EXPECTATIONS FOR A SUCCESSFUL REGULATORY AUDIT

PURPOSE OF AUDIT

- To verify compliance with federal regulations for the protection of human research subjects through the review of IRB documents, consent form content and signed patient consent forms.

AUDIT PREPARATION

- Well organized records are easier to review and ensures all documentation can be located
- Tagging records facilitates the ease of locating documents
- Allows the site to be proactive in fixing errors and implementing corrective action plans
- Review of electronic records is acceptable

IRB REVIEW

Regulatory Binder Contents

- IRB approvals
- Annual progress reports and continuing review approvals
- All versions of IRB-approved consent forms or comprehensive list of all approved versions
- Acknowledgement of internal Serious Adverse Events (SAEs), if applicable
- Acknowledgement of Safety reports (distributed by sponsor), if applicable
- Reports of serious non-compliance
- Correspondence
- SOPs if applicable to audit process (e.g. submission of external Safety Reports)

Verification of IRB Approval of:

- Initial approval, annual approvals, and approvals of protocol modifications (amendments, revisions, action letters, memos, etc.) and associated consent forms, if applicable
- Letters or minutes for documentation (No IRB Certification Forms)
- Documentation should provide details on date of meeting, item approved, consent versions, etc.
- Submission of external safety reports reportable per OHRP policy within 90 days (10% verified at audit)
- Submission of internal Serious Adverse Events

CIRB

- All documentation of CIRB approvals must be provided by the local site
- Documentation of CIRB as IRB of Record (or Independent Model Approval Letter)
- Documentation of approval of boilerplate language for local consents (“Annual Signatory Institution Worksheet About Local Context”)
- Documentation of date of local activation or implementation of protocol changes/consent versions
- Reports of serious non-compliance to the CIRB

Examples of IRB Deficiencies

- Protocol updates not approved within 90 days of distribution (date of SWOG/CTSU bi-monthly email)

- Failure to update consent forms with updates within 90 days of distribution
- Delays in annual review of active or long term follow-up protocols
- Failure to submit external safety reports according to local SOP
- Failure to provide adequate documentation of IRB actions
- Failure to provide documentation of implementation dates of consents when using the CIRB

Recommendations

- Routinely monitor bi-monthly SWOG/CTSU distributions in order to submit protocol modifications to the IRB as soon as possible
- Verify IRB approvals of long term follow-up protocols against your list of patients on long term follow-up (refer to the CRA Workbench for a list of patients in follow-up at your site)
- Create a system for tracking submission of external safety reports, if applicable
- Alternatively, you are encouraged to work with your IRB to implement alternate procedures for handling external safety reports in accordance with FDA and OHRP guidance
- Monitor the List of Applicable Protocols for S9808-Long Term Follow-up Protocol and List of Protocols with No Required Follow-up available on the CRA Workbench
- IRB oversight of a study must continue until all registered patients are deceased or have met the follow-up requirements outlined in the protocol. A study should not be closed out until verification that all data submission is complete and there are no outstanding queries for any of these patients.

CONSENT FORM CONTENT REVIEW

Verification of the Following Content Items:

- Contains all essential elements required by federal regulations
- Compared to the model consent to ensure intent of the content is the same
- Deletions or substantive modifications to the risks or alternatives sections approved by SWOG/CTSU
- Updated by protocol modifications
- Specimen and other correlative study questions identical to the model

Examples of Consent Form Deficiencies

- Missing required