AUDA-NEPAD
AFRICAN UNION DEVELOPMENT AGENCY

World Health Organization

Evaluation of Medicinal Products Technical Committee (EMP-TC)
Continental Procedure

Acronyms

AMA	African Medicines Agency
AMQF-TC	African Medicines Quality Forum – Technical Committee
AMRH	African Medicine Regulatory Harmonisation
API	Active Pharmaceutical Ingredient
AU	African Union
AUDA-NEPAD	African Union Development Agency-New Partnership for Africa's Development
AVAREF	African Vaccine Regulatory Forum
CD	Calendar days
CDC	Center for Disease Control
CTD	Common Technical Document
CRO	Contract Research Organisation
CROMF	Contract Research Organisation Master File
CRP	Collaborative Registration Process
COPD	Chronic Obstructive Pulmonary Disease
DG	Director General
EAC	East African Community
ECOWAS	Economic Community of West African States
EMP-TC	Evaluation of Medicinal Products – Technical Committee
EoI	Expression of Interest
FPP	Finished Pharmaceutical Product
FPR	Facilitated Product Registration
GCP	Good Clinical Practices
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
GMP-TC	Good Manufacturing Practices Technical Committee
ICH	International Conference on Harmonisation
IP	Immunological Product
IS	Immunogenic Substance
MA	Marketing Authorisation
ML3	Maturity level 3
NCD	Noncommunicable Diseases
NCE	New Chemical Entity
NEPAD	New Partnership for Africa's Development
NRAs	National Regulatory Authorities
NTD	Neglected Tropical Disease
PAR	Public Assessment report
PIR	Public Inspection Report
PMPA	Pharmaceutical Manufacturing Plan for Africa
QA	Quality Assurance
QMS	Quality Management System
REC	Regional Economic Community
SADC	Southern African Development Community
SMF	Site Master File
SOP	Standard Operating Procedure
SmPC	Summary of Product Characteristics
SRA	Stringent Regulatory Authorities
TC	Technical Committee
WHO	World Health Organization
WHO PQ	World Health Organization Prequalification Programme
WHO TRS	World Health Organization Technical Report Series
WLA	WHO Listed Authority

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Introduction

The African Medicines Regulatory Harmonisation (AMRH) Initiative was established in 2009 as an African Union (AU) Programme to support the implementation of the Pharmaceutical Manufacturing Plan for Africa (PMPA) under the New Partnership for Africa's Development (NEPAD) Framework. The AMRH Initiative aims to address the disparate regulatory systems on the continent working through regional economic communities (RECs).

The development, adoption by the AU Assembly and subsequent coming into force of the Treaty for the establishment of the AMA is a result of the foundation built by the AMRH Initiative as part of the PMPA framework[1]. The creation of AMA is the final component of the AU vision of a strengthened medicines regulatory ecosystem on the continent, which, among others, will play a critical role in support of the AU plan to advance vaccines manufacturing.

Under AMRH, several Technical Committees have been put in place. These committees will also be necessary for the AMA as described in the AMA Treaty[2]. They could become the TCs for AMA when fully established and will be responsible for conducting scientific assessments and providing scientific opinions.

The Evaluation of Medicinal Products[3] Technical Committee (EMP-TC) established by the AMRH Steering Committee (and which may be transferred under AMA) plays a vital role in the scientific evaluation of human medicinal products at continental level and harmonising assessment, registration and marketing authorisation activities at REC and NRA levels.

Among its specific objectives, this committee is to develop continental medicinal product evaluation processes to support registration by countries and devise a mechanism for submission of applications for continental assessment for priority products. It is also expected to organise the assessment of applications for the list of priority medicinal products assessed at continental level, provide final scientific recommendations on medicinal products (positive or negative) based on assessment reports, and share them with NRAs to support registration and marketing authorisations.

This procedure describes the process proposed to undertake a comprehensive evaluation of the quality, safety, and efficacy of medicinal priority products based on information submitted by the applicants of such products (manufacturers or suppliers) and on an inspection of the corresponding manufacturing facilities and clinical sites. This will be done through a standardised procedure based on quality standards applicable for continental evaluation. These standards will be mainly based on WHO standards and, if not existing, ICH standards or any other relevant standards until customised African standards are developed and adopted.

This guideline has been developed after a review of the WHO Prequalification Procedure WHO TRS N°961 untitled (who.int), 2011 and the European Medicine Agency (EMA) centralised procedure Marketing authorisation | European Medicines Agency (europa.eu). Flowcharts and Procedures used for joint assessments and inspections of medicinal products by Regional Economic Communities have also been reviewed (in particular, EAC, ECOWAS and ZAZIBONA/SADC).

When operating under the AMRH or when the AMA is fully operational under the current AMA Treaty, the medicinal products found to meet AMRH standards after evaluation by the EMP-TC will be included in the list of medicines recommended by AMRH/AMA and published on the website to facilitate reliance and pooled procurement through the AU. However, EMP-TC recommendations do not imply any approval of products/manufacturing sites by AMRH/AMA, which is the only prerogative of NRAs of concerned member states.

African countries can decide to adopt EMP-TC recommendations for granting a national marketing authorisation through a reliance mechanism after accessing the product assessment and inspection reports produced by the EMP-TC.

In addition, as a specialised agency of the African Union, AMA is expected to also play a role in the global space in alignment with AU agenda 2063 by establishing a pathway for evaluating and publishing

1 AU Executive Council Decision, {EX.CL/Dec.857 (XXVI)} of January 2015

2 36892-treaty-0069_-_ama_treaty_e.pdf (au.int)

3 "Medicinal products" terminology is equivalent to "medicines" and include all medicines including biologicals, vaccines.

its scientific opinion on medicinal products for human use when manufacturers, sponsors or applicants intend to use the AMA opinion in applying for marketing authorisation of any product even if the intended market is not Africa.

Glossary of terms

Abridged regulatory pathway

Regulatory procedures are facilitated by reliance, whereby a regulatory decision is solely or partially based on the application of reliance. It is expected that reliance on these pathways will save resources and time compared with standard pathways while ensuring that the standards of regulatory oversight are maintained.

Immunological Product (IP)

An immunological product is the finished dosage form of the immunogenic substance. The immunological product contains the immunogenic substance(s) formulated with other ingredients in the finished dosage form ready for marketing. Other active or inactive ingredients may include adjuvants, preservatives, stabilisers, and/or excipients.

Immunogenic Substance (IS)

An immunogenic substance is an unformulated active substance which may be subsequently formulated with excipients to produce a medicinal product. Immunogenic substances may be whole bacterial cells, viruses, or parasites (live or killed), split bacterial cells, viruses, or parasites, crude or purified antigens isolated from killed or living cells; crude or purified antigens secreted from living cells, recombinant or synthetic carbohydrate, protein or peptide antigens, polynucleotides (as in plasmid DNA vaccines) or conjugates.

