

## MEDVANCE FACT SHEET No 1 **EN ISO 14155:2003 Part 1&2**

### **What is EN ISO 14155?**

Guidance for conducting medical device clinical investigations to the required **standard** to meet global national regulations.

### **When should EN ISO 14155 be used?**

This standard should be used to support the medical device directives **MDD93/42/EEC** and **AIMDD 90/385/EEC**. Not IVDD98/79/EEC.

### **Format of EN ISO 14155**

EN ISO14155 currently consists of two parts: EN ISO14155-1:2003 Part 1: General Requirements and EN ISO14155-2:2003 Part 2: Clinical Investigation Plans. The format however is being revised for publication in 2009.

### **Part 1: General Requirements**

Part 1 of EN ISO 14155 defines the procedures for the conduct of clinical investigations with special reference to the protection of human subjects, ensuring scientific conduct of the clinical investigation and assisting sponsors, monitors, investigators, Research Ethics Committees and Regulatory Authorities involved in conformity assessment of devices. In order to determine the **justification** and **optimal design** for a clinical investigation, an objective **literature review** of published and available unpublished medical and scientific data and information should be conducted. This should also include **risk / benefit analysis**. The following **ethical considerations** are required:

- The clinical investigation should be carried out in accordance with the principles of the Declaration of Helsinki.
- The Sponsor and Investigator must avoid improper influence or inducement of subject, monitor or other parties.
- Provision for compensation and continuing health care to patients should be included.
- All parties involved share the responsibility for the ethical conduct of the clinical investigation.

**Agreements** should be in writing and signed by all participants. All parties must be **qualified** for their role in the investigation. A **clinical investigation plan**, designed to obtain **clinically relevant data** with **scientific validity**, is written as outlined in EN ISO 14155-2.

**Confidentiality** shall be observed and preserved by all parties, and any information which identifies patients shall be stored separately from the case report forms (CRFs).

All patients must sign an **informed consent** form before any study related procedures take place. This process must avoid any coercion, not waive the patient's legal rights, use non-technical language and the patient must be given a reasonable time to consider participation.

**Documents** and **data** should be produced and maintained in a way which assures control of documents and data and protect subject's privacy. All **subjects** enrolled **must be accounted for** and documented including those withdrawn or lost to follow-up. **Investigators** have a right to **preclinical information**. **Monitors** should have access to **source documents** and other information to ensure compliance and assess progress of the clinical investigation. The Investigator shall allow **auditing** of their clinical investigation procedures. A **Clinical Investigation Brochure** should be compiled to include information on: the description of the medical device, safety data, pre-clinical scientific data, method of manufacture and manufacturers details. This should be updated as new information becomes available. A **Clinical Investigation File** must be compiled before the start of a clinical investigation to contain relevant documentation. The minimum documents required are as follows:

- Clinical Investigation Plan / Protocol
- Signed and dated CV of Investigator
- Investigational institution details
- Research Ethics Committee opinion
- Correspondence with authorities
- Agreements
- Certificates of insurance
- Case report forms
- Informed consent and patient information sheet
- Adverse event (AE) and adverse device event (ADE) forms
- Monitor contact details
- Investigator brochure

The **responsibilities** of the **Sponsor, Monitor** and **Investigator** are outlined. The **Sponsor's** responsibilities include:

- Selection of Investigators, institutions and Monitors
- Compiling Clinical Investigation Plan (CIP) and Investigator Brochure (IB)
- Documenting Investigator and Monitor compliance / deviation from CIP

- Informing all Investigators when investigation is terminated
- Ensuring Investigators are fully trained and have appropriate information regarding the device under investigation
- Informing all Investigators on developmental status of the device
- Supplying devices and ensure device accountability and traceability systems
- Reviewing deviations and approve any amendments
- Documenting all amendments and all applicable regulatory requirements through a quality system
- Ensuring all AE's and ADE's are reported and reviewed and reported to the ethics committee
- Informing all Investigators in the study of AE's and ADE's

The **Monitor** should confirm:

- The CIP is adhered to
- CRFs have been completed correctly
- Informed consent has been obtained
- Subject recruitment rate is sufficient
- Facilities and staff are adequate
- AE and ADE procedures are complied with
- Device accountability and traceability
- Withdrawal/non-compliance, by patients, is reported to the Sponsor
- Reviews and reports are forwarded to the Sponsor, regarding any non-compliance or modifications to the CIP

For the purpose of the clinical investigation, the **Investigator** should:

- Be appropriately qualified and experienced
- Thoroughly understand and be practiced on the procedures in the CIP
- Ensure the CIP is followed and document any deviations
- Make any necessary emergency contingency plans to ensure the well being of the patient
- Attempt to recruit sufficient patients
- Ensure the Research Ethics Committee has given a favourable opinion for the clinical investigation and communicate all correspondence to the Sponsor
- Submit any substantial amendments to the Ethics Committee
- Advise the Research Ethics Committees of all ADEs.
- Advise the Sponsor of all AEs and ADEs
- Fully explain the procedure, to the patient, before obtaining informed consent
- Obtain and document informed consent for all patients
- Ensure that any new information is passed on to the patient
- Inform the patient of any early termination of the clinical investigation

- Label patient clinical records declaring their participation in the clinical study
- Take principle responsibility for all clinical investigation documentation
- Ensure data is kept for minimum time as stated in the CIP
- Supervise and assign study related tasks and encourage correct conduct of the clinical investigation
- Ensure all the devices are accounted for

A **final report** should be written, even if the investigation has terminated prematurely. This should be signed by all parties and disseminated to all participating Investigators, and the Research Ethics Committee. The final report should include device name, study methodology, clinical investigation design, deviations, statistical analysis and critical appraisal. No patients should be identifiable. All clinical Investigators should be given the opportunity to comment.

## **Part 2: Clinical Investigational Plans**

Part 2 of EN ISO 14155 provides the requirements for the preparation of the Clinical Investigation Plan (CIP). Required sections include:

- Title and reference number, version/issue number and date
- Names, addresses of professional persons and their institutions
- Name and address of Sponsor
- Monitoring arrangements
- Description of data and quality management
- Synopsis of clinical investigation
- Approval and agreement of CIP
- Identification and description of medical device to be investigated
- Literature review
- Preclinical testing
- Previous clinical experience
- Device risk analysis and risk assessment
- Objectives of the clinical investigation
- Design of the clinical investigation
- Statistical considerations
- Deviations from the CIP
- Amendments to the CIP
- Adverse event and adverse device effects
- Early termination of the investigation
- Case report forms – appendix I outlines the contents of the CRF

EN ISO 14155-2 is intended for Clinical Investigations only. However most of the general structure and advice can be used for Post Marketing Surveillance Studies.