South African Health Products
Regulatory Authority
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GUIDELINE ON CLINICAL INVESTIGATION OF MEDICAL DEVICES

This guideline is intended to clarify the requirements of conducting a clinical investigation in a medical device in South Africa. It represents the South African Health Products Regulatory Authority's (SAHPRA)'s current thinking on the safety, quality and performance of medical devices under clinical investigation. It is not intended as an exclusive approach. The Authority reserves the right to request any additional information to establish the safety, quality and performance of a medical device in keeping with the knowledge current at the time of evaluation. Alternative approaches may be used but these should be scientifically and technically justified. The Authority is committed to ensuring that all registered medical devices will be of the required acceptable quality, safety and performance.

Document History

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Glossary

Abbreviation/ Term	Meaning
CI	Clinical Investigation
CIMD	Clinical Investigation of a Medical Device
GHTF	Global Harmonization Task Force
IMDRF	International Medical Devices Regulators Forum
ISO	International Organization for Standardization
PMS	Post Marketing Surveillance
RIMS	Regulatory Information Management System
SAHPRA	South African Health Products Regulatory Authority

Definition of terms

Adverse Event: Means any untoward medical occurrence or undesirable incident that may occur in association with the use of a medical device which—

(a) does not necessarily have a causal relationship with its use; or

(b) may occur due to its malfunction, its deterioration of safety, quality, or performance, or an error of its use.

Clinical Data: Safety, clinical performance, and/or effective information that is generated from the clinical use of a medical device.

Clinical Evaluation: A set of ongoing activities that use scientifically sound methods for the assessment and analysis of clinical data to verify the safety, clinical performance, and/or effectiveness of the medical device when used as intended by the manufacturer.

Clinical Evidence: The clinical data and its clinical evaluation of a medical device.

Clinical Investigation: Any systematic investigation or study in or on one or more human subjects, undertaken to assess the safety, clinical performance, and/or effectiveness of a medical device.

Clinical Investigation Plan: Document that states the rationale, objectives, design, and pre-specified analysis, methodology, monitoring, conduct, and record-keeping of the clinical investigation.

Clinical Performance: The ability of a medical device to achieve its intended clinical purpose as claimed by the manufacturer.

Clinical Performance Study: Means a study undertaken to establish or confirm the clinical performance of a medical device, including IVD, focusing on the actual performance of the device in real-world clinical conditions, often involving the collection of data on how well the device performs its intended function and the clinical benefits it provides to patients.

Conformity Assessment: Relevant testing, calibration, inspection, or certification of a medical device or a quality management system.

Effectiveness: The ability of a medical device to achieve clinically meaningful outcome(s) in its intended use as claimed by the manufacturer.

Endpoint: An indicator used for providing the evidence for safety, clinical performance, and/or effectiveness in a clinical investigation (ISO 14155:2011, modified).

Ethics Committee: Independent body whose responsibility it is to review clinical investigations to protect the rights, safety, and well-being of human subjects participating in a clinical investigation.

Investigator: Individual member of the investigation site team designated and supervised by the principal investigator at an investigation site to perform critical clinical investigation–related procedures or to make important clinical investigation-related decisions. *NOTE 1:* An individual member of the investigation site team can also be called 'sub-investigator' or 'co-investigator'.

Multi-Regional Clinical Investigation: A clinical investigation conducted in more than one region under a single protocol.

Region: A geographical region, country, or regulatory region.

Regulatory Region: A region comprised of jurisdictions for which common sets of regulatory requirements apply.

Residual Risk: Risk remaining after risk control measures have been taken (ISO 14971:2007).

Risk Management: The systematic application of management policies, procedures, and practices to the tasks of analysing, evaluating, controlling, and monitoring risk (ISO 14971).

Safety: Acceptability of risks as weighed against benefits, when using the medical device according to the manufacturer's labelling.