Active Pharmaceutical Ingredient (API)

A substance used in a finished pharmaceutical product (FPP) intended to furnish pharmacological activity or to otherwise directly affect the diagnosis, cure, mitigation or prevention of diseases or to have immediate effect in restoring, correcting or modifying physiological functions in human beings.

Applicant

The person or entity who submits an expression of interest (EoI) to participate in this procedure in respect of the product(s) listed in the invitation, together with the required documentation on such product(s).

Assessment
This document covers any evaluation conducted for a regulatory function (e.g., evaluation of a clinical trial application or an initial marketing authorisation for a medical product or any subsequent post-authorisation changes, evaluation of safety data, evaluation as part of an inspection).

Biologicals
Biologicals are that class of medicines which are grown and then purified from large-scale cell cultures of bacteria or yeast, or plant or animal cells. Biologicals are diverse medicines, including vaccines, growth factors, immune modulators, monoclonal antibodies, and products derived from human blood and plasma. What distinguishes biologicals from other medicines is that these are generally proteins purified from living culture systems or blood. In contrast, other medicines are considered 'small molecules' made synthetically or purified from plants.

Common Technical Document
A standard format for submitting scientific information when applying for marketing authorisations was initially created in the European Union, Japan, and the United States and is now used by many NRAs worldwide.

Contract Research Organisation (CRO)
An organisation (commercial, academic, or other) to which an applicant may have transferred some of its tasks and obligations concerning the conduct of clinical studies with the product submitted to AMRH/AMA for assessment under the current procedure.

Finished Pharmaceutical Product (FPP)
A finished dosage form of a pharmaceutical product has undergone all stages of manufacture, including packaging in its final container and labelling.

Good Clinical Practices (GCP)
That part of quality assurance ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorisation.

Good Laboratory Practices (GLP)
That part of quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorisation.

Good Manufacturing Practices (GMP)
That part of quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorisation.

Innovator product
Generally, the pharmaceutical product which was first authorised for marketing (typically as a patented product) based on documentation of efficacy, safety, and quality according to requirements at the time of the authorisation. When a substance has been available for many years, identifying an innovative pharmaceutical product may not be possible.

Invitation for Expressions of Interest (EoI)
Invitation calling upon interested parties (e.g., manufacturers or suppliers) to submit an expression of interest (EoI) to AMRH/AMA to participate in the EMP TC continental procedure in respect of the product(s) listed in the invitation. Such an EoI should be accompanied by the required documentation on the product(s) in question.

Manufacture
All operations of purchase of materials and starting materials, preparation of the active pharmaceutical ingredient (API) and the medicinal product, including packaging and repackaging, labelling, relabelling, quality control, release, storage and distribution and the related management.

Manufacturer
A company that produces, packages, repackages, labels and/or relabels medicinal products.

Marketing Authorisation
A legal document issued by a competent agency/authority for marketing or free distribution of a product which has been approved after evaluation for safety, efficacy, and quality.

Medicinal products (equivalent to medicines).
Any substance or mixture of substances used or purporting to be suitable for use or manufactured or sold for use in:

- The diagnosis, treatment, mitigation, modification, or prevention of diseases, abnormal physical or mental state or the symptoms thereof in humans; or

- Restoring, correcting, or modifying any somatic, psychic or organic function in humans.

Member State
Member States of the African Union.

Multisource products
Pharmaceutically equivalent or pharmaceutically alternative products that may or may not be therapeutically equivalent. Multisource pharmaceutical products that are therapeutically equivalent are interchangeable.

New chemical entity (NCE)
Actives that have not previously been authorised for marketing as medicine for use in humans in the country in question.

Prequalification (PQ)
Standardised quality assessment procedure of WHO to evaluate the acceptability, in principle, of pharmaceutical products for purchase by UN agencies.

Public Assessment Report (PAR)
A set of documents describing the evaluation of medicine authorised through the AMRH/AMA procedure and including the product information published on the AMRH/AMA website.

Public Inspection Report (PIR)
A Public Inspection Report is a publicly available summary of an on-site inspection report or a desk assessment indicating that the site or study is compliant with international standards and norms and in adherence with dossier information.

Quality control
Embraces all measures taken, including setting specifications, sampling, testing and analytical clearance, to ensure that raw material, intermediates, packaging materials and finished pharmaceutical products conform with established specifications for identification, strength, purity and other pharmaceutical characteristics.

Quality Overall Summary
The Quality Overall Summary (QOS) is a summary that follows the scope and the outline of the Body of Data in Module 3 of the CTD.

Regulatory Authorities
Regulatory authority is meant to cover all the institutions, working together in an integrated and effective manner, responsible for regulatory oversight of medical products in a given country or region.

Reliance
The act in which the regulatory authority in one jurisdiction considers and gives significant weight to assessments performed by another regulatory authority, trusted institution, or any other authoritative information in reaching its own decision. The relying authority remains independent, responsible, and accountable for the decisions taken, even when it depends on the decisions, assessments, and information of others.

Standard Operating Procedure (SOP)
An authorised written procedure giving instructions for performing operations not necessarily specific to a given product or material (e.g., equipment operation, maintenance, and cleaning; validation; cleaning of premises and environmental control; sampling and inspection). Specific SOPs may be used to supplement product-specific master and batch production documentation.

Stringent Regulatory Authorities
A regulatory authority which is: (a) a member of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), being 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 (as before 23 October 2015); or (b) an ICH observer, being the European Free Trade Association, as represented by Swissmedic, and Health Canada (as before 23 October 2015); or (c) 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).

Summary of Product Characteristics (SmPC)
A document describing the properties and the officially approved conditions of use of a medicine. Summaries of product characteristics form the basis of information for healthcare professionals on how to use the medicine safely and effectively.

Supplier
A company (pharmaceutical entity) authorised to become a marketing authorisation holder.

Treaty
The treaty establishing the African Medicines Agency.

Vaccine
A biological preparation that improves immunity to a particular disease. A vaccine typically contains an agent that resembles a disease-causing microorganism and is often made from weakened or killed forms of the microbe, its toxins, one of its surface proteins or genetically engineered material. The agent stimulates the body's immune system to recognise the agent as foreign, destroy it and "remember" it so that the immune system can more easily recognise and destroy any of these microorganisms it later encounters.

Variations
A change to any aspect of a pharmaceutical product, including but not limited to the change of use of a starting material, a change in formulation, method or site of manufacture, specifications for the finished product and ingredients, container and container labelling and product information.

WHO-Listed Authorities (WLA)
A WHO Listed Authority (WLA) is a regulatory authority or a regional regulatory system (RRS) which has been documented to comply with all the relevant indicators and requirements specified by WHO for the requested scope of listing based on an established benchmarking and performance evaluation process.

