ETHIOPIAN FOOD AND DRUG AUTHORITY

Medicine Evaluation and Marketing Authorization Led Executive office

Guideline for describing the role and responsibly of Market authorization Lead executive Office

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Acronyms

LEO	Lead Executive Officer
CTD	Common technical documents
EFDA	Ethiopian Food and Drug Administration Authority
EFMHACA	Ethiopian Food, Medicine and Healthcare Administration and control Authority
ICH	International council on Harmonization
MEMA	Medicine Evaluation and Market Authorization Lead Executive Office
SOP	Standard Operating Procedure
SPC	Summary of product characteristics

Acknowledgment

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Definitions

The following definitions are provided to facilitate understanding of the Guideline; they apply only to the words and phrases used in this Guideline. Although every effort has been made to use standard definitions, the words and phrases used here may have different meanings in other contexts and other documents.

Assessor

An expert employed as per EFDA recruitment criteria for the assessment of dossier application submitted for marketing authorization, successfully completed the theoretical and practical session of the training on dossier assessment and whose competency evaluated by the Executive Office

Advanced Therapy Medicinal Products (ATMPs)

Are biological medicinal products including gene therapy and somatic cell therapy medicinal products and tissue engineered products, for which the starting materials involve genes and their vectors (viruses, plasmids) and viable cells/ tissues.

Biological medicinal products

Are medicinal products of which active substance is a biological substance including vaccines, blood products (e.g. coagulation factors), allergens and products manufactured using recombinant technology (proteins, e.g. insulin and antibodies), advanced therapy medicinal products (ATMPs)(gene- and cell therapy medicinal products and tissue engineered products) and bio similar products. These products are also referred to as biopharmaceuticals

Biological substances

Is active substance that is produced by or extracted from a biological source, characterized and determined for its quality by a combination of physico-chemical and biological testing, together with the production process and its control.

Bio similar products

Are the generic form of the biopharmaceuticals, however, diverge from common generic products in that their marketing authorization requires more extensive assessment than only quality and

bioequivalence studies. This is due to the heterogeneity of biological, the analysis and control of which requires several analytical methods.

Lead assessor

An expert employed as per EFDA recruitment criteria for the assessment of dossier application submitted for marketing authorization, successfully completed the theoretical and practical session of the training on dossier assessment and with a minimum of 4 years of experience in dossier assessment and capable of developing regulatory tools required for dossier assessment, and supervising and /or training others.

Non biological Medicinal products

Are medicinal products of which active substance is a chemical substance defined by a single molecular structure that is not a protein or nucleic acid substance and are generally considered "small" molecules which have associated salts, solvates or ions and may be described using a single definitive or representative structure.

Primary assessor

An expert employed as per EFDA recruitment criteria for the assessment of dossier application submitted for marketing authorization, successfully completed the theoretical and practical session of the training on dossier assessment.

Regulatory dossier/Dossier

A package of documents, which include all information, required by regulatory authorities regarding newly developed drug products and/or generics, for granting marketing authorization

Traditional medicine

Is the sum total of the knowledge, skills, and practices based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement, or treatment of physical and mental illness.

1. Introduction

The Ethiopia food and Drug Authority is established by Regulation number 531/2023. It is mandated to ensure safety, efficacy and quality of medicinal products and granting Market authorization based on article 20 (1) of the Food and Medicine Administration Proclamation No. 1112/2019.

Medicine Evaluation and Market Authorization Executive Office is the EFDA regulatory unit responsible for marketing Authorization of medicine. Therefore, it is the responsibility of this Executive Office to conduct activities related to the registration and marketing authorization including screening of application, pre and post market assessment of application submitted for the marketing authorization of medicines, grant approval for import of registered medicine, renewal of market Authorization for registered medicine, evaluation of post approval variation to the information accepted by the Authority.

The Executive Office is also responsible for other related activities such as approval of an agency agreement between the applicant and the local agent and registry of the license holders and local agents, approval of purchase order, issuing pre import permits of non-routine market authorization of medicine under emergency situation and other related services requested by the applicants.

