Purpose

Monitoring is necessary to assure adequate protection of the rights of human subjects and the safety of all subjects involved in clinical investigations and the quality and integrity of the resulting data submitted.

The objectives the monitoring procedures are:

• To ensure that the study is being carried out in accordance with the approved protocol.
• To identify any problems and suggest / seek solutions.

Overall the monitor should be seen (and behave) as a supportive extension of the study team. They have a professional duty to be impartial and their role is to ‘monitor’, and NOT audit. Therefore, the monitor should not be perceived as an outside threat but part of the team and there to identify any problems affecting the conduct and quality of data collected.

The purpose of this Standard Operating Procedure (SOP) is to describe the standard procedures to be followed in a monitoring plan related to clinical research conducted in the 2nd Department of Internal Medicine, University Hospital of Ioannina, Greece.

Scope

This SOP is applicable to the Principal Investigator (PI), study management group, the monitors and all other research team members at 2nd Department of Internal Medicine, University Hospital of Ioannina, Greece.

Definitions

1. 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.

2. Essential Documents

Essential documents are those documents that individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. Essential
documents include the Trial Master File, source documents and Case Report Forms (CRFs).

3. Monitoring
The act of overseeing the progress of a clinical study, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, SOPs, Good Clinical Practice (GCP), and the applicable regulatory requirement(s).

4. Investigator Site file (ISF)
The repository for the essential documents for the conduct of a clinical trial. These documents individually and collectively permit evaluation of the conduct of the study and the quality of the data produced. These documents demonstrate the compliance of the sponsor-investigator and of the monitor with standards of GCP and with all applicable regulatory requirements.

5. Principal Investigator (PI)
The person responsible to the sponsor for the conduct of the clinical trial at the clinical trial site, who is entitled to provide health care under the laws of the province where that clinical trial site is located, and who is

   a. in the case of a clinical trial respecting a drug to be used for dental purposes only; a physician or dentist and a member of good standing of a professional medical or dental association; and

   b. in any other case, a physician and a member of good standing of a professional medical association.

6. Sub-investigator
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).

7. Clinical Research Associates (CRAs)
Part of the sponsor team who ensure compliance with the Regulations, GCP, SOPs and the protocol of the clinical trial, by monitoring clinical trials.

8. Case Report Forms (CRFs)
A printed, optical or electronic document designed to record all of the protocol required information on each trial subject.
Responsibility

Description of study monitoring arrangement…… e.g. The CRA will be responsible for conducting trial monitoring. The CRA will appoint an appropriately qualified person(s) to monitor the trial (a sub-investigator or the PI). The monitor(s) will be trained on the study protocol and will be familiar with all study procedures.

Site monitoring schedule

Ordinarily, a pre study, initiation, routine and close out monitoring are planned and conducted in the life span of a study. The site initiation visit will be conducted as soon as:

- All the necessary approvals have been obtained
- Staff recruited
- Investigational product has been delivered to site (is about to be delivered to site)
- CRF and source documents are ready
- Laboratory is ready to start storing study samples

The first routine monitoring visit will occur as soon as the first participant is recruited or within 2 weeks of the first participant being recruited. The table below provides an estimate of what will be needed in terms of time on site for the monitor. This needs to be continually assessed by the study management team and the monitors. The monitoring frequency may need to increase if recruitment is faster than predicted, at times of data entry deadlines (such as interim analysis or if the DSMB request a safety report) then two or more people can attend the visit.
Procedure

Monitoring will focus on the following key processes of the study so as to ensure protection of rights and well-being of study participants and integrity of data:

1. Informed consent process.
2. Study eligibility criteria met for all participants.
3. Timely completion of Study CRFs.
4. Accurate abstraction of data from clinical and laboratory forms.
5. Sample collection and handling in accordance to Protocol and SOP(s).
6. Review of data management procedure i.e. data entry, handling of data discrepancies and data backup.
7. Reporting of adverse events and protocols violations according to SOP(s).
8. Drug accountability.
9. Follow up assessments and procedures.
10. Measures to ensure complete participant follow up.

For each site visit the monitor will work according to an agreed schedule of tasks, including the following that will be given as specifics in the monitoring form and guidelines:
MONITORING PLAN

- Schedule a date with the study investigator for the monitoring procedure and provide them with a list or shell of the study sections that will be monitored in this particular visit.

- Review last monitoring procedure report.

- Review the Site study File: ensuring that it is updated appropriately.

- Verify written informed consents were given for every subject entered into the study and obtained according to the consent SOP.

- Review current status of the study’s participant enrolment vs. anticipated enrolment, losses to follow up, outstanding data issues, reported serious adverse events, outstanding laboratory issues.

- Review the study forms and database ensuring that the participants were eligible and note any safety issues and protocol violations or deviations.

- Review laboratory issues: Handling, storage and shipment of samples.

- Source data verification - abstraction of data from clinical and laboratory forms.

During the initial visits the monitors will review 100% of the fields of all the study forms. Subsequently the monitors will review 100% data contributing to the primary endpoint and 100% of fields for a randomly selected sample of study forms. All forms monitored during a visit will be detailed in the monitoring visit report. A data base check for accuracy of data entry will be performed at regular intervals. The data points to be checked will be end point data and safety data.

After each monitoring visit the monitor will debrief the study team i.e. praise them where they are getting it right and highlight areas which need improvement. The monitor will then write up a
monitoring report citing all findings and status of such findings (resolved or not) and forward a signed copy to the sponsor and/or sponsor appointed project manager. The monitoring report may be shared with the Principal investigator.

At close out visit(s) the monitor will ensure all queries are resolved; the study product is accounted for and returned or destroyed according to sponsor SOP; and study documents are properly archived. The comprehensive list of activities during this visit(s) will be detailed in a study close out SOP.

References

Health Canada Good Clinical Practice (GCP) – ICH: International Conference on Harmonisation (E6)

EU Directive 2001/20/EC
EU Directive 2005/28/EC


07. Oct. 2004 National Ethics Committee Composition & Operating procedures Official Governments’ Gazette (FEK) 1503


Associated Documents

None
SOP Revision History

<table>
<thead>
<tr>
<th>Revision No.</th>
<th>Revision Date</th>
<th>Description of Change</th>
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<tr>
<td>01</td>
<td>25 JAN 2014</td>
<td>New SOP</td>
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Signatories

Prepared by: Dr Fotios Barkas MD  
Print Name

Date: 25 JAN 2015  
DD MMM YYYY

Signature:  
Title: Subinvestigator

Time: 10:00  
24 hr clock

Approved by: Dr Evangelos Liberopoulos MD  
Print Name

Date: 25 JAN 2015  
DD MMM YYYY

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Time: 13:00  
24 hr clock

Add more approvers as required.
Three-year Review

(To be completed only if the SOP has reached the three year timeline for revision)

Reviewed by: ___________________________ Date: ____________

Print Name ___________________________________ DD MMM YYYY

Signature: ___________________________

Time: ___________________________

Title: ___________________________

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