Purpose and principles

The purpose of this procedure is to establish processes for the evaluation of quality, safety, efficacy and compliance with current requirements of Good Manufacturing Practices (hereafter referred to as GMP) as defined by the AMRH/AMA of priority medicinal products identified for continental assessment (as defined in the priority products eligibility guidance for continental assessment by the AMRH published and updated from time to time).

This procedure, established by the AMRH Initiative, is based on the following principles:

- The priority medicinal products eligible for EMP-TC assessment are listed in an Expression of Interest published on the AMRH website. Product dossiers for these priority products should be submitted only at continental level starting from the publication date of the first EoI.
- General understanding of the production and quality control activities of the manufacturer
- Assessment of medicinal product data (quality, efficacious, and safe data) received in a Common Technical Document (CTD) format.
- Inspection of Finished Pharmaceutical Product (FPP)/Immunological Product (IP) and Active Pharmaceutical Ingredient (API)/ Immunogenic Substance (IS) manufacturing sites (GMP).
- Inspection of clinical testing units or contract research organisations (CROs) with Good Clinical Practices (GCP) and Good Laboratory Practices (GLP).
- Reliance on the information provided from WHO Prequalification (WHO PQ)[4], Stringent Regulatory Authorities (SRAs)[5] and WHO Listed Authorities (WLAs)[6].
- Random sampling and testing of medicinal products supplied to countries.
- Handling of complaints and recalls reported to the AMRH Secretariat (AMA, when operational)
- Product lifecycle management involves monitoring changes in the product dossier and managing variations.

The EMP-TC, or sub-TCs created under EMP-TC for specific categories of products, such as the sub-TC for vaccines and other biological products, will assess product dossiers with a pool of continental assessors and inspectors respectively coming from the African continent NRAs. However, the EMP-TC and the GMP-TC may also collaborate with assessors and inspectors from WHO PQ/SRAs/WLAs when necessary or until the required expertise is available on the continent as set out in the Terms of Reference of the EMP TC.

Steps of the procedure

The EMP-TC will comprehensively evaluate the quality, safety, and efficacy of the medicinal products based on information submitted by the applicants (being manufacturers or suppliers) and inspection of the relevant manufacturing and clinical sites.

Flowcharts showing the EMP-TC process under AMRH (and AMA, when operational) are provided as Annex 1.

A call for Expression of Interest (EoI) to interested parties will be published on the AMRH website (AMA website, once operational), requesting them to voluntarily participate in this procedure with respect to the priority products identified for continental assessment and any other products as it is deemed fit by the AMRH governance structures or the AMA from time to time. This EoI will also propose to applicants several pathways:

- Pathway 1: An EMP-TC Independent opinion leading to an EMP-TC recommendation by AMRH/AMA when operational that NRAs can use to grant a marketing authorisation through reliance, based on assessment and inspection reports shared by the EMP-TC with NRAs. This pathway, once the AMA is fully operational, could be used to give an opinion on any products, even if

4 WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control) | WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control)

5 Stringent Regulatory Authorities (SRAs) as defined in the WHO Technical Report Series 1003 TRS 1003 - 51st report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations

6 List of WHO Listed Authorities WLAs

not on the priority list, through voluntary requests by applicants to assist in their submissions in interested markets, such as evaluation and opinion to medicines with an orphan status in other jurisdiction outside Africa.

- Pathway 2: An EMP-TC facilitated product registration (FPR) if a similar application is submitted to at least 10 NRAs from at least 3 RECs for a product not in the scope of regional joint assessments.

By submitting an EoI, the applicant undertakes to share information with the AMRH Secretariat (AMA, when operational) on all relevant aspects of manufacture and control of the specified products, along with changes made and/or planned. Interested applicants provide the necessary information to the AMRH Secretariat by submitting a product dossier in a CTD format and other information requested.

In the EoI, the applicant will need to specify the pathway to be used by the EMP-TC.

The procedure will typically include:

- An assessment of the product dossier must include product data and information as specified in the guidelines for submitting dossiers.

- The GMP-TC will inspect manufacturing sites of FPP/AIP and API/AIS (if applicable) to assess compliance with GMP.

- An inspection of clinical sites (if applicable) to assess compliance with GCP and GLP, as appropriate, will be performed by AVAREF.

Should the evaluation demonstrate that the medicinal product meets continental recommended/ recognised standards of quality, safety and efficacy, the product will be included in the list of medicinal products recommended by the EMP-TC and recommended by EMP-TC. The products will then be listed on the AMRH/AMA website.

The EMP-TC reserves the right to terminate the evaluation of any medicinal product if the applicant cannot provide the required information and/or implement any corrective actions that EMP-TC may require within a specific period or when the information supplied is inadequate to complete the procedure.

The EMP-TC recognises the importance of reliance work done by other competent bodies such as WHO PQ, EDQM, SRAs or WLAs, which apply quality, safety, and efficacy standards equivalent to those recommended by AMRH/AMA. Providing WHO PQ, EDQM, SRAs and WLAs are willing to share certain information with AMRH/AMA, the EMP-TC may consider abridged or verification evaluations route of such products and eventually inclusion in the list of products recommended by the EMP-TC.

Inspecting manufacturing site(s) or CRO by AMRH or AMA once operational through GMP TC or AVAREF is a prerequisite before any conclusion can be taken on a medicinal product by EMP-TC. However, it may not be required after a review of the documents received by the GMP-TC and AVAREF if:

- There has been an inspection by WHO PQ or an SRA/WLA where the AMRH can access inspection reports.

- The inspection was conducted within the last three years by WHO PQ, SRA/WLA by AMRH/ AMA GMP TC or AVAREF where necessary.

- Information on the inspection (including inspection report and responses to any deficiencies) is available for review by GMP-TC and AVAREF and

- Based on this and other available information, it is determined that the site(s) in question meet the applicable AMRH/AMA standards.

To coordinate inspection activities, avoid duplication, and promote information sharing without prejudice to the protection of any confidential and or proprietary information of the applicants and manufacturers under the terms of this procedure, the AMRH Secretariat/ AMA may disclose inspection-related information to NRAs in Africa and outside of the continent. This will require obtaining consent from applicants/marketing authorisation holders.

Invitation for expressions of interest

A permanent, open and transparent EoI will be published on the AMRH website (AMA website, when operational) requesting applicants (manufacturers or suppliers) to voluntarily participate in this procedure with respect to the priority products listed in the EoI. This EoI will also be circulated to pharmaceutical association networks and will include the instructions for submission and the guidance on priority product eligibility criteria for continental assessment as published by the AMRH or AMA once operational. When sending their Expression of Interest, applicants should provide EMP-TC with their strategy for introducing the products on the continent and where they intend to market their products (country list).