Sponsor: Individual or organisation taking responsibility and liability for the initiation or implementation of a clinical investigation.

Note: All other definitions in alignment with Act 101 of 1965 and MD regulations.

1. INTRODUCTION

A clinical investigation (CI) of a medical device is defined as any systematic investigation or study in or on one or more human subjects, undertaken to assess the safety, clinical performance, and/or effectiveness of a medical device.

The undertaking of a clinical investigation is a scientific process that represents one method of generating clinical data. The objective of a clinical investigation is to assess the safety, clinical performance, and/or effectiveness of a medical device for a particular indication or intended use. ISO 14155: 2020 Clinical Investigation of Medical Devices for Human Subjects — Good Clinical Practice details the requirements for the conduct of clinical investigations. This is an international standard that addresses good clinical practice for the design, conduct, recording, and reporting of CIs carried out in human subjects to assess the safety or performance of medical devices for regulatory purposes.

Thirteen principles are included, such as adherence to ethical principles (as per the Declaration of Helsinki), subjects' rights, a determination that benefits outweigh risks, and oversight by an independent ethics committee. The two main CIs relevant to the regulation of medical devices are those conducted during premarket and post-market assessments.

A CI must consider scientific principles underlying the collection of clinical data, along with accepted ethical standards surrounding the use of human subjects. Every medical device requires clinical evidence, appropriate for the use and classification of the device, demonstrating that the device complies with the applicable provisions of the Essential Principles of Safety and Performance of medical devices.

In general, CIs of investigational medical devices require two types of assessment, from a national regulatory authority for medical devices and from a relevant research ethics committee prior to beginning the study.

1.1 Purpose

The purpose of this document is to provide an overview of the medical device regulations and guidance on how to submit applications to conduct CIs within the Republic of South Africa. Given the wide diversity of medical devices and their associated risks, this document is not intended to provide comprehensive guidance for clinical investigations of specific medical devices

1.2 Scope

The intention is to be a dynamic document that supplements the medical devices regulations. This guideline applies to all applicants intending to conduct clinical investigations for medical devices, including in vitro diagnostics (IVDs).

1.3 Ethical Considerations for Clinical Investigations

As a general principle, “the rights, safety and wellbeing of clinical investigation subjects shall be protected consistent with the ethical principles laid down in the Declaration of Helsinki” and the applicable regulatory requirements or other relevant standards (ISO 14155:2020). It is ethically important in deciding to conduct a clinical investigation that it should generate new data and answer specific safety, clinical performance, and/or effectiveness questions that remain unanswered by the most current body of knowledge.

The desire to protect human subjects from unnecessary or inappropriate experimentation must be balanced with the need to protect public health using CI where they are indicated. In all cases, however, care must be taken to ensure that the necessary data is obtained through a scientific and ethical investigational process that does not expose subjects to undue risks or discomfort. The rights, safety, and well-being of subjects are paramount, and appropriate trial design and conduct are essential to generate meaningful data.

2. LEGAL PROVISION

Regulations relating to medical device, Government Gazette.

3. INTERNATIONAL STANDARDS

- ISO 14155:2020 Clinical investigation of Medical Devices for human subjects - Good Clinical Practice
- ISO 14971:2019 Application of risk management to medical devices
- Clinical investigation of medical devices shall comply with the requirements established by the National Ethics Review Board

4. REQUIREMENTS TO CONDUCT CLINICAL INVESTIGATION

Any Clinical Investigation of a Medical Device (CIMD) to be conducted within the Republic of South Africa shall be approved by the Authority before commencement. Investigational medical devices can only be imported for clinical investigations if approval is obtained from the Authority. Any person or body intending to conduct clinical investigation should submit their applications through the SAHPRA Regulatory Information Management System (RIMS). Applications should be accompanied by the prescribed fees as per the gazetted fee Regulations applied and the following information: -

