Good Clinical Practice (GCP)
Basic Information for Researchers

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What is Good Clinical Practice, GCP? GCP is an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects. Compliance with GCP assures that the rights, safety, and well-being of trial subject are protected; consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trail data are credible.

"The Good Clinical Practice: Consolidated Guidance" was issued by DHHS, FDA, CDER, and CBER in April 1996 and became effective in May 1997

Statement from DHHS: The Good Clinical Practice Guidance should be followed when generating clinical trial data that are intended to be submitted to regulatory authorities.

1. The first basic principle of Good Clinical Practice is the protection of the patient/subject/volunteer.

2. The second basic principle is that the data obtained are correct and reproducible.

The GCP guidance document is broken down into eight sections.
The eight sections are:

1. Glossary
2. The Principles of GCP
3. The IRB
4. The Investigator
5. The Sponsor
6. The Trial & Protocol
7. Investigator's Brochure

Section 8 of the guidelines deals with Record Management – Essential documents for the conduct of a Clinical Trial:

8.1 Essential documents

- Permit the evaluation of the conduct of a trial and the quality of the data produced.
- Serve to demonstrate the compliance of the investigator with the standards of GCP and all regulatory requirements.
- Confirm validity of the trial data

8.2 Before the trial commences all the documents required for the trial should be compiled into a Regulatory Binder.

- IRB Approved Protocol (retain all communication)
- Approved and stamped Informed Consent (retain original to make copies)

- Advertisements to be used for recruitment
- Financial agreements, contracts and/or other agreements
- Regulatory authority authorization/approval (retain all pertinent communication)
- CV's of investigators
- Certification of mandatory human subject protection training for PI and staff

And also, if applicable:

- Investigator's Brochure, IB
- Case Report forms (CRFs)
- Normal lab values and/or tests included in the protocol
- Certification, accreditation or validation of labs/facility/procedures/tests
- Sample of label for device
- Instructions for handling product and trial related material if not in IB
- Shipping records of products for trial
- Decoding procedures for blinded trials and master randomization list
- Pre-trial monitoring report and trial initiation monitoring report

8.3 The following documents should be added as they become required:

- Any revisions to Protocol, CRFs, Informed Consent, Ads, etc
- Correspondence with IRB, updated ICF, Continuing Review
- Notification to Regulatory Authorities re any revisions to above
- Updates to Investigator's Brochure, IB
- CV of investigators, update every 2-3 years at least, add any new people
- Updates to normal lab values, procedures, etc
- Updates to any lab/medical/technical certifications, accreditations, QA or validations
- Certificates of analysis for any new batches of investigational products
- Monitoring visit reports. If monitor identifies issues such as deviations or AEs reports should be sent to sponsor and IRB Communications, i.e., AE reports, deviation reports, letters, meeting minutes, notes of telephone calls
- Source documents
- Certification of any new staff regarding mandatory Human Subject Protection training as well as HIPAA for Research training
- Signed, dated and completed case report forms, CRFs. If electronic records perform routine QA on study including CRFs and have PI or study coordinator sign report
- Documentation of corrections to CRFs. If CRFs are electronic records and changes need to be made archive old record, make changes and save as new. Write up note to file explaining correction and have PI or study coordinator sign and date.
- Notification of PI to sponsor of AEs, Deviation reports, letters/notes from IRB
- Notification by sponsor and/or PI to regulatory authorities and IRB of unanticipated problems involving risk to subjects or others, reportable adverse events (SAEs) and/or any other safety information
- Notification by sponsor to PI of safety information
- Interim or annual reports to IRB, sponsor, Regulatory authority
- Subject Screening log

- Subject ID code list
- Subject enrollment log
- Investigational product accountability at site
- Staff Signature log
- Record of any retained body fluids/tissue samples if applicable

8.4 After Completion or termination of the trial, all the documents in Section 8.2 and 8.3 should be in the file together with the following

- Investigational Product accountability
- Documentation of investigational product destruction
- Completed subject ID code list
- Audit certificate, if required
- Final trial close-out monitoring report
- Treatment allocation and decoding documentation
- Final report by PI/Institution to IRB where required and if applicable, to Regulatory authority
- Clinical study report

Q & A on GCP

Q	What are source documents? And, what are Case Report Forms (CRFs)?
A	Source documents are original documents, data, and records. They can exist prior to the study such as medical records or lab results, etc. Or, they can be created during a study such as your subject completes a survey. CRFs are printed, optical or electronic documents designed to record all of the protocol-required information of each trial subject
Q	When you view an electronic medical record and then transfer study data to an electronic record do you still have a source document and a case report form?
A	Yes, the electronic medical record remains the source document, electronic or otherwise, and the electronic record where study data was transferred to becomes the case report form, CRF, albeit an electronic CRF. Keep in mind the term case report form, CRF, is only a term. You can call these records your study data records or whatever you want to call them. **See ICH GCP 4.9.2.**
Q	When you make corrections on a CRF, or electronic study data file, do you need to save those changes?
A	Yes, GCP states you should document any CRF corrections, **see ICH GCP 8.3.15**. You should make note that you changed something on your study file. There are several ways you can do this. You can archive your old study file and save the edited version as the new file. Or, you can print out the old file, save the new edited file and delete the old. Keep the copy of the old data and write a note to file as to what you changed and why. You must have the PI or designee sign this paper copy.
Q	How do you sign and date CRF's that are electronic files?

A	GCP's state you should sign and date CRFs, **see ICH GCP 8.3.14**. The key to this requirement is making sure the data is correct. In other words are you capturing the data your protocol state(s) you want to capture? This checking of CRFs targets principle 2 - your data are credible and accurate. To that end you can do a QA on the electronic CRFs (study data) and then have an appropriate person check the data. Not just that the data fields are filled but do the fields have the data you are looking for. IF this is in a report then you should save these reports with the study file and have either the PI or designee sign and date the report.
Q	Why would we need a staff signature sheet when we only have electronic records?
A	The staff signature log is used to verify the signature of research staff who obtain informed consent (sign the ICF) or who enter data into the study file. QA reports should be completed to verify the accuracy and completeness of electronic records. QA reports should be reviewed by the PI or study coordinator. Once reviewed they should be signed and dated. A signature sheet documents signatures and initials of all persons authorized to obtain informed consent or make entries and/or corrections on CRFs. **See ICH GCP 8.3.24**. Any notes to file that explain changes to electronic CRF or any other documents should be signed and dated by PI.
Q	If my study requires subjects to purchase a product over the counter for the study would this involve the FDA?
A	Yes, the FDA reserves the right to regulate any clinical investigation of a product regulated by the FDA. This includes foods, dietary supplements that bear a nutrient content claim or health claim, infant formulas, food and color additives, drugs for human use, medical devices and electronic products. **See CFR21§50.1.** The definition of Clinical Investigation can be found at **21CFR§50.3(25)(c)**. This definition states: Clinical investigation means any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the FDA or is not subject to requirements for prior submission to the FDA but the results of which are intended to be submitted later to, or held for inspection by the FDA as part of an application for a research or marketing permit. (The reason the FDA reserves the right to regulate **any** clinical investigation is there is always the possibility the manufacturer of the product may want to make a marketing claim after a clinical investigation even if that was not the initial intent. If the trial is held to the standards of GCP the data would be credible for such a submission to the FDA).

Have a Question about GCP? Contact Jacqui Poore Research Compliance Program Administrator at (401)444-5843 or JPoore@lifespan.org

Links to Additional Information

FDA Regulations relating to CGP and Clinical Trials
http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/default.htm

Good Clinical Practice
http://ichgcp.net/