I. Purpose

This document aims to standardize the process of submitting and receiving amendments to ERB-approved protocols, assigning reviewers, consolidating reviews and providing approvals by the MSF Ethics Review Board.

II. Definitions

A. Amendment – any significant changes that are made to an ERB-approved protocol. These changes may be classified as major or minor.

1. Major amendments involve *substantial alterations* in the study protocol that may *affect ethical soundness, scientific validity* or *alter the risk-benefit profile of the study*, such as:
    a. Modifications to the primary hypothesis that is being tested.
    b. Changes in the research design or the methodology.
    c. Addition of outcomes or exposures, which may be unrelated to the main focus.
    d. Changes in the study site(s) and/or modifications in the facilities that support safe conduct of the study.
    e. Changes in the definition of the study population.
    f. Major adjustments in the sample size.
    g. New information on the efficacy or safety profile on an investigational product
    h. Addition of new laboratory/medical procedures
    i. Changes in the duration of the follow-up period
    j. Changes in or addition of data collection methods and tools.
    k. Introduction of new plans involving interactions with health professionals and/or patients and/or prospective or current study participants.
    l. Major revisions in the analysis plan.
    m. Changes in data sharing terms and conditions; addition of linkages with other data bases; addition of or changes in linkages with stored biological material.
    n. Changes in collection, analysis, transport, storage and/or access to biological material, including: changes in or addition of source(s) of biological material; modifications in or addition of biological material collected, analysed, transported and/or stored; modifications in or addition of tests to be conducted; etc.

o. The introduced amendment(s) to the protocol potentially alters the presumed willingness of current study participants to continue their involvement in the study.
p. Substantial changes in the qualifications of the research team.
q. A change in the Principal Investigator.
r. Considerable changes in collaborating institutions/organizations and/or collaborators.
s. Other changes which may be deemed as more than minor by the Executive Officer, in concurrence with the Chair or the Vice Chair.

2. Examples of amendments which may be considered as minor include:
   a. Changes in the research staff other than the principal investigator, provided the necessary expertise for the research remains unchanged
   b. Adjustments in the study time schedule brought about by delays in study initiation, provided the reasons for delay are presented.
   c. Limited additional analysis suggested by unexpected findings, provided these are clearly presented as post-hoc.
   d. Additional statistical methods to further control for confounding or sensitivity analysis provided these are to be reported as secondary to the main findings.

B. ERB-approved protocol – a research protocol, identified by a date and version number, which has been reviewed and approved by the MSF ERB.

III. Abbreviations

ERB	Ethics Review Board
MSF	*Médecins Sans Frontières*
MSF ERB ID	Identification number (The identification number assigned to the protocol by the ERB Secretariat)
OC	Operational Centre

IV. Responsible person for the submission

All requests for approval of amendments to ERB-approved protocols must be addressed to the Chair of the ERB through the Operational Centre's Medical Director or the Director General of Epicentre (in case the research is carried out by Epicentre without MSF). The Medical Director or the Director General will be the contact person of the ERB regarding said request for approval of amendment.

V. Documents required at the time of submission

Submissions should include the following:

A. Duly accomplished MSF ERB Application for Amendment Template[1]

B. The amended protocol, in "*tracked changes*" (the proposed changes highlighted or in another font color, and showing the deletions) and labeled with its version number, date, and the assigned MSF ERB ID number.

C. Disclosure of previous reviews by other ethics or scientific boards or committees or independent peer reviewers and copies of the approvals or conclusions and/or recommendations.[2]

D. Documents related to but not incorporated in the amended protocol that would be changed by the amendment or are introduced with the amendment (such as amended or new patent information sheets; amended or new consent or assent forms; amended or new study SOPs, MTA etc).

E. Any other documents as required by the ERB.

VI. Submitting the request for amendment and the amended protocol

The accomplished MSF ERB Application for Amendment Template, the amended protocol and other documents must be submitted electronically by the Medical Director/Director General to the MSF ERB Secretariat at msferb-secretariat@msf.org. The Medical Director/Director General should mention the MSFERB ID number of the ERB-approved protocol in the communication. The Secretariat, through the ERB Executive Officer, will acknowledge the Medical Director/Director General of the documents received. The ERB will not review incomplete submissions. The review will only commence once all required documents are received.

The Executive Officer shall record details of the request in the ERB database and upload the MSF ERB Application for Amendment Template, the amended protocol and any other accompanying documents to the MSF ERB online repository.

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[1] Available from http://fieldresearch.msf.org/msf/handle/10144/618702

[2] This includes any reviews or advice provided by individual MSF ERB member(s) consulted independently. Approvals from other Ethics Committees may be submitted on a later date / once available.

VII. Ethics review

The Executive Officer will conduct the initial ethics review to determine whether the change(s) to the research are minor or major and whether a further review is warranted. These decisions are made with the Chair or the Vice-Chair. Should a further review be necessary, the amended protocol will be reviewed by the same ERB members who reviewed the original protocol (if available).

The ERB's evaluation of amendments to ERB-approved protocols shall be guided by the MSF ERB Ethics Framework for Review and various international reference documents for ethics review, as mentioned in the MSF ERB Terms of Reference.

The Executive Officer will compile individual reviews. The Chair or Vice-Chair shall facilitate discussion between the different ERB members in case of divergent reviews. A consolidated ethics review will be prepared by the Executive Officer, and will be revised as needed and validated by the Chair and/or Vice-Chair. The time frame for review will depend on the quantity and extent of modifications in the amended protocol and if further review was conducted or not, and may range from one to three weeks.

The ERB review of the amended protocol, which may include clarification questions and suggestions and requirements for improving the ethical aspects of the amended protocol, will be sent by the Chair or Vice-Chair to the Medical Director of the MSF OC concerned or to the Director General of Epicentre. All ERB members who participated in the review will receive a copy.

The Medical Director/Director General shall submit the investigators' replies and revisions made to the amended protocol (in tracked changes) to the Chair through the ERB Secretariat.

Although uncommon, several cycles of ERB comments and MSF replies and revisions to the amended protocol may be needed before a decision is reached by the Board.

VIII. Decisions of the ERB

Decisions of the ERB are made by consensus.
The review of amendments to an ERB-approved protocol will result in one of the following actions:

A. ***Approved***: The submitted version of the amended protocol is approved.

B. ***Conditionally approved***: The amended protocol has not yet been approved; it requires the completion of one or more requirements before approval can be granted. When the requirements are met, a letter of approval will be issued.

C. ***Not approved***: The amended protocol is not approved because the changes introduced are not ethically sound.

The ERB has an advisory role; it has no enforcement powers with regards to any decisions in implementing the amendments made to the research. It is the responsibility of the Medical Director of the MSF operational centre concerned or the Director General of Epicentre to decide about this. The ERB should be informed if MSF or Epicentre acts contrary to its advice. The ERB cannot be held accountable for any amendments implemented against or without its advice.

The Board will not retrospectively review any amendments to previously approved research protocols that has been started or that has taken place without prior ERB approval.

IX. Interfaces

A. MSF ERB Application for Amendment Template, version 1 October 2016 and further updates

B. MSF ERB Amendment Approval Form

X. Revision history

SOP NUMBER	TITLE	REVISION VERSION	DATE
2	Review process for amendments to previously approved protocols	1	November 2016

XI. Approved:

Doris Schopper, Chair Person

Date: November 2016