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GOLDEN ISO14155 RULES

for Medical Device Trials

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Rule 4

Ensure Device Application and Trial Equipment are Adequate

The trial sponsor will want to verify that the method of application of the trial device is according to the instructions of use. Certainly with a new device the sponsor will provide written instructions as well as hands-on training facilities. A proctor or instructor might be present during the first case(s).

The trial monitor will want to make sure that any other equipment that needs to be used in the trial (eg. fluoroscopy, Doppler, ultrasound, spirometers, fridges) is adequate. The investigator can use the acronym “SMAC” to check that trial equipment meets requirements.



* **Suitable**

Read the CIP to check that the correct equipment is being used.

* **Maintained**

All equipment should be regularly maintained. Records should be available for inspection by the monitor.

* **Available**

Make sure that equipment is available for use in the trial from start to finish – it may already be overused!

Do not assume that everyone knows how to use a piece of equipment correctly. Training should be given to ensure proper use in the trial.

Summaries of ISO14155 requirements

A clinical investigator's brochure should be prepared by the sponsor. This should describe the device, how it functions and its correct use [3.7 and 7.2, especially c].

The sponsor must ensure that the investigator receives adequate information on the use of the device and any other information requested by the investigator [8.2 g, 10.3 c].

The monitor should check that any equipment being used in the trial is properly maintained and calibrated [9.1 i].

* **Calibrated and checked**

Some instruments require regular calibration to ensure that they perform correctly (eg. spirometers, patient-controlled analgesia equipment). Calibration records should be available for inspection.

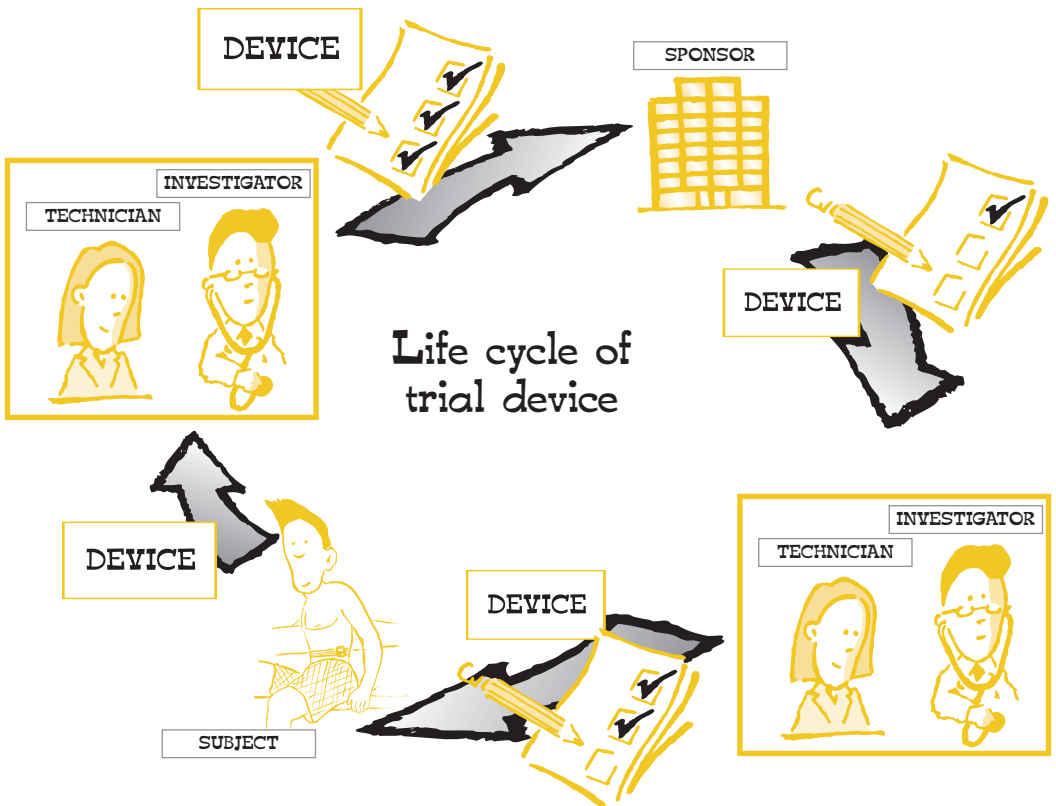


**Equipment
Maintenance
Records**

Rule 7

Document Device Accountability

- Keep detailed records of medical devices:
 - received from the sponsor
 - used for each subject
 - returned from each subject
 - returned to the sponsor.
- Record precisely the number and lot number for devices used with a patient. For ancillary devices, even when these are not studied, it is wise to record their numbers or lot numbers, certainly when they are to be in contact with the device during application or afterwards.



Summaries of ISO14155 requirements

- If the subject has to operate the device him/herself, take time to explain how and when – ensuring good treatment compliance is important in trials.
- Encourage subjects to return both device and unused device pack – this can be used to measure compliance.
- Follow the instructions relating to storage of the medical device.
- Do not destroy or dispose of unused or returned devices – the trial sponsor will advise you what to do.

The investigator must ensure that all devices used in the trial are accounted for [10.3 y].

Devices, as required by the CIP, should be supplied by the sponsor [8.2 f].

The trial monitor should check that the device is being used as per the CIP and in accordance with instructions [9.1 b]. The monitor will also check that the investigator's supply of devices is adequate [9.1 d].

Sponsors should have systems in place to ensure that devices are tracked and accounted for [8.2 o].

Carefully document every transaction.

