African Medicines Regulatory Harmonisation (AMRH)

EVALUATION OF MEDICINAL PRODUCTS TECHNICAL COMMITTEE (EMP-TC)

GUIDELINES ON PROCEDURAL ASPECTS FOR SUBMISSION OF APPLICATIONS TO THE EMP TC DURING THE PILOT

ABBREVIATIONS AND ACRONYMS

BMGF	-	Bill and Melinda Gates Foundation
BMR	-	Batch Manufacturing Record
AU	-	African Union
AMRH	-	African Medicines Regulatory Harmonization
EMA	-	European Pharmaceutical products Agency
FEAPM	-	Federation of East African Pharmaceutical Manufacturers
GCP	-	Good Clinical Practice
GMP	-	Good Manufacturing Practice
ICH	-	International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
LH	-	Listing Holder
MER	-	Medicines Evaluation and Registration
NEPAD	-	New Partnership for African Development
WHO	-	World Health Organization

1. INTRODUCTION

The guideline covers the steps that are followed from the submission of a dossier to the final outcome, the timeframe and procedure for the EMP TC to amend, where necessary the conditions of listing of a particular product.

2. SCOPE

The guideline is applicable for all types of application submitted to EMP TC that include new application, renewal of application and application for variation of a listed medicinal product.

3. TYPES OF APPLICATIONS

3.1 For purposes of submission, applications are classified into new application, application for variation of a listed Medicinal product and renewal application.

3.2 A new application is an application for listing of a medicinal product that is intended to be evaluated by the EMP TC for the first time. A new application may only be made by the applicant and shall be the person who signs the application form.

3.3 A new application shall include submission of relevant documentation as provided in the main guidelines issued by the EMP TC from time to time.

4. GENERAL REQUIREMENTS AND APPLICATION PROCEDURES FOR MEDICINAL PRODUCT LISTING

4.1 All Application shall be submitted to the South African Health Products Regulatory Authority (SAHPRA) which receives applications on behalf of the EMP-TC in accordance with its procedures for submission.

4.2 All applications and supporting documents shall be in English. All submitted documents which are in any language other than English must be accompanied by a certified or notarized English translation.

4.3 The responsibility of applying for product listing rests with the company responsible for the introduction of the product into the AU concerned markets through the EMP TC.

4.4 Applications must be duly completed and supported by all the required documents i.e., Module I to Module V in accordance with the EMP-TCs guidelines on submission of documentation for listing. The submitted application will be screened for completeness within 15 calendar days. Dossiers which are incomplete will not be accepted for evaluation.

4.5 A dossier is a file that contains detailed scientific information on the chemistry, manufacturing and control, non-clinical and clinical studies that demonstrates quality, safety and efficacy of active pharmaceutical ingredient(s) and the corresponding finished pharmaceutical product.

Different sections of the dossier shall be distinctly marked, and page numbered in the style: **page x of y** and have a table of contents indicating the sections and page numbers. Where information is required in the application forms its location shall be cross referenced in dossier.

4.6 The covering letter or EoI shall be submitted expressing interest for continental assessment via the SAHPRA online system. Upon acceptance the entire application shall be electronically submitted to EMP TC through the SAHPRA's e-CTD system.

4.7 Application must be accompanied by two samples of the finished product as packaged for sale, submitted as per SAHPRA's sample submission guidelines. The EMP TC may request for additional samples when need arises.

4.8 There will be no fees paid for products submitted for the purpose of the pilot.

5. PROCESSING OF APPLICATIONS (MANAGEMENT OF APPLICATIONS)

5.1 Upon acceptance of an application, an acknowledgement for the receipt of the application will be issued within 5 calendar days and a reference number will be generated. The reference number shown in this acknowledgement should be used in all subsequent correspondences relating to the application.

5.2 The EMP-TC secretariat shall complete screening of the dossier for completeness within 15 calendar days from receiving such application.

5.3 In the event that the dossier is incomplete, the applicant will be notified of the deficiencies and requested to address the same.

5.4 In case of a positive outcome following screening, the application shall be placed in the evaluation queue.

5.5 Review of application for Listing of a Product will follow the appropriate evaluation queue. Priority review may be granted to products meant for public health emergencies. Evaluation of priority product shall be carried out as per the EMP-TC continental overarching procedures [insert reference link].

5.6 Abridged evaluation **may** be carried out to medicinal products that are registered in any of the EMP-TC recognized agencies. [insert reference link to of agencies recognized by EMP-TC].

5.7 During product evaluation, the EMP TC may request for further information and additional supporting documents from the applicant.