4.1 Documents

CHECKLIST -*Documents Submitted with Application (Circle or shade applicable)*	
Signed and dated Cover letter	*YES / NO*
Application form *(Annexure A)*	*YES / NO*
Checklist completed	*YES / NO*
Protocol (version and date)	*YES / NO*
Clinical investigation plan or clinical trial or clinical performance assessment for the medical device/IVD protocol	*YES / NO*
Clinical investigation agreement between sponsor and Clinical Research Organisation (CRO) if applicable	*YES / NO*
Clinical investigation agreement between sponsor and clinical investigation site(s)/principal investigator(s)	*YES / NO*
Investigator Brochure	*YES / NO*
Informed consent documents	*YES / NO*
Instructions for use	*YES / NO*
Curriculum vitae of the investigator/s (SAHPRA format)	*YES / NO*
Investigator/s proof of GCP training certificates (not more than 3 years old)	*YES / NO*
Investigator/s proof of current malpractice insurance (Certificate/ Card)	*YES / NO*
Disclosure of Principal Investigator Conflict of Interests	*YES / NO*
Signed declaration by investigator/s	*YES / NO*
National Principal Investigator (CV/GCP/Malp/Declaration)	*YES / NO*
Participant insurance & expiry date (where relevant)	*YES / NO*
Proof of sponsor indemnity for investigators and trial sites	*YES / NO*
Proof of application to register the trial/investigation/performance assessment on SANCTR	*YES / NO*
Workloads for investigators	*YES / NO*
Copy of ethics committee approval	*YES / NO*

Copy of letter submitted to Ethics Committee	*YES / NO*
Reimbursement for patients	*YES / NO*
Remuneration to investigators	*YES / NO*
Study budget	*YES / NO*
Patients' questionnaire(s)	*YES / NO*
Proof of registration with Professional Statutory Body(ies)	*YES / NO*
Additional information, i.e. Cert. of analysis (where relevant)	*YES / NO*

4.2 Notifications and Reports

- Notification for withdrawal of ethics committee within five (5) working days
- Notification for suspension or termination of clinical investigation within five (5) working days
- Major deviations from the investigational plan
- Change of principal investigator
- Progress reports every six (6) months
- Serious adverse events that have led to serious adverse effects
- Clinical investigational final report

Note: The Authority reserves the right to inspect the ongoing clinical investigation without prior notice.

5. GENERAL PRINCIPLES WHEN CONSIDERING THE NEED FOR A CLINICAL INVESTIGATION

The investigation should be appropriate to the device under evaluation, its specific properties, and its intended purpose. Benefits and risks should be specified, e.g., as to their nature, probability, extent, duration and frequency. Core issues are the proper determination of the benefit/risk profile in the intended target groups and medical indications, and demonstration of acceptability of that profile based on current knowledge/the state of the art in the medical fields concerned.

Clinical investigation is a responsibility of the manufacturer, and its report is an element of the technical documentation of a medical device, including In vitro diagnostics. Conformity to the Essential Principles can only be assumed when the following items are aligned with each other:

- The information materials supplied by the manufacturer (the labelling, instructions for use, available promotional materials, including accompanying documents foreseen by the manufacturer),
- The clinical investigation (the device description used for the clinical investigation, other contents of the clinical investigation report),
- Available clinical data (such as results of Clinical Investigations, publications, PMS studies, etc.). Particularly, evaluators should address the following points to decide if these are adequately supported by sufficient clinical evidence:
- The intended purpose described in the information materials supplied by the manufacturer (including for all medical indications);
- The clinical performance and benefits described in the information materials supplied by the manufacturer (including, for example, any claims on product performance and safety);
- Measures for risk avoidance and risk mitigation described in the information materials supplied by the manufacturer (including, for example, the declaration of the residual risks, - contraindications, precautions, warnings, instructions for managing foreseeable unwanted situations);
- The usability of the device for the intended users and the suitability of the information materials supplied by the manufacturer for the intended users (including, if applicable, for lay or disabled persons);
- Instructions for target population groups (including, for example, pregnant women, paediatric populations).