In situations of high public concern or public health emergencies, as determined by Africa CDC, any other recognised competent body by the AU or WHO, the AMRH Secretariat or AMA may also directly invite relevant parties to submit specified product dossiers for evaluation by EMP-TC under this procedure without publication of an invitation for EoI.

Data and information to be submitted.

Applicants are expected to submit documentation on the medicinal products as called for in the invitation for EOI and as prescribed by the guidelines on application submission as published by the EMP-TC from time to time. For Pathway 1, applicants should submit their product dossiers with the required information at any time to the AMRH Secretariat/ AMA (when operational) or directly to a minimum of 10 NRAs in at least 3 RECs for the Pathway 2, with a letter and copy of the dossier to the AMRH Secretariat/AMA to enable coordination of evaluation through EMP TC. The applicants should submit the documentation in electronic format defined by the EMP-TC in close collaboration with the IMS-TC and specified in the EoI.

Usually, the applicants who approach the AMRH Secretariat/AMA are manufacturers but could also be suppliers. In the case an applicant is not the manufacturer of the FPP/AIP, all relevant documentation, including (but not limited to) contract manufacturing documentation, should be submitted, demonstrating that the applicant is in

complete control of the manufacturing process for and quality assurance of, the products submitted for prequalification. For suppliers, a formal relationship between the supplier and manufacturer should be demonstrated, and the manufacturer should confirm the supplier can submit the dossier at the continental level.

In case of doubt, and before applying, applicants can send an Eligibility request to AMRH/AMA to confirm their product is eligible for EMP-TC evaluation.

In submitting an EoI for product evaluation by the EMP-TC, the applicant should send the following to the EMP-TC Secretariat:

- A cover letter expressing interest in participating in the EMP-TC procedure, confirming that the information submitted in the product dossier is complete and correct and indicating the pathway to use.
- The applicant's strategy for introducing the products on the continent and where they intend to market their products (country list).
- A product dossier in a CTD format.
- Product samples to enable visual examination and potentially chemical, pharmaceutical, or biological analysis.
- A site master file (SMF) for each manufacturing site listed in the product dossier, in the format specified in AMRH/AMA guidance documents, upon request from GMP-TC.
- A contract research organisation master file (CROMF) for each clinical site listed in the dossier, in the format specified in the AMRH/AMA guidance documents, upon request from AVAREF.

All documentation should be submitted in English.

For the purposes of this procedure, different requirements for documentation to be submitted apply to the following categories of products:

- Multisource (generic) FPPs/AIPs to be assessed by EMP-TC
- New chemical entities/novel products to be assessed by EMP-TC
- Biologicals, including vaccines to be assessed by EMP-TC
- Innovator FPPs/AIPs approved by WHO PQ/SRAs and WLAs
- Multisource (generic) FPPs/AIPs approved by WHO PQ/SRAs and WLAs

The guidelines on submission of dossiers and documentation requirements for each category above can be found on the AMRH (AMA, when operational) websites. These requirements may be revised from time to time.

If considered necessary or desirable by either party, and before the actual evaluation process starts, a discussion may be held between the applicant and EMP-TC. This meeting should be scheduled as early as possible with a predefined agenda to address questions sent in advance to the EMP-TC Secretariat by the applicant.

Screening of dossiers submitted

The EMP-TC Secretariat will screen each product dossier submitted by an applicant according to an internal Standard Operating Procedure (SOP) before the evaluation can start, for completeness of dossiers, selected pathway, and eligibility as part of priority products for continental assessment. The EMP-TC secretariat will have 15 calendar days (CD) to screen the dossiers.

Dossiers submitted for products not meeting the eligibility criteria for the priority product list will not be accepted for continental assessment. Once the AMA is fully operational, other products, on a case-by-case basis, may be accepted and assessed for the AMA to issue an independent opinion like the EU-M4All pathway[7].

Similarly, the EMP-TC Secretariat will not consider incomplete dossiers. The EMP-TC Secretariat will inform the applicant that an incomplete dossier has

7 Medicines assessed under the 'EU-M4all' procedure | European Medicines Agency (europa.eu)

been received and will be requested to complete the dossier within 15 calendar days. In the event of non-compliance, the dossier may be rejected for incompleteness and returned to the applicant.

Dossiers considered complete as the results of the screening done by the EMP-TC Secretariat will be retained by the EMP-TC Secretariat for assessment.

After screening, if the dossier is accepted for assessment, the applicant will be informed of this and will receive a letter including a dossier reference number. This letter will serve as an agreement between the EMP-TC and the applicant for participation in the continental procedure and a commitment to comply with the provisions of the EMP-TC procedure.

Dossier evaluation

Selection of the Rapporteur and Co-Rapporteur:

As stated in the EMP-TC Terms of Reference, for each product dossier, a rapporteur and co-rapporteur will be appointed from amongst the members of the TC or alternates. The appointment of the rapporteur will be made based on objective criteria, which will allow the use of the best available expertise in Africa in the relevant scientific area. The EMP-TC may also want to consider EMP-TC co-opted members with specific profiles.

The rapporteur and co-rapporteur will select the assessors doing the assessments and prepare and present the final assessment report in English, including a proposed recommendation, to the EMP-TC, based on the assessors' reports and the feedback from the GMP-TC or AVAREF if applicable.

From the twenty (20) EMP-TC members and alternates, the selection of rapporteurs and co-rapporteurs will be made on a rotational basis by the EMP-TC Secretariat, with the possibility for members/alternates to refuse.

The EMP-TC secretariat will ensure the selection of co-rapporteurs to support the capacity building of members from less mature NRAs.

Selection of assessors

The assessors will be selected by the rapporteur/co-rapporteur from the pool of experts put in place by the AMRH Secretariat and experts identified for each part of the dossier (quality for API/AIS and FPP/AIP and efficacy/safety) for primary review and secondary review. The assessors must have the relevant qualifications and experience in pharmaceutical and biological development and quality assessment of medicinal products. The EMP-TC Secretariat will assign the dossier to experts and a work agreement (timelines and allowance stated in the agreement).

Although affiliated with the NRAs of AU member states, assessors will be working for AMRH/AMA individually and will be paid an allowance. Information will be sent to the NRAs/institutions from where the assessors come, and the latter will be expected to obtain a no-objection from their NRA or employer to perform the product assessments for AMRH (or AMA, when operational).

The EMP-TC may consult additional ad-hoc experts for specific questions when expertise is unavailable in the EMP-TC and its pool of experts. These additional experts will be identified through the Partnership Platform Technical Group, going through their chair if needed.

When operational, the assessors must comply with the confidentiality and conflict of interest rules of the AMRH Secretariat/AMA.

Evaluation process

According to an internal SOP for evaluation process management, the EMP-TC will assess the product information submitted in the dossiers.

