STANDARD OPERATING PROCEDURES
MSF ETHICS REVIEW BOARD

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1. BACKGROUND

Médecins Sans Frontières (MSF) aims at providing medical care to victims of natural and man made disaster. However, what counts as the best intervention is not always established or clear. As a result MSF is committed to trying new approaches, learning from experiences and pro-actively researching new intervention strategies. While doing so it is imperative that MSF's research activities follow relevant ethical principles drawn from medical, public health, humanitarian and research ethics. This aim is particularly important given MSF's role as both a provider of medical humanitarian assistance and a promoter of research in this area.

Although MSF often works in close collaboration with scientific institutes that have their own ethical review mechanisms, MSF as an organisation has the obligation to endorse with confidence any research proposed to take place under its responsibility. It is for this reason that it was decided in 1999 to organise an ethics review board (ERB) specifically for MSF.

Epicentre is an association affiliated to Médecins Sans Frontières that seeks to improve the quality of medical field interventions through research activities. While Epicentre carries out research on behalf of MSF, it may also act as sponsor of research projects implemented independently from MSF. In some instances, Epicentre may thus directly request advice from the MSF ERB. Unless otherwise stated, MSF research refers to research carried out by MSF and/or Epicentre.

2. OBJECTIVE

To ensure that research carried out by or with MSF is ethically sound, thus safeguarding the dignity, rights, safety and well-being of all actual or potential research participants and of their communities.

This is achieved through the review of proposals of research to be carried out by or in cooperation with an MSF mission or team by an independent and competent ethics review board. In addition, the ERB has a role in sensitizing and educating MSF researchers in research ethics.

3. COMPOSITION OF THE ETHICS REVIEW BOARD

3.1. The ERB consists of a fixed chair and at least 5 regular members. Regular members shall fulfil the following conditions[1]:

- The members must have the professional competence to review the research;
- The majority of members should be health professionals or health researchers, at least one of these having ethical expertise;
- The board may not consist of members from only one profession;
- At least one member should have a professional legal background;
- At least one member should be expert in the discipline of ethics;
- At least one member should be a social scientist;
- The board must consist of both men and women;

[1] Some members may satisfy more than one criterion, for example a female lawyer with knowledge of ethics may meet three requirements for a board composed otherwise of four male scientists.

- Since MSF research often involves vulnerable populations, one or more member(s) must be knowledgeable and experienced in working with such populations.

3.2. The chair of the ERB is appointed by the MSF medical directors. The duration of appointment is six years, renewable. New regular members of the ERB are appointed by consensus by current ERB members. The duration of the appointment of regular members is three years, renewable by consensus. Concerning research proposals requiring specific expertise not available from its regular members, the ERB chair can appoint one or two ad hoc members for the duration of the review. If an expert is hired to review proposals, his/her CV should be provided to the medical directors.

3.3. To avoid conflict of interest and to promote independence, members should not have a working or governance (associative) relationship with MSF or Epicentre during the time of their appointment. This implies that:

- ERB members should not be employed by MSF or Epicentre during the time of their appointment;
- They cannot be members of the board of an operational centre or Epicentre or of any other MSF or Epicentre entity (partner section, branch office, delegate office, etc.) during the time of their appointment;
- If an ERB member has an interest in a research proposal or a matter under consideration by ERB, he or she must disclose all information regarding his or her interest (notably any personal interest or affiliation with a co-investing institution should be disclosed, e.g. employment or consulting arrangements, memberships on boards, other research relationships etc.) and shall abstain from that particular review.

4. Working procedures

4.1. The standards of the MSF ERB will be consistent with, and build upon, established international standards for the ethical conduct of research (Annex 1). The review of research proposals will address the main issues as outlined in the framework appended (Annex 2).

4.2. The language of communication within the ERB and between the ERB and MSF will be English.

4.3. MSF line managers and medical advisors are responsible for the timely submission of research proposals to the chair of the ERB through the medical director of their own operational centre.

