

## Tip Sheet 11: Following the Guideline of the International Conference on Harmonization – Good Clinical Practice (E6)

### Related Accreditation Elements: I.1.D., I.1.F., I-2, I.7.B., II.2.E., II.2.F., II.4.A., II.4.C., III.1.C., III.1.E., III.1.F., and III.2.A.

ICH-GCP is an ethical and scientific quality guidance document that is used internationally in the conduct of clinical trials. It includes areas for designing, conducting, recording and reporting research that involve the participation of human participants. The guidance has its origins in the Declaration of Helsinki and was developed with consideration of the current good clinical practices of the European Union, Japan, and the United States, as well as those of Australia, Canada, the Nordic countries and the World Health Organization (WHO).

In addition to general principles of good clinical practice, the document has sections for the Institutional Review Board (IRB or EC) or Independent Ethics Committee (EC), Researcher, and Sponsor. All of these sections have requirements that are unique to this guideline and above those required by following the DHHS and FDA regulations. AAHRPP has identified those unique ICH-GCP (E6) requirements and have included them in its Standards for those organizations that follow ICH-GCP (E6).

### Recommended Content:

*Policies and procedures should describe the extent to which ICH-GCP is followed:*

1. ICH-GCP (E6) is applied to all research conducted by the organization or limited to certain types of research (e.g., international clinical trials).
2. All requirements of ICH-GCP (E6) are followed or limited to certain areas (e.g. IRB/IEC section only).
3. Sponsors that require ICH-GCP (E6) be followed, should be notified to what extent the organization follows ICH-GCP (E6). If there is a contract or funding agreement that requires ICH-GCP (E6) be followed, the contract should include the extent or limit that the organization follows ICH-GCP (E6).
4. Indicate how IRB or EC chairs, vice-chairs, IRB or EC members, IRB or EC staff, and Researchers and Research Staff are educated about ICH-GCP (E6) requirements and to which research ICH-GCP (E6) is applied.
5. The items below are those that are not found in the DHHS or FDA regulations and represent additional requirements to the DHHS and FDA regulations.

*ICH-GCP requirements to be included in policies and procedures:*

1. Policies and procedures include a statement that clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with GCP and the applicable regulatory requirements. (AAHRPP Element I.1.D.; ICH-GCP 2.1)
2. Policies and procedures include the evaluation of the available nonclinical and clinical information on an investigational product is adequate to support the proposed clinical trial. (AAHRPP Element I.1.F.; ICH-GCP 2.4)
3. Clinical trials are scientifically sound and describe in a clear, detailed protocol. (AAHRPP Element I.1.F.; ICH-GCP 2.5)
4. The Organization provides (or assures) for each research study the resources necessary to protect participants including: (AAHRPP Element I-2; ICH-GCP 4.2.3)
  - a. Adequate numbers of qualified staff.
  - b. Adequate facilities.
5. Where allowed or required, the Researcher may assign some or all duties for investigational articles accountability at the trial sites to an appropriate pharmacist or another appropriate individual who is under the supervision of the Researcher. (AAHRPP Element I.7.B.; ICH-GCP 4.6.2)
6. The Researcher, pharmacist, or other designated individual will maintain records of the product's delivery to the trial site, the inventory at the site, the use by each participant, and the return to the sponsor or alternative disposition of unused products. These records will include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational products and trial participants. Researchers should maintain records that document adequately that the participants are provided the doses specified by the protocol and reconcile all investigational products received from the sponsor. (AAHRPP Element I.7.B.; ICH-GCP 4.6.3)
7. The reviewer is provided and reviews the Researcher's current curriculum vitae or other documentation evidencing qualifications. (AAHRPP Element II.2.E.; ICH-GCP 3.1.2)
8. Policies and procedures define the problems Researchers have to report to the IRB or EC to include: (AAHRPP Element II.2.F.; ICH-GCP 3.3.8)
  - a. New information that may affect adversely the safety of the participants or the conduct of the clinical trial.
  - b. Any changes significantly affecting the conduct of the clinical trial or increasing the risk to participants.
9. For ICH-GCP consent disclosure includes: (AAHRPP Element II.3.F.; ICH-GCP 4.8.10)
  - a. For alternative procedures or treatment that may be available to the participant, include their important potential benefits and risks.

- b. That the monitor, the auditor, the IRB or EC, and the regulatory authority will be granted direct access to the participant's original medical records for verification of clinical trial procedures or data, without violating the confidentiality of the participant, to the extent permitted by the applicable laws and regulations and that, by signing a written consent form, the participant or the participant's legally acceptable representative is authorizing such access.
  - c. The approval of the IRB or EC.
10. When adults are unable to consent, policies and procedures have the IRB or EC determine: (AAHRPP Element II.4.A.; ICH-GCP 4.8.14)
- a. A non-therapeutic clinical trial (i.e. a trial in which there is no anticipated direct clinical benefit to the participant) should be conducted in participants who personally give consent and who sign and date the written consent document.
  - b. Non-therapeutic clinical trials may be conducted in participants with consent of a legally acceptable representative provided the following conditions are fulfilled:
    - i. The objectives of the clinical trial cannot be met by means of a trial in participants who can give consent personally.
    - ii. The foreseeable risks to the participants are low.
    - iii. The negative impact on the participant's wellbeing is minimized and low.
    - iv. The clinical trial is not prohibited by law.
    - v. The opinion of the IRB or EC is expressly sought on the inclusion of such participants, and the written opinion covers this aspect.
    - vi. Such trials, unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. Participants in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.
11. Policies and procedures require that the participant or the participant's legally authorized representative is informed about the clinical trial as soon as possible and provides consent if the participant wishes to continue. (AAHRPP Element II.4.C.; ICH-GCP 4.8.12)

The following requirements are those of Researchers. Policies and procedures must contain the following Researcher responsibilities in a form accessible or provided to Researchers.

