

Good Clinical Practice

- International ethical & scientific standard for design, conduct, recording and reporting of human clinical trials.
- Unified standard to facilitate mutual acceptance of clinical data by regulatory agencies (FDA, EU, Japan).
- Applicable standard for FDA regulated research.

- <http://www.ifpma.org/pdf/ifpma/e6.pdf>
- <http://www.ifpma.org/pdf/ifpma/e2.pdf>

Good Clinical Practice

- Differences between HHS and ICH guidelines
 - Participation in life-threatening situations
 - Enrollment of vulnerable populations
- Trial Initiation Requirements
- Definition of Source Documents
- Changes in source documents and CRF
- Adverse event reporting

Vulnerable Populations Defined in USA

- Title 45 Code of Federal Regulations Part 46
- HHS- Subpart B: pregnant women, human fetuses and neonates
- HHS- Subpart C: prisoners (no prisoner research can currently be approved at USC)
- HHS- Subpart D: children

Vulnerable Populations International Definition (ICH)

- Students
- Employees
- Armed forces
- Detainees
- Incurable diseases
- Nursing homes
- Impoverished
- Ethnic minorities
- Homeless
- Nomads
- Refugees
- Minors
- Incapacitated
- OHRP accepts ICH as a procedural standard

Life-threatening Situations

- HHS – does not permit enrollment of a subject into a clinical trial in the absence of consent of the subject or legally authorized representative.
- ICH – provides exception in life-threatening situations.
- The HHS rule applies in the USA.

Trial Initiation

- Investigator's Brochure
- Protocol Detail
- Informed Consent
- Budget Agreement
- Indemnification Clause
- Signed Agreement
- IRB Approval
- FDA Form 1572 or CV
- Laboratory standards
- Trial initiation report

Continuation of the Trial

- Amendments, revisions and updates
- IRB approval of same
- Shipping & dispensing logs
- Monitoring visit reports
- Signed consents
- Source documents
- Case record forms
- SAE reports
- IRB response to serious SAE reports
- Interim reports
- IRB continuation approval(s)

Completion of Study

- Investigational product accountability
- Subject identification code list
- Final IRB report
- Clinical study report

Source Documents (The CRF is not a source document)

- Hospital Records
- Clinic/Office Charts
- Laboratory Notes
- Subject's Diaries
- Evaluation Checklists
- Pharmacy Records
- Recorded data from automated instruments
- Microfiches
- Photographic negatives
- X-rays
- Transcriptions certified after verification as being accurate

Changes in the Case Record File (CRF)

- Changes: dated, initialed, & explained
- Should not obscure original entry
- Applies to both written & electronic media
- Investigator is responsible for retaining records of the changes and corrections

Adverse Event

- “Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product [device] and which does not necessarily have to have a causal relationship with this treatment.”

Adverse Drug Reaction

- “All noxious and unintended responses to a medicinal product [device] related to any dose should be considered adverse drug reactions”

Unexpected Adverse Drug Reaction

- “An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g., Investigator’s Brochure)

Serious Adverse Event (SAE)

- Death
- Life-threatening
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability
- Is a congenital anomaly/birth defect
- Medical judgement should be exercised

Adverse Event Reports

- Required to report all serious adverse events (SAE) not just serious adverse drug reactions (serious ADR)
 - Death and life-threatening events to be reported within 15 days of event unless expedited reporting required
- Expedited reporting required for:
 - Serious, unexpected and related events
 - Initial report within 7 days of event
 - Follow-up report within 15 days of event
- USC IRB has external and internal SAE forms

Recent Audit Experience

- CFR has personal identifiers (name, PF #)
 - Use codes
- Enrolled subject's did not meet eligibility criteria defined in protocol detail
 - Use eligibility checklists
- Use of expired consent documents
 - Signature page has expiration date of the consent
- Frequent failed follow-up appointments & failure of investigator to document attempts to contact subject
 - Document attempts to contact subject

Health Science IRB

- New Vice Chair: Alexander Burnett, M.D
Obstetrics and Gynecology
- Trailer 25 has been closed
- IRB Offices now located in the Intern & Resident Dormitory (IRD), 4th Floor
 - 2020 Zonal Ave., IRD Room 423
 - Los Angeles, CA 90033
 - Phone number unchanged: 323-223-2340
