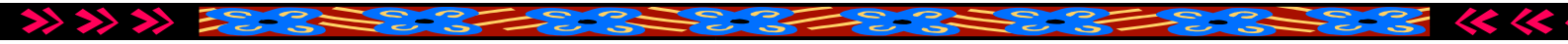


REPUBLIC OF NAMIBIA



MINISTRY OF HEALTH AND SOCIAL SERVICES

**GUIDELINES
ON
CLINICAL TRIALS IN HUMAN SUBJECTS**



MINISTRY OF HEALTH AND SOCIAL SERVICES

GUIDELINES

ON

CLINICAL TRIALS IN HUMAN SUBJECTS

DIRECTORATE: POLICY, PLANNING AND HRD
DIVISION: PLANNING
SUBDIVISION: MANAGEMENT INFORMATION AND RESEARCH

Private Bag 13198
Windhoek
Republic of Namibia

Tel: 203 25 38
Fax: 27 2286
E-mail: doccentre@mhss.gov.na

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Foreword

Since Independence, the Ministry of Health and Social Services (MoHSS) has been committed to and is actively involved in the implementation of the global Health for All strategy, and to rendering services in line with the tenets of this initiative. In the provision of these services, my Ministry aims to ensure that this commitment extends to and includes the need for ongoing scientific, medical research and development, while aware that the rights, interests and well-being of the patient or trial subject remain paramount.

The Ministry has recognised the importance of clinical trials for assessing the effects of particular intervention on defined outcome measures. However, in the past few years, an increase in the number of reports related to serious adverse drugs reaction amongst clinical trial participants has been reported worldwide. Therefore, as the co-ordinating body for health research, the Ministry need to be assured that those who conduct research/trials involving human participants adhere to guidelines to safeguard study participants and ensure that the data gathered are of high quality. These guidelines are closely related to the regulations of the Medicines Control Council of Namibia and are based on the International Conference on Harmonisation's Good Clinical Practice (ICH GCP) Guideline.

Given the significance of research and clinical trials and the potential for positive impact thereof, it is hoped that this guideline will be conducive to informing and improving health services. It is also intended to ensure that trials are conducted in accordance with good practice and those requirements, which safeguard the subjects and their best interest. Therefore, it is essential that researchers, trial participants, principal investigators of trials, trial sponsors, general public and all those who have an interest in clinical trial research use these guideline as a reference to ensure a standardised and ethical approach to clinical trial activities in the country.

It is envisaged that researchers and trial sponsors will take into consideration issues surrounding disadvantaged groups and communities such as women, children, HIV/AIDS patients and the poor when planning and executing trials to ensure that they safeguard their rights, safety and well-being. When establishing research agenda, it is also important to ensure that the focus of research funding is oriented towards the needs of the majority of the people in Namibia. This guideline provides the Ministry's first attempt at addressing issues related to clinical trial research in Namibia. I therefore believe that it will contribute significantly to ensuring good health and promoting the health of all Namibians

DR L AMATHILA
MINISTER

Preface

This guideline on clinical trials in human subjects was produced to provide persons controlling or performing clinical trials with a reference document to be utilised when planning, executing and reporting clinical trial research. The necessary structures and environment, within the Namibian legal and ethical framework, to promote and enable the trials necessary for valuable research that is also relevant to local realities and context are provided in this guideline. It introduces a re-structured notification procedure, which covers all sectors of clinical trial research. Another new feature is the parallel execution of ethical and scientific-technical review, according to set deadlines. The guideline is designed to be used in any prospective study involving human participants and administration of a treatment or type of management, including diagnosis or the provision of lifestyle advice.

The current Namibian legislation should be observed when conducting clinical trials on medicinal products in human subjects. In addition, the International Conference on Harmonisation (ICH) Guideline for Good Clinical Practice shall be followed (Topic E 6) and research projects shall conform to the current contents on the Declaration of Helsinki of the World Medical Association.

The guideline is divided into several parts; it covers different aspects of clinical trials on human subjects. The prerequisites of clinical trials, documents to be submitted, ethical aspect related to the trial and the right of the study subjects are all covered in this guideline. This guideline however, should be used in conjunction with the MoHSS Research Management Policy.

The process to this clinical trial guideline started in 1997, with the development of the draft research policy. The Ministry is grateful to all those who contributed to the preparation of this document, in particular, staff in the Directorate Policy, Planning and HRD, for initiating and co-ordinating the process of development until its final stage. The Medicine Control Council of Namibia, various departments, regions and districts in the Ministry are hereby acknowledged for their pivotal role in providing input into the finalisation of this important document. My gratitude goes to the Managing Director of PSR consultancy LTD, Finland, who edited the text and the Government of Finland supported Health and Social Sector Support Programme, Phase II for their financial contribution towards this whole process.

DR K. SHANGULA
PERMANENT SECRETARY

ABBREVIATIONS

BREC	Biomedical Research Ethics Committee
GCP	Good Clinical Practice
GMP	Good Manufacturing Practice
HRD	Human Resources Development
HSSSP II	Health and Social Sector Support Programme, Phase II
IB	Investigator's Brochure
ICH	International Conference on Harmonisation
IDMC	Independent Data Monitoring Committee
IRB	Institutional Review Board (Ethics Committee)
RMC	Research Management Committee
MCC	Medicines Control Council
MoHSS	Ministry of Health and Social Services
NDP	National Drug Policy
PIC	Pharmaceutical Inspection Convention
SAE	Serious Adverse Event
SUADR	Serious Unexpected Adverse Drug Reaction (s)
UADR	Unexpected Adverse Drug Reaction
WMA	World Medical Association

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Clinical Trials in Human Subjects

1. INTRODUCTION

This guideline covers all clinical research projects in human subjects performed in Namibia, either as single country studies or as part of international multi-centre studies. All studies will be subjected to ethical review in a Biomedical Research Ethics Committee (BREC) and to technical review in the Research Management Committee (RMC).

Before any trial is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual trial subject and society. A trial should be initiated and continued only if the anticipated benefits justify the risks. The rights, safety and wellbeing of the study subjects are the most important considerations and should prevail over the interests of science and society.

2. GENERAL PREREQUISITES OF CLINICAL TRIALS ON MEDICINAL PRODUCTS

A clinical trial must be conducted in circumstances where there are prerequisites for its appropriate, safe and qualified execution. General prerequisites for a medical research project have been laid down in the MoHSS *Research Management Policy*, and in Chapter 11 of the *National Drug Policy*. Briefly, it is required that the research proposals conform to the *Declaration of Helsinki* of the World Medical Association and that studies are conducted according to specified principles of Good Clinical Practice and in particular, that they follow the ICH Guidelines.

The person responsible for clinical drug trials in human subjects shall be an authorised medical practitioner or dentist. Further instructions on the qualifications of the investigator are included in Section 7. – The person responsible for the trial shall be responsible for ensuring that the clinical trial complies with the current legislation and with other relevant regulations and guidelines.

It shall be a prerequisite that before any clinical drug trial is conducted the purpose of the trial is medically and ethically justified and that sufficient pharmacological, toxicological, pharmaceutical / chemical and biological data on the medicinal product are available. The sponsor has the primary responsibility for the adequacy of the data. The person responsible for the trial has responsibility for the professional competence of those conducting the trial, for the appropriateness of the trial protocol and for the safety of trial subjects.

The sponsor shall supply the medical practitioner or dentist intending to conduct the clinical trial with all the above information before notification (defined in more detail below) of a clinical trial on medicinal products in human subjects is submitted to the Permanent Secretary (PS) of the MoHSS. The sponsor shall also supply any other information that may affect the trial, usually in the form of an Investigator's Brochure. If the sponsor is not an organisation, the person responsible for the trial shall also bear responsibility for the availability of sufficient and reliable pharmacological, toxicological, pharmaceutical / chemical and biological data on the medicinal product or substance to be investigated.

The person responsible for the investigation shall ensure that the data on the disease, treatment and monitoring of the patient are available to those treating the patient in the case of an emergency.

The first clinical trials on a new product or particularly extensive clinical trials shall usually be performed at, or under the control of, clinics or clinical departments of teaching hospitals or university.

3. NOTIFICATION OF A CLINICAL TRIAL ON A MEDICINAL PRODUCT

The investigator, or sponsor, or manufacturer, or applicant for a marketing authorisation shall submit an advance notification to the PS of the MoHSS at least 90 days before the intended commencement of the investigation. The Research Unit will inspect the documentation and, if found correct and complete, will submit for parallel review by the BREC and the RMC.

A multi-centre trial shall be considered one trial, for which one complete notification shall be filed including the trial protocol as well as data on the medicinal product and earlier trials on the product. Each research centre participating in a multi-centre trial shall, in addition, complete a notification form confirming its participation in the trial. If the investigation forms part of an international multi-centre trial, the other participating countries shall be stated in the notification. In addition, an estimate shall be presented as to the part of the trial to be conducted in Namibia (number of recruited subjects).

