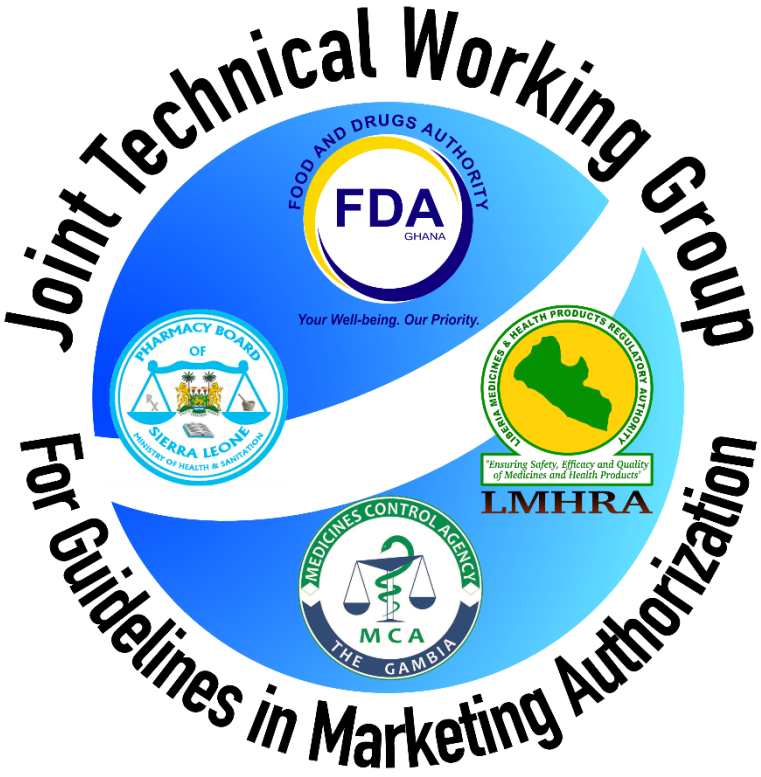

Guideline on Withdrawal, Suspension, Revocation or Cancellation of Marketing Authorization

For the National Medicines Regulatory Authorities of Ghana, Liberia, Sierra Leone, and The Gambia

Updated December 2, 2022

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<02 December 2022>
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Guideline on Withdrawal, Suspension, Revocation or Cancellation of Marketing Authorization, Version 1, Updated December 2, 2022

Draft written by LMHRA Liberia	November 2021
Draft reviewed and agreed by LMHRA, MCA The Gambia, PBSL, FDA Ghana, GHPP PharmTrain	14 September 2022
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Adopted by <Committee/Board> for release for consultation	<DD Month YYYY>[1]
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Adopted by <Committee/Board>	<DD Month YYYY>
Date of coming into effect	<DD Month YYYY>[4]

This guideline replaces '<guideline>' (NMRA/…/…).[5]

Comments should be provided using the template for submission of comments. The completed comments form should be sent to <as appropriate (NMRA's Email)>

Keywords	**Withdrawal, Suspension, Revocation, Cancellation, Marketing Authorization**

[1]Last day of relevant Committee meeting.
[2]Date of publication on the NRA public website/1st day of the month following adoption of the guideline.
[3]Last day of the month concerned.
[4]First day of coming into effect. Latest 3 months after adoption.
[5]If this supersedes a previous guideline – otherwise delete.

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Guideline on Withdrawal, Suspension, Revocation, or Cancellation of Marketing Authorization (MA), Version 1, Updated December 2, 2022

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Style notes for this draft version:

[ ] Comments to be removed with finalization

< > Placeholder to be filled with specific information or to be decided if kept or deleted.

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Executive summary

The development of this guideline is based on the outcomes and consensus of the meetings convened in January / February 2020 by GHPP-PharmTrain Project team of the Federal Institute for Drugs and Medical Devices (BfArM, Germany) with participants from the national medicines regulatory authorities (NMRA) of Liberia (LMHRA, Liberia Medicines and Health Products Regulatory Authority), Sierra Leone (PBSL, Pharmacy Board of Sierra Leone), and The Gambia (MCA, Medicines Control Agency).