- 12. A qualified physician (or dentist, when appropriate), who is an Researcher or a Co-Researcher for the clinical trial, is responsible for all clinical trial-related medical (or dental) decisions. [Does not apply to independent IRB or ECs] (AAHRPP Element III.1.C.; ICH-GCP 4.3.1)
- 13. During and following a participant's participation in a clinical trial, the Researcher ensures that adequate medical care is provided to a participant for any adverse events, including clinically significant laboratory values, related to the clinical trial. [Does not apply to independent IRB or ECs] (AAHRPP Element III.1.C.; ICH-GCP 4.3.2)
- 14. Researchers inform participants when medical care is needed for other illnesses of which

- the Researchers become aware. [Does not apply to independent IRB or ECs] (AAHRPP Element III.1.C.; ICH-GCP 4.3.2)
15. The Researcher follows the clinical trial's randomization procedures, if any, and ensures that the code is broken only in accordance with the protocol. If the clinical trial is blinded, the Researcher promptly documents and explains to the Sponsor any premature unblinding. [Does not apply to independent IRB or ECs] (AAHRPP Element III.1.C.; ICH-GCP 4.7)
  16. The Researcher informs the participant's primary physician about the participant's participation in the clinical trial if the participant has a primary physician and if the participant agrees to the primary physician being informed. [Does not apply to independent IRB or ECs] (AAHRPP Element III.1.E.; ICH-GCP 4.3.3)
  17. Although a participant is not obliged to give his or her reasons for withdrawing prematurely from a clinical trial, the Researcher makes a reasonable effort to ascertain the reason, while fully respecting the participant's rights. (AAHRPP Element III.1.E.; ICH-GCP 4.3.4)
  18. Policies and procedures describe that Researchers and Research Staff provide all the disclosures and follow the requirements pertaining to consent covered by ICH-GCP. (AAHRPP Element III.1.F.; ICH-GCP 4.8)
  19. The Researcher provides evidence of his or her qualifications through up-to-date curriculum vitae or other relevant documentation requested by the Sponsor, the IRB or EC, or the regulatory authority. (AAHRPP Element III.2.A.; ICH-GCP 4.1.1)
  20. The Researcher is familiar with the appropriate use of the investigational product, as described in the protocol, in the current Researcher brochure, in the product information, and in other information sources provided by the Sponsor. (AAHRPP Element III.2.A.; ICH-GCP 4.1.2)
  21. The Researcher permits monitoring and auditing by the Sponsor and inspection by the appropriate regulatory authority. [Does not apply to independent IRB or ECs or if FDA regulations are followed] (AAHRPP Element III.2.A.; ICH-GCP 4.1.4)
  22. The Researcher ensures the accuracy, completeness, legibility, and timeliness of the data reported to the Sponsor. [Does not apply to independent IRB or ECs] (AAHRPP Element III.2.A.; ICH-GCP 4.9.1)
  23. The Researcher maintains the clinical trial documents as specified in Essential Documents for the Conduct of a Clinical Trial and as required by the applicable regulatory requirements. [Does not apply to independent IRB or ECs or if FDA regulations are followed] (AAHRPP Element III.2.A.; ICH-GCP 4.9.4)
  24. Essential documents are retained until at least two years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least two years have elapsed since the formal discontinuation of clinical development of the investigational product. [Does not apply to independent IRB or ECs or if FDA regulations are followed] (AAHRPP Element

III.2.A.; ICH-GCP 4.9.5)

25. The Researcher must maintain a list of appropriately qualified persons to whom they have delegated significant clinical trial-related duties. [Does not apply if FDA regulations are followed] (AAHRPP Element III.2.B.; ICH-GCP 4.1.5)
26. The Researcher reports all serious adverse events (SAEs) to the Sponsor except for those SAEs that the protocol or other document (e.g., Researcher's brochure) identifies as not needing immediate reporting. The Researcher follows regulatory requirements related to the reporting of unexpected serious adverse drug reactions to the regulatory authority and the IRB or EC. (AAHRPP Element III.2.D.; ICH-GCP 4.11.1)
27. The Researcher reports adverse events or laboratory abnormalities identified in the protocol as critical to safety evaluations to the Sponsor according to the reporting requirements and within the time periods specified by the Sponsor in the protocol. [Does not apply to independent IRB or ECs or if FDA regulations are followed] (AAHRPP Element III.2.D.; ICH-GCP 4.11.2)
28. For reported deaths, the Researcher supplies the Sponsor and the IRB or EC with any additional requested information (e.g., autopsy reports and terminal medical reports). [Does not apply if FDA regulations are followed] (AAHRPP Element III.2.D.; ICH-GCP 4.11.3)
29. The Researcher provides written reports to the Sponsor, the IRB or EC, and, where applicable, the Organization on any changes significantly affecting the conduct of the clinical trial or increasing the risk to participants. (AAHRPP Element III.2.D.; ICH-GCP 4.10.2)
30. If the Researcher terminates or suspends a clinical trial without prior agreement of the Sponsor, the Researcher informs the Organization, Sponsor, and the IRB or EC. (AAHRPP Element III.2.D.; ICH-GCP 4.12.1)
31. If the IRB or EC terminates or suspends approval of the clinical trial, the Researcher promptly notifies the Sponsor. (AAHRPP Element III.2.D.; ICH-GCP 4.12.3)
32. Upon completion of the clinical trial, the Researcher informs the Organization; the IRB or EC with a summary of the trial's outcome; and the regulatory authority with any reports required. (AAHRPP Element III.2.D.; ICH-GCP 4.13)