Sometimes trial subjects and patients need to be monitored after termination of the trial itself, although a continuation trial is not included in the trial protocol. If no new patients are admitted and no interventions on trial subjects are performed, no new trial notification is needed. The continuation trial is in that case notified to the Research Unit in the MoHSS, as an amendment of the protocol. The amendment must be accompanied by a new patient information leaflet and patient consent. These will be re-reviewed by the BREC. A new notification must be made regarding the situation if new patients are admitted to the continuation trial, or if interventions on trial subjects are performed.

The sponsor or its representative shall submit the notification, together with its appendices, to the Research Unit in the MoHSS. The notification shall be accompanied by the particulars and documents listed in the Notification Form as well as in Section 4 below and the documentation shall be in the English language.

3.1 Documents to be Appended to the Notification

The notification shall be accompanied by the following documents:

- **A cover letter**, listing the documents accompanying the notification:
 - notification form,
 - copy of processing fee receipt,
 - study protocol,
 - subject information leaflet,
 - informed consent form,
 - description of subject recruitment procedures,
 - case record forms, and
 - a copy of the insurance policy.

3.1.1 Notification form

In the case of a multi-centre trial, notification forms are submitted for all trial centres. If this is not possible at the time of the notification, at least half of the notification forms must be submitted. A trial should not be commenced at a centre from which a notification form has not been submitted to the MoHSS Research Unit.

3.1.2 Copy of processing fee receipt

The notification must be accompanied by a receipt for payment in accordance with the current MoHSS decision relating to the notification procedures subject to a charge, or else by a request for exemption from payment. Payment must be made to the MoHSS, Commercial Bank, Frans Indongo

Street, Windhoek Main Branch, Account Name: NDHS Project, Account Number: 1609 095537. Payment details must clearly indicate to which clinical trial the payment relates. A single fee of not less than US\$ 5000.00 (Five Thousand US Dollars) is payable for a multi-centre trial. The fee might be waived for clinical trials conducted by an individual investigator, a trial team, a local university institute, or a local teaching hospital without outside financing or with financing by a non-profit organization, or a study commissioned by the MoHSS. If a waiver is desired, the notification of a trial must be accompanied by an informal statement to the effect that the investigation will not receive external funding. Medicinal products received free of charge for the purpose of an investigation are not regarded as external funding, but must be reported, preferably already in the protocol.

3.1.3 Study protocol

The trial protocol shall contain at least the following information:

1. The purpose of the investigation and the justification for its performance.
2. A description of the research method (controlled, uncontrolled), the trial arrangement (the parallel groups, alternating investigation), randomisation (the method and procedure), blinding method (double blinding, simple blinding). This should include an account of the method for ensuring that the reference product cannot be distinguished from the investigational product (masking procedure).
3. A description of the study population: the inclusion and exclusion criteria of the study subjects. An estimate of the representativeness of the study subjects, i.e. to what extent disease of the selected patients represents the disease in general clinical practice.
4. The estimated number of patients to be included in the trial, which must be justified using documented statistical methods. The methods used must be properly specified and referenced. A concluding statement as to whether the sample size is appropriate to test the study hypothesis, at the set type error levels I and II.
5. The method of administration, dose and dosing schedule of the investigational medicinal product and the comparison product as well as the treatment period.
6. The control groups and control treatment (placebo, other treatment etc).
7. Other concurrent treatment, if any.
8. Monitoring of the effects. Result variables, primary result variable, description and evaluation of measurement methods. Measurement dates.
9. Monitoring of trial safety and related laboratory and other tests.
10. Monitoring methods of adverse events: a description of the registration of adverse events as well as of any systematic follow-up questionnaire of adverse events. A description of the methods used in the monitoring of adverse events. Include precautions for emergencies and criteria for the breaking of the trial code and suspension of the trial.
11. Any adverse effects that the investigational medicinal product may cause and that may be caused by the trial to patients' relatives, to nursing staff and to the surroundings. Measures to prevent these.
12. Reports on the maintenance of specific trial protocols, patient monitoring forms and other patient files on the subjects participating in the trial. The list shall, where necessary, allow the identification of each patient/subject. Information on the storage location of the trial

code, as well as instructions for breaking it in the case of an emergency. Information on monitoring, if any.

13. Measures ensuring the safe handling of medicinal products and aimed at promoting and controlling maximal compliance with the instructions/orders given.
14. Analysis of the results: a description of the research methods and statistical methods, and handling of data on patients/subjects who have interrupted the trial.
15. Estimated schedule of the trial.
16. Information on the advance information to be given to the trial subjects/patients and on the method for obtaining the informed consent of the trial subjects (cf. Section 4, Informed consent of the trial subject).
17. Ethical aspects relating to the trial (cf. Section 5, Ethical evaluation).
18. Arrangements for the treatment of the patients after the trial (such as gradual discontinuation of the investigated medicinal product, possible change over to other medication, etc.). An account of the arrangements for the treatment of patients with good results from the medicinal product investigated.
19. A description of how changes in the trial protocol are recorded and notified to the MoHSS Research Unit.
20. A transparent description of the financing of the trial, including all funding sources, fees to be paid to the researchers and eventual compensation for loss of income or other appropriate and verifiable expenses to the study subjects.

The sponsor or person responsible for the trial shall inform the MoHSS Research Unit in writing of any essential changes that may have been made in a trial protocol submitted earlier. If a new version of the trial protocol is later submitted to the MoHSS Research Unit, essential changes in comparison with the earlier version shall be clearly detailed.

3.1.4 Subject information leaflet

See discussion in Chapter 4.

3.1.5 Informed consent form

See discussion in Chapter 4.

3.1.6 Description of subject recruitment procedures

For example, a copy of a newspaper announcement, if subjects are sought by newspaper or similar advertising.

3.1.7 Case record forms

In the case of a clinical trial on a medicinal product that has been granted a marketing authorisation or whose application for a marketing authorisation is pending at the Medicines Control Council, reference to the material submitted in connection with the application for marketing authorisation will be sufficient. If earlier trials on an investigational medicinal product have been conducted in Namibia, reference may be made to the material accompanying that earlier trial notification. In other cases the following information must also be supplied (see Annex 1, for a detailed description of the required information):

- information on the pharmaceutical, chemical and biological properties of the medicinal product,

-
- information on the pharmacology and pre-clinical toxicology of the medicinal product,
 - information on earlier trials in human subjects, and
 - Investigator’s Brochure, if one has been prepared.

The notification shall be made in English using the Research Unit in the MoHSS form entitled: *Notification of a clinical trial in human subjects*.¹ The notification shall be signed by the medical practitioner or dentist responsible for the performance of the trial at the trial site in question.

For contact relating to a clinical trial on medicinal products, a foreign sponsor should have a representative in Namibia. Both international and Namibian multi-centre trials shall have a contact person in Namibia, who is responsible for communicating and liaison between the different trial centres and the MoHSS Research Unit.

3.1.8 Insurance policy

See discussion in Chapter 6.

4. Informed Consent

A medical trial in human subjects cannot be performed without the free and informed consent of the trial subjects (a detailed explanation of the trial must be given before consent is requested). An exception may only be made if, owing to the emergency and the patient’s state of health, consent cannot be obtained and the measure is expected to be of immediate benefit to the health of the patient. Even in such cases, if at all feasible, efforts should be made to obtain consent from the legal representative of the patient. The biological parent, guardian or legal representative of the subject shall give consent if, in the case of an investigation involving treatment for a disease, the patient is a minor or unable to decide on his/her treatment owing to a mental problem or mental handicap, or is for some other reason unable to decide on his/her treatment.

The trial subject must be given a satisfactory explanation of his/her rights, of the purpose and nature of the trial and of the procedures used therein. He/she must also be given a satisfactory explanation of the potential disadvantages and risks. The explanation must be provided in such a way that the subject is capable of reaching a decision concerning consent while aware of the trial-related circumstances that affect this decision. Whenever possible, the explanation in question shall be given both verbally and in writing (subject information leaflet).

An information leaflet and consent form intended for a trial subject shall be available in English and in a language that the trial subjects understand well, i.e. usually their mother tongue. The consent document should contain the name, place of birth and address of the trial subject. The consent document must be dated and signed by the consenting person, or an independent person who has established the consent of the trial subject, and by the receiver of consent. A copy of the document must be given to the consenting person. The written or oral explanation, which is to be given to the trial subject shall be appended to the notification, which is sent to the MoHSS Research Unit and the method of obtaining consent must be described in the protocol.

If it is necessary to deviate from the above, the recommendations of the *Declaration of Helsinki* of the WMA (Annex 2) must be observed and procedures must be subjected to evaluation by the BREC.

The trial subject has the right to withdraw his/her consent, even without stating the reason, at any time prior to his/her scheduled end of participation in the trial. He/she must be informed of this right

¹ The notification form is available from the Research Unit (see annex 4)*

before commencement of the trial, with a reassurance than an eventual withdrawal will not affect his/her care in the future.

The subject shall, where necessary, be asked for written consent permitting a person appointed by the Permanent Secretary or the sponsor with approval from the PS, to familiarise himself/herself with the original patient records and trial materials to the extent required for verification of the authenticity of data collected in connection with the trial. A person appointed by the Permanent Secretary of the MoHSS has this right, but neither monitors appointed by the sponsor nor foreign authorities have this right without the written consent of the trial subject.