This document has been discussed and adapted in exchange between LMHRA, PBSL, The Gambia MCA, Ghana (FDA, Food and Drugs Authority) and the GHPP-PharmTrain project team from November 2021 to September 2022.

From January 2022 the Joint Technical Working Group for Guidelines in Marketing Authorization (TWG-MAG), with the above-mentioned members, was established to continue the successful development of regulatory guidelines.

<This document should be read in conjunction with the accompanying notice and the relevant sections of other applicable guidance.>

1. Introduction (background)

This guideline describes the conditions under which a marketing authorization (MA) can be withdrawn, suspended, revoked or cancelled. When medicinal products are suspected of being potentially harmful to users due to their defective quality, safety or efficacy, or administrative issues or malpractice of the manufacturer, importer, distributor or marketing authorization holder (MAH) of the medicinal product their marketing authorization may be subjected to a withdrawal, suspension, revocation or cancellation process. This in the worst case can trigger the recall of the product (find details on the recall process in <NMRA> specific Guideline). All related information must be reported to the <NMRA>. MAHs are required, in all circumstances, to notify the <NMRA> immediately of unanticipated adverse effects that could possibly be associated with an authorized product and that might call for restrictive regulatory action. This document provides guidance to ensure that the respective operations are effectively and efficiently carried out by all actors involved. The <NMRA> is responsible to assess are the nature of complaints/product defect and decide whether a regulatory consequence is warranted, which can be a suspension, revocation or cancellation of the MA.

1.1. Objectives:

This guideline provides guidance and clarification on what conditions a marketing authorization can be withdrawn, suspended, revoked or cancelled and what measures need to be taken in any of these processes.

All final decisions on the status of the marketing authorization of medicinal products and, if indicated, any subsequent action related to it will be taken by <NMRA>.

2. Scope

The guideline provides guidance regarding the withdrawal, suspension, revocation and cancellation of a marketing authorization of medicinal products. The term “medicinal products” in the context of this TWG-MAG guideline includes finished pharmaceutical products (FPPs), biotherapeutics, and vaccines.

3. Legal basis

[Where applicable, i.e. for scientific guidelines in relation to quality, safety and efficacy.]

This guideline is coherent with national/regional frameworks and policies. The usage of this guideline by the NMRA and the MAH is supported/embedded in the legal provision <quote title of national medicines Act and section, if applicable>. MAHs are encouraged to familiarize themselves with this document and the above law.

4. Various post-marketing authorization scenarios resulting in withdrawal, suspension, revocation or cancellation of MA

Withdrawal → The permanent discontinuation of the marketing authorization by the marketing authorization holder (MAH). Reasons for withdrawal could be manifold, including administrative or commercial. The MAH shall declare the reason for withdrawal, particularly if his/her action concerns the quality, safety and/or efficacy of the medicinal product.

Suspension → Action taken by the NMRA, if a ground for refusal as defined in the legal provision developed or if one of the conditions imposed pursuant to maintaining the marketing authorization has not been met and the flaw has not been corrected within a reasonable period of time that is to be specified by the NMRA.

Revocation → Action taken by the NMRA, if a marketing authorization was granted unlawfully from the outset, e.g., due to deception or the like.

Cancellation → Action taken by the NMRA for the invalidation of a marketing authorization that was lawful at the time of its granting and for which the reason for invalidation occurred subsequently (e.g. due to additional [post-marketing] information about the medicinal product).

5. Classification of scenarios

Marketing authorization of an authorized product may be withdrawn, suspended, revoked or cancelled in various circumstances that can be allocated into three classes:

Circumstances related to

5.1. Administrative issues

5.2. Malpractice of the manufacturer, importer, distributor or MAH of the medicinal product

5.3. Issues related to quality, safety or efficacy of the medicinal product

5.1. Administrative issues

5.1.1. Suspension of marketing authorization

Marketing authorization may be suspended under the following circumstances;

a. Where the MAH failed to pay maintenance fees, where applicable.

b. Where a conditional marketing authorization has been issued and the MAH could not meet the condition on time

For imported products, if marketing authorization is suspended or withdrawn in the country of origin, the MAH is obliged to report this to <NMRA>, by stating the reasons. The MAH should indicate whether the quality, safety or efficacy of the product or Good Manufacturing Practices (GMP) certification of the sites of manufacture are affected.