4.4. In exceptional cases, where Epicentre is planning research with no direct MSF involvement, Epicentre can directly submit research protocols to the ERB. In this case, research proposals will be submitted to the chair of the ERB through the Director General of Epicentre.

4.5. At submission the proposal should be accompanied by a duly completed MSF ERB Ethics Review Research Template and the advice(s) of the competent ethics committee(s) of each country where the research takes place or where the data used originates from. If the latter is not yet available, the ERB should be

guaranteed that a review by locally constituted ethics committees and, if applicable, by regulatory authorities in each of the countries where the research will take place or where the data used originates from, is being sought. A copy of the approvals by local ethics committees and, if applicable, regulatory authorities must be provided in due time.

4.6. The chair will send the proposal and all supportive documents to the members of the ERB through e-mail and ask for their comments within four weeks. The chair will compile individual comments and facilitate discussion between the different ERB members in case of disagreement. A consolidated ethical review will be prepared by the chair usually within six weeks of initial reception of the research proposal.

4.7. The decision of the ERB, including suggestions for improving the ethical aspects of the proposal and basic pre-conditions that must be met will usually be sent within six weeks of initial reception of the proposal to the medical director (head of medical/public health department) of the MSF operational centre concerned. All ERB members having participated in the review will receive a copy.

4.8. Several cycles of ERB comments and MSF replies may be needed before the ERB can reach a final decision of approval or rejection. Clearly stated reasons for approval, conditional approval or rejection will be sent to the medical director (head of medical/public health department) of the MSF operational centre concerned.

4.9. The ERB has an advisory role, but no decision making power. It is the responsibility of the Medical Director of the MSF operational centre concerned or the Director General of Epicentre (in case the research is carried out by Epicentre without MSF) to decide about the implementation of the research. The ERB would like to be informed if MSF or Epicentre acts contrary to its advice. The ERB cannot be held accountable for any research carried out against (or without) its advice.

4.10. A copy of the MSF ethical review and final decision should be sent to the local ethics committee that reviewed the proposal. Review and comments from national/local ethics committee, in addition to the final decision, should be shared with the MSF ERB.

4.11. If any significant changes occur to the initial protocol reviewed by the ERB, the ERB should be informed and asked for approval. If relevant, a second review may be initiated by the ERB chair.

4.12. Anything that may occur during the research that may affect ethical acceptability of the project, including adverse effects on participants or unforeseen events, must be reported immediately to the ERB.

4.13. ERB approval of any study is only given for a 12 month period. If the study is not initiated within 12 months after approval, the approval of the protocol is no longer valid. Where any study is not completed during one year, a request for extension must be submitted to the ERB in order to protect the subjects that are

involved in the study (Form "Request for extension of erb approval"). A study is completed when there is no more contact with patients and when data are collected, cleaned and analysed. For low risk studies, the ERB can consider extending the initial approval to 18 months instead of 12 months.

4.14. The ERB expects MSF to send all reports, publications etc. to document dissemination of the results as well as to be informed of the study impact.

4.15. Medical Directors and the Director General of Epicentre are responsible for reporting on progress of research approved by the ERB on an annual basis.

5. REVIEW CATEGORIES

The ERB recognizes different types of ethical review requirements.

5.1. Full review, requiring participation of all ERB members, is warranted if the effectiveness, efficacy or safety of a given procedure or therapy is tested on human subjects and/or if the research involves collecting body/tissue samples with hypothesis testing (e.g. all clinical trials and some operational research projects).

5.2. Expedited review, requiring participation of two or three ERB members, is deemed sufficient if the research carries only minimal risks to human subjects. This includes descriptive studies involving monitoring and evaluation as a means to test a new approach, social science research in health and health systems, prevalence and incidence studies, other surveys.

5.3. In case of emergency research (research that is more than minimal risk in nature but which is urgent and time-sensitive), the ERB is willing to pre-approve generic proposals. The details will then be filled in for rapid expedited review (chair plus 2 reviewers, with a turn-around time of 48 hours) when operationalizing the protocol in a specific setting.