The Executive Office also acts as an information center for the customers in relation to the above regulatory services. Therefore, this guidance is developed to describe the structure, roles, responsibility of the Executive Office in executing these regulatory activities.

2. The organizational Structure of the Executive Office

The Medicine Evaluation and Market Authorization Executive Office are accountable to the EFDA deputy director general for Medicine. As per the newly approved structure of the authority the Executive Office is organized in to the assessment desks as indicated in the figure 1 below:

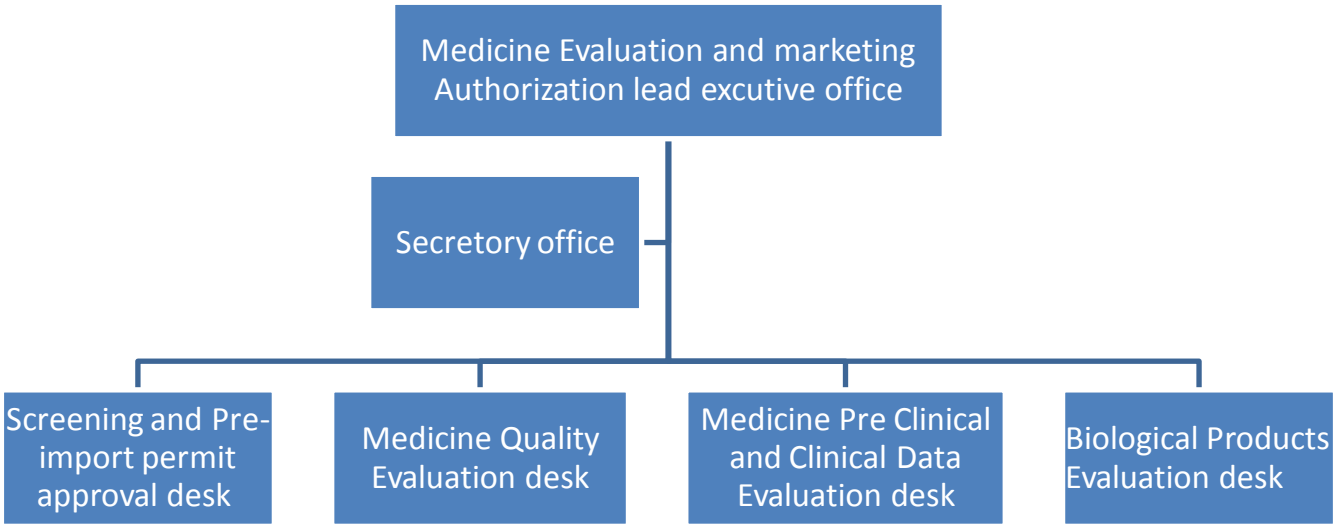

Figure1:-Structure of Medicine Evaluation and Marketing Authorization lead Executive Office.

2.1 Lead Executive Officer (LEO)

The Lead Executive officer is directly accountable to the deputy director general and it is the responsibility of this LEO to ensure that activities are planned and executed and proper services are delivered as per the applicable standards and guidelines. Therefore, the LEO is responsible to

- Identify the authority's focus areas and strategic directions, bottle necks for improvements and good governance and implement as applicable
- Prepare annual Executive Office plan based on the strategic plan of the authority, enrich the plan with his/her desk, request budget, prepare plan of action for implementation, ensure cascading of the plan in to desks and individual experts, monitor and evaluate the implementation of the plan, take necessary corrective actions as required, prepare report and submit to the responsible bodies
- Measure the performance of each desks, identify the knowledge and skill gaps, organize capacity building training where required
- Ensure that effective work communication exists where and when at appropriate frequency between the desks within the Executive Office and other appropriate units of the authority

and decide on matters beyond the mandate of the desk heads including communicating other parallel Executive Offices and higher decision makers of the EFDA.

- Represent the Executive Office in communication with the other Executive Offices, higher level managements, stakeholders and other official correspondences
- Identify and adopt the systems, strategies, standards, guidance, working procedures etc to strengthen the national registration and marketing authorization system of the country
- Identify human and material resources required for the successful execution of the plan of the Executive Office and submitted request for the responsible body for their availability
- Establish virtual team for the registration of tradition medicine and tradition medicine registration related activities.