The assessment of product dossiers will be done by the assessors following guidance developed by EMP-TC and in accordance with the SOP established by the EMP-TC describing the evaluation process (including templates to be used by assessors and Quality Overall Summary) to ensure uniformity in evaluation and timeliness of assessment activities. They will also benefit from technical support from the other committees (GMP-TC, AMQF-TC, etc.). If needed, EMP-TC may provide training to assessors.
The initial evaluation of a product dossier by assessors should take a maximum of 80 calendar days. Following this initial assessment, a report on each part of the dossier will be consolidated by the EMP-TC Secretariat for quality assurance and consolidation of the final list of queries to the applicant.

The applicant will then have a maximum of 60 calendar days to respond to queries from the assessors (two times) and to send the additional information to the EMP-TC Secretariat. The assessors should assess the applicants' responses within 60 additional days. If necessary, a second round of questions may be sent to the applicants with similar timelines. When the applicant has provided the final responses, the assessors and rapporteur/co-rapporteur will have 60 additional calendar days to give a final opinion. The total timeline for an EMP-TC process will be 260 calendar days maximum (not considering the stop clock of evaluation pending additional information from applicants).
A fast-track evaluation process with shorter timelines may be applied for medicinal products needed for emergencies, orphan medicines, or WHO/SRA/WLA-approved products.

Applicants may request longer timelines for responding to assessor queries, providing strong justifications to the AMRH Secretariat/AMA. This will be done through a negotiation between applicants and the EMP-TC Secretariat.

If necessary, each applicant may also request a meeting with EMP-TC experts involved in the assessment to clarify issues identified by assessors.

The EMP-TC Secretariat will oversee the quality assurance of the assessment process according to the SOP established by the EMP-TC.

Site inspections

GMP status

When EMP-TC receives a product dossier, the GMP-TC will be informed after screening and acceptance, and manufacturing site information in the CTD will be shared with them for assessment.

Then, GMP-TC will provide feedback to the EMP-TC Secretariat on the outcome of the GMP compliance (after desk review or site inspection).

The assessors will consolidate GMP TC recommendations as part of their consolidated reports to the Rapporteur/ Co-Rapporteur to prepare final consolidated reports with all inputs.

GCP status, when applicable

AVAREF will provide similar support to EMP-TC to assess GCP at the clinical sites, the sponsor and/ or CROs when needed. Then, AVAREF will give feedback to the EMP-TC Secretariat on the outcome of the GCP compliance scrutiny (after desk review or site inspection).

The processes will be guided by the following:

- SOP existing under GMP-TC/AVAREF for GMP and GCP/GLP inspections.
- Norms and standards applicable as developed and adopted.
- Procedures for continental inspections.
- Compliance of inspectors selected by the AMRH Secretariat with the confidentiality and conflict of interest policy from AMRH /AMA.

Reporting and communication of the results of the evaluation

For each product dossier, the assessors and inspectors will finalise their reports according to the established EMP-TC SOP and templates, describing the findings and queries to the applicant, manufacturer and/or CROs as relevant.

The queries from the dossier assessment, based on the documentation and data submitted, will be communicated in writing to the applicant by the EMP-TC Secretariat requesting submission of the missing data and information, as appropriate, within 60 days.

GMP-TC will also communicate the inspection report to the manufacturer or CRO. If the applicant is not a manufacturer, with the written agreement from the manufacturer or CRO, a copy of the inspection report may also be provided to the applicant. Should any additional information be required or if the manufacturer or CRO must take correction actions, GMP-TC will postpone its decision on the acceptability of the site(s) concerned until such information has been evaluated or the corrective action has been taken and found satisfactory in light of the specified standards. This will also postpone the finalisation of the evaluation of the product dossier by the assessors.

When the assessors' and inspectors' reports are finalised, including their recommendations and GMP-TC/AVAREF recommendations are available, the EMP-TC Secretariat will share them with the Rapporteur and Co-Rapporteur, who will then produce a final assessment report in English and a summary report in French that will be tabled to the EMP-TC for final recommendation.

EMP-TC reserves the right to terminate the assessment for a specific product if the applicant cannot provide the required information, implement the corrective actions within a specified period, or if the information supplied is inadequate to complete this procedure.

In a disagreement between an applicant and EMP-TC, handling such disputes will be managed according to an internal SOP with the possibility of re-examining a product dossier.

As AMRH/AMA is responsible for the EMP-TC evaluation process, the ownership of the reports lies with AMRH Secretariat/AMA. Thus, the AMRH Secretariat/AMA will be entitled to use and publish such reports subject to the protection of any commercially sensitive and confidential information of the applicant/manufacturer.

Confidentiality provisions will be contained in the exchange of letters, to be concluded before the assessment of the product dossier or inspection of the manufacturing and clinical sites, between the EMP-TC Secretariat and each applicant, manufacturer or CRO.

Outcome of the evaluation procedure

Based on the presentation of the final assessment report from the Rapporteur and Co-Rapporteur during an EMP-TC meeting, EMP-TC Members will agree on a final recommendation for each product dossier assessed. This final recommendation can be positive or negative.

Positive Outcome

Once EMP-TC is satisfied that the procedure is complete for the relevant product, as manufactured at the specified manufacturing site(s), and that required standards are met, the product will be considered as recommended by the EMP-TC and will be included in the list of products recommended at continental level.

Each applicant will receive a letter from the EMP-TC Secretariat informing it of the outcome of the assessment process of the specific medicinal product submitted. Once the product is included in the list of products recommended at continental level, the applicant will be responsible for keeping continuously the EMP-TC Secretariat updated on all relevant aspects of the manufacture and rollout of such product and to meet any requirements, as agreed with AMRH/AMA.

In **countries that have ratified the AMA Treaty,** the EMP-TC positive recommendations are expected to be communicated immediately, and the public assessment reports made available automatically through a dedicated AMRH/AMA platform. Countries will then have a maximum of 60 calendar days to issue a marketing authorisation and to include the product in their NRA registers, including labelling in local languages. These countries will receive special attention from the AMRH Secretariat/AMA to facilitate this process.

In **countries that have not yet ratified the AMA Treaty, and based on voluntary participation from governments,** a Memorandum of Understanding with the AMRH Secretariat/AMA will be put in place to give them access to the EMP-TC assessment report available. The WHO Collaborative Registration Processes (CRP) can serve as a reference. Applicants will be asked to consent to sharing assessment reports with these countries. Countries will be given a maximum of 90 calendar days to issue an MA in countries following the EMP TC positive recommendation.

In all cases, AMRH Secretariat/AMA will publish a Public Assessment Report (PAR) on the product dossier assessments, Public GMP/GCP Inspection Reports (PIR), if applicable, that were found compliant with AMRH/AMA guidelines and standards and a Summary of Product Characteristics (SmPC) in English, French and other official African Union languages, as appropriate. These reports will be published on the AMRH/AMA website.
After a product has been listed on the AMRH/AMA website, and if new information is shared with EMP-TC and confirmed that should impact EMP-TC's initial recommendation, it will be possible for the EMP-TC to publish notices of concern or notices of suspension, when appropriate.

