on the legal meaning of a concerned AU member state where the manufacturer is located on what is considered "local."

Category 4: Medicinal Products Outside the scope of recognised international regulatory/ quality assurance systems (QA)

Any other medicinal product may be considered eligible through a continental assessment even if it does not meet criteria under **Categories 1, 2 and 3** where there is no regulatory or QA mechanism to do the following in respect of such products:

- Conduct a risk-benefit assessment in the African populations, including the suitability of product information for African markets
- Assess the suitability of use in African populations, including stability and local use
- Involve African regulators in the review mechanisms
- Address the (on-site inspections) GMP for the manufacturing sites intended for supply in African markets
- Does not have the capacity for sharing all unredacted full assessment and inspection reports and is available for regulatory consultations and exchange of information through the product life cycle with all interested national African regulators
- Address the post-approval changes for the product
- Equivalence of the regulatory standards to the standards adopted for continental assessments.

Note:
Examples of Internationally Recognised Regulatory or Quality Assurance Systems are WHO PQ, EUM4all, Swissmedic Marketing Authorisations for Global Health Products Procedures and the like.

General Guidance Note

It should be noted that this document guides eligibility criteria that prioritise human medicinal products that qualify to use the EMP-TC continental route. The list has considered all factors existing at country and REC levels, the AMA treaty and existing international mechanisms to establish a continental regulatory route that will build a foundation for reliance and recognition of EMP-TC recommendations.

This document does not provide an exhaustive list of priority products but rather provides guiding principles on criteria for defining the eligibility of medicinal products for the continental regulatory route as it was defined at the start of the EMP-TC and is subject to amendments or updates based on new priorities and information as considered appropriate from time to time.

Applications are welcome, and applicants are encouraged to approach the EMP-TC Secretariat to confirm if a product could be eligible for continental assessment by the committee, even if not explicitly mentioned in this Guidance. This information will also be provided in the Call for Expression of Interest, which will be published occasionally and defined by the TC.

Further, it should be noted that the EMP-TC route for product assessment is optional.

Annex 1: Example of Complex Products extracted from the WHO EML 2021

- Amphotericin B liposomal complex 50mg injection.
- Copper containing device.
- Levonorgestrel-releasing intrauterine system (WHO PQ scope RH)
- 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 and auto-injectors.

Annex 2

WHO EML 2021- Biological Products

Biological Medicines in WHO EML 2021	
	Included as part of the complementary list in WHO EML
	In the scope of the 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	Immunological > Sera, immunoglobulins, and monoclonal antibodies
Anti-tetanus immunoglobulin	Human immunoglobulins
Antivenom immunoglobulin	Immunological > 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	Antianemia medicines
Diphtheria antitoxin	Immunological > Sera, immunoglobulins, and monoclonal antibodies
Enoxaparin	Medicines affecting coagulation
Epoetin alfa	Antianemia medicines
Epoetin beta	Antianemia medicines
Epoetin theta	Antianemia medicines
Equine rabies immunoglobulin	Immunological > Sera, immunoglobulins, and monoclonal antibodies
Erythropoiesis-stimulating agents	Antianemia 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	Vaccines

Annex 3

Vaccines for diseases prioritised by Africa CDC (PAVM)

Exhibit 11: 22 diseases prioritized for the FFA

Archetype	Disease	Does a vaccine exist?	African doses volume by 2040 (Mn)	DALYS 2040 (Mn)
Legacy	Hepatitis B, Diphtheria, Tetanus, Whooping Cough	✓	~370	6
	Tuberculosis	✓	~140	12
	Measles	✓	~240	2
	Yellow Fever	✓	~50	<1
	Cholera	✓	~30	1
	Typhoid	✓	~20	1
	Meningococcus[1]	✓	~60	5
Expanding	Human papillomavirus	✓	~30	4
	Pneumococcus	✓	~140	13
	Rotavirus	✓	~120	9
	COVID-19	✓	~710	TBD
	Malaria	✓	~120	20
	HIV	✗	~110	10
Outbreak	Ebola	✓	~1	9
	Influenza[2]	✓	~10	1
	Chikungunya	✗	~1	<1
	Rift Valley fever	✗	~1	<1
	Lassa fever	✗	~1	<1
	Disease X	✗	N/A	N/A
	Total		~2,200	

1. Including key serogroups found in Africa (A, C, W and X)
2. Considering here outbreak influenza

AUDA-NEPAD
AFRICAN UNION DEVELOPMENT AGENCY