2.2 Secretary and administrative assistant

This office is organized under the Lead Executive Officer and is responsible for the facilitation of any secretarial and administrative services required for the performance; in addition of he/she is also responsible for getting the print out of the certificates to be granted for the MA holders

2.3 The-Lead executive officer and the desk heads shared responsibilities

The Lead executive officer and desk heads have a shared responsibility to

- Identify and develop or adopt the systems, strategies, standards, guidance, working procedures to strengthen the national registration and marketing authorization system of the country
- Conduct activities related to the development and implementation of the QMS:
    - Prepare and implement the annual plan of the Executive Office, and report performance related to QMS to the deputy director and the QMS Executive Office;
    - Liaison the QMS development and implementation of the Executive Office with QMS Executive Office which leads and coordinates the implementation of Authority's QMS roadmap;
    - Participate and support in the implementation of the overall QMS of the Authority;
    - Develop, review and manage documentations related to QMS in executive Offices documents;

  - Represent the executive Office in relation to the QMS and Work as technical experts for any Technical Working Groups organized by the Authority on QMS;

- Facilitate and Evaluate subcontracting systems, processes and agreements;
- Conduct periodic performance audit, identify the quality of work for the marketing authorization activities, the knowledge and skill gaps, organize capacity building training where required
- Identify human and material resources required for the successful performance of the registration and marketing authorization activities
- Conduct periodic work load analysis and request the Authority additional expert as required, train and evaluate the hired experts together with HR personnel,
- The Drug Evaluation and Market authorization LEO/ Desk heads and QA officers will develop and periodically revise a job description in consultation with office for human resource development management
- Establish effective work communication within the registration and marketing authorization function
- The lead executive office and desk heads may delegate lead assessors or other appropriate experts to perform the above shared responsibilities
- The lead executive officer and the desk leaders are responsible for organizing expert group for the preparation and publication of SPC-like information and the public assessment reports for the accepted or differed applications

2.4 The Screening and Pre-import permit approval Desk responsibilities

The Screening and Pre-import permit desk is independent from the dossier assessment desks and has its own desk head accountable to the LEO of the Executive Office

The role and responsibility of the desk will be the following

2.4.1.Consultation service for applicants as an information desk of the Executive Office

The Screening and Pre-import permit desk should provide consultation services to the customers regarding the requirements and procedures for the marketing authorization approval of new medicine and the post approval services including variation and renewal of marketing Authorization certificate.

To render this type

of consultation service the desk head may communicate other desk heads of the respective desks or the LEO, when needed.

2.4.2.Receiving and screening of applications

The Screening and Pre-import permit desk should

- Ensure that applicants have submitted dossier application only online on electronic regulatory information system not by the manual hard copy application unless required by the authority to do so.
- Conduct screening of online new medicine dossier application (for new molecule applications, new generic medicine, radiopharmaceuticals, medicinal gases, vaccines and other biological medicines) variation application and renewal applications to verify that the dossiers applications are submitted as per the medicine registration guideline of EFDA. The screener should use the most current versions of the guideline, SOPs and checklists prepared for the same purpose.
- In addition, he/she confirm that necessary service payments were made per application.

2.4.3. Assessment and Approval of Pre import permits

It is also the responsibility of the Screening and Pre-import permit desk to

- Ensure that applicant have submitted the pre-import application only via online application procedure unless justified for unseen circumstances or requested by the authority to do so.
- Review the applications as per the most current versions of the applicable directive, guideline, SOPs and checklists prepared for the same purpose and issue pre import approvals and purchase orders of the medicines.

2.4.4. Agency agreement management

It is also the responsibility of this desk to verify that the agency agreement is compiled and submitted in line with the EFDA guidance for the registration of medicines with respect to the requirements of the agency agreement. The assessment of agency agreement approval shall be made as per the SOP for the management of the agency agreement.