If serious safety and/or quality concerns arise concerning a recommended medicinal product, the EMP-TC may delist the product after it evaluates the new evidence and based on a risk-benefit assessment. Alternatively, it might suspend its positive recommendation until it can evaluate the results of further investigations.

Negative outcome

In case of a negative outcome following the EMP-TC meeting, the EMP-TC Secretariat will send the applicant a letter stating the reasons for not recommending the product assessed and indicating that the applicant can request a re-examination. This information will not be published on the AMRH/AMA

website and will only be communicated to concerned parties (applicants and NRAs in countries under Pathway 2).

An appeal system will be provided to allow applicants to raise concerns about an unfavourable decision taken by the EMP TC. A procedure for this appeal system will be implemented and made available to applicants on the AMRH/AMA website.

Maintenance of the continental recommendation

Applicants must communicate to the EMP-TC any changes (variations) that may impact the safety, efficacy and quality of a medicinal product recommended by the EMP-TC.

Guidelines on variations to EMP-recommended medicinal products can be found on AMRH/AMA website. These requirements may be revised from time to time.

It is the applicant's responsibility to provide the EMP-TC with the appropriate documentation (referring to relevant parts of the dossier) to prove that any intended or implemented variation will not have a negative impact on the quality, safety and efficacy of the product that has been recommended. The EMP-TC will evaluate variations according to the established EMP-TC guidelines and SOPs and communicate the outcome to the applicant within the prescribed timelines. Adherence to the reporting requirements will be verified during the inspections performed by the GMP-TC.

Manufacturers of EMP-TC-recommended medicinal products and associated API manufacturers will be re-inspected at regular intervals as defined by the GMP-TC but at least every three years. Re-inspections are conducted to verify compliance with GMP as the GMP-TC recommends and include data verification. Furthermore, to maintain their EMP-TC recommended status, AMRH/AMA will arrange for medicinal products to be re-assessed at regular intervals and at least every five years. The procedure and guidelines for re-assessing EMP-TC recommended products can be found on the AMRH/AMA website. These requirements may be revised from time to time. Re-inspection or re-assessment may also be performed:

- If any fraud or omissions by the applicant in the initial assessment procedure or during the follow-up activities become evident.

- And if an NRA or a country considers that a batch or batches supplied EMP-TC recommended products are not in compliance with the specifications found to be applicable at the time of the initial assessment performed by the EMP-TC.

If, because of a re-inspection or re-assessment, it is found that a medicinal product and/or specified manufacturing site no longer complies with the AMRH/AMA recommended standards, such products and manufacturing sites may be suspended or removed from the list of products recommended by the EMP-TC. Failure of an applicant to participate in re-inspection or re-assessment (as applicable) may also lead to suspension or removal from this list.

Post-marketing surveillance of continentally approved products

Post-marketing surveillance of products recommended by EMP-TC will be done in close collaboration with NRAs, RECs and AMQF TC.

Random samples of EMP-TC recommended products supplied will be taken for independent testing of final product characteristics. Certificate of analysis of FPP/AIP released by the manufacturer and specifications for test methods should be provided by the manufacturer or applicant to EMP-TC for review by the AMQF-TC upon request. In the event of failure to meet the established criteria for testing, EMP-TC will investigate the problem and communicate the outcome of this investigation to the manufacturer and applicant, if other than the manufacturer.

Complaints concerning EMP-TC-recommended products communicated to the EMP-TC Secretariat will be investigated according to an internal SOP established for that purpose and in close collaboration with the AMQF-TC and GMP-TC as appropriate. After investigation, the EMP-TC will provide a written report of the problem and include recommendations for action where relevant. The EMP-TC will make the report available to the applicant and the NRA of the country where the manufacturing site is located. Subject to protecting the commercially sensitive information referred to above, AMRH Secretariat/ AMA reserves the right to share the full report with the relevant authorities of interested Member States.

Monitoring of the implementation of the EMP-TC recommendations in countries

The EMP-TC Secretariat should regularly monitor and evaluate the implementation of the EMP-TC recommendations by countries.

Cost recovery

To ensure sustainability in implementing this procedure, a fee will be required for applicants applying for continental assessment. The fee will include a fee to cover the costs for product assessment and an annual fee for covering the cost of the EMP-TC Secretariat.

Through Pathway 1, a fee will be paid to AMRH Secretariat. Manufacturers must also pay NRA fees if they want to market their products in particular countries.

Through the EMP-TC facilitated registration process (Pathway 2), a fee will be paid at the central level to support the cost of the assessment, and a reduced NRA fee will be paid at country level using the EMP-TC recommendations to grant an MA.

Confidentiality undertaking

When implementing this procedure, the EMP-TC members, rapporteur/co-rapporteur and experts will work under the confidentiality undertaking policy from AUDA NEPAD or AMA when operational.

Conflict of interest

When implementing this procedure, the EMP-TC members, rapporteur/co-rapporteur and experts will work under the conflict-of-interest policy from AUDA NEPAD or AMA when operational.

Advocacy plan and implementation of the procedure

A roadmap should be developed to implement this procedure, including the development of guidelines, SOPs and templates to support the implementation of this procedure.

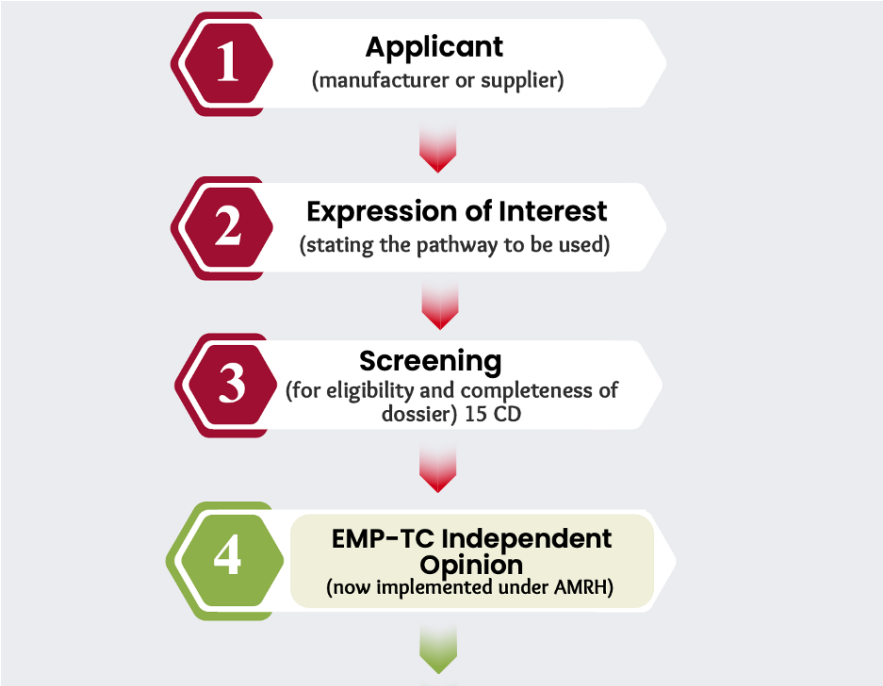
When this procedure is finalised and approved by the EMP-TC and then endorsed by the AMRH Steering Committee, it is proposed to pilot the implementation with a pool of experts identified through Regional Economic Communities Medicine Regulatory Harmonization (MRH) projects if the AMRH Secretariat pool of experts is not yet in place. An evaluation of the pilot will inform further amendments to the procedure, guidelines, and SOPs, if necessary.

