SOP #	CRSC-105
Effective Date	10-22-2013
Version #	1
Version Date	7-30-2013

Standard Operating Procedures
Guidelines for Good Clinical Practice

Purpose:

This SOP outlines the steps required to follow FDA and GCP Guidelines.

Procedure

A. General Regulatory Information

1. Regulations and Guidelines that Apply to Clinical Research Using FDA Regulated Drugs or Biologics
   a. U.S. Code of Federal Regulations (21 CFR)
   b. ICH E6 Good Clinical Practice (GCP) Guidelines
   c. Applicable State Laws
   d. FDA Guidance documents
2. PIs are required to follow the U.S. Code of Federal Regulations
   a. 21 CFR 11: Electronic Records and Signature
   b. 21 CFR 50: Informed Consent
   c. 21 CFR 54: Financial Disclosures
   d. 21 CFR 56: Institutional Review Board (IRB)
   e. 21 CFR 312: Investigational New Drug (IND)
   f. 21 CFR 812: Investigational Device Exemptions (IDE)
3. U.S. Code of Federal Regulations must be followed at a minimum
4. Many sponsors require that GCP guidelines be followed in addition to FDA regulations since many studies are done internationally. PIs should verify this with their sponsor.
5. All studies involving a clinical investigation of a drug or biologic under FDA purview must have a FDA Form 1572 completed.
6. Clinical Trial agreements with sponsors are negotiated with Grants and Contracts.
7. All aspects of a clinical investigation must be reported to the IRB, sponsor and/or the lead site.
8. If the holder of an IND/IDE is the sponsor-investigator, he/she is accountable for all responsibilities of both the sponsor and the investigator.

B. Study Conduct

9. The PI is responsible for protecting the rights, safety, and welfare of participants.
10. The investigation cannot be started until it has received final IRB approval and must be scientifically sound and described in a clear, detailed protocol.

11. The informed consent must be freely signed and dated by the participant prior to any research procedures being performed.
12. The investigation must be conducted according to the approved protocol.
13. The PI is responsible for overseeing and supervising the conduct of the investigation.
14. All information obtained in a trial must follow HIPAA regulations.
15. All adverse events, unanticipated adverse device effects and unanticipated problems must be reported to the sponsor, lead site and IRB as per the approved protocol.
16. Accurate and complete case histories and records must be prepared and maintained to ensure they are complete and accurate.
17. The IRB must be notified of any changes in the research as per the IRB policy.
18. No changes to the research must be implemented without prospective IRB approval unless required to eliminate immediate hazard to participants.
19. Each individual involved in conducting a trial should be qualified by education, training and experience to perform his or her respective tasks.
20. The PI must comply with the requirements of the Controlled Substances Act and all FDA test article requirements.
21. All test articles (drugs and devices) must be appropriately tracked.
22. The PI or sub-investigator must supervise the use and disposition of the test articles.
23. Relevant financial and non-financial conflict of interest must be reported as per UCD or affiliate policy.
24. All personnel involved in the investigation must complete and receive adequate training and this training must be documented on the delegation of duties log and training logs.
25. Records must be retained for two years following the date the marketing application is approved or withdrawn or according to the sponsor requirements.
26. Investigational products should follow good manufacturing practice (GMP).

C. Essential Documents

- All sites should have an essential documents binder which includes the following:

1. FDA Forms and Correspondence
2. Protocol (Investigational Plan)
3. Consent Forms
4. IRB Correspondence including amendments, change forms, etc.
5. Site Approval Letters (including approval from other sites if multi-center sites)
6. Investigator Brochure/Package Inserts
7. DSMB/IDEC/DMC Charter (If applicable)
8. Manual of Operations (if applicable)
9. Screening Log
10. Enrollment Log
11. Delegation Log
12. Training Log
13. Compliance Review or Audit Reports
14. Drug/Device Accountability Logs
15. Curricula Vitae/ Medical Licenses (if multi-center trial include PI and sub-investigator from other sties)
16. Laboratory Information/Certifications/Abnormal and Normal Lab Values
17. AE and UAP logs
18. Monitor Reports
19. Notes to File/Waivers