2.5. The role and responsibilities of the Dossier assessment Desks

These desks are responsible for the assessment of the application dossiers for conventional medicines of non-biological origins and biological origins which may include the traditional medicines to ensure that they are safe, effective and of good quality. It is based on the positive assessment outcome of these desks that the marketing authorization is issued for the products.

The desk heads shall assign application by first-in-first-out principle based on their verification date for new, renewals and variation applications. However, for additional data submission the assessment should be based on reply date.

The primary assessor are responsible for detailed evaluation or assessment of the medicine dossier application in depth possible to avoid duplication of effort as per relevant Directives, guidelines and SOPs as well EFDA recognized official monographs so that the lead assessor may not necessarily dig in the bulk of the data, unless required and then write and communicate the assessment report to the respective quality, clinical or biological lead assessors.

The respective lead assessor shall review the first assessment report, discuss with the first assessor and may go in to the dossier application, as required, before preparing assessment summary report and sending the assessment report to the desk head. In addition, the lead assessor may return the first assessment report to the primary assessor when observations in the dossier were not discussed in depth by the primary assessor or the assessment was not conducted as per the respective registration guideline, SOPs and checklist.

The assessment outcome or report could be requesting additional information, or rejection or acceptance of the application. These reports will be submitted to the respective desk heads. Moreover the lead assessor shall prepare assessment summary report for approved applications and public assessment report for publication.

The respective Desk heads will verify the assessment reports submitted by the responsible lead assessors including conclusion for the request for acceptance or rejection of the provided information for every application. Incomplete assessment reports will be returned to the respective lead assessor(s). The report reviewed by the desk lead should be submitted to the Lead executive officer

The dossier assessment Desk is also responsible for the assessment of promotional material.

The Medicine Quality data assessment desk head is responsible to compile assessment outcomes (product information, quality and Pre-clinical and clinical data assessment outcomes) to have a single complied assessment report for the application of small molecule application dossiers to be communicated to the LEO or the applicant as applicable.

The data to be evaluated by these desks will cover; the quality data, preclinical and clinical data and the product information, biological product assessment. Based on the nature of these data these desks are organized as follows

2.5.1. Medicine Quality data assessment Desk:

Responsible for the assessment of the quality part of the dossier including review of relevant sections of the product information (Summary of Product Characteristics and Patient Information Leaflets and labels) and correspondence with the applicant. This also covers preparation of draft SPC-like information and public assessment summary report; in addition the desk is responsible to conduct the following activity;

2.5.1.1. Medicinal gases and radiopharmaceuticals

Medicinal gasses and radiopharmaceutical application dossiers will be evaluated and assessment summary report and public assessment report will be prepared as required.

2.5.1.2. Renewal of marketing Authorization

Any marketing authorization certificates issued by the Lead Executive Office for the import, distribution and sale of pharmaceutical products in Ethiopian territory should be renewed every five year. For this purpose applicant should organize and submit renewal application and it is the responsibility of the Medicine Quality data assessment desk to evaluate and approve such

application except for the biological product as this will be the responsibility of the relevant desk. The assessors should use the most current versions of the marketing authorization renewal guideline, SOPs and checklists prepared for the same purpose.

2.5.1.3. Assessment and Approval of variation application

Applications with a variation from the conditions of the previous registration will be assessed and approved by Medicine Quality data assessment desk for products of non-biological origins, medical gases and radiopharmaceuticals. The assessors should use the most current versions of the relevant marketing authorization guideline, SOPs and checklists prepared for the approval of post market changes or variations.

2.5.1.4. Assessment of Low risk products

It is also the responsibility of Medicine Quality data assessment desk to handle, evaluate and issue marketing authorization approvals for the low risk products including Antiseptic, disinfectant, Oral and skin care products, and other products designated as low risk products by the authority. The assessors should use the most current versions of the guideline, SOPs and checklists prepared for the same purpose.

2.5.2. Preclinical and Clinical data assessment Desk

Responsible for the assessment of the clinical part of the dossier, including review of relevant sections of the product information (Summary of Product Characteristics and Patient Information Leaflets and labels) and correspondence with the applicant. This also covers drafting information relevant to be included to the SPC-like information and public assessment summary report.