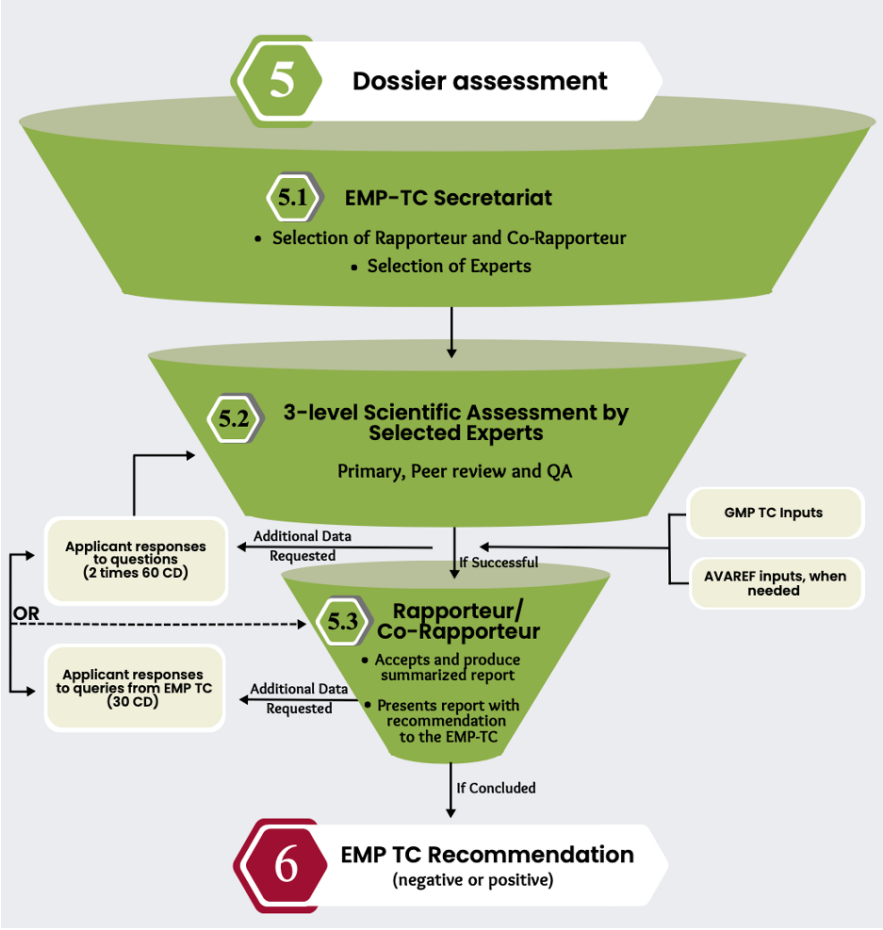
Then, after approval of the new version of the procedure by the EMP-TC and endorsement by the AMRH Steering Committee, the new procedure will be implemented under the AMRH Secretariat and proposed for adoption when AMA is operational.