ISO14155 for Investigators:

Executive Summary

- The ISO14155 Standard has become the principle by which medical device trials should be performed. The ISO14155 is a legal standard in all ISO member states and compliance will be checked by inspections of sponsors, investigators and laboratories. Investigators should therefore work in accordance with this standard.
- Investigators must be properly qualified and have adequate experience to do the trial. An up-to-date CV will be required (usually dated and signed) to allow the sponsor of the trial and Ethics Committee (EC) to confirm suitability. The investigator team must be informed about the test product – the sponsor provides a clinical investigator’s brochure (IB) for this purpose.
- Trial-related duties may be delegated to appropriately qualified and trained staff. CVs will be required for any staff member who sees trial subjects, records data and obtains consent. The principal investigator retains overall responsibility for the trial. A log of trial site personnel must be kept – this should detail who, when and what the person did.
- The investigator must have sufficient time to do the trial (find patients, undertake screening, perform trial, meet with monitor and other sponsor personnel, allow auditing) and have an adequate number of potential subjects. The facilities at the trial site must be adequate and available for the duration of the trial.
- The investigator must set up trial files in which essential documentation is kept. ISO14155 requires a large number of documents to be generated and retained in order to show that the trial is being performed in accordance with ISO14155. Monitors, auditors and inspectors will use the file to evaluate ISO14155 compliance. “Good” investigators will ensure that files contain the correct documentation and are up to date. Access to the trial files needs to be regulated. A trial administrator can be appointed to look after trial files.
- The investigator must ensure that acceptable EC approval is obtained and documented. The EC must “approve” the CIP, consent form, patient information and recruitment procedures. Investigators should also ensure that trial subjects are adequately informed (there are 19 essential items described in ISO 14155-1 part 6.7.3, that need to be discussed verbally and in writing). Consent must be obtained before any trial-related procedures (including screening) are undertaken.
- The investigator must read the trial CIP carefully and agree to work in accordance with it. Sponsors and inspectors deem CIP violation (no matter how trivial) unacceptable. CIPs can only be amended by following established standard operating procedures. The EC needs to approve CIP amendments (unless they are of an administrative nature or needed to eliminate an immediate hazard) before implementation.

Summary of ISO14155 trial-related responsibilities

Sponsor

- Select suitable trial investigator(s) and sites(s).
- Appoint a trial monitor.
- Prepare and update the clinical investigator's brochure.
- Undertake a review of available data to ensure the trial is justified and the design appropriate.
- Prepare a Clinical Investigation Plan (CIP); obtain investigator's input, agree and sign-off approved CIP.
- Provide pre-clinical and clinical information as required by the investigator, including information on the regulatory status of the device.
- Provide suitable investigational product (devices) and ensure that each device is fully accounted for in the trial.
- Discuss with investigator and review deviations from CIP.
- Collect, review and report adverse events and adverse device effects as required.
- Provide investigators and Ethics Committees with information about serious adverse events and device effects.
- Ensure that essential trial documents are produced, completed, collected, stored and archived.
- Inform investigators, regulatory authorities and Ethics Committees if the trial is terminated early and the reason for this.

Monitor

- Make sure that the investigator is following CIP and using the device in accordance with instructions.
- Discuss with investigator and document any deviation from CIP.
- Check that the site has adequate resources (staff, facilities and available subjects) to fulfil its responsibilities before and during the trial.
- Ensure that any equipment used in the trial is maintained and calibrated.
- Check that informed consent is obtained from all subjects before any trial-related procedures are undertaken.
- Check data in the case report forms and ensure their validity by undertaking source data/document verification.
- Check that all adverse events are being properly recorded and reported to the sponsor in accordance with the requirements in the CIP.
- Ensure that all devices used in the trial are being accounted for by the investigator.
- Meet with the investigator to discuss trial progress, including the number of recruited subjects, withdrawals and subject/CIP violations.
- Ensure that all monitoring activities are documented in a report.

Investigator

- Has the time, staff, facilities, subjects and other vital resources to do the study properly.
- Ensure that there is no conflict of interest.
- Obtain from the sponsor the clinical investigator's brochure and any other information required to attain suitable knowledge of the device being investigated to ensure subjects are protected.
- Review and agree the CIP. The investigator should sign the final version.
- Obtain Ethics Committee approval/favourable opinion before starting the study.
- Try hard to recruit the planned number of suitable subjects to the trial.
- Informed consent should be obtained from each subject prior to any trial-related procedures. The investigator should ensure that the subject has received sufficient information (verbally and in writing) and has understood it. Consent should be documented by the investigator's and subject's dated signature.
- Ensure that the clinical records of any subjects taking part in the trial are clearly marked. With the subjects' consent, inform their primary physician of trial participation.
- Follow the CIP and ensure that any staff working on the trial are fully informed about the trial and the relevant requirements. The investigator retains overall responsibility for supervision and assignment of tasks.
- Make sure that all trial data are correctly, accurately and legibly recorded and allow verification of the data by monitors and auditors.
- Ensure that adverse events and adverse device effects are appropriately reported to the sponsor and Ethics Committee.
- Account for all devices used in the trial.
- Make arrangements for the emergency care of trial subjects should the need arise. Provide subjects with contact points and instructions in the event of questions or problems.
- Appropriately inform the sponsor, subject and/or subject's primary physician of any information arising as a result of the trial that may be of importance to the health of the subject.
- Keep trial documents safely and securely for the required amount of time.
- Inform subjects and their physician if the trial is terminated early.
- Review and sign final study report.