5.1 When should a clinical investigation be undertaken?

Clinical investigations are necessary to provide data not available through other sources (such as literature or nonclinical testing) required to demonstrate compliance with the relevant Essential Principles (including safety, clinical performance and acceptability of benefit/risk associated with its use). When a clinical investigation is conducted, the data obtained is used in the clinical evaluation process and is part of the clinical evidence for the medical device.

When considering the need for a clinical investigation, one should consider whether there are new questions of safety, clinical performance, and/or effectiveness for the particular medical device and intended use that need to be addressed in a clinical investigation. Generally, such questions are more likely to be generated for high risk and/or novel medical devices.

For long-established technologies, the clinical investigation data that might be required for novel technologies may not be necessary. The available clinical data in the form of, for example, published literature, reports of clinical experience, post-market reports and adverse event data may, in principle, be adequate to establish the safety, clinical performance, and/or effectiveness of the medical device, provided that new risks have not been identified, and that the intended use(s)/purpose(s) has/have not changed.

5.2 What are the key considerations in clarifying the need for clinical investigations?

- Identifying relevant clinical Essential Principles (for example, specifics of safety, clinical performance, acceptability of benefit/risk) for the medical device and its intended use/purpose(s).
- Performing risk management (ISO 14971:2019) activities, such as a risk analysis, will help in identifying the clinical data necessary to address residual risks and aspects of clinical performance not completely resolved by available information (e.g., design solutions, nonclinical and material/technical evaluation, conformity with relevant standards, labelling).
- Risk control measures include inherent safety by design, protective measures in the medical device itself or in the manufacturing process, and information for safety. The decision to use a medical device in the context of a clinical procedure requires the residual risk to be balanced against the anticipated benefits of the procedure. A clinical investigation may be required to further elucidate the benefit/risk in a defined patient population;

- Conducting a proper clinical evaluation will demonstrate which clinical data are necessary, and can be adequately contributed to by sources such as literature searching, prior clinical investigations (including clinical data generated in other jurisdictions), clinical experience, or clinical data available from comparable devices, and which clinical data should be generated from clinical investigation(s) when data are unavailable or insufficient to demonstrate conformity to the Essential Principles. Available clinical data from comparable devices should be carefully examined for comparability and adequacy.

5.3 Clinical investigation evaluation undertaken for the development of a medical device

Premarket research and development are guided by clinical investigation and risk management. Typically, manufacturers carry out clinical investigations to define needs regarding clinical safety and clinical performance of the device.

In case of possible equivalence to an existing device, evaluate if there are clinical data available and determine equivalence; carry out a gap analysis and define which data still need to be generated with the device under evaluation, whether clinical investigations are necessary and if so, define the study design for additional information. As the initial clinical evaluation identifies the questions to be answered by a clinical investigation, the clinical evaluation process should generally commence in advance of any clinical investigation.

5.4 Clinical investigation for initial Registration

Clinical evaluation is required to be carried out for the conformity assessment process leading to the product registration and placing on the market of a medical device. **The purpose is to:**

- Document that there is sufficient clinical evidence to demonstrate conformity with the Essential Principles covering clinical performance and clinical safety;
- Identify aspects that need to be addressed systematically during post-market surveillance (PMS), e.g., in post-market clinical follow-up studies (PMCF Studies) required under the relevant medical device regulations.

Typically, these aspects include estimation of residual risks and uncertainties or unanswered questions (such as rare complications, uncertainties regarding long-term performance, safety under widespread use).

6. GENERAL PRINCIPLES OF CLINICAL INVESTIGATION DESIGN

6.1 Compliance of Clinical Investigation

Any clinical investigation must;-

- Be based on the results of the clinical evaluation process;
- Follow a proper risk management procedure to avoid undue risks;
- Be compliant with all relevant legal and regulatory requirements;
- Be appropriately planned, conducted, analysed, and reported;
- Follow appropriate ethical principles.