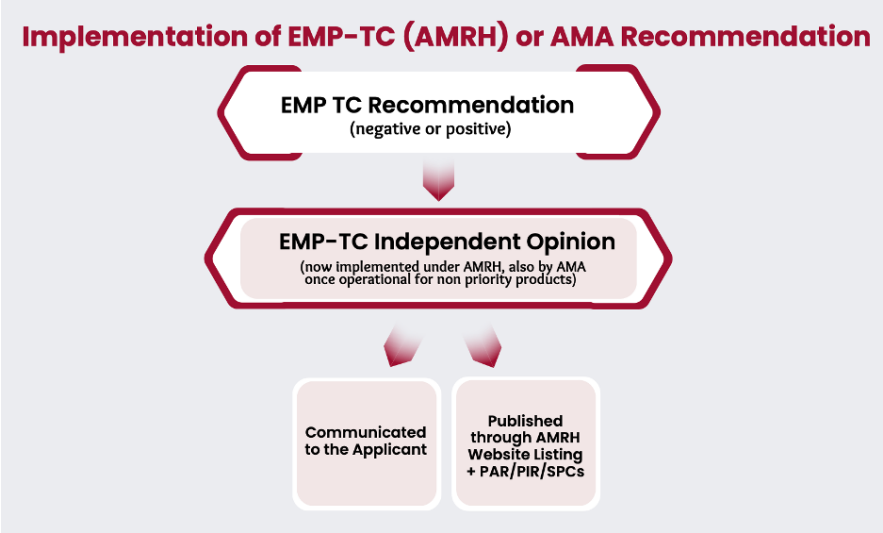
Annex 1

Flowcharts of evaluation of medicinal products at continental level

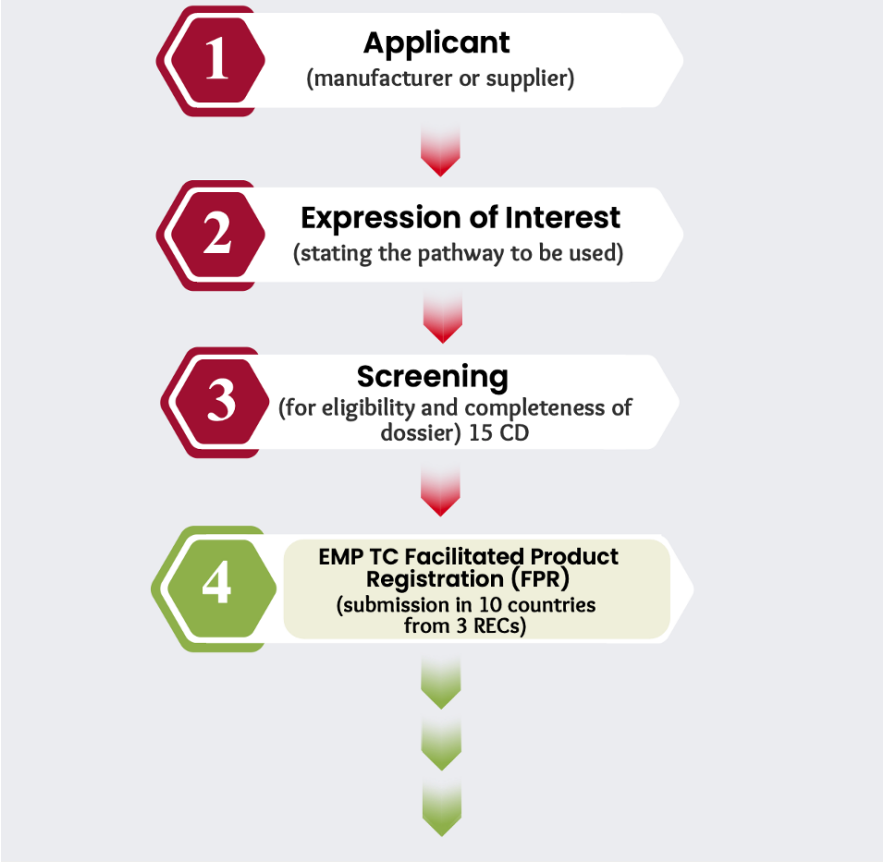
1 - EMP-TC Independent opinion

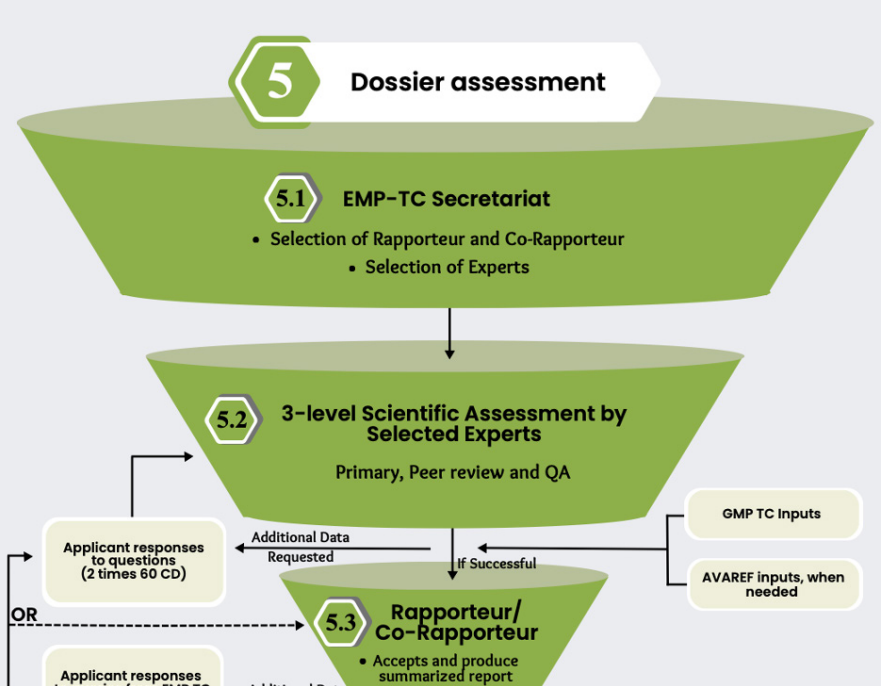


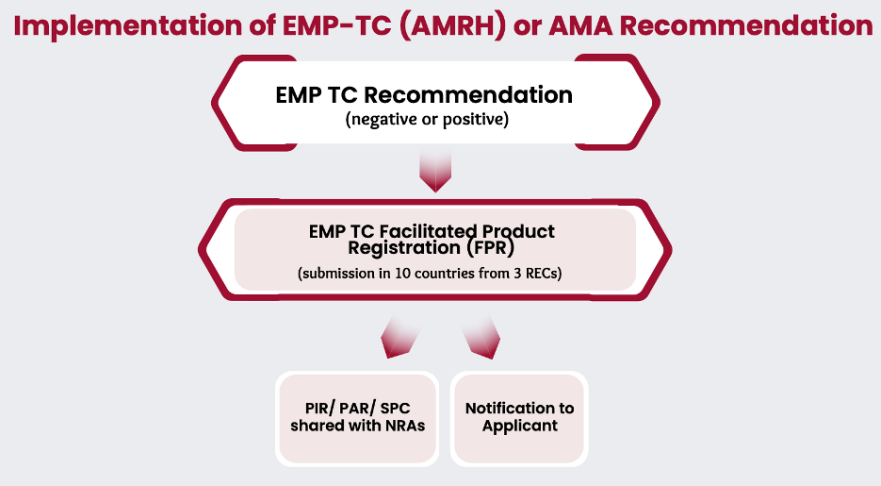




2 - EMP-TC facilitated product registration (FPR)




5
Dossier assessment
5.1
EMP-TC Secretariat
• Selection of Rapporteur and Co-Rapporteur
• Selection of Experts
5.2
3-level Scientific Assessment by Selected Experts
Primary, Peer review and QA
GMP TC Inputs
AVAREF inputs, when needed
Applicant responses to questions (2 times 60 CD)
Additional Data Requested
If Successful
OR
5.3
Rapporteur/ Co-Rapporteur
• Accepts and produce summarized report
Applicant responses


Implementation of EMP-TC (AMRH) or AMA Recommendation
EMP TC Recommendation
(negative or positive)
EMP TC Facilitated Product Registration (FPR)
(submission in 10 countries from 3 RECs)
PIR/ PAR/ SPC shared with NRAs
Notification to Applicant

Annex 2

Compendium of documents developed or under development which supports the implementation of this Procedure.

1. Call of Expression of Interest, including the instructions for submission of applications to AMRH/AMA Secretariat
2. Guidelines for Submission of a Product Dossier in a CTD Format
3. SOP for screening of applications
4. Template of letter of acceptance of a dossier after screening
5. SOP for evaluation process management
6. AMRH/AMA Policy for the management of Conflict of Interests and Confidentiality Undertaking and templates to be used (AMRH Secretariat document)
7. Guidance document for assessors, including templates to be used to produce assessment reports.
8. Guidance document for EMP-TC Members including templates for final assessment reports.
9. SOP for the EMP TC interaction with the GMP-TC, AVAREF and other relevant Committees in the evaluation process
10. SOP for management of an appeal system and the possibility to re-examine an application.
11. Template of letter to share with applicants the outcome of the evaluation process (positive and negative opinion)
12. Template for a Public Assessment Reports
13. Template for a Summary of Product Characteristics
14. Guidelines on variations to EMP-recommended medicinal products.
15. SOP for the management of complaints concerning EMP-TC recommended products, including a template for quality concern notification.
16. Notification letter template to NRAs on the outcome of the EMP TC assessments

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