For a trial involving healthy volunteers, the consent must always be obtained in writing. Special provisions must be taken into consideration where the trial subject is handicapped, a minor, pregnant, breast-feeding or a prisoner.

Study subjects shall not be paid any fees or other incentives for their participation in the study. This does not exclude small tokens without significant value, which may be given at specific milestones of the study, however, not when the consent is being obtained, or at the first study visit. Loss of income to the subjects or other appropriate and verifiable expenses may be reimbursed.

5. Ethical Evaluation

After receipt of correct and complete notification documents, the MoHSS Research Unit will submit all research proposals for review by the BREC (see Research Management Policy). This review covers the study protocol, the proposed subject information leaflet and informed consent form and draft Case Record Forms.

The committee meets at least monthly, if required, and the PS of the MoHSS must receive notifications and protocols at least 90 days in advance of the proposed starting date of the trial. The committee will respond by issuing a written opinion, which may endorse the trial, or suggest amendments to the protocol or to other study documents. The committee may request a resubmission of the protocol after the changes have been effected.

The primary task of BREC is the review of research proposals and their supporting documents, with special attention given to the informed consent process, documentation, suitability and feasibility of the protocol. BREC needs to take into account prior scientific reviews, if any, and the applicable laws and regulations. The *Declaration of Helsinki* of the World Medical Association (Annex 2) and *international GCP guidelines* must be observed, when undertaking ethical evaluation. Elements of the review process are detailed in Annex 3. Briefly, the committee should consider:

- 1) scientific design and conduct of the study,
- 2) recruitment of study subjects,
- 3) care and protection of study participants,
- 4) protection of confidentiality,
- 5) informed consent process,
- 6) community considerations.

The technical evaluation in the RMC will take place [partly] in parallel with the ethical evaluation. However, the final decision-making will be pending on the opinion of the BREC. Should the BREC suggest amendments to the protocol or to other study documents and request a resubmission of the protocol, the RMC decision will be pending until the changes have been effected and/or the documents have been re-evaluated by the BREC.

6. Insurance

Before a clinical trial on a medicinal product is commenced, the investigators shall ensure that the trial subjects are adequately covered by an insurance policy for the event of adverse events and accidents possibly occurring during the course of the investigation. The insurance shall also cover the necessary medico-legal and other appropriate related expenses that may arise as a consequence of the adverse event after the trial has been completed. A copy of the insurance policy must be submitted to the PS of the MoHSS before commencement of the trial, as an enclosure to the notification documents.

7. Qualifications of the Investigator

The person responsible for a clinical trial on a medicinal product shall have good familiarity with clinical trials on medicinal products and preferably be a qualified specialist in the clinical field comprising the investigation and the disease being treated in the investigation. In trials that so require, one of the investigators shall hold the qualification of associate professor (lecturer) in the field of research in question. The person responsible for the trial who has signed the notification form shall be responsible for ensuring that the trial is performed expertly and competently.

In all clinical drug trials the investigators are required to be thoroughly familiar with the properties, effects and adverse effects of the investigational medicinal product. The minimum requirement is that all have read the Investigator's Brochure and attended team-briefing meetings. The trial team must have access to the expertise in clinical pharmacology, biology and statistics that is necessary for qualified performance of the trial.

The smaller the number of clinical trials performed with the medicinal product or substance in question, the higher the level of pharmacological and clinical pharmacological expertise within the trial team should be. This is because the particular competence is required to detect and interpret signals that may be significant regarding the safety of the product.

An Independent Data Monitoring Committee (IDMC) shall, if necessary, be created by the trial team for the purpose of monitoring trials that last more than a year, which are conducted with large numbers of patients and trials relating to new, potentially dangerous, treatments. The committee shall monitor trial progress, safety data and critical result variables, and may, if necessary, recommend continuation, modification or suspension of the trial.

8. Trial Site

The investigation shall be performed in circumstances that make it possible to perform it in an appropriate, safe and qualified manner. When choosing the trial site, attention shall be given to the phase of the clinical trial in question, as well as any risks that may be associated with the use of the medicinal product. An official written permission to conduct the study is a prerequisite for notification and commencement of the trial and should be obtained from the superintendent of the hospital or the director of the institute (trial site).

The first clinical trials on a new medicinal product (Phases I and II) shall ordinarily be performed at, or under the control of, teaching or university hospitals. When the aim of a clinical trial on medicinal products is to investigate the effects of a new medicinal product in patients in a clinical situation corresponding to outpatient care, the trial may be performed at a hospital out-patient clinic or another out-patient unit, under strict control of the relevant clinical department.

9. Informing the Personnel

The personnel participating in a clinical trial (such as the personnel of a pharmacy, hospital pharmacy, laboratory, patient wards, etc.) shall be given appropriate information on the investigation planned. It shall be the responsibility of the investigating medical practitioner or dentist to give this information. The person responsible for the trial shall have the responsibility of giving this information. All participating personnel should be familiar with the provisions of the *Declaration of Helsinki* (Annex 2). The investigating medical officer or dentist shall ensure that the trial is conducted according to the plan. Personnel in the wards can only assist and their ward routine should not be compromised or disrupted.

10. NOTIFICATION OF ADVERSE EVENTS AND REACTIONS

This provision, and the notification of adverse events and reactions, refers to clinical trials on medicinal products conducted in Namibia. Study organisations do not need to notify the MoHSS Research Unit of adverse effects observed in multi-centre studies at foreign trial centres, unless the adverse effect leads to other measures, such as changes in the trial protocol, additional updating of the Investigator's Brochure etc. In which case appropriate notification shall be made.

The sponsor shall provide the MoHSS Research Unit with significant data as quickly as possible, and within not more than 7 days, when a fatal or life-threatening serious adverse event (SAE) or serious unexpected adverse reaction (SUADR) is suspected. Well-founded information relating to continuation measures is to be provided within the subsequent 7-day period. SAEs and SUADRs that are not life threatening or fatal, must be reported to the MoHSS Research Unit as quickly as possible, and in any case within 15 days from the date on which the sponsor was informed of the events for the first time. The notifications should be made in writing.

The front page of the notification shall carry a clear indication of the number assigned to the trial by the MoHSS Research Unit, the investigational medicinal product or products,, the diagnosis of treated patients (or information to the effect that healthy volunteers were investigated) and the observed adverse reaction.

If the occurrence of adverse events is a result variable of the trial, e.g. in extensive follow-up trials examining mortality and morbidity, summaries of adverse effects relating to result variables may be supplied to the Research Unit in the MoHSS at regular intervals, for example, quarterly or biannually. In that case, the procedure shall be defined in the trial protocol. Such trials usually need an IDMC, whose reports must be submitted to the MoHSS Research Unit within 7 days of their preparation.

Adverse events that are not serious or unexpected need not be reported separately to the MoHSS Research Unit. They must, however, be covered by the final study report.

In respect of fatalities, the investigator shall provide the sponsor and the PS of the MoHSS with all requested additional information.

The sponsor shall inform the investigators of any new significant observations relating to the safety of the investigational medicinal product.

The sponsor shall annually submit to the MoHSS Research Unit a list of all the serious adverse events and unexpected adverse drug reactions and SUADRs, which have occurred during the period in question, together with an account of the safety of persons participating in the clinical trial. This obligation remains in force throughout the period of the clinical trial.

Notification of the sponsor

The investigator shall inform the sponsor immediately of all SAEs and UADR and SUADRs, excepting those SAEs that, according to the trial protocol or to the Investigator's Brochure, do not need to be reported immediately. Exceptions may include, for example, hospitalisations for an elective diagnostic or therapeutic procedure. Immediate notification is followed by a detailed written report. The trial subjects shall be identified by code numbers in the immediate notification and in the subsequent report to be submitted.

Adverse events and deviant laboratory results, which are defined in the trial protocol as significant with regard to the safety evaluation, shall be reported to the sponsor in accordance with the trial protocol.

The sponsor shall keep a detailed record of all adverse events, which have been reported to him by the investigator(s). This record shall be supplied upon request to the competent authorities of those participating countries, on whose territory the clinical trial is performed.

11. MEDICINAL PRODUCTS USED IN THE TRIAL

Regulations relating to the manufacture of the investigational medicinal product are specified in Annex 1. The import, storage and distribution of medicinal products to be used in the trial shall occur in accordance with the provisions of the Medicines and Related Substances Control Act Number 13 of 2003.

A pharmaceutical manufacturer, wholesale distributor as well as a pharmacy may supply a medical practitioner or dentist performing a clinical trial on a medicinal product with the medicinal products necessary for the trial against a written receipt. When so supplying, information on received investigational medicinal products shall also be delivered to the hospital pharmacy. If a pharmacy, hospital pharmacy is responsible for storage of the investigational medicinal products, the personnel responsible at these units must acknowledge receipt of the investigational medicinal products in writing.

Packages which are used for clinical trials, and also placebo packages, shall be marked 'Only for clinical trials'. The package label should include the:

- trial code,
- batch number,
- manufacturer and/or sponsor,
- name of the doctor or dentist responsible for the trial,
- patient identifier,
- pharmaceutical form,
- method and/or route of administration,
- number of doses,
- instructions for storage (if special storage instructions are necessary),
- expiry date, and, if necessary,
- technical handling instructions.

