Chapter 19
Monitoring the Trial

19.1 Purpose

'The purposes of trial monitoring are to verify that':

(a) 'The rights and well being of human subjects are protected'.

(b) 'The reported trial data are accurate, complete, and verifiable from source documents'.

(c) 'The conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with applicable regulatory requirement(s) [1–3]'.

19.2 Selection and Qualifications of Monitors

(a) 'Monitors should be appointed by the sponsor'.

(b) 'Monitors should be appropriately trained, and should have the scientific and/or clinical knowledge needed to monitor the trial adequately. A monitor's qualifications should be documented'.

C. Cingi, N. Bayar Muluk, *Quick Guide to Good Clinical Practice*,
DOI 10.1007/978-3-319-44344-7_19,

(c) 'Monitors should be thoroughly familiar with the investigational product(s), the protocol, written ICF and any other written information to be provided to subjects, the sponsor's SOPs, GCP, and the applicable regulatory requirement(s) [1–3]'.

19.3 Extent and Nature of Monitoring

'The sponsor should ensure that trials are adequately monitored. The sponsor should determine the appropriate extent and nature of monitoring. The determination of the extent and nature of monitoring should be based on considerations such as the objective, purpose, design, complexity, blinding, size, and endpoints of the trial. In general, there is a need for on-site monitoring before, during, and after the trial; however, in exceptional circumstances, the sponsor may determine that central monitoring in conjunction with procedures such as investigators' training and meetings, and extensive written guidance, can assure appropriate conduct of the trial in accordance with GCP. Statistically controlled sampling may be an acceptable method for selecting the data to be verified [1–3]'.

19.4 Monitor's Responsibilities

'The monitor(s), in accordance with the sponsor's requirements, should ensure that the trial is conducted and documented properly by carrying out the following activities when relevant and necessary to the trial and the trial site':

1. 'Acting as the main line of communication between the sponsor and the investigator'.

2. 'Verifying that the investigator has adequate qualifications and resources (and that these remain adequate throughout the trial period, and that the staff and facilities, including laboratories and equipment, are adequate to safely and properly conduct the trial and that they remain adequate throughout the trial period)'.
3. 'Verifying, for the investigational product(s)':
   (a) 'That storage times and conditions are acceptable, and that supplies are sufficient throughout the trial'.
   (b) 'That the investigational product(s) is supplied only to subjects who are eligible to receive it and at the protocol-specified dose(s)'.
   (c) 'That subjects are provided with necessary instruction on properly using, handling, storing, and returning the investigational product(s)'.
   (d) 'That the receipt, use, and return of the investigational product(s) at the trial sites are controlled and documented adequately'.
   (e) 'That the disposition of unused investigational product(s) at the trial sites complies with applicable regulatory requirement(s) and is in accordance with the sponsor's authorised procedures'.
4. 'Verifying that the investigator follows the approved protocol and all approved amendment(s), if any'.
5. 'Verifying that written informed consent was obtained before each subject's participation in the trial'.
6. 'Ensuring that the investigator receives the current IB, all documents, and all trial supplies needed to conduct the trial properly and to comply with the applicable regulatory requirement(s)'.
7. 'Ensuring that the investigator and the investigator's trial staff are adequately informed about the trial'.

8. ‘Verifying that the investigator and the investigator’s trial staff are performing the specified trial functions, in accordance with the protocol and any other written agreement between the sponsor and the investigator/institution, and have not delegated these functions to unauthorised individuals’.
9. ‘Verifying that the investigator is enrolling only eligible subjects’.
10. ‘Reporting the subject recruitment rate’.
11. ‘Verifying that source data/documents and other trial records are accurate, complete, kept up-to-date, and maintained’.
12. ‘Verifying that the investigator provides all the required reports, notifications, applications, and submissions, and that these documents are accurate, complete, timely, legible, dated, and identify the trial’.
13. ‘Checking the accuracy and completeness of CRF entries, source data/documents, and other trial-related records against each other. The monitor, specifically, should verify that’:

    (a) ‘The data required by the protocol are reported accurately on CRFs and are consistent with the source data/documents’.
    (b) ‘Any dose and/or therapy modifications are well documented for each of the trial subjects’.
    (c) ‘Adverse events, concomitant medications, and intercurrent illnesses are reported in accordance with the protocol on the CRFs’.
    (d) ‘Visits that the subjects fail to make, tests that are not conducted, and examinations that are not performed are clearly reported as such on the CRFs’.
    (e) ‘All withdrawals and dropouts of enrolled subjects from the trial are reported and explained on the CRFs’.

14. ‘Informing the investigator of any CRF entry error, omission, or illegibility. The monitor should ensure that appro-

priate corrections, additions, or deletions are made, dated, explained (if necessary), and initialled by the investigator or by a member of the investigator's trial staff who is authorised to initial CRF changes for the investigator. This authorisation should be documented'.

15. 'Determining whether all AEs are appropriately reported within the time periods required by GCP, the ICH Guidance for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting, the protocol, the IRB/IEC, the sponsor, and the applicable regulatory requirement(s)'.
16. 'Determining whether the investigator is maintaining the essential documents'
17. 'Communicating deviations from the protocol, SOPs, GCP, and the applicable regulatory requirements to the investigator and taking appropriate action designed to prevent recurrence of the detected deviations [1–3]'.

19.5 Monitoring Procedures

'The monitor(s) should follow the sponsor's established written SOPs as well as the procedures that are specified by the sponsor for monitoring a specific trial [1–3]'.

19.6 Monitoring Report

(a) 'The monitor should submit a written report to the sponsor after each trial-site visit or trial-related communication'.
(b) 'Reports should include the date, site, name of the monitor, and name of the investigator or other individual(s) contacted'.
(c) 'Reports should include a summary of what the monitor reviewed and the monitor's statements concerning the sig-

nificant findings/facts, deviations and deficiencies, conclusions, actions taken or to be taken, and/or actions recommended to secure compliance'.

(d) 'The review and follow-up of the monitoring report by the sponsor should be documented by the sponsor's designated representative [1–3]'.

References

1. Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER). ICH, Apr 1996.
2. Hutchinson D. The trial investigator's GCP handbook: a practical guide to ICH requirements. Brookwood Medical Publications Ltd. Surrey, UK, 1997.
3. Committee: ICHS: ICH Harmonised Tripartite Guideline for Good Clinical Practice. Second publication, Brookwood Medical Publications Ltd.; Richmond, Surrey, UK, 1997.