1. PURPOSE

1.1. This guidance outlines the additional obligations of investigators conducting a <Clinical Trial> subject to ISO 14155.

2. GUIDANCE

2.1. General

2.1.1. The role of the principal investigator is to implement and manage the day-to-day conduct of the clinical investigation as well as ensure data integrity and the rights, safety and well-being of the subjects involved in the clinical investigation.

2.1.2. If the sponsor contracts an institution to conduct the clinical investigation, the institution shall appoint an appropriately qualified person to be the principal investigator.

2.2. Qualification of the principal investigator: The principal investigator shall

2.2.1. Be qualified by education, training and experience to assume responsibility for the proper conduct of the clinical investigation in accordance with this International Standard; evidence of such qualifications of the principal investigator and key members of the investigation site team shall be provided to the sponsor through up-to-date cvs or other relevant documentation.

2.2.2. Be experienced in the field of application and trained in the use of the investigational device under consideration.

2.2.3. Disclose potential conflicts of interest, including financial, that interfere with the conduct of the clinical investigation or interpretation of results.

2.2.4. Be knowledgeable with the method of obtaining informed consent.

2.3. Qualification of investigation site: The principal investigator shall be able to demonstrate that the proposed investigation site

2.3.1. Has the required number of eligible subjects needed within the agreed recruitment period.

2.3.2. Has one or more qualified investigators, a qualified investigation site team and adequate facilities for the foreseen duration of the clinical investigation.

2.4. Communication with the IRB: The principal investigator shall

2.4.1. Provide the sponsor with copies of any clinical-investigation-related communications between the principal investigator and the IRB.

2.4.2. Comply with the requirements to communicate with the IRB.

2.4.3. Obtain the written and dated approval/favourable opinion of the IRB for the clinical investigation before recruiting subjects and implementing all subsequent amendments, if required.

2.4.4. Perform safety reporting as specified below.

2.4.5. Promptly report any deviations from the clinical investigational plan that affect the rights, safety or well-being of the subject or the scientific integrity of the clinical investigation, including those which occur under emergency circumstances, if required by the IRB, clinical investigational plan or national regulations.

2.4.6. In particular circumstances, the communication with the IRB can be performed by the sponsor, partly or in full, in which case the sponsor shall keep the principal investigator informed.

2.5. Informed consent process: The principal investigator shall

2.5.1. Comply with the requirements specified by the IRB to obtain informed consent.

2.5.2. Ensure compliance with the applicable regulatory requirements and ethical principles for the process of obtaining informed consent.

2.5.3. Ensure and document appropriate training if an authorized designee is appointed to conduct the informed consent process.

2.6. Compliance with the clinical investigational plan: The principal investigator shall

2.6.1. Indicate his/her acceptance of the clinical investigational plan in writing.
2.6.2. Conduct the clinical investigation in compliance with the clinical investigational plan.
2.6.3. Create and maintain source documents throughout the clinical investigation and make them available as requested during monitoring visits or audits.
2.6.4. Ensure that the investigational device is used solely by authorized users as specified in 6.2, and in accordance with the clinical investigational plan and instructions for use.
2.6.5. Propose to the sponsor any appropriate modification(s) of the clinical investigational plan or investigational device or of the use of the investigational device.
2.6.6. Refrain from implementing any modifications to the clinical investigational plan without agreement from the sponsor, IRB and regulatory authorities, if required.
2.6.7. Document and explain any deviation from the approved clinical investigational plan that occurred during the course of the clinical investigation.
2.6.8. Ensure that an adequate investigation site team and facilities exist and are maintained and documented during the clinical investigation.
2.6.9. Ensure that maintenance and calibration of the equipment relevant for the assessment of the clinical investigation is appropriately performed and documented, where applicable.
2.6.10. Ensure the accuracy, completeness, legibility and timeliness of the data reported to the sponsor in the case report forms and in all required reports.
2.6.11. Maintain the device accountability records.
2.6.12. Allow and support the sponsor to perform monitoring and auditing activities.
2.6.13. Be accessible to the monitor and respond to questions during monitoring visits.
2.6.14. Allow and support regulatory authorities and the IRB when performing auditing activities.
2.6.15. Ensure that all clinical-investigation-related records are retained as required.
2.6.16.
2.6.17. Sign the clinical investigation report.

2.7. Medical care of subjects: The principal investigator shall

2.7.1. Provide adequate medical care to a subject during and after a subject's participation in a clinical investigation in the case of adverse events, as described in the informed consent.
2.7.2. Inform the subject of the nature and possible cause of any adverse events experienced.
2.7.3. Provide the subject with the necessary instructions on proper use, handling, storage and return of the investigational device, when it is used or operated by the subject.
2.7.4. Inform the subject of any new significant findings occurring during the clinical investigation, including the need for additional medical care that may be required.
2.7.5. Provide the subject with well-defined procedures for possible emergency situations related to the clinical investigation, and make the necessary arrangements for emergency treatment, including decoding procedures for blinded/masked clinical investigations, as needed.
2.7.6. Ensure that clinical records are clearly marked to indicate that the subject is enrolled in a particular clinical investigation.
2.7.7. If appropriate, subjects enrolled in the clinical investigation shall be provided with some means of showing their participation in the clinical investigation, together

with identification and compliance information for concomitant treatment measures (contact address and telephone numbers shall be provided).

2.7.8. Inform, with the subject's approval or when required by national regulations, the subject's personal physician about the subject's participation in the clinical investigation.

2.7.9. Make all reasonable efforts to ascertain the reason(s) for a subject's premature withdrawal from the clinical investigation while fully respecting the subject's rights.

2.8. Safety reporting: The principal investigator shall

2.8.1. Record every adverse event and observed device deficiency, together with an assessment.

2.8.2. Report to the sponsor, without unjustified delay, all serious adverse events and device deficiencies that could have led to a serious adverse device effect; this information shall be promptly followed by detailed

2.8.3. Written reports, as specified in the clinical investigational plan.

2.8.4. Report to the IRB serious adverse events and device deficiencies that could have led to a serious adverse device effect, if required by the national regulations or clinical investigational plan or by the IRB.

2.8.5. Report to regulatory authorities serious adverse events and device deficiencies that could have led to a serious adverse device effect, as required by the national regulations.

2.8.6. \supply the sponsor, upon sponsor's request, with any additional information related to the safety reporting of a particular event.

3. REFERENCES

3.1. ISO 14155 Clinical investigation of medical devices for human subjects — Good clinical practice