The person responsible for the trial shall also bear responsibility for the return or the proper disposal of investigational medicinal products that remain unused in accordance with separate written instructions.

12. COMMENCEMENT AND ENDING OF THE TRIAL

In all cases, before commencement of a trial, the MoHSS Research Unit shall obtain an opinion of the trial from the BREC. If the BREC has suggested changes to the study design, protocol, patient

information leaflet or patient consent form, all revised documents shall be re-submitted to the MoHSS Research Unit revised to conform to the opinion of the ethics committee.

The MoHSS Research Unit shall examine the notification of a clinical trial on medicinal products with its appendices and, whenever necessary, may request additional information. If on preliminary examination the notification is found to be deficient or incorrect, the MoHSS Research Unit shall request supplementation of the notification before commencement of handling thereof. The sponsor shall be provided with an acknowledgement of receipt of a notification, showing the process starting date and the MoHSS Research Unit number assigned to the investigation. This number is to be used as a reference in correspondence regarding the trial.

In parallel with the ethical review, the MoHSS Research Unit will submit the documentation for review by the RMC, which may reject the study proposal or request additional explanations. If such explanations are requested, the party that has submitted the notification shall be informed thereof in writing within 60 days from the process starting date. In its request for further clarifications, the RMC may grant permission to commence the trial as soon as the additional explanations have arrived at the MoHSS Research Unit or only after the opinion of the RMC on the additional explanations has been made known. If additional explanations are not requested, the trial may be commenced, when 60 days have elapsed since the date of commencement of handling.

The RMC and the PS of the MoHSS may, if necessary, order that a clinical trial on medicinal products be suspended.

The sponsor shall notify the PS of the MoHSS within 90 days of a decision that a clinical trial on medicinal products should not be commenced, that the trial has been suspended or cancelled, and also when the clinical phase of trial has ended. If a clinical trial has been terminated prematurely, termination of the trial and the reasons which led to termination shall be reported within 15 days.

13. INSPECTIONS AT THE TRIAL SITE

A person appointed by the MoHSS RMC, shall have the right if necessary to inspect the trial site and trial documents. If an authority from a foreign country intends to inspect the trial site and trial documents, the sponsor shall notify the MoHSS Research Unit of the inspection in writing within 7 days of the date on which notification of the intended inspection reached the sponsor.

14. TRIAL DOCUMENTATION AND MAINTENANCE OF THE DOCUMENTATION

The storage of the investigation files shall be governed by the rules set out in specified *Guidelines for Good Clinical Practice*. These rules normally comprise the verification of case report forms, changes in their information content, the verification of information in an electronic medium with dated and signed hard copies and backup copies, the inclusion of reference values in laboratory results, etc. The original trial results and codes shall be maintained for at least 15 years from the end of the trial. The general provisions and regulations thereon, shall govern the maintenance of patient files.

15. REPORT ON THE TRIAL RESULTS

The sponsor or the person responsible for the investigation shall submit a complete Final Report on the results of the trial to the MoHSS Research Unit not later than 1 year after the end of the investigation.

16. GUIDANCE AND ADVICE

The MoHSS Research Unit shall, on request, provide additional guidance and advice on the interpretation and practical application of this guideline.

17. GLOSSARY

Terms that have not been defined here, shall have the same meaning in this regulation, as in the ICH Topic E 6 'Guideline for Good Clinical Practice' (Section 1. Glossary).

Adverse drug reaction (ADR). In the pre-approval clinical experience with a new medicinal product or its new usages, particularly as therapeutic dose(s) may not be established, all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions.

The phrase 'responses to a medicinal product' means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e., the relationship cannot be ruled out.

Regarding marketed medicinal products:

A response to a drug that is noxious and unintended and that occurs at doses normally used in man for prophylaxis, diagnosis or therapy of diseases or for modification of physiological function (see the ICH guidance for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting).

Adverse event (AE). An AE is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product (see the ICH guidance for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting).

Amendment (to the protocol). See Protocol Amendment.

Applicable regulatory requirement(s). Any law(s) and regulation(s) addressing the conduct of clinical trials of investigational products of the jurisdiction where trial is conducted.

Approval (in relation to ethical review). The affirmative decision of the IRB that the clinical trial has been reviewed and may be conducted at the institution site within the constraints set forth by the IRB, the institution, good clinical practice (GCP), and the applicable regulatory requirements.

Audit certificate. A declaration of confirmation by the auditor that an audit has taken place.

Audit report. A written evaluation by the sponsor's auditor of the results of the audit.

Audit trail. Documentation that allows reconstruction of the course of events.

Audit. A systematic and independent examination of trial-related activities and documents to determine

whether the evaluated trial-related activities were conducted, and the data were recorded, analysed, and accurately reported according to the protocol, sponsor's standard operating procedures (SOPs), good clinical practice (GCP), and the applicable regulatory requirement(s).

Blinding/masking. A procedure in which one or more parties to the trial are kept unaware of the treatment assignment(s). Single blinding usually refers to the subject(s) being unaware, and double blinding usually refers to the subject(s), investigator(s), monitor, and, in some cases, data analyst(s) being unaware of the treatment assignment(s).

Case record form (CRF). A printed, optical, or electronic document designed to record all of the protocol-required information to be reported to the sponsor on each trial subject.

Clinical trial/study report. A written description of a trial/study of any therapeutic, prophylactic, or diagnostic agent conducted in human subjects, in which the clinical and statistical description, presentations, and analyses are fully integrated into a single report (see the ICH Guidance for Structure and Content of Clinical Study Reports).

Clinical trial/study. Any investigation in human subjects intended to discover or verify the clinical, pharmacological, and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy. The terms clinical trial and clinical study are synonymous.

Commencement and termination of the trial. A trial shall be regarded as having commenced when the first trial subject signs a consent document. A trial is regarded as having terminated when the entire clinical phase of the trial is over as far as the last trial subject is concerned.

Comparator (product). An investigational or marketed product (i.e., active control), or placebo, used as a reference in a clinical trial.

Competent authority. The authority, which at any given time has the current legal right to perform regulatory actions.

Compliance (in relation to trials). Adherence to all the trial-related requirements, good clinical practice (GCP) requirements, and the applicable regulatory requirements.

Confidentiality. Prevention of disclosure, to other than authorised individuals, of a sponsor's proprietary information or of a subject's identity.

Consent document. A document which contains an explanation for the trial subject of his/her rights, of the purpose and nature of the trial and procedures to be used therein and of any associated risks and disadvantages, and which is signed by the consent giver and consent receiver. The document may be independent or may form part of trial subject information leaflet (or patient information leaflet) and consent form.

Contract Research Organisation (CRO). A person or an organisation (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions.

Contract. A written, dated, and signed agreement between two or more involved parties that sets out any arrangements on delegation and distribution of tasks and obligations and, if appropriate, on financial matters. The protocol may serve as the basis of a contract.

Co-ordinating committee. A committee that a sponsor may organise to co-ordinate the conduct of a multi-centre trial.

Co-ordinating investigator. An investigator who is responsible for co-ordination of the work of the investigators at different trial centres participating in a multi-centre trial.

Co-ordinating Investigator. An investigator assigned the responsibility for the co-ordination of investigators at different centres participating in a multi-centre trial.

Direct access. Permission to examine, analyse, verify, and reproduce any records and reports that are important to evaluation of a clinical trial. Any party (e.g., domestic and foreign regulatory authorities, sponsors, monitors, and auditors) with direct access should take all reasonable precautions within the constraints of the applicable regulatory requirement(s) to maintain the confidentiality of subjects' identities and sponsor's proprietary information.

Documentation. All records, in any form (including, but not limited to, written, electronic, magnetic, and optical records; and scans, x-rays, and electrocardiograms) that describe or record the methods, conduct, and/or results of a trial, the factors affecting a trial, and the actions taken.

Essential change in the trial protocol. A change which affects the selection, treatment or safety of the trial subjects or the measures directed towards them or which fundamentally changes the interpretation of the trial results.

Essential documents. Documents that individually and collectively permit evaluation of the conduct of a study and the quality of the data produced (see section 8. 'Essential Documents for the Conduct of a Clinical Trial').

Excipient. Is an inert substance that is added to a medicine to make it of a more suitable consistency or form for administration (and production)

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 data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

Impartial witness. A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the subject or the subject's legally acceptable representative cannot read, and who reads the informed consent form and any other written information supplied to the subject.

Independent Data Monitoring Committee (IDMC) (Data and Safety Monitoring Board, Monitoring Committee, Data Monitoring Committee). An independent data monitoring committee that may be established by the sponsor to assess at intervals the progress of a clinical trial, the safety data, and the critical efficacy endpoints, and to recommend to the sponsor whether to continue, modify, or stop a trial.

