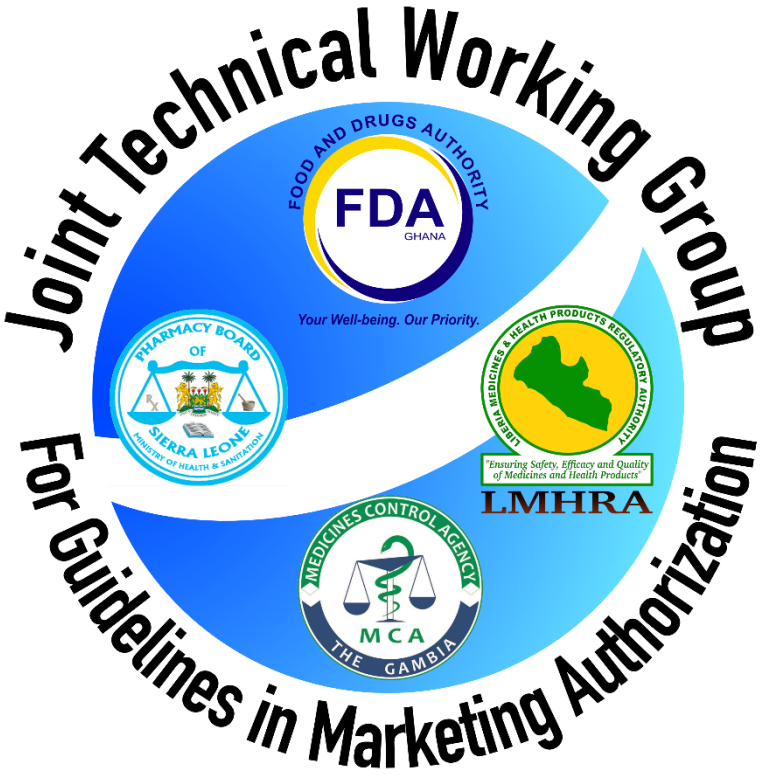

Guideline on

the Investigation of Bioequivalence

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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The Guideline on the Investigation of Bioequivalence, Version 1, Updated December 2, 2022

This Guideline (GL) is an adaptation of the Guideline on the Investigation of Bioequivalence, EMA, Rev 1, 2010, with all 3 annexes whereby region, country, and national medicines regulatory authorities (NMRA) specific requirements as well as improvements of certain aspects that differ from the adopted GL are specified by <NMRA> annotations in the following document.

Draft written by FDA Ghana and MCA The Gambia	October 2021
Draft annotations reviewed and agreed by TWG-MAG: LMHRA, MCA The Gambia, PBSL, FDA Ghana, GHPP PharmTrain	10 May 2022
Updated by LMHRA, MCA The Gambia, PBSL, FDA Ghana, GHPP PharmTrain	02 December 2022
Adopted by <Committee/Board> for release for consultation	<DD Month YYYY>[1]
Start of public consultation	<DD Month YYYY>[2]
End of consultation (deadline for comments)	<DD Month YYYY>[3]
Agreed by <Working group(s)/Departments>	<Month YYYY>
Adopted by <Committee/Board>	<DD Month YYYY>
Date of coming into effect	<DD Month YYYY>[4]

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

[1]Last day of relevant Committee meeting.
[2]Date of publication on the NMRA 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.

<Street of the NMRA> • <Region> • <City> • <Country>
Telephone < > **Facsimile** < >
Send a question via our website www.<NMRA>…
An agency of the <……>.

Country logo

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	*bioequivalence, pharmacokinetics, biowaiver, in vitro dissolution, generic*

Guideline on the Investigation of Bioequivalence, Version 1.0, Updated December 2, 2022

Table of contents

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.

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 October 2021 to May 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.>

Information on the adopted Guideline on the Investigation of Bioequivalence

Title: Guideline On The Investigation Of Bioequivalence

Title(s) of Annexes/Appendixes:

APPENDIX I-Dissolution testing and Similarity of Dissolution Profiles

APPENDIX II-Bioequivalence study requirements for different dosage form

APPENDIX III- BCS-based Biowaiver

Author(s): European Medicines Agencies (EMA), Committee For Medicinal Products For Human Use (CHMP)

Document No: Doc. Ref.: CPMP/EWP/QWP/1401/98 Rev. 1/ Corr **

Version No:

Date of issue: 20 January 2010

Source (e.g. website link): https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-investigation-bioequivalence-rev1_en.pdf

1. <NMRA> annotations on the adopted Guideline on the Investigation of Bioequivalence

1.1. Concerning Section 1.3 Other Types Of Application

Annotation: Hybrid application need to be excluded from the list of other applications that this GL is applicable to.

Rationale: Hybrid application is not applicable to the registration process of <NMRA>.