5.1.2. Cancellation of marketing authorization

a. If applicable: Where the product is not available on the market after one year of marketing authorization

b. Where the MAH failed to apply for renewal within time (if applicable).

c. Where there is change in the treatment policy for public health programmes.

d. The circumstances under which the medicinal product was registered no longer exist

5.2. Malpractice of the manufacturer, importer, distributor or certificate holder of the medicinal product

5.2.1. Revocation of marketing authorization

Marketing authorization may be revoked under the following circumstances

a. The premises, in which the medicine or part thereof is manufactured, packaged or stored by or on behalf of the holder of the Marketing Authorization Certificate is unsuitable for the manufacture, packaging or storage of the medicines

b. Unauthorized variation (e.g. mis-labelling, change of applicant, manufacturer, labelling, product information or other registered particulars)

c. Importation without permission and/or through unapproved route

d. Distribution of products to unauthorized facilities/premises, where applicable.

e. the product is found to have been promoted (by MAH, distributor, any other stakeholder…) in an inappropriate or unethical manner

5.3. Defective quality, safety or efficacy

5.3.1. Suspension of marketing authorization

The NMRA may suspend the marketing authorization where a complaint is received from the MAH, the public or through NMRA's post market activities, and where the under listed issues are reported, investigated and found to be credible:

a. Product defect (e.g., quality defect) affecting public health

b. The quantitative or qualitative composition is not as specified in the marketing authorization;

c. lack of compliance to cGMP

d. accumulation of reported unanticipated adverse effects/ reactions

e. The product is not in compliance with the conditions of marketing authorization

f. It is strongly suspected that the product is unsafe in the normal conditions of use.

In the event where a product is suspended in any country because of safety, quality, efficacy issues, the MAH shall notify the NMRA within one month of the suspension, failure to do so may lead to cancellation of the MA.

5.3.2. Cancellation of marketing authorization

The <NMRA> may cancel the marketing authorization where a complaint is received from the public or through its post market activities, and where the under listed issues are reported, investigated and found to be credible:

a. Product defect (e.g., quality defect) affecting public health

b. The quantitative or qualitative composition is not as specified in the marketing authorization;

c. lack of compliance to cGMP

d. accumulation of reported unanticipated adverse effects/ reactions

e. new published research findings stating irreversible quality, safety or efficacy concerns

f. The standard of quality, safety and efficacy as prescribed in the documentation for marketing authorization is not being complied with.

g. The product is not in compliance with the conditions of marketing authorization

h. The product has proven to be ineffective for the approved indication(s);

i. It is proven that the product is unsafe in the normal conditions of use

j. If during the lifecycle of the generic product it is confirmed that the risk-benefit balance of the reference medicinal product is not favourable and the marketing authorization of that reference medicinal product is cancelled, the same action would be required also towards the generic medicinal products of that reference medicinal product.

In the event where a product is cancelled in any country because of safety, quality, efficacy issues, the MAH shall notify the NMRA within one month of the cancellation, failure to do so will lead to cancellation of the MA.

6. **Processing withdrawal, suspension, revocation and cancellation of MA.**

Withdrawal

The MAH will officially write to the NMRA the reason(s) for withdrawing the MA. The MAH must notify the NMRA of any actions taken to withdraw the authorization of a medicinal product from the market, to request the withdrawal or to not request the renewal of a marketing authorization together with the reasons for such action. He must in particular declare if his action concerns the quality, safety or efficacy of the medicinal product or if it is based on an administrative or commercial decision. A template for voluntary withdrawal by the MAH is attached in the Annex I.

After resolving the issue that led to the withdrawal, the MAH may apply for marketing authorization again, if applicable, with a revised dossier and all problems concerning the medicinal product sorted. The NMRA will respond upon this request and archive the product's / companies' history.