6.2 Clinical data requirements

The design of the clinical investigation, including the study objectives and statistical considerations, should provide the clinical data necessary to address the residual risks, including aspects of clinical performance.

Factors that may influence include;-

- Type of medical device and/or regulatory classification
- Novel technology/relevant previous experience
- Clinical application/indications
- Nature of exposure to the product (e.g., surface contact, implantation, ingestion)
- Risks inherent in the use of the product (e.g., risk associated with the procedure)
- Performance claims made in the medical device labeling (including instructions for use) and/or promotional materials
- Component materials or substances
- Disease process (including severity) and patient population being treated
- Demographic, geographic, and cultural considerations (e.g., age, ethnicity, gender)
- Potential impact of device failure
- Period of exposure to the medical device
- Expected lifetime of the medical device
- Availability of alternative treatments and the current standard of care
- Ethical considerations

6.3 Considerations for Medical Device Study Protocols

Factors needing consideration in study protocols include:-

- Clear statement of objectives
- Minimisation of risk to subjects and those involved with the conduct of the investigation
- Adverse event definitions and reporting
- Study endpoints
- Appropriate subject population(s)
- Minimisation of bias (e.g., randomisation, blinding/masking, concealment of allocation)
- Identification of confounding factors (e.g., concurrent therapies, co-morbidities)
- Choice of appropriate controls (e.g., active control, sham, historical)
- Design configuration (e.g., parallel, crossover, cohort study, single arm)
- Type of comparison (e.g., superiority, non-inferiority, equivalence)
- Follow-up duration and monitoring

6.4 Statistical requirements

In designing the study, statistical considerations should be prospectively specified and be based on sound scientific principles and methodology. **Development of a statistical plan should include consideration of the following:**

- Clinically relevant endpoints
- Analysis of population
- Statistical significance levels, power
- Sample size calculation and justification
- Analysis methodology
- Management of potential confounding factors
- Procedures for multiplicity control and adjustment of error probabilities
- Procedures for handling missing, unused or spurious data, including drop-outs
- Procedures for handling deviations from the original statistical analysis plan

6.5 Conduct of Clinical Investigations

A properly conducted clinical investigation, including compliance with the clinical investigation plan and local laws and regulations, ensures the protection of human subjects, the integrity of the data and that the data obtained is acceptable for the purpose of demonstrating conformity to the Essential Principles. ISO 14155 outlines good clinical practice for clinical investigations of medical devices.

6.6 Final Study Report

The outcome of a clinical investigation should be documented in a final study report. This then forms part of the clinical data that is included in the clinical evaluation process and ultimately becomes integrated into the clinical evaluation report for the purposes of conformity assessment.

7. ETHICAL CONSIDERATIONS FOR CLINICAL INVESTIGATIONS

The rights, safety, and well-being of clinical investigation subjects shall be protected consistent with the ethical principles laid down in the Declaration of Helsinki" and the applicable regulatory requirements or other relevant standards (ISO 14155:2020).

It is ethically important in deciding to conduct a clinical investigation that it should generate new data and answer specific safety, clinical performance, and/or effectiveness questions that remain unanswered by the current body of knowledge. The desire to protect human subjects from unnecessary or inappropriate experimentation must be balanced with the need to protect public health using clinical investigations where they are indicated. In all cases, however, care must be taken to ensure that the necessary data are obtained through a scientific and ethical investigational process that does not expose subjects to undue risks or discomfort. The rights, safety, and well-being of subjects are paramount, and appropriate trial design and conduct are essential to generate meaningful data.