5.8 Applicant should make available such information or documentation requested after the first round of evaluation within 60 calendar days from the date of receipt of the request.

5.9 Applicant should make available any information or documentation requested after the second round which is the final round of evaluation within 60 calendar days from the date of receipt of the request.

5.10 If no response is received from applicant after the timelines described in 5.9 and 5.10 above (section to be revised), the clock stops and the application will be cancelled if no formal request for extension of deadline has been made. A new application will have to be submitted if the Applicant wishes to pursue Listing of the Product by the EMP TC.

5.11 Evaluation of the additional information shall be carried out within 60 calendar days from receiving such information. This shall be considered as the first round of

evaluation and subsequent submission of additional information shall be considered as the final round of evaluation.

5.12 Evaluation of one application shall not exceed three rounds of evaluation with the exception of administrative queries.

5.13 The Applicant will be informed of the decision in writing as to whether the application has received an EMP-TC positive or negative opinion.

5.14 A listing number will be given when a product is recommended. The listing number is specific for the product recommended by the EMP-TC. A letter of positive opinion shall be issued for the listed product.

5.15 For a product to be issued with a positive opinion/recommended by the EMP TC, it must be manufactured in a GMP compliant facility and studies conducted following GCP. The GMP and GCP status will be determined by the AMRH GMP-TC and AVAREF (if needed)

5.16 For a product to be issued MA in concerned AU countries, the applicant will be required to submit the final dossiers with all amendments along with letter of positive opinion to the concerned NRAs as per each country's requirement.

6. MAINTENANCE OF PRODUCTS IN THE EMP-TC LIST OF RECOMMENDED MEDICINAL PRODUCTS

6.1 The conditions for Listing of medicinal products are as follows: -

6.1.1 The product listed by the EMP-TC shall have the name, composition, characteristics, specifications and origin as specified in the letter of positive opinion.

6.1.2 The applicant must supply such documents, items, samples, particulars or information as the EMP-TC may require in relation to the listed product.

6.1.3 Changes in name, composition, characteristics, origin, specifications, manufacturer, packing, indications, labelling, package insert, product literature or any other particulars of the listed product shall not be made without prior notification and/ or approval from the EMP-TC.

6.1.4 The labels for the listed product must comply with all of the labelling requirements as specified by the guidelines for labelling by the EMP-TC.

6.1.5 The listed product must only be indicated for use as recommended by the EMP-TC.

6.1.6 The Applicant must inform the Continental PV-TC of any adverse reactions or complaints on quality, safety and efficacy of the listed product immediately after becoming aware of such adverse reactions or complaints, in addition to notice in the registered countries.

6.1.7 The applicant must notify in writing to the EMP-TC of any decision to withdraw the product from the list and shall state the reasons for the decision.

6.2 The listing of a product shall be valid for 5 years or such period as specified in the letter of positive opinion (unless suspended or cancelled by the EMP-TC).

6.3 The renewal of product listing should be done not later than three months prior to expiry. Applications for renewal of listing shall be made by submitting documents as outlines in guidelines on submission of documentation for renewal.

7. CANCELLATION OR SUSPENSION OF LISTING

7.1 The EMP-TC may cancel or suspend the Listing of any product if there are deficiencies in safety, quality or efficacy of the product or failure to comply with the Listing requirements or due to changes in continental, regional or national policies.

8. APPEALS AGAINST EMP-TC'S DECISIONS ON PRODUCT LISTING

8.1 For products that have been suspended and cancelled by the EMP-TC, applicant may appeal in writing to the Secretariat for the EMP-TC to review its decision.

8.2 All notice of appeals must be made within thirty (30) calendar days from the date of the notification.

8.3 Applicants shall make appeal by giving grounds for review of each reason given for the negative opinion of their product. The grounds for the request shall be based on the information that was submitted in the product dossier. Any additional or new information that was not earlier submitted will not be accepted. The EMP-TC may review or uphold its earlier decision.

9. VARIATIONS IN PARTICULARS OF LISTED PRODUCTS

All variations to listed products shall be made to the concerned AU countries according to requirements stipulated in the variation guidelines of a specific country.

9.1 EXTENSION APPLICATIONS

9.1.1 An extension application is an application that is a modification of already listed medicinal products. The modification shall be such that it does not fulfil criteria for minor or major variations but is similar enough to the original product in terms of quality, safety and efficacy.

9.1.2 An applicant may apply for extension of Listing of an already listed product as an extension application. Such an application should be submitted as a new application however an abridged evaluation will be carried out.