Independent Ethics Committee (IEC). An independent body (a review board or a committee, institutional, regional, national, or supranational), constituted of medical / scientific professionals and non-medical/non-scientific members, whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in a trial and to provide public assurance of that protection, by, among other things, reviewing and approving / providing favourable opinion on the trial protocol, the suitability of the investigator(s), facilities, and the methods and material to be used in obtaining and documenting informed consent of the trial subjects. – The legal status, composition, function, operations, and regulatory requirements pertaining to Independent Ethics Committees may differ among countries, but should allow the Independent Ethics Committee to act in agreement with GCP as described in this guidance.

Informed consent. A process by which a subject voluntarily confirms his/her or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed, and dated informed consent form.

Inspection. The act by a regulatory authority(ies) of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority(ies) to be related to the clinical trial and that may be located at the site of the trial, at the sponsor's and/or contract research organisation's (CROs) facilities,

or at other establishments deemed appropriate by the regulatory authority(ies).

Institution (medical). Any public or private entity or agency or medical or dental facility where clinical trials are conducted.

Institutional Review Board (IRB). An independent body constituted of medical, scientific, and non-scientific members, whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trials, of protocols and amendments, and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects.

Interim clinical trial/study report. A report of intermediate results and their evaluation based on analyses performed during the course of a trial.

Investigational product. A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorisation when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.

Investigator. The person who is responsible for performance of the clinical trial at the trial site.

Investigator. A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator. See also Subinvestigator.

Investigator/Institution. An expression meaning ‘the investigator and/or institution, where required by the applicable regulatory requirements.’

Investigator’s Brochure. A compilation of the clinical and non-clinical data on the investigational product(s) that is relevant to the study of the investigational product(s) in human subjects.

Legally Acceptable Representative. An individual or juridical or other body authorised under applicable law to consent, on behalf of a prospective subject, to the subject’s participation in the clinical trial.

Medicinal product. A product or substance intended to be used internally or externally to cure, alleviate or prevent a disease or its symptoms in a human or animal subject. (*Medicines and Related Substances Control Act). A medicinal product shall also mean a product or substance referred to above and intended to be used internally or externally to determine the state of health of a person or the cause of a disease or to restore, improve or change his/her physiological functions (*Medicines and Related Substances Control Act).

Monitoring report. A written report from the monitor to the sponsor after each site visit and/or other trial-related communication according to the sponsor’s SOPs.

Monitoring. The act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, standard operating procedures (SOPs), GCP, and the applicable regulatory requirement(s).

Multi-centre trial. A trial which, according to the trial protocol, is to be conducted at more than one trial site.

Multi-centre trial. A clinical trial conducted according to a single protocol but at more than one site, and, therefore, carried out by more than one investigator.

Non-clinical study. Biomedical studies not performed on human subjects.

Opinion (in relation to Independent Ethics Committee). The judgement and/or the advice provided by an Independent Ethics Committee (IEC).

Original medical record. See Source Documents.

Other than intervention trial. A trial in which a medicinal product or products is/are prescribed in the normal way in accordance with the prerequisites set out in the marketing authorisation. The trial protocol does not contain advance specification of a patient’s particular treatment programme, but the trial forms part of normal medical practice and a decision regarding prescription of the medicinal product is completely independent of a decision on admission to the trial. Patients must not be subjected to excessive diagnostic or monitoring procedures.

Principal investigator. If the trial is conducted by a group, the investigator responsible for management of the group shall be designated the principal investigator.

Protocol amendment. A written description of a change(s) to or formal clarification of a protocol.

Protocol. A document that describes the objective(s), design, methodology, statistical considerations, and organisation of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents. In ICH GCP Guidance, the term protocol refers to protocol and protocol amendments.

Quality assurance (QA). All those planned and systematic actions that are established to ensure that the trial is performed and the data are generated, documented (recorded), and reported in compliance with GCP and the applicable regulatory requirement(s).

Quality control (QC). The operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial related activities have been fulfilled.

Randomisation. The process of assigning trial subjects to treatment or control groups using an element of chance to determine the assignments in order to reduce bias.

Regulatory Authorities. Bodies having the power to regulate. In the ICH GCP guidance, the expression ‘Regulatory Authorities’ includes the authorities that review submitted clinical data and those that conduct inspections (see section 1.29). These bodies are sometimes referred to as competent authorities.

Serious Adverse Event (SAE) or Serious Adverse Drug Reaction (Serious ADR). Any untoward medical occurrence that at any dose:

- results in death,
- is life-threatening,
- requires inpatient hospitalisation or prolongation of existing hospitalisation,
- results in persistent or significant disability/incapacity, or
- is a congenital anomaly/birth defect.

(See the ICH guidance for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting.)

Source data. All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies).

Source documents. Original documents, data, and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the clinical trial).

Sponsor. An individual, company, institution, or organisation that takes responsibility for the initiation, management, and/or financing of a clinical trial.

Sponsor-Investigator. An individual who both initiates and conducts, alone or with others, a clinical trial, and under whose immediate direction the investigational product is administered to, dispensed to, or used by a subject. The term does not include any person other than an individual (e.g., it does not include a corporation or an agency). The obligations of a sponsor-investigator include both those of a sponsor and those of an investigator.

Standard Operating Procedures (SOPs). Detailed, written instructions to achieve uniformity of the performance of a specific function.

Subinvestigator. Any individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions (e.g.,

associates, residents, research fellows). See also Investigator.

Subject Identification Code. A unique identifier assigned by the investigator to each trial subject to protect the subject’s identity and used in lieu of the subject’s name when the investigator reports adverse events and/or other trial-related data.

Subject/trial subject. An individual who participates in a clinical trial, either as a recipient of the investigational product(s) or as a control.

Trial protocol. A document setting out the objective or objectives, protocol, procedure and statistical considerations of the trial and the trial organisation. The trial protocol shall mean the trial protocol, its subsequent versions and amendments thereof.

Trial site. The location(s) where trial-related activities are actually conducted.

Trial subject. A person who participates in a trial, either as a recipient of the investigational medicinal product or as a control patient.

Unexpected Adverse Drug Reaction. An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g., Investigator’s Brochure for an unapproved investigational product or package insert/summary of product characteristics for an approved product). (See the ICH Guidance for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting.)

Vulnerable subjects. Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental, and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention. Other vulnerable subjects include patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors, and those incapable of giving consent.

Well-being (of the trial subjects). The physical and mental integrity of the subjects participating in a clinical trial.

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Annex 1. Documents to be submitted for clinical trials on medicinal products

This appendix sets out the information which, where applicable, should accompany the notification that has to be submitted in respect of clinical trials on medicinal products. The extent of the material may vary depending on the nature of the trial.

Summarising documentation should be submitted on the following topics:

1. Pharmaceutical, chemical and biological information
2. Manufacture and manufacturer of investigational medicinal products
3. Toxicological characteristics
4. Pharmacological properties
5. Human pharmacological and clinical particulars

Where necessary, the Research Unit in the MoHSS may request full trial reports or other supplementary information.

In the case of a medicinal product that has been granted a marketing authorisation referred to in the Medicines and Related Substances Control Act, or whose application for a marketing authorisation is pending at the Medicines Control Council, just making a reference to the documentation that was submitted in connection with the application for marketing authorisation will usually be sufficient.

1. PHARMACEUTICAL, CHEMICAL AND BIOLOGICAL INFORMATION

The pharmaceutical, chemical and biological information shall, where applicable, be presented in accordance with the rules issued to applicants for marketing authorisation for a medicinal product. The information may, however, be preliminary, and need not be as detailed as the information presented in the application for marketing authorisation. The extent of the information shall depend upon the trial phase in question. When transferring from one clinical trial phase to another, additional information may be requested from the manufacturer.

Pharmaceutical or other changes in a medicinal product being used for a trial already in progress, which substantially affect the absorption or excretion of the medicinal product, shall be reported without delay to the MoHSS Research Unit. If the pharmaceutical, chemical and/or biological characteristics of the medicinal product have changed compared with the characteristics of the medicinal product used in animal tests or in earlier clinical trials, the nature of this change shall be explained and the reason for the change shall be stated.

Composition of the medicinal product. The detailed quantitative composition of the medicinal product shall be declared.

Manufacturing process. A brief description of the manufacturing process shall be given, unless it is self-evident. The process for the manufacture of medicinal products which are to be administered parenterally, in particular the sterilisation process and other critical stages of manufacture, shall in all cases be described.

Active ingredient(s). Data which are presented in relation to the active ingredient(s) shall essentially correspond to the data provided in the application for a marketing authorisation.

For an active ingredient the structural formula, the empirical formula, the chemical and generic name, possibly the internal name and the laboratory code must be provided. In the case of products of biological origin, the starting materials should also be specified.

The description of the active ingredient should be as full as possible. Attention should in particular be given to information relating to molecular structure and to accounts relating to impurities. The extent of accounts relating to impurities shall be determined according to the trial phase in question. Impurities in the active ingredient should be fully examined not later than in Phase III.

In the information relating to substances of biological origin, special attention should be paid to the manufacturing process for the active ingredient and to ensuring virus safety therein. The quality requirements for the active ingredient shall always be set out. In addition, analysis results from one or more batches must be included.