8. REFERENCES

- IMDRF: 2018- Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices
- IMDRF: 2019 Principles of Labeling for Medical Devices and IVD Medical Devices document, when released
- IMDRF:2019 Clinical Evidence – Key definitions and Concepts
- GHTF:2008 Summary Technical Documentation for Demonstrating Conformity to the Essential Principles of Safety and Performance of Medical Devices (STED)

- ISO 14155:2020 – Clinical investigation of medical devices for human subjects — Good clinical practice.
- ISO 14971:2019 – Medical devices - Application of risk management to medical devices

9. VALIDITY

This guideline is valid for a period of five (5) years from the effective date of revision and replaces the previous version. It will be reviewed within this timeframe or as and when required.

Annex 1: Application Form for Clinical Investigation of Medical Devices

	Date Received **……**	For SAHPRA Use	
		For SAHPRA Use	
Status			
1.1	**Aim of Study**	☐ Pre-marketing approval for new device ☐ Pre-marketing approval for new claims ☐ Post-Marketing study ☐ Non-Marketing study	
1.2	**Type of Study**	☐ Observational study ☐ Interventional study	
1.3	**Does this clinical investigation involves first-in-human use?**	☐ Yes ☐ No	
1.4	**Will the investigational device be imported into South Africa**	☐ Yes ☐ No	
Sponsor details			
2.1	**Type of Sponsorship**	☐ Commercial ☐ Non-commercial	
2.2	**Type of sponsor**	☐ Manufacturer ☐ Authorised Representative ☐ Hospital ☐ Independent individuals ☐ Foundation ☐ University or Institution ☐ Other, please specify: ----------	
2.3	**Type of aid**	☐ Material support ☐ Funding support ☐ Other, please specify: ----------	
2.4	**Sponsor Details**	Name _____ _____ Address _____ Phone _____ E-mail _____ Contact person name _____ Contact person phone_____	

		Contact person e-mail _____	
2.5	**Person responsible for completing the application**	Name _____ Position _____ Phone _____ E- mail _____	
3. CRO Details	**Clinical Research Organisation, if applicable**	Name _____ SAHPRA's license (if applicable) _____ Address_____ Phone_____ E- mail_____ Contact person name _____ Contact person phone _____ Contact person e-mail _____	
4. Investigational Device Information			
4.1	**Is the device registered by SAHPRA?**	☐ Yes, where applicable: ☐ No: _____ ☐ No, but registered in: ☐ Australia ☐ Canada ☐ Japan ☐ USA ☐ EU ☐ Other, please specify: …….. ☐ Not registered anywhere	
4.2	**Investigational Device Name**	_____	
4.3	**Device Category**	☐ Active implantable devices ☐ Anaesthetic and respiratory devices ☐ Dental devices ☐ Electromechanical medical devices ☐ Hospital hardware ☐ Non-active implantable devices ☐ Ophthalmic and optical devices ☐ Reusable devices ☐ Single use devices ☐ Assistive products for persons with disability	

		☐ Diagnostic and therapeutic radiating devices ☐ Complementary therapy devices ☐ Biologically derived devices ☐ Healthcare facility products and Adaptations ☐ Laboratory equipment ☐ Other: …….	
4.4	**Is the device an implantable?**	☐ No ☐ Yes, brief description: …….. …… ☐ Is the device intended to remain permanently implanted in the patient: ☐ No ☐ Yes	
4.5	**Whether the device is intended to be used for cosmetic rather than medical purposes**	☐ No ☐ Yes, Select: ☐ A non-corrective contact lens ☐ An implant for augmentation, fixation, or sculpting of body parts ☐ A facial or other skin filler ☐ Equipment for liposuction ☐ Surgical laser equipment	
4.6	**Does the device incorporate, as an integral part or substance, a medicinal product in achieving its primary intended action?**	☐ No ☐ Yes ☐ Brand name of drug: ……	
4.7	**Does the device incorporate a substance of animal origin?**	☐ No ☐ Yes ☐ Type of tissue, cell, or substance: ……	
4.8	**Does the device incorporate human tissue, cell, or substance?**	☐ No ☐ Yes Type of tissue, cell, or substance: ……	
4.9	**Does the device incorporate cells or substance of microbial origin?**	☐ No ☐ Yes Type of microorganism: ……	