Suspension, revocation or cancellation

a. An issue that may lead to suspension, revocation or cancellation as per Chapter 5 is detected by the NMRA, filed in or received from either the MAH or the public.
b. The report is processed and investigated by the NMRA. NMRA specific timelines for processing are specified in <Annex XX>.
c. Based upon case specific outcomes, once guilty, MAH is notified of the appropriate regulatory actions (suspension of MA).

Annexes

Annex I

Withdrawal letter template

(< FROM MAH ON HEADED PAPER >)

Date: <dd mmmm yyyy>

<NMRA address>

Subject: Withdrawal of <Product Name>, (INN), strength(s), pharmaceutical form(s)> -

<EMEA/H/product No.> OR <EMEA/H/product No./X or II/nn>

Dear <NMRA>,

For the withdrawal of initial marketing authorization application

I would like to inform you that, at this point of time, <MAH's name> has taken the decision to withdraw the application for Marketing Authorization of <Product Name>, (INN), strength(s), pharmaceutical form(s)>, which was intended to be used for <applied for MAH's proposed indication>.

OR

For the withdrawal of Type II variation/ Annex I (Regulation 1234/2008) application linked to an extension of indication for a medicinal product already authorized I would like to inform you that, at this point of time, <MAH name> has taken the decision to withdraw the application for <a new indication> <a change to the marketing authorization> for <name of the product>, <to add <a <strength><pharmaceutical form>,> in the <treatment of /prophylaxis against/diagnosis of> <disease>.

This withdrawal is based on the following reasons

<Please state the reasons for the withdrawal. The following is included as possible examples, amongst others>:

<identification of major manufacturing issues>

<identification of major pre-clinical issue>

<identification of major clinical issues>

<identification of major GxP issues>

<the NMRA considers that the data provided do not allow the committee to conclude on a positive benefit risk balance>

<Company's marketing strategy>

Other: <please elaborate>

<Please provide any further detailed comment as appropriate>

<Provide information on the consequences of the withdrawal on ongoing clinical trials and

compassionate use programme>

<Provide additional information on any future plan for development of the product>

We reserve the right to make further submissions at a future date in this or other therapeutic

indication(s).

I agree for this letter to be published on the NMRA website.

Yours sincerely,

<Signature from the MAH>

Definitions

Applicant (for MA)

A person or entity who has applied for regulatory approval of a product or a change thereof. All applicants are to own the product. Representatives of product owners may not hold themselves as applicants unless they own the product.

In some jurisdictions this term is used in a wider sense (see “Marketing authorization holder)”.

Marketing Authorization (MA)

Approval to market a medicinal product in the NMRA’s country. MA is issued by the NMRA with a legal document for the purpose of marketing or distribution of a product within the country after evaluation for safety, efficacy and quality in the marketing authorization assessment process.

Marketing Authorization Holder (MAH)

A person or entity whose product has been authorized by a national medicines regulatory authority to be on the market.

Medicinal Product

Any substance or combination of substances prepared, sold or presented for use in the diagnosis, treatment, mitigation or prevention of disease, disorder of abnormal physical state or the symptoms of it or restoring, correcting or modifying organic functions in human beings

The term Medicinal products in the context of these guidelines include finished pharmaceutical products, biotherapeutics, and vaccines. Not included are medical devices, in-vitro diagnostics, blood products and animal products, if not indicated otherwise.

Recall

The removal of specific batch/batches of a medicinal product or related product from the market for reasons relating to deficiencies in the quality, safety or efficacy.

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This guideline template is based on the structure of the Guideline on Guidelines V1, February 2021 developed by the joint working group of Food and Drugs Authority (<NMRA>, Ghana), Liberia Medicines & Health Products Regulatory Authority (LMHRA, Liberia), Medicines Control Agency (MCA, The Gambia), Pharmacy Board of Sierra Leone (PBSL, Sierra Leone), and the Global Health Protection Programme (GHPP) PharmTrain-Project of the Federal Institute for Drugs and Medical Devices (BfArM, Germany).