[The annotation "concerning Section 1.3 Other Type of Application" should be deleted, if hybrid application are processed in the registration process of the respective NMRA. In view of the fact that not all member NMRAs recognise hybrid applications the applicability of this guideline to hybrid applications will be country specific.]

1.2. Concerning Section 3 Legal Requirements

Annotation: Replacement of the EMA legal requirement with the <NMRA> specific legal requirement <quote title of regulation/ national medicines Act if applicable>. This amendment includes all references to "Directive 2001/83/EC" in the guideline.

Rationale:

The EMA legal requirement "Directive 2001/83/EC" is not applicable to the <NMRA>.

1.3. Concerning Section 4.1 Design, conduct and evaluation of bioequivalence studies

Annotation: In the sentence

"Module 2.7.1 should list all relevant studies carried out with the product applied for, i.e. bioequivalence studies comparing the formulation applied for (i.e. same composition and manufacturing process) with a reference medicinal product marketed in EU"

"EU" was replaced by *"countries of regulatory agencies and institutions classified as group B in the WHO framework" (https://www.who.int/publications/m/item/list-of-transitional-wlas)* and complemented with an additional sentence.

"*Module 2.7.1 should list all relevant studies carried out with the product applied for, i.e. bioequivalence studies comparing the formulation applied for (i.e. same composition and manufacturing process) with a reference medicinal product marketed in countries with regulatory agencies and institutions classified as group B in the WHO framework* (https://www.who.int/publications/m/item/list-of-transitional-wlas). *In the event that there is no innovator brand available applicant should contact the NMRA.*"

Rationale:

Since the EU is not applicable for West Africa the "*EU*" could be replaced by *"countries with regulatory agencies institutions classified as group B in the WHO framework"* to expand the scope of the source of reference to well-resourced agencies and institutions.

Definitions

Bioequivalence

The absence of a significant difference in the rate and extent to which the active pharmaceutical ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study.

Clinical Trial

A clinical trial is any systematic study on a medicinal product in human subjects, whether in patients or other volunteers, in order to discover or verify the effects of, and/or identify any adverse reaction to, an investigational product, and/or to study the absorption, distribution, metabolism and excretion of the product with the object of ascertaining its efficacy and safety.

Clinical Trial Protocol

A document that describes the objective, design, methodology, statistical considerations, and organization of a clinical trial/study.

Comparator product

A medicinal product with which the generic product is intended to be interchangeable in clinical practice

Extension application / line extension

An extension application is an application for a marketing authorization in the name of the same marketing authorization holder, for example if the pharmaceutical form and/or strength, therapeutic indication of the product differs from one or more other medicinal products having the same active ingredients, for which this marketing authorization holder already has a marketing authorization.

Generic medicinal product

Is a medicinal product, which has the same qualitative and quantitative composition in active pharmaceutical ingredients and the same pharmaceutical form as the authorized reference medicinal product and which bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies.

Good Clinical Practice (GCP)

A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the study data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

Good Manufacturing Practices (GMP)

A standard concerning the production, processing, packing, release, and holding of a medicine which ensure that medicinal products are consistently produced and controlled according to quality standards appropriate to their intended use and as required by marketing authorization.

Hybrid application

Hybrid medicines are medicinal products whose authorization depends partly on the results of tests on the reference medicine and partly on new data from clinical trials. This happens when a manufacturer develops a generic medicine that is based on a reference medicine, but has a different strength, a different route of administration or a slightly different indication from the reference medicine.

Protocol Amendment

A written description of a change or formal clarification of a clinical trial protocol

Reference Medicinal Product

Pharmaceutical product with which the new product is intended to be interchangeable in clinical practice. The reference product will normally be the innovator product for which efficacy, safety and quality have been established. Where the innovator product is not available, the product, which is the market leader may be used as a reference product, provided that it has been authorized for marketing and its efficacy, safety, and quality have been established and documented.

Reference Institution (RI) / Reference Regulatory Authority

An authority or institution which assessment and its outcome serve as basis for regulatory reliance. As per WHO guidance (https://www.who.int/news/item/29-04-2021-who-publishes-new-guidance-to-promote-strong-efficient-and-sustainable-regulatory-systems) this encompasses different levels of reliance.

In this document this term relates to a list of authorities/institutions determined by the NMRA including the transitional WHO listed authorities referred to as group B (https://www.who.int/publications/m/item/list-of-transitional-wlas) and WHO Prequalification Programme.

References

WHO. 51th report of the World Health Organization Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP), WHO Technical Report Series No. 1003, 2017.

This guideline template is based on the structure of the adoption approach of the Guideline on Guidelines V1, February 2021 developed by the joint working group of Food and Drugs Authority (FDA, 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).