9.1.3 Extension applications shall be applicable in the following situations: -

a) Changes or addition of a pharmaceutical form from multi-dose to single dose of the finished product or vice versa.

b) Change or addition of strength of the finished product.

c) Change or addition of a route of administration of the finished product for products of the same pharmaceutical form.

d) Inclusion of medical devices that result in change of strength, pharmaceutical form or route of administration of the finished product.

9.1.4 An extension application shall be accompanied by the following: -

a) A dully filled in applicant form with the extension application box clearly marked (ticked).

b) A full dossier submitted in accordance to the requirements stipulated in the EMP-TC guidelines for submission of documentation for human medicinal products.

c) A cover letter declaring the following:
   i. The name and listing number of the relevant product from which the extension is applied.
   ii. The Applicant for both products shall remain the same.

d) An overview of the nature of the extension being made.

e) Supporting data related to the proposed extension.

9.1.5 The final decision on whether an application meets the criteria for extension applications will lie with the EMP-TC. In case of any doubt the applicant may contact the Secretariat of the EMP-TC before filing for an extension application.

9.2 Duplicate Listing

9.2.1 The EMP-TC shall authorize the same applicant to submit more than one application for a finished product when there are objective verifiable reasons on public health grounds regarding the availability of finished products to health-care professionals and/or patients, or for co-marketing reasons and/or for Export purposes.

9.2.2 Additionally, the Applicant can grant the use of product information to another Applicant , whereby the original Applicant acts as a contract manufacturer.

9.2.3 The assessment on whether the conditions of a duplicate application are met shall be done on a case-by-case basis, having regard to the facts of each application. The overall objectives being preservation of public health.

9.2.4 To assess whether an application refers to a particular finished product that has already been listed , and consequently, whose application for Listing qualifies for a duplicate license, the composition in active substance(s) and the pharmaceutical form shall be considered. Thus, any finished product with the same qualitative and quantitative composition in active pharmaceutical ingredient (i.e., the same strength) and the same pharmaceutical form are to be considered as the same relevant product.

9.2.5 A duplicate product shall be identical in all Listing requirements with the exception of brand name and any other specific requirements on labelling. Additionally, any variation made to the original Listing should be applied for the duplicate listing.

9.2.6 Conditions for a Duplicate Listing are outlined hereafter: -

a) That the duplicate application shall be submitted by the same applicant that submitted and/or holds the Listing that is being duplicated (hereafter “original Listing”).

b) That the original Listing is valid. This step does not apply in case of duplicate applications that are submitted in parallel with the original Listing application (i.e., in cases where the application for the original Listing is still pending).

c) In cases where the duplicate Listing is submitted on the basis of an informed consent application, there should be a letter of (no objection) from the Applicant that owns the dossier that is referred to.

d) The original Listing to which the duplicate application relates has to be valid at the time of the submission of the duplicate application.

9.2.7 The applicant for a duplicate list may fall under the following categories: -

a) Applicant is the same entity that applied for the original Listing.

b) Applicant belongs to the same group of companies as the applicant of the original Listing.

c) Applicant is an independent entity that has agreed to placing on the market the product with the applicant of the original Listing (evidence of license agreement or other agreements that can be identified are required).

d) Applicant is an independent entity whereby there are license agreements with the Listing holder of the product in respect of which the duplicate is asked but not for the placing on the market of that product.

e) Applicant is an independent entity that has got an agreement to purchase and/or use data from the company that has applied for a Listing for the product for the first time but there is not an agreement regarding the placing on the market of the product.

9.2.8 All documents in accordance to the EMP-TC guidelines on submission of documentation for new applications should be submitted however an abridged evaluation shall be applied. In addition, the following shall be submitted when making a duplicate application: -

a) A dully filled in application form (Annex II) with the duplicate list box clearly marked (ticked).

b) A cover letter detailing the following: -

i. The name of the Listing holder relevant for the duplicate application.
ii. The name of the product relevant for the duplicate application.
iii. The proposed brand name for the duplicate application.
iv. The proposed Listing holder for the duplicate application.

c) For co-marketing reasons, the co-marketing evidence (contract or letter of agreement between the companies).

d) For duplicates asked on grounds of the existence of patents protecting certain therapeutic indications or pharmaceutical forms, the applicant shall provide a commitment undertaking to extend the therapeutic indication(s)/ pharmaceutical form(s) of the duplicate Listing as soon as the patent restrictions no longer exist. Alternatively, the applicant may also commit to withdraw the Listing with restricted indications/pharmaceutical forms after the relevant patents are no longer in force.

The SmPC shall be harmonized. The commitment letter shall be submitted alongside the Listing Application Dossier.

e) Letter of no objection where applicable.