Excipients. In addition to the active ingredient, the excipients used in the medicinal product and the quality requirements relating thereto shall also be declared. If the medicinal product contains new excipients which have not previously been used in medicinal products, or substances which may affect the efficacy of the medicinal product, the information relating to them should essentially correspond to the information required in connection with the

application for a marketing authorisation. In the case of excipients and colorants which are commonly used, a statement of the name and quantity will suffice.

Packaging materials. An account shall be given of the package type and of the quality of the package material for parenterally administered medicinal products and ophthalmic medicinal products. The structure and function of new and new-type packages should be described in detail.

Final product. With regard to the final product (a medicinal product for use in a clinical trial on a medicinal product), the name of the product and/or the code used in the clinical trial shall be specified, along with its pharmaceutical form and strength.

A brief description shall be provided concerning pharmaceutical characteristics such as half-life, solubility, viscosity, crystalline form, particle size, etc., as well as possible reasons. Quality requirements must always be presented. They should at least comprise confirmatory tests, concentration determinations and tests to demonstrate the fundamental technical characteristics of the product. The quality requirements may be preliminary. Analysis results from one or more batches should also be included.

Shelf life studies. Investigations into the shelf life of the active ingredient should indicate whether they are of essential significance for shelf life evaluation of the final medicinal product.

An account of the shelf life of the final product should be provided. It should be based upon the results of shelf life investigations commenced on the final product.

Virological documentation. In respect of products containing substances of biological origin an account should be included of the virus safety of the product and of measures carried out for prevention of transmissible spongiform encephalopathies (TSE).

Reference products. If a placebo or some other reference product is used in the trial, an adequate account must be provided of its composition, appearance and taste.

2. MANUFACTURE AND MANUFACTURER OF INVESTIGATIONAL MEDICINAL PRODUCTS

Manufacture. Medicinal products which are used in clinical trials (investigational medicinal products) should be manufactured in accordance with specified guidelines on Good Manufacturing Practices (GMP), and also observing the rules separately issued concerning investigational medicinal products.

Manufacturer in Namibia. In Namibia, investigational medicinal products should be manufactured at a pharmaceutical company, a pharmacy or a hospital pharmacy. If the manufacturer is a pharmaceutical company, the operating licence should cover the pharmaceutical form used in the trial. Medicinal products prepared in a hospital pharmacy may be produced only for the hospital's own use. The supply of medicinal products prepared in a hospital pharmacy for some purpose other than for internal use by the hospital concerned requires the consent of the Medicines Control Council.

In the case of the above-mentioned manufacturers in Namibia conforming to the provisions of the Medicines and Related Substances Control Act, there is no need to send a licence or GMP certificate to the MoHSS Research Unit.

Manufacturer abroad. If the investigational medicinal products are manufactured in a country which has ratified the Pharmaceutical Inspection Convention (PIC) agreement either a current pharmaceutical factory operating licence or a GMP certificate issued by an authority supervising the activity shall be submitted in respect of the manufacturer. They should contain mention of the pharmaceutical form used in the trial.

In order that investigational medicinal products prepared somewhere other than in the above-mentioned countries may be approved for use in a clinical trial on a medicinal product in Namibia, the GMP conformity of the place of manufacture of the medicinal product shall be evaluated on the basis of a GMP inspection carried out by the Medicines Control Council, or an inspection authority in the country concerned. In exceptional cases other reliable reports may be accepted as the basis for evaluation of GMP conformity.

Operating licence decisions or GMP certificates and inspection reports (including reports mentioned in the above sections) shall be submitted to the MoHSS Research Unit in English.

3. TOXICOLOGICAL CHARACTERISTICS

A new medicinal product may only be administered to humans when adequate toxicological data relating to it are available. Toxicological investigations shall be planned in such a way that they correspond as closely as possible to the intended clinical use of the medicinal product. There are instructions regarding the required investigations: ICH topic M3. *Non-Clinical Safety Studies for the Conduct of Human Clinical Trials for Pharmaceuticals (CPMP/ICH/286/95)*.

4. PHARMACOLOGICAL PROPERTIES

Trials prior to Phase I and II. The material should be based upon tests conducted in relevant animal test models, in which preferably more than one animal species has been used.

Pharmacodynamic properties. Information about the effects of the medicinal product on the most important organs and organ groups shall be supplied where possible. In particular the most important effect of all (the anticipated therapeutic effect) must be properly analysed. An account of the essential features of the mechanism of action must also be provided. At the same time tests shall generally also be conducted with a known reference product. Simple screening tests are rarely satisfactory. If a drug substance occurs as several different stereo isomers in a medicinal product, the effects of these should be examined separately. – Attention shall be given to possible interactions with other drug substances.

Pharmacokinetic properties. The following pharmacokinetic information shall be presented concerning the intended method of administration: absorption distribution metabolism elimination. If a drug substance occurs as several different stereo isomers in a medicinal product, the kinetic properties of these should be examined separately. – Any occurrence of active metabolites should be examined.

Trials prior to Phase III and IV. An account of the Phase I and Phase II clinical trials on medicinal products which have been performed shall generally be submitted to the MoHSS Research Unit before proceeding to Phase III. The results of Phase I and Phase II trials in human subjects may render it necessary for additional pharmacodynamic and pharmacokinetic data to be obtained before Phase III and Phase IV trials are commenced.

5. HUMAN PHARMACOLOGICAL AND CLINICAL PARTICULARS

Prior to Phase II clinical trials the results of earlier human pharmacological investigations must be submitted to the MoHSS Research Unit. These will show, for example, not only the effects on target organs and the desired therapeutic effects but also any effects on other important systems when the dose levels in question are used. At the same time an account shall be given of the results of kinetic studies conducted with the medicinal product and also of the distribution and excretion of the medicinal product when other methods of administration are used. Also to be submitted are the results of other such investigations upon which the choice of dosage is based, that is to say dose-effect studies, studies on the correlation of effects upon quantities of the medicinal product measured in the tissues and tolerance studies.

The results of earlier human pharmacological and clinical trials must be submitted to the MoHSS Research Unit.

Annex 2. 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 1975, 35th WMA General Assembly, Venice, Italy, October 1983, 41st WMA General Assembly, Hong Kong, September 1989, 48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996 and the 52nd WMA General Assembly, Edinburgh, Scotland, October 2000

A. INTRODUCTION

1. The World Medical Association has developed the Declaration of Helsinki as a statement of ethical principles to provide guidance to medical practitioners and other participants in medical research involving human subjects. Medical research involving human subjects includes research on identifiable human material or identifiable data.
2. It is the duty of the medical practitioner to promote and safeguard the health of the people. The medical practitioner's knowledge and conscience are dedicated to the fulfilment of this duty.
3. The Declaration of Geneva of the World Medical Association binds the medical practitioner with the words, '*The health of my patient will be my first consideration*', and the International Code of Medical Ethics declares that, '*A medical practitioner shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient.*'
4. Medical progress is based on research that ultimately must rest in part on experimentation involving human subjects.
5. In medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society.
6. The primary purpose of medical research involving human subjects is to improve prophylactic, diagnostic and therapeutic procedures and the understanding of the aetiology and pathogenesis of disease. Even the best proven prophylactic, diagnostic and therapeutic methods must continuously be challenged through research for their effectiveness, efficiency, accessibility and quality.
7. In current medical practice and in medical research, most prophylactic, diagnostic and therapeutic procedures involve risks and burdens.
8. Medical research is subject to ethical standards that promote respect for all human beings and protect their health and rights. Some research populations are vulnerable and need special protection. The particular needs of the economically and medically disadvantaged must be recognised. Special attention is also required for those who cannot give or refuse consent for themselves, for those who may be subject to giving consent under duress, for those who will not benefit personally from the research and for those for whom the research is combined with care.
9. Research Investigators should be aware of the ethical, legal and regulatory requirements for research on human subjects in their own countries as well as applicable international requirements. No national ethical, legal or regulatory requirement should be allowed to reduce or eliminate any of the protections for human subjects set forth in this Declaration.

B. BASIC PRINCIPLES FOR ALL MEDICAL RESEARCH

10. It is the duty of the medical practitioner in medical research to protect the life, health, privacy, and dignity of the human subject.
11. 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 on adequate laboratory and, where appropriate, animal experimentation.
12. Appropriate caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected.
13. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol. This protocol should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee, which must be independent of the investigator, the sponsor or any other kind of undue influence. This independent committee should be in conformity with the laws

and regulations of the country in which the research experiment is performed. The committee has the right to monitor ongoing trials. The researcher has the obligation to provide monitoring information to the committee, especially any serious adverse events. The researcher should also submit to the committee, for review, information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest and incentives for subjects.

14. The research protocol should always contain a statement of the ethical considerations involved and should indicate that there is compliance with the principles enunciated in this Declaration.

15. Medical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given consent.

16. Every medical research project involving human subjects should be preceded by careful assessment of predictable risks and burdens in comparison with foreseeable benefits to the subject or to others. This does not preclude the participation of healthy volunteers in medical research. The design of all studies should be publicly available.

17. Medical practitioners should abstain from engaging in research projects involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Medical practitioners should cease any investigation if the risks are found to outweigh the potential benefits or if there is conclusive proof of positive and beneficial results.

18. Medical research involving human subjects should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the subject. This is especially important when the human subjects are healthy volunteers.