5.4. A posteriori analyses of routinely collected clinical data do not require ERB review, if the medical directors take responsibility for addressing the ethics issues. The following criteria must be fulfilled to qualify for exemption from ERB review:

- Studies/articles are based on routinely-collected program data.
- They are either descriptive/evaluative or targeted evaluations.
- Confidentiality is respected; no individual patient identifiers are revealed.
- Harm is minimal but acknowledged where relevant.
- Potential benefits to both the programme and the community are described. Since the goal is publication, the relevance to a wider audience is described.
- Collaborative involvement and, if applicable, authorship from a local authority or partner (Ministry of Health, DHO, other NGO) is encouraged. If relevant and possible, consultation with a body representing the community is desirable.
- If the decision for exemption from review is taken by the medical directors, the responsibility to ensure that ethical requirements are met lies with MSF.

This, however, does not exempt MSF to comply with regulatory requirements in the country from where the data originate. In some countries, local ethical review may still be required.

5.5. Review exemption applies to routine programme implementation and assessment related work. Monitoring and evaluation as part of normal implementation of projects does not need ethical review.

Any MSF research not exempt from review should be submitted to the ERB.

The ERB will not retrospectively review any research that has been started or taken place without ERB submission/approval.

6. DOCUMENTATION AND ARCHIVING

All documentation and communication of the ERB will be filed and archived by the chair. All ERB members should have access to these archives[2].

Documents to be filed include:

- Curriculum vitae of all ERB members
- Identity and Curriculum vitae of ad hoc experts appointed;
- Standard operating procedures of the ERB
- Framework for ethical review
- One copy of all research proposals submitted
- Deliberations of the ERB
- A copy of the decisions, advice and requirements sent to applicants and their reply
- One copy of the final, approved research proposal and related documentation (incl. local ethics and other regulatory approvals)
- All written documentation received during follow-up (e.g. resubmission, amendments, extension request, premature suspension, protocol violations or termination of study)
- Final (summary) report of study and/or publication(s)

7. REIMBURSEMENT OF COSTS

All direct costs related to the review will be charged to the operational centre (or Epicentre) that sends in the proposal (these include postage, telephone and other direct costs). Most communication is done through e-mail with no additional costs attached. Travel expenses of ERB members will be covered by MSF. The chair person will be offered a stipend per review coordinated. Time investment of individual ERB members is considered to be on a voluntary basis and will not be reimbursed.

[2] The International Office will provide such a common/accessible archiving space as decided at the 6th ERB meeting in Amsterdam, March 2012.

Annex 1. International reference documents for Ethical Review

The Nuremberg Code
[http://ohsr.od.nih.gov/guidelines/nuremberg.html]

World Medical Association Declaration of Helsinki. Ethical Principles for Medical Research Involving Human Subjects. Revised version October 2013
[http://www.wma.net/en/30publications/10policies/b3/]

The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research
The (US) National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, National Institutes of Health 1979
[http://ohsr.od.nih.gov/guidelines/belmont.html]

International Ethical Guidelines for Epidemiological Studies,
Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO), CIOMS Geneva 2009.
[http://www.ufrgs.br/bioetica/cioms2008.pdf]

International Ethical Guidelines for Biomedical Research Involving Human Subjects
Prepared by the Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO), CIOMS Geneva 2002. [http://www.fhi.org/training/fr/retc/pdf_files/cioms.pdf]

Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants. World Health Organization 2011
[http://www.who.int/ethics/publications/research_standards_9789241502948/en/index.html]

Annex 2. MSF ERB Ethics Framework for review

(version 1, November 2013)

The framework is based on accepted ethical principles for research involving humans and builds upon the most influential international guidelines. It attempts to capture the diversity of research carried out by MSF.

The framework consists of twelve questions, structured into three broad sections following a temporal logic. Section 1 addresses issues to be considered in defining the research and developing the methodology. Section 2 asks questions related to the implementation phase of the research. Finally, section 3 is concerned with what will occur once research has been completed or stopped.

Section 1. Research Question and Methodology (5 main questions)
Section 2. Respecting and Protecting Research Participants and Communities (4 main questions)
Section 3. Implications and Implementation of the Research Findings (3 main questions)

The format of using questions is adopted as a way to help MSF researchers and ERB members in their deliberations about ethical issues. Each main question is followed by a short explanatory statement and a further series of sub-questions. The latter sub-questions are for illustration only and are not supposed to be an exhaustive list of relevant considerations. Which of these questions are most relevant will depend upon the detail of the proposed protocol's research question and methods. All relevant questions should be considered and used to shape the answers to the questions when filling out the ethics review research template.

1. Research Question and Methodology

(1.1) What is the research question? Why is it important?

The research question should be the central element in any protocol. Where there is more than one question they should be presented in a logical order.

a. Why is the research question(s) scientifically important? What knowledge gap will it fill?

b. Why is the research question(s) important to the community affected?

c. If other alternative research questions are possible, why was the particular question selected?

d. What potential harms might arise if the research is not conducted?

(1.2) How is the methodology and proposed analysis appropriate given the research question(s)?

It is important that the proposed method and analysis will not only allow the researchers to answer the question that they have set, but that it is the best way to do so.

a. How will the research design and analysis provide the best means of answering the proposed question (e.g. sample size and method, selection of study population etc.)?

b. What scientific/methodology review has been obtained prior to submission for ethical review?

c. How have ethical considerations shaped the proposed methodology? For example, what justification exists for any standard of care in the proposed research?

(1.3) What is the context in which the research will be conducted? How has this influenced the research design? The protocol must include details about existing and planned community engagement and collaborative partnerships and how they have influenced or shaped the proposed research[3].

a. How have the community's views about their needs and research priorities been taken into account? What is the researchers' strategy to engage the community as part of the research process?

b. What collaborative research partnerships or agreements exist in relation to this project? What engagement has occurred with local or national health authorities?

c. To what extent can partnerships be structured in a fair and equitable manner?

[3] The **concept of 'community'** can be used in a number of different ways. Most commonly, it is used in a descriptive sense to pick out a particular geographic, linguistic, functional or socio-cultural entity with characteristics such as shared interests and experiences, values, common fate or cultural affinity. Sometimes a community will have a pre-existing structure, such as a village committee, that may be used as a means of engagement. However, care needs to be taken to avoid assuming that such structures represent all relevant interests in the community; otherwise there is a danger of reflecting prior repressive or coercive structures, potentially interfering with the voluntariness of decisions about participation. In some conflict-ridden environments where MSF works, the social structure has been damaged or destroyed. In such contexts it is especially important to consider carefully who would best represent the interests of the relevant population.

d. How will the researchers enhance local research capacity with this project?
e. Has research ethics review been obtained by all appropriate ethics review boards at the local/regional/national level?

(1.4) Are there any other parties involved in the research? What potential interests of these parties might conflict with MSF's mission and values?

a. Who may benefit directly and indirectly from the research?
b. Where other parties (e.g. companies) benefit from the research, how will the interests of participants, community and MSF be protected?
c. What are the potential benefits relating to spin-off interests or intellectual property etc.? How will they be apportioned?

(1.5) Are all relevant resources for the research secured?

a. What is the budget for the research? Is it secured?
b. What additional infrastructure is required? Is it secured?
c. What possible changes might occur in the field? What plans are in place to respond to such alterations?
d. Is there an operational commitment for the expected time of the study?

(1.6) Have the research staff the relevant training and protections?

a. Have the research staff the required expertise to carry out the research?
b. What training has been conducted with the research staff, or how will this be provided?
c. What risks of harm might researchers be exposed to? How can this be minimised?
d. Have any of the research staff double allegiances (being both carer and researcher)? How will potential conflicts of interest be avoided?

2. Respecting and Protecting Research Participants and Communities

(2.1) What are the anticipated harms and benefits?

Considering all relevant harms and benefits is an essential part of assessing whether a proposed piece of research is ethical. As MSF works mostly with populations at risk, there are multiple opportunities for considerable harm.

a. Given the best available evidence and any relevant experience what are the anticipated harms and benefits of the research? How likely and how significant are any harms and benefits to research participants?
b. What are the potential wider social harms and benefits to communities?
c. What protections will be put in place to avoid or mitigate anticipated harms?
d. Benefits and burdens of research may be unequally distributed between sub-groups. How are harms and benefits distributed between participants and communities? Have researchers ensured that any proposed inclusion/exclusion criteria are fair?
e. What is the process to monitor unknown harms/new information arising in the study? Will a data and safety monitoring committee be needed?

(2.2) What are your plans for obtaining consent?

A requirement to inform participants is often seen as being an important way to show respect and promote patient autonomy and welfare.

a. What information ought to be provided? This will usually include the following elements: the reasons for doing research, details about who is doing the research, why the potential participant is being asked to be involved, details about what any intervention might involve and any on-going commitments of participation, details about anticipated risks and benefits, the fact that participants are free to refuse or withdraw, that any findings will be communicated back to the participants etc. The information given should be proportionate to any risks, but this does not mean that the higher the risk, the more information ought to be provided. Sometimes, calling attention clearly to a common or significant particular risk is more important than listing every possible remote risk.
b. Providing information does not guarantee it has been understood. How can information be provided at an appropriate linguistic level, without jargon or technical terms, and appropriate to the local language and culture?
c. Should information be provided in oral and/or written form?
d. How will the consent process be conducted? You may want to consider issues such as: who will consent, where they will do so (is the place appropriate to allow a confidential discussion), will a witness to the consent be required, how much time will be offered to consider whether to be involved? Prior engagement with communities can be a useful way to ensure that the consent process meets local expectations and sensitivities. How will the act of consent be recorded (e.g. signed and witnessed document, thumb print etc.)?

e. Alternative or additional consent procedures may need to be developed where potential participants are minors, minor parents, or suffering from short or long-term incapacities etc.

f. It should not be assumed that a long and complicated information sheet is always necessary and in exceptional cases it may be justifiable not to seek informed consent. Where researchers believe that this is appropriate, they should be careful to provide reasons for this in the protocol.

(2.3) How do you plan to protect confidentiality?

Data will include all information (medical and non-medical) about or derived from participants.

a. What data security policies are in place?

b. Where will data be gathered and stored? Who will have access to it? Where will it go?

c. Will it be anonymised or coded? Will it be linked, or could it be linked, to other data sets? If so, are adequate protections in place?

d. Will data be placed in the public domain (in line with the MSF data sharing policy)? How will confidentiality be protected?

(2.4) How do you plan to access, store and distribute any collected biological material?

a. Will biological material be collected, retained, stored, exported or destroyed? If so, how will this be done? If collected for one purpose, could it be used for other purposes?

b. Is the relevant consent obtained?

c. Where transfer of material is planned what national or international regulations are relevant? Have the necessary authorisations been sought? Is there a material transfer agreement in place? If so, what does this say?

3. Implications and Implementation of the Research Findings

(3.1) What will happen when the research is either stopped or is complete?

Good planning for a project will consider how it will end.

a. Under what conditions would you consider stopping the project earlier than planned?
b. What will happen to investments in infrastructure, human and other resources, when the research is complete or ends early?

(3.2) How will the findings be disseminated?

a. How will the results be disseminated? Through publication? Where? Will they be available through open access or on the MSF web site?
b. How will MSF communicate the results of the research directly to the community/participants involved?
c. What is the plan for dissemination if the research findings are negative?

(3.3) How will the findings be implemented?

It will not be possible, before results are known, to establish all the details about implementation. However, it is often possible to think about such issues in advance.

a. What is MSF's obligation to the research participants?
b. What is MSF's obligation to others in the immediate programme or community where the research occurred?
c. What is MSF's obligation to others in the same situation elsewhere?
d. How will MSF fulfil any post-research obligations entailed by the results of the research?
e. Is there an (advocacy) plan in place to assure access to benefits of the study results if applicable? This is particularly important where individuals and communities are unable to access an intervention for some reasons (e.g. it is too expensive).