20. General Correspondence
21. Final (Closeout) Report

D. Source Documents

- Information that will be collected in the Source Documents include:

1. Original, signed ICF (copies go to patient and to medical records)
2. Documentation of ICF process (checklist)
3. Original, signed HIPAA form, if applicable (copy goes to patient and to medical records)
4. Subject demographic information (date of birth, sex, ethnicity)
5. Medical history, physical exam, laboratory values, diagnostic procedures and tests, current and concomitant medication (these are ongoing data capture points and will be re-evaluated at each subject visit)
6. Inclusion and exclusion criteria (best practice for PI or delegated sub-I to sign, verifying these criteria were met at time of enrollment and continue to be met for the duration of the study)
7. AE/UAP/UADE logs
8. Medication Log (this contains ongoing data capture points that will be re-evaluated at each subject visit)
9. Drug accountability log (this contains ongoing data capture points that will be re-evaluated at each subject visit)
10. Device Log (see device SOP)
11. Visit specific and subject specific Source Documents including (see tip sheet):
    a. Specific time points (i.e., EKG timing, PK blood draws)
    b. Relevant observations, information and data on the condition of the subject (this will be followed and updated throughout the duration of the subject's participation)
    c. Topics discussed with the subject including e-mail communication
    d. Progress notes from the PI or designated investigator, as specified in the delegation log (i.e., clinic notes)
    e. Any protocol deviations
    f. Any other protocol specific data capture points

- Source Document Maintenance

1. Source documents will be accurate, legible, correct and current.
2. Corrections to data will be made with a single line through the error, as to not cover up the initial entry. The correction will be initialed and dated to provide an audit trail. If needed, a brief explanation of the reason for the correction will be included.
3. Source documents will be signed as reviewed by the PI or designee in a timely manner. When applicable, the indication of Not Clinically Significant (NCS) or Clinically Significant (CS) results will be included, per site specifications.
4. Source documents will be filed in one binder per subject, per study.
5. Subject source document binders will be stored in a secure location (i.e. locked file cabinet) with limited accessibility.

Applicable Regulations and Guidelines

Food and Drug Administration	21 CFR 11; 21 CFR 50; 21 CFR 54; 21 CFR 56; 21 CFR 312; 21 CFR 812
ICH Good Clinical Practice	E6 Good Clinical Practice: Consolidated Guidance
US Department of Health and Human Services	45 CFR 46

Definitions

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 is protected.
Investigator	A person responsible for the conduct of the clinical trial at the trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.
Sub investigator	Any individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform clinical trial-related procedures and/or to make important trial-related decisions (e.g. associates, residents, research fellows).
Sponsor-Investigator	An individual who both initiates and conducts, alone or with others, a clinical trial, and under whose immediate direction the investigational product is administered to, dispensed to, placed in or used by a subject. The obligations of a sponsor-investigator include both those of a sponsor and those of an investigator.
Investigational Product	A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.
Medical Device	A diagnostic or therapeutic article that does not achieve any of its principal intended purpose through chemical action and/or is not metabolized within or on the body.

Protocol Amendment	A written description of a change(s) to or form clarification of a protocol.
Investigator's Brochure	A compilation of the clinical and nonclinical data on the investigational product(s) that is relevant to the study of the investigational product(s) in human subjects.
Institutional Review Board (IRB)	An independent body constituted of medical, scientific, and nonscientific members, whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trials, of protocols and amendments, and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects.
Informed Consent	A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed and dated informed consent form.
Essential Documents	Documents that individually and collectively permit evaluation of the conduct of a study and the quality of the data produced.
Source Documents	Original documents, data, and records (e.g. hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, computer data, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the labs, and at the medico-technical departments involved in the clinical trial).
Unanticipated Adverse Device Effect (UADE)	Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.
Adverse Event (AE)	An AE is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment.

Unanticipated Problem (UAP)	The phrase “unanticipated problems involving risks to subjects or others” is found but not defined in the HHS regulations at 45 CFR part 46. OHRP considers *unanticipated problems*, in general, to include any incident, experience, or outcome that meets **all** of the following criteria: 1. unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied; 2. related or possibly related to participation in the research (in this guidance document, *possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and 3. suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.