For new chemical entity both the preclinical and clinical data should be assessed whereas only the bioequivalence or the bio-waiver data will be the center of attention for assessment for the generic/multisource products.

2.5.3. Biological Medicinal product application dossier assessment Desk

The marketing authorizations of the biological medicinal products require special attention due to the fact that these products differ from other medicinal products with regards to their composition, manufacturing processes and associated risk. The active substances of biological medicinal products

are often heterogeneous mixtures, because of their starting materials (live cells) and complex manufacturing and purification processes.

This desk is organized separately due to this complex nature of these products that require professional mixes including pharmacologists, biochemists, cell and molecular biologist, microbiologist, virologist and immunologist and additional specialized and specific training related to the manufacturing and regulatory standards of biological medicinal products in addition to the basic dossier assessment training. Here, it is important to be mentioned that authority may use the external experts with respect to the mentioned specialties in this regards.

This desk is responsible for the assessment of the application dossiers for medicines of biological origins such as vaccines, plasma derived medicinal products, blood products (e.g. coagulation factors), allergens and products manufactured using recombinant technology (proteins, e.g. insulin and antibodies), advanced therapy medicinal products (ATMPs)(gene- and cell therapy medicinal products and tissue engineered products) and bio similar products; to ensure that they are safe, effective and of good quality. It is also based on the positive assessment outcome of this desk that the marketing authorization is issued for the products.

The evaluation of biological application dossier will be as per the respective biological dossier registration guideline of the Authority and other independent guideline such as WHO and ICH guideline.

Similar to the other medicines application dossiers, the biological medicine dossier shall also evaluated by two assessor (primary and lead assessors) and the similar procedure described above under 2.5 for the non-biological medicinal products including assigning of dossier for assessment by desk head, assessment of dossier by the assigned assessor including review of product information (Summary of Product Characteristics and Patient Information Leaflets and labels) and correspondence with the applicant. This also covers drafting information relevant to be included to the SPC-like information and public assessment summary, However, the assessment by these two assigned assessors will be end to end as it covers the quality data, clinical data and the product information; in addition the following activities will be carried out

2.5.3.1. Renewal of marketing Authorization

Any marketing authorization certificates issued by the Executive Office for the import, distribution and sale of pharmaceutical products in Ethiopian territory should be renewed every five year. For this purpose applicant should organize and submit renewal application and it is the responsibility of the Biological Medicinal product application dossier assessment desk to evaluate and approve Biological Medicinal product application. The assessors should use the most current versions of the relevant guideline, SOPs and checklists prepared for the same purpose.

2.5.3.2. Assessment and Approval of variation application

Biological Medicinal product applications with a variation from the conditions of the previous registration will be assessed and approved by Biological Medicinal product application dossier assessment desk. The assessors should use the most current versions of the relevant guideline, SOPs and checklists prepared for the same purpose.

2.6. The responsibility for traditional medicine dossier assessment

The traditional medicine registration is an area yet not touched by the authority. Therefore, it will be the responsibility of this Executive Office to take initiative to

- Design and develop a national regulatory system for the approval of traditional medicines including the national strategy, directives, guidelines, standard operating procedures and any other related regulatory tools that will facilitate the registration of traditional medicines.
- Support the Anthropological and ethnological studies that will help in the development of national ethno-pharmacopoeias
- Generate and implement other initiatives that will help in strengthening the traditional medicines endogenous knowledge and practices
- Train and capacitate the traditional medicines practitioners on the compilation of regulatory information and data required for the national registration of traditional medicines
- Prepare and publish the information on the safety and use of approved traditional medicines

Assessment of traditional medicine application dossier will be as per the established registration strategy and guideline of the Authority and other national, regional and international body regulatory standards recognized by EFDA.

Once established system is in place, traditional medicines shall also be evaluated by two assessor (primary and secondary assessors) and the similar procedure flow described above under 2.5 including assigning of dossier for assessment by desk head, assessment of dossier by the assigned assessor, assessment report compilation and public summary report preparation etc; will be followed for the assessment and approval of these products. However, the assessment by these two assigned assessors will be end to end as it covers the quality data, clinical data and the product information.

3. References

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