19. Medical research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the results of the research.

20. The subjects must be volunteers and informed participants in the research project.

21. The right of research subjects to safeguard their integrity must always be respected. Every precaution should be taken to respect the privacy of the subject, the confidentiality of the patient's information and to minimise the impact of the study on the subject's physical and mental integrity and on the personality of the subject.

22. In any research on human beings, 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. The subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. After ensuring that the subject has understood the information, the medical practitioner should then obtain the subject's freely-given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed.

23. When obtaining informed consent for the research project the medical practitioner should be particularly cautious if the subject is in a dependent relationship with the medical practitioner or may consent under duress. In that case the informed consent should be obtained by a well-informed medical practitioner who is not engaged in the investigation and who is completely independent of this relationship.

24. For a research subject who is legally incompetent, physically or mentally incapable of giving consent or is a legally incompetent minor, the investigator must obtain informed consent from the legally authorised representative in accordance with applicable law. These groups should not be included in research unless the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons.

25. When a subject deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the investigator must obtain that assent in addition to the consent of the legally authorised representative.

26. Research on individuals from whom it is not possible to obtain consent, including proxy or advance consent, should be done only if the physical/mental condition that prevents obtaining informed consent is a necessary characteristic of the research population. The specific reasons for involving research subjects with a condition that renders them unable to give informed consent should be stated in the experimental protocol for consideration and approval of the review committee. The protocol should state that consent to remain in the research should be obtained as soon as possible from the individual or a legally authorised surrogate.

27. Both authors and publishers have ethical obligations. In publication of the results of research, the investigators are obliged to preserve the accuracy of the results. Negative as well as positive results should be published or otherwise publicly available. Sources of funding, institutional affiliations and any possible conflicts of interest should be declared in the publication. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.

C. ADDITIONAL PRINCIPLES FOR MEDICAL RESEARCH COMBINED WITH MEDICAL CARE

28. The medical practitioner may combine medical research with medical care, only to the extent that the research is justified by its potential prophylactic, diagnostic or therapeutic value. When medical research is combined with medical care, additional standards apply to protect the patients who are research subjects.

29. The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists.

30. At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study.

31. The medical practitioner should fully inform the patient which aspects of the care are related to the research. The refusal of a patient to participate in a study must never interfere with the patient-medical practitioner relationship.

32. In the treatment of a patient, where proven prophylactic, diagnostic and therapeutic methods do not exist or have been ineffective, the medical practitioner, with informed consent from the patient, must be free to use unproven or new prophylactic, diagnostic and therapeutic measures, if in the medical practitioner's judgement it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, these measures should be made the object of research, designed to evaluate their safety and efficacy. In all cases, new information should be recorded and, where appropriate, published. The other relevant guidelines of this Declaration should be followed.

Annex 3. Biomedical Research Ethics Committee

Review of research proposals and follow-up of clinical research

The Biomedical Research Ethics Committee (BREC) shall review or require modifications in ethical aspects of all clinical research activities conducted in Namibia.

The BREC shall require that all information given to subjects as part of informed consent is in accordance with the Guidelines on Clinical Trials in Human Subjects. The BREC may require that specific additional information be given to the subjects, when in the BREC's judgement the information would meaningfully add to the protection of the rights and welfare of subjects.

In specific justified cases the BREC may recommend to waive the requirement of written informed consent (e.g. if the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context; or in emergency research). In such cases, the BREC may require that the investigator provides the subjects with a written statement regarding the research.

BREC may recommend approval of the trial to RMC. BREC shall notify RMC in writing of its decision to approve or disapprove the proposed research activity, or modifications required to secure BREC approval. If the BREC decides to disapprove a research activity, it shall include in its written notification a statement of reasons for its decision, and give the investigator an opportunity to respond in person or writing.

The BREC shall conduct continuing review of research in Namibia at intervals appropriate to the degree of risk, but not less than once per year, and shall have authority to observe or have a third party observe the consent process and the research.

Functions and operations

To ensure impartial and high quality review of research proposals, the Biomedical Research Ethics Committee shall follow written procedures:

- for conducting its initial and continuing review of research, and for reporting its findings and actions to the investigator and the institution;
- for determining which projects require review more often than annually and which projects need verification from sources other than the investigator that no material changes have occurred since previous BREC review;
- for ensuring prompt reporting to the BREC of changes in research activity; and
- for ensuring that changes in approved research, during the period for which the BREC approval has already been given, may not be initiated without BREC review and approval except where necessary to eliminate apparent immediate hazards to the human subjects.

The BREC shall also follow written procedures for ensuring prompt reporting to appropriate institutional officials, and the Medicines Control Council:

- any unanticipated problems involving risks to human subjects or others;
- any instance of serious or continuing non-compliance with the regulations or the requirements or determinations of the BREC; or
- any suspension or termination of BREC approval.

With the exception of resubmitted research documents containing changes proposed by the BREC, the committee shall review the proposals at convened meetings at which a majority of the committee members are present, including at least one member, whose primary concerns are in non-scientific areas. For the research to be approved, it shall receive the approval of a majority of those members present at the meeting. – Resubmitted research documents may be reviewed by the BREC chairperson, who may decide on their acceptability independently. Such decisions shall be copied for other BREC members for information.

Meeting requirements

The BREC should meet regularly on pre-scheduled dates. Meetings should be planned in accordance with the needs of the workload, minutes should be kept in all meetings, and there must be an approval system for the minutes. The applicant, sponsor, and/or investigator or independent consultants may be invited to present the protocol or other specific issues in the meeting, or in writing.

Elements of the review

The primary task of BREC is the review of research proposals and their supporting documents, with special attention given to the informed consent process, documentation, suitability and feasibility of the protocol. BREC needs to take into account prior scientific reviews, if any, and the applicable laws and regulations. The committee should consider:

- 1) Scientific design and conduct of the study:
 - a. the appropriateness of the study design in relation to the objectives of the study, statistical methodology, including sample size calculation, and the potential for reaching sound conclusions with the smallest number of study subjects.
 - b. the justification of predictable risks and inconveniences weighed against the anticipated benefits for the study subjects and for the concerned communities.
 - c. the justification for the use of control arms.
 - d. criteria for withdrawing study subjects.
 - e. criteria for suspending or terminating the study.
 - f. the adequacy of monitoring and auditing arrangements.
 - g. the adequacy of the study sites, facilities, supporting staff, and emergency procedures, and
 - h. the manner of reporting and publishing of study results.
- 2) Recruitment of study subjects:
 - a. study population characteristics,
 - b. the means of making the initial contact and recruitment,
 - c. the means of conveying information to the potential participants, and
 - d. inclusion and exclusion criteria.
- 3) Care and protection of study participants:
 - a. investigators' qualifications and experience,
 - b. plans to withdraw or withhold standard therapies for the purposes of research,
 - c. medical care to be provided to the participants during and after the study,
 - d. steps to be taken, if the participants discontinue their participation in the study,
 - e. criteria for emergency use of study preparations,
 - f. the arrangements, if appropriate, for informing the subjects' own medical practitioner, including procedures for seeking the participant's consent to do so,
 - g. plans to make the study product available to the study participants after completion of the trial (compassionate use),
 - h. costs to the participants,
 - i. rewards and reimbursements to the study subjects,
 - j. provisions for compensation in case of injury, disability or death attributable to participation in the research, and
 - k. the insurance and indemnity arrangements.
- 4) Protection of confidentiality:
 - a. a description of the persons who have access to personal data of the study subjects, including medical records and biological samples, and
 - b. the measures taken to ensure the confidentiality and security of personal information concerning research participants.
- 5) Informed consent process:
 - a. a full description of the process for obtaining informed consent, including the identification of those responsible for obtaining consent,
 - b. the adequacy, completeness and understandability of written and oral information to be given to the study subjects, and, when appropriate, to their legal representative(s)
 - c. clear justification for the intention to include individuals who cannot consent
 - d. assurances that the study subjects will receive relevant new information that becomes available during the course of the trial (including their rights, safety and well-being), and
 - e. the provisions made for receiving and responding to queries and complaints from the study participants or their representatives.
- 6) Community considerations:
 - a. the impact and relevance of the research on the communities from which the research participants are drawn,
 - b. the steps taken to consult with the concerned communities during the planning phase of the study,

- c. the influence of the community on the consent of the individuals,
- d. proposed community consultation during the course of the trial,
- e. the extent to which the research contributes to capacity building, such as the enhancement of local healthcare, research, and the ability to respond to public health needs,
- f. a description of the availability and affordability of any successful study product to the concerned communities after completion of the study, and
- g. the manner in which the study results will be made available to the study subjects and the concerned communities.

Membership in the Biomedical Research Ethics Committee

The Biomedical Research Ethics Committee shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities. The BREC shall be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, cultural backgrounds, and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.

In addition to the professional competence necessary to review the specific research activities, the BREC shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards or professional conduct and practice. The BREC shall therefore include persons knowledgeable in these areas. If the BREC regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, consideration shall be given to the inclusion of one or more individuals, who are knowledgeable about and experienced in working with those subjects.

