Collection of samples for lumefantrine/desbutyl-lumefantrine pharmacology analysis v2.0

Procedure

WorldWide Antimalarial Resistance Network (WWARN)



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Version History

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| Version number  | Revision(s) & reason for amendment | Release Date |
| 1.0 | Creation of procedure | 02Oct2015 (Chris Lourens, Joel Tarning) |
| 2.0 | Updated nomenclature, other minor administrative changes | 14Sep2018 |

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# 1. Purpose

The purpose of this document is to standardize the sample collection procedure during clinical studies of lumefantrine / desbutyl-lumefantrine antimalarial drugs. This should be considered as a recommendation or as a definition of minimum requirements, created by the Worldwide Antimalarial Resistance Network (WWARN), aiming to achieve homogeneous quality in the pre-analytical phase of studies and to provide guidelines in the processes of collection, processing, preserving, storage, shipment and safe handling of samples from human origin.

# 2. Scope

This document applies to those sites wishing to conduct clinical trials to assess the pharmacokinetics/pharmacodynamics of lumefantrine / desbutyl-lumefantrine to support antimalarial drug investigation.

**NOTE: It is crucial to contact the analytical laboratory before commencement of the study to inquire about specific requirements of that particular laboratory.**

# 3. Abbreviations

WWARN Worldwide Antimalarial Resistance Network

QA/QC Quality assurance / quality control

LF Lumefantrine

LFm Desbutyl-lumefantrine

# 4. Duties and responsibilities

The tasks to be completed for this procedure are listed below. Each of these must be assigned to an individual(s) who has been trained to perform these tasks and in the use of relevant health and safety precautions.

* Proper identification of patient and matching samples
* Collection of samples
* Processing of samples

# 5. Materials

Samples for pharmacology analysis of LF / LFm must be collected in plastic containers and transferred to screw cap polypropylene cryovials for transportation and storage. The tube should be at room temperature (18°- 25° C) prior to use. Use of plastic sampling and storage containers minimizes the risk for analyte adsorption and improves safety at the site. The recovery of LF / LFm is unaffected when plasma is taken pre- or post-prandially.

Choice of the paper used to collect dried blood spot samples must be made in consultation with the analytical laboratory.

EDTA or sodium or lithium heparin must be used as an anticoagulant. (1)

# 6. Procedure

Analysis of LF / LFm may be done in whole blood, plasma or dried blood spots per the validated bioanalytical method used for the analyses. Plasma and whole blood matrices are the most commonly used sampling procedures.

* Collect the required volume of whole blood following the local protocol for the collection of blood.

Note: A catheter may be needed for dense sampling to reduce venipunctures. The minimum volume required may differ for individual laboratory methods. Please contact the laboratory first to obtain more information on specific needs. Mass spectrometry-based methods commonly require smaller volumes in the range of 100-500 microliters, and UV-based methods commonly require volumes in the range of 500-1000 microliters.

* Whole blood: Transfer whole blood directly into pre-labelled (Patient ID, date and clock time of collection) polypropylene cryovials with added EDTA or sodium or lithium heparin as anticoagulant. Store frozen (see section 8 below), do not thaw the sample after freezing.
* Plasma: Centrifuge EDTA or sodium or lithium heparin anticoagulated whole blood within 60 minutes of sampling at 1000 – 3000 x g for 7 – 15 minutes. Transfer the plasma into pre-labelled (Patient ID, date and clock time of collection) polypropylene cryovials. Store frozen (see section 8 below), do not thaw the sample after freezing.
* Dried blood spots: Apply whole blood directly to pre-labelled (Patient ID, date and clock time of collection) filter paper. If dried spot methodology is used, contact the laboratory to obtain more information on paper specifications, drying and storage conditions.

# 7. Sampling times

Sampling times should be verified by a pharmacologist to ensure an informative clinical trial design. The sampling times vary depending on intended analysis technique (i.e. model-independent or model-based analysis) and also with the specific aim of the study (1).

Suggested dense sampling times (1):

Six doses (0, 8, 24, 36, 48, 60 h) Hour: 0, 1, 2, 4, 6, 12, 16, 28, 52, 64

Days: 3, 4, 7, 14

# 8. Stability

LF / LFm is stable in plasma at 4oC for up to 48 hours. Venous blood samples should not be stored for more than 1 hour at room temperature. It can also be stored at -20oC for up to three months. Long term storage at -80oC is usually sufficient for at least 1 year.

# 9. Reference

1. Methods and techniques for assessing exposure to antimalarial drugs in clinical field studies. *WHO*. ISBN 978 92 4 150206 1, p43.