4.10	**The intended purpose of the investigational device**	…… ……	
5. Design of the Clinical Investigation			
5.1	**Clinical Investigational Plan (CIP) information**	Scientific title ……	
5.2	**Clinical Investigational Plan title**	Insert the following information: Abbreviated title Clinical Investigation Plan number Clinical Investigation Plan date Clinical Investigation Plan version Planned start date Planned completion date	
5.3	**Type of Design**	☐ Open-label non-randomised clinical investigation ☐ Randomisation, Randomised controlled clinical investigation Parallel group: …… Cross over: …… ☐ Blinding ☐ Single blinded ☐ Double blinded ☐ Other ☐ Comparator used ☐ Placebo ☐ Comparator device, identify: ……	
5.4	**Does this study include vulnerable subjects?**	☐ No ☐ Yes	
5.5	**Size of the sample population**	Planned total number of subjects involved in the clinical investigation …… Planned number of subjects involved in South Africa ……	
5.6	**Number of study centres in South Africa**	----------	
5.7	**Other countries where this clinical investigation is carried out**	---------- ---------- ----------	
5.8	**Is there a Data Safety Monitoring Committee**	☐ Yes ☐ No	

	for this study?		
6.	**Investigation Site(s) in South Africa**		
	Site 1	Name _____ Address_____ Phone_____ E-mail _____ Name of principal investigator _____ EC name _____ EC address_____ EC phone_____ EC E-mail_____ Protocol number approved by EC _____	
	Site 2	Name_____ Address_____ Phone _____ E-mail _____ Name of principal investigator _____ EC name _____ EC address _____ EC phone _____ EC E-mail _____ Protocol number approved by EC	
	More sites if applicable can be added using the same format as in #6		
7	**Declaration by Sponsor**		
	I as the sponsor defined in this application: ☐ undertake that I comply with the Ethics Committee requirements. ☐ undertake that I will report to the Authority any Adverse device event of which I become aware for the investigational device without delay but not later than <10> working days of occurrence/becoming aware of the event. ☐ undertake that I will provide the documents specified in section 4 in the SAHPRA'S guidance entitled Guidelines on Clinical Investigations of Medical Devices. ☐ undertake to notify Ethics Committee and Principal investigators in case of withdrawal of SAHPRA's approval, or part of it, within five working days of receiving the withdrawal notice. ☐ undertake, under any request from the SAHPRA, to respond by providing accurate, current, and complete information about any aspect of the study.		

	☐ declare that SAHPRA has the right to inspect the study at any time without prior notification. ☐ declare that all information provided in this application is true and complete. ☐ declare that I will maintain if applicable, an appropriate process for the safe return or disposal of investigational devices. **Name: _____** **Position: _____** **Date:** **Signature: _____**

Annex II: Disclosure of Principal Investigator Conflict of Interests

Title of Clinical Investigation Plan	
Date received:	
Clinical Investigation Application Number:	

I disclose the following regarding my involvement in the investigation in the submitted application:

☐ any significant payments of other type made from the sponsor, including but not limited to a grant to fund ongoing research, compensation in the form of equipment, retainer, or ongoing consultation, or honoraria;

☐ any proprietary interest in the investigational product held by the clinical investigator;

☐ any considerable equity interest (including but not limited to any ownership interest, stock deal, or other financial interest) held by the clinical investigator in the sponsor of the covered study.

Details of the disclosable financial arrangements and interests are attached, along with a description of steps taken to minimise the potential bias of clinical study results by any of the disclosed arrangements or interests.

Name of Principal Investigator: _____

Date: _____

Signature: _____

Note: In case of Multicentre Study, a separate form shall be filled for each Principal Investigator.