Every non-discriminatory effort shall be made to ensure that the BREC does not consist entirely of men or entirely of women, including full consideration of qualified persons of both sexes, so long as no selection is made to the BREC on the basis of gender. The BREC may consist entirely of members of one profession.

The BREC shall include at least one member whose primary concerns are in the scientific area and at least one member whose primary concerns are in non-scientific areas.

The BREC shall include at least one member who is not affiliated with government institutions and who is not part of the immediate family of a person who is affiliated with such institutions.

The BREC may not have a member participate in initial or continuing review of any project, in which the member has a conflicting interest, except to provide information requested by the BREC.

The BREC may, in its discretion, invite individuals with competence in special areas to assist in the review of complex issues, which require expertise beyond or in addition to that available on the BREC. However, these individuals may not vote with the BREC.

Institutional Review Boards

Research institutions may form Institutional Review Boards to conduct internal review of clinical studies conducted within the institution. The IRBs should comply with the provisions specified above. Internal IRB review does not make BREC review redundant. IRB decisions may be submitted to the BREC, for information.

Annex 4. Notification Form

FOR OFFICIAL USE

Clinical trial number	Notification received	Supplementary information requested	Notification accepted
Additional information requested		Additional information received	
Commencement of the trial allowed	Trial rejected	Trial ended	
Trial interrupted	Trial cancelled or suspended	Safety update	Study report received

INFORMATION FROM THE SPONSOR / RESEARCH INSTITUTE

Name of the trial	
Number, code or other study identifier	
Processing fee paid to Bank of Namibia, Account: *	
Fee amount (NAD):	Payment date:
<input type="checkbox"/> Receipt copy enclosed	<input type="checkbox"/> Exemption from the processing fee requested

Manufacturer of the investigational product, if no marketing authorisation in Namibia

Name	Manufacturing licence enclosed	GMP certificate enclosed
Street address	Postal code and city	Country

Manufacturer of the active substance (if not the same as the manufacturer of the investigational product)

Name	Manufacturing licence enclosed	GMP certificate enclosed
Street address	Postal code and city	Country

Sponsor

Name		
Street address	Postal code and city	Country

Contact person

Name	Company	P.O. Box
Street address	Postal code and city	Country
Telephone	Fax	E-mail

Agent of the pharmaceutical company in Namibia

Name	Company	P.O. Box
Street address	Postal code and city	Country
Telephone	Fax	E-mail

Distribution of the investigational product (pharmaceutical company, wholesale distributor or pharmacy)

Importer	Stock keeper	Distributor
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Signature of the agent or contact person

I hereby confirm that the above information given on the trial and the medicinal product is correct. We shall submit a study report of the clinical trial to the MoHSS, Research Unit, and shall inform without delay if the trial is suspended or cancelled.		
Date	Signature	Name in print

FOR CLINICAL DRUG TRIALS

The investigational product is:		
<input type="checkbox"/> New substance	<input type="checkbox"/> New combination product	<input type="checkbox"/> Other:
<input type="checkbox"/> Formerly known substance	<input type="checkbox"/> New route of administration	
<input type="checkbox"/> New pharmaceutical form	<input type="checkbox"/> New synonym product	
<input type="checkbox"/> New strength	<input type="checkbox"/> New combination treatment	
ATC Code:		
Investigational product		Comparator product
Active substance		Active substance
Generic name		Generic name
Code name (if given)		Code name (if given)
Pharmaceutical form		Pharmaceutical form
Strength		Strength
Route of administration		Route of administration
The product has a marketing authorisation in:		The product has a marketing authorisation in:
<input type="checkbox"/> Namibia, trade name:		<input type="checkbox"/> Namibia, trade name:
<input type="checkbox"/> Elsewhere, trade name and country:		<input type="checkbox"/> Elsewhere, trade name and country:
<input type="checkbox"/> Nowhere		<input type="checkbox"/> Nowhere
The product does not have a marketing authorisation, but an application the authorisation has been submitted in:		The product does not have a marketing authorisation, but an application the authorisation has been submitted in:
<input type="checkbox"/> Namibia, date:		<input type="checkbox"/> Namibia, date:
<input type="checkbox"/> Elsewhere, date and country:		<input type="checkbox"/> Elsewhere, date and country:
<input type="checkbox"/> Nowhere		<input type="checkbox"/> Nowhere
Another product containing the same active ingredient has a marketing authorisation in:		Another product containing the same active ingredient has a marketing authorisation in:

<input type="checkbox"/> Namibia, trade name: <input type="checkbox"/> Elsewhere, trade name and country: <input type="checkbox"/> Nowhere	<input type="checkbox"/> Namibia, trade name: <input type="checkbox"/> Elsewhere, trade name and country: <input type="checkbox"/> Nowhere
Additional information:	

STUDY

Summary of the investigational plan
Purpose of the trial
<input type="checkbox"/> Treatment, in: <input type="checkbox"/> an approved indication <input type="checkbox"/> a new indication <input type="checkbox"/> Non-interventional trial <input type="checkbox"/> Kinetics <input type="checkbox"/> Interactions <input type="checkbox"/> Basic science study <input type="checkbox"/> Other, specify:
Study phase
<input type="checkbox"/> I <input type="checkbox"/> II <input type="checkbox"/> III <input type="checkbox"/> IV
Study design
<input type="checkbox"/> No comparator group <input type="checkbox"/> Parallel groups <input type="checkbox"/> Cross-over <input type="checkbox"/> Other, specify:
Blinding
<input type="checkbox"/> Open <input type="checkbox"/> Only patient blinded <input type="checkbox"/> Double-blind <input type="checkbox"/> Other, specify:
Study subjects
<input type="checkbox"/> Healthy volunteers <input type="checkbox"/> Patients, diagnosis:
If patients, the target group is
<input type="checkbox"/> Treatment according to the current practice <input type="checkbox"/> New group (e.g. children, elderly):
Will the current treatment of the patients be changed
<input type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> Previously untreated patients
Schedule of the trial in Namibia
The estimated start of enrolment
The estimated end of study
Other countries involved in the trial

STUDY CENTRE

Name				
Address				
Number of study subjects	Subjects receiving the investigational product	Subjects receiving the comparator product	Subjects receiving placebo	Total
At this centre				
In Namibia				
Study total				
Physicians or dentists or other scientists involved in the trial at this centre				
Name	Degree	Speciality		
Signature				
I am familiar with the information on the study, and on the medicinal product in question given by the manufacturer (agent). I shall comply with the investigational plan and ensure that the possible essential changes to be made in the investigational plan and any serious adverse events will be informed to the Ministry of Health and Social Services, Research Unit.				
I have the permission of the director of the trial site or institute to perform the trial.				
Date, signature and printed name of the physician or dentist responsible for the performance of the trial at this centre				
Enclosures				
– to be submitted always		– to be submitted if needed, see the Clinical Trials Guideline		
<input type="checkbox"/> Investigational plan (study protocol)	<input type="checkbox"/> Patient information leaflet and informed consent form	<input type="checkbox"/> Processing fee receipt copy (or justification for exemption)	<input type="checkbox"/> Opinion of the Biomedical Research Ethics Committee	<input type="checkbox"/> Pharmaceutical, chemical and biological information <input type="checkbox"/> Pharmacological and toxicological information <input type="checkbox"/> Clinical study results <input type="checkbox"/> Manufacturing licence or GMP certificate

Additional form to be used in case of several investigational products	
The investigational product is:	
<input type="checkbox"/> New substance <input type="checkbox"/> Formerly known substance <input type="checkbox"/> New pharmaceutical form <input type="checkbox"/> New strength	<input type="checkbox"/> New combination product <input type="checkbox"/> New route of administration <input type="checkbox"/> New synonym product <input type="checkbox"/> New combination treatment
<input type="checkbox"/> Other:	
ATC Code:	
Investigational product	Comparator product
Active substance	Active substance
Generic name	Generic name
Code name (if given)	Code name (if given)
Pharmaceutical form	Pharmaceutical form
Strength	Strength
Route of administration	Route of administration
The product has a marketing authorisation in:	The product has a marketing authorisation in:
<input type="checkbox"/> Namibia, trade name: <input type="checkbox"/> Elsewhere, trade name and country: <input type="checkbox"/> Nowhere	<input type="checkbox"/> Namibia, trade name: <input type="checkbox"/> Elsewhere, trade name and country: <input type="checkbox"/> Nowhere
The product does not have a marketing authorisation, but an application the authorisation has been submitted in:	The product does not have a marketing authorisation, but an application the authorisation has been submitted in:
<input type="checkbox"/> Namibia, date: <input type="checkbox"/> Elsewhere, date and country: <input type="checkbox"/> Nowhere	<input type="checkbox"/> Namibia, date: <input type="checkbox"/> Elsewhere, date and country: <input type="checkbox"/> Nowhere
Another product containing the same active ingredient has a marketing authorisation in:	Another product containing the same active ingredient has a marketing authorisation in:
<input type="checkbox"/> Namibia, trade name: <input type="checkbox"/> Elsewhere, trade name and country:	<input type="checkbox"/> Namibia, trade name: <input type="checkbox"/> Elsewhere, trade name and country:

