**Clinical Study Protocol**

**Title**

**Protocol No:**

**Brief Title**

**Other Number(s)**

**Protocol Version – Date**

**Sponsor** Medical Research Council Unit, The Gambia
Atlantic Road, Fajara

PO Box 273 Banjul,
The Gambia, West Africa

**Principal Investigator**

Protocol amendment(s)

Amendment #:

|  |  |  |
| --- | --- | --- |
| **Principal Investigator:**  Name, Title  | **Signature:**  | **Date:**  |

|  |  |  |
| --- | --- | --- |
| **Sponsor’s representative:**  Name, Title  | **Signature:**  | **Date:**  |

Signature page

The study will be carried out in accordance with the protocol, the principles of good clinical practice as laid down in the ICH Harmonised Tripartite Guideline for Good Clinical Practice, the MRC Guidelines for Good Clinical Practice in Clinical Trials, <<*insert other regulations if applicable>>*, and in accordance to local legal and regulatory requirements.

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| --- | --- | --- |
| **Principal Investigator:**  *Name, Title*  | **Signature:**  | **Date:**  |

|  |  |  |
| --- | --- | --- |
| **Sponsor’s representative:**  *Name, Title*  | **Signature:**  | **Date:**  |

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Key roles

For questions regarding this protocol, contact <<*insert name of appropriate MRC staff>>* at MRC << *insert address, email, phone(s), fax, >>*.

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| --- | --- |
| **Author:**  |  |
| **Sponsor’s representative:**  |  |
| **Principal Investigator(s):**  |  |
| **Investigator(s):**  |  |
| **Trial Physician:**  |  |
| **Sponsor’s Medical Expert:**  |  |
| **Trial monitor(s):**  |  |
| **Local Safety Monitor:** |  |
| **Chair of DMC/DMSB:**  |  |
| **Statistician:**  |  |
| **Data Manager:**  |  |

|  |  |
| --- | --- |
| **External Adviser:**  |  |
| **Clinical Laboratory/ies:**  |  |
| **Other institutions:**  |  |
| **Ethics Committee** | Gambia Government/MRC Joint Ethics Committee, c/o MRC Unit, The Gambia, PO Box 273, Banjul, The Gambia, West Africa  |

List of abbreviations

|  |  |
| --- | --- |
| AE | Adverse Event/Adverse Experience |
| AR | Adverse Reaction |
| CIOMS | Council for International Organizations of Medical Sciences |
| CRF | Case Report Form |
| DMC | Data Monitoring Committee  |
| GCP | Good Clinical Practice |
| IB | Investigator’s Brochure |
| ICF | Informed Consent Form |
| ICH | International Conference on Harmonization |
| IEC | Independent or Institutional Ethics Committee |
| IMP | Investigational Medicinal Product |
| INN | International Nonproprietary Name |
| MRC | Medical Research Council; represents Medical Research Council Laboratories (UK) Unit in The Gambia |
| PI | Principal Investigator |
| SAE | Serious Adverse Event |
| SAR | Serious Adverse Reaction |
| SCC | Scientific Coordinating Committee |
| SIS | Subject Information Sheet |
| SmPC | Summary of Product Characteristics |
| SOP | Standard Operating Procedure |
| TMF | Trial (site) Master File (Regulatory File) |
| TSC | Trial Steering Committee |
| WHO | World Health Organization |

Protocol summary

|  |  |
| --- | --- |
| **Title:** |  |
| **Brief title** |  |
| **Phase** (if applicable) |  |
| **Population:** |  |
| **Number of Sites:** |  |
| **Study Duration:****- Clinical Phase****- Whole study** |  |
| **Subject Participation Duration:** |  |
| **Description of Products or Intervention:** |  |
| **Objectives:**  |  |
| **Description of Study Design:** |  |

# Background information and rationale

## Background information

References of literature and data are listed in Section 14.

## Rationale

## Potential risks and benefits

The potential risks to human subjects and known benefits, if any, are summarised in Section “Human Subject Protection”.

# Study objectives

## Study endpoints

# Study design

## Type of study and design

## Randomisation and blinding procedures

### Randomisation

### Blinding

## Sub-studies

## Investigational products or interventions

### Description of product or intervention

### Formulation, packaging and labelling

### Product storage and stability

## Dosage, preparation and administration of investigational productor intervention

## Concomitant medications/treatments

# Selection and withdrawal of participants

## Selection of participants

## Eligibility of participants

Participants must meet all of the inclusion criteria and none of the exclusion criteria to be eligible to participate in the trial.

### Inclusion criteria

### Exclusion criteria

## Withdrawal of participants

A study participant will be discontinued from participation in the study if:

* Any clinical significant adverse event (AE), laboratory abnormality, intercurrent illness, or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the subject.
* Development of any exclusion criteria.

For further details on participant’s premature termination see corresponding section below.

Participants are free to withdraw from the study at any time without giving a reason.

# Study procedures and evaluations

For an overview see annex “Schedule of Events”.

## Study schedule

### Screening

### Enrollment (Baseline)

### Follow-up

### Final study visit

### Early termination visit

## Study evaluations

### Clinical evaluations

### Laboratory evaluations

# Safety considerations

## Methods and timing for assessing, recording, and analysingsafety parameters

### Adverse events

### Reactogenicity

### Serious adverse events (SAEs)

## Reporting procedures

## Safety oversight

# Discontinuation criteria

## Participant’s premature termination

## Study discontinuation

# Statistical considerations

# Data handling and record keeping

## Data management and processing

## Source documents and access to source data

The Principal Investigators will maintain appropriate medical and research records for this study in compliance with the principles of good clinical practice and regulatory and institutional requirements for the protection of confidentiality of participants. The study team members will have access to records.

The authorised representatives of the sponsor, the ethics committee(s) or regulatory bodies may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) for the subjects in this study. The clinical study site will permit access to such records.

## Protocol deviations

A protocol deviation (PD) is any noncompliance with the clinical trial protocol, good clinical practice (GCP), or other protocol-specific requirements. The noncompliance may be either on the part of the participant or the investigator including the study team members, and may result in significant added risk to the study participant. As a result of a deviation, corrective actions will be developed and implemented promptly.

If a deviation from, or a change of, the protocol is implemented to eliminate an immediate hazard(s) to trial participant without prior ethics approval, the PI or designee will submit the implemented deviation or change, the reasons for it, and, if appropriate, the proposed protocol amendment(s) as soon as possible to the relevant ethics committee(s) for review and approval and to the sponsor for agreement.

The PI or designee will document and explain any deviation from the approved protocol on the CRF, where appropriate, and record and explain any deviation in a file note or deviation form that will be maintained as an essential document. Deviations from the protocol, GCP or trial specific requirements that might have an impact on the conduct of the trial or the safety of participants will be reported within 5 working days to the sponsor and relevant EC, as appropriate.

# Quality control and quality assurance

## Study monitoring

# Ethical considerations

This study is conducted in accordance with the principles set forth in the ICH Harmonised Tripartite Guideline for Good Clinical Practice and the Declaration of Helsinki in its current version (see appendix), whichever affords the greater protection to the participants.

## General considerations on human subject protection

### Rationale for participant selection

### Evaluation of risks and benefits

## Informed consent

## Participant confidentiality

## Future use of stored specimen

# Financing and insurance

# Publication policy

# References

Supplements, appendices and other documents

**\*Schematic of Study Design**:

Appendix: Schedule of events

**Appendix:**

**World Medical Association Declaration of Helsinki**

**Ethical Principles for Medical Research Involving Human Subjects**

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964 and amended by the:29th WMA General Assembly, Tokyo, Japan, October 197535th WMA General Assembly, Venice, Italy, October 198341st WMA General Assembly, Hong Kong, September 198948th WMA General Assembly, Somerset West, South Africa, October 199652nd WMA General Assembly, Edinburgh, Scotland, October 2000 53rd WMA General Assembly, Washington, DC, USA, October 2002(Note of Clarification on paragraph 29 added)55th WMA General Assembly, Tokyo, Japan, October 2004(Note of Clarification on Paragraph 30 added)59th WMA General Assembly, Seoul, Korea, October 2008

**A. INTRODUCTION**

1. The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects**,** includingresearch on identifiable human material and data. The Declaration is intended to be read as a whole and each of its constituent paragraphs should not be applied without consideration of all other relevant paragraphs.

2. Although the Declaration is addressed primarily to physicians, the WMA encourages other participants in medical research involving human subjects to adopt these principles.

3. It is the duty of the physician to promote and safeguard the health of patients, including those who are involved in medical research. The physician's knowledge and conscience are dedicated to the fulfilment of this duty.

4. The Declaration of Geneva of the WMA binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act in the patient's best interest when providing medical care."

5. Medical progress is based on research that ultimately must include studies involving human subjects. Populations that are underrepresented in medical research should be provided appropriate access to participation in research.

6. In medical research involving human subjects, the well-being of the individual research subject must take precedence over all other interests.

7. The primary purpose of medical research involving human subjects is to understand the causes, development and effects of diseases and improve preventive, diagnostic and therapeutic interventions (methods, procedures and treatments). Even the best current interventions must be evaluated continually through research for their safety, effectiveness, efficiency, accessibility and quality.

8. In medical practice and in medical research, most interventions involve risks and burdens.

9. Medical research is subject to ethical standards that promote respect for all human subjects and protect their health and rights. Some research populations are particularly vulnerable and need special protection. These include those who cannot give or refuse consent for themselves and those who may be vulnerable to coercion or undue influence.

10. Physicians should consider the ethical, legal and regulatory norms and standards for research involving human subjects in their own countries as well as applicable international norms and standards. No national or international ethical, legal or regulatory requirement should reduce or eliminate any of the protections for research subjects set forth in this Declaration.

**B. PRINCIPLES FOR ALL MEDICAL RESEARCH**

11. It is the duty of physicians who participate in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects.

12. Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and adequate laboratory and, as appropriate, animal experimentation. The welfare of animals used for research must be respected.

13. Appropriate caution must be exercised in the conduct of medical research that may harm the environment.

14. The design and performance of each research study involving human subjects must be clearly described in a research protocol. The protocol should contain a statement of the ethical considerations involved and should indicate how the principles in this Declaration have been addressed. The protocol should include information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest, incentives for subjects and provisions for treating and/or compensating subjects who are harmed as a consequence of participation in the research study. The protocol should describe arrangements for post-study access by study subjects to interventions identified as beneficial in the study or access to other appropriate care or benefits.

15. The research protocol must be submitted for consideration, comment, guidance and approval to a research ethics committee before the study begins. This committee must be independent of the researcher, the sponsor and any other undue influence. It must take into consideration the laws and regulations of the country or countries in which the research is to be performed as well as applicable international norms and standards but these must not be allowed to reduce or eliminate any of the protections for research subjects set forth in this Declaration. The committee must have the right to monitor ongoing studies. The researcher must provide monitoring information to the committee, especially information about any serious adverse events. No change to the protocol may be made without consideration and approval by the committee.

16. Medical research involving human subjects must be conducted only by individuals with the appropriate scientific training and qualifications. Research on patients or healthy volunteers requires the supervision of a competent and appropriately qualified physician or other health care professional. The responsibility for the protection of research subjects must always rest with the physician or other health care professional and never the research subjects, even though they have given consent.

17. Medical research involving a disadvantaged or vulnerable population or community is only justified if the research is responsive to the health needs and priorities of this population or community and if there is a reasonable likelihood that this population or community stands to benefit from the results of the research.

18. Every medical research study involving human subjects must be preceded by careful assessment of predictable risks and burdens to the individuals and communities involved in the research in comparison with foreseeable benefits to them and to other individuals or communities affected by the condition under investigation.

19. Every clinical trial must be registered in a publicly accessible database before recruitment of the first subject.

20. Physicians may not participate in a research study involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians must immediately stop a study when the risks are found to outweigh the potential benefits or when there is conclusive proof of positive and beneficial results.

21. Medical research involving human subjects may only be conducted if the importance of the objective outweighs the inherent risks and burdens to the research subjects.

22. Participation by competent individuals as subjects in medical research must be voluntary. Although it may be appropriate to consult family members or community leaders, no competent individual may be enrolled in a research study unless he or she freely agrees.

23. Every precaution must be taken to protect the privacy of research subjects and the confidentiality of their personal information and to minimize the impact of the study on their physical, mental and social integrity.

24. In medical research involving competent human subjects, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, and any other relevant aspects of the study. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal. Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information. After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely-given informed consent, preferably in writing. If the consent cannot be expressed in writing, the non-written consent must be formally documented and witnessed.

25. For medical research using identifiable human material or data, physicians must normally seek consent for the collection, analysis, storage and/or reuse. There may be situations where consent would be impossible or impractical to obtain for such research or would pose a threat to the validity of the research. In such situations the research may be done only after consideration and approval of a research ethics committee.

26. When seeking informed consent for participation in a research study the physician should be particularly cautious if the potential subject is in a dependent relationship with the physician or may consent under duress. In such situations the informed consent should be sought by an appropriately qualified individual who is completely independent of this relationship.

27. For a potential research subject who is incompetent, the physician must seek informed consent from the legally authorized representative. These individuals must not be included in a research study that has no likelihood of benefit for them unless it is intended to promote the health of the population represented by the potential subject, the research cannot instead be performed with competent persons, and the research entails only minimal risk and minimal burden.

28. When a potential research subject who is deemed incompetent is able to give assent to decisions about participation in research, the physician must seek that assent in addition to the consent of the legally authorized representative. The potential subject's dissent should be respected.

29. Research involving subjects who are physically or mentally incapable of giving consent, for example, unconscious patients, may be done only if the physical or mental condition that prevents giving informed consent is a necessary characteristic of the research population. In such circumstances the physician should seek informed consent from the legally authorized representative. If no such representative is available and if the research cannot be delayed, the study may proceed without informed consent provided that the specific reasons for involving subjects with a condition that renders them unable to give informed consent have been stated in the research protocol and the study has been approved by a research ethics committee. Consent to remain in the research should be obtained as soon as possible from the subject or a legally authorized representative.

30. Authors, editors and publishers all have ethical obligations with regard to the publication of the results of research. Authors have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports. They should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results should be published or otherwise made publicly available. Sources of funding, institutional affiliations and conflicts of interest should be declared in the publication. Reports of research not in accordance with the principles of this Declaration should not be accepted for publication.

**C. ADDITIONAL PRINCIPLES FOR MEDICAL RESEARCH COMBINED WITH MEDICAL CARE**

31. The physician may combine medical research with medical care only to the extent that the research is justified by its potential preventive, diagnostic or therapeutic value and if the physician has good reason to believe that participation in the research study will not adversely affect the health of the patients who serve as research subjects.

32. The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best current proven intervention, except in the following circumstances:

* The use of placebo, or no treatment, is acceptable in studies where no current proven intervention exists; or
* Where for compelling and scientifically sound methodological reasons the use of placebo is necessary to determine the efficacy or safety of an intervention and the patients who receive placebo or no treatment will not be subject to any risk of serious or irreversible harm. Extreme care must be taken to avoid abuse of this option.

33. At the conclusion of the study, patients entered into the study are entitled to be informed about the outcome of the study and to share any benefits that result from it, for example, access to interventions identified as beneficial in the study or to other appropriate care or benefits.

34. The physician must fully inform the patient which aspects of the care are related to the research. The refusal of a patient to participate in a study or the patient's decision to withdraw from the study must never interfere with the patient-physician relationship.

35. In the treatment of a patient, where proven interventions do not exist or have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorized representative, may use an unproven intervention if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, this intervention should be made the object of research, designed to evaluate its safety and efficacy. In all cases, new information should be recorded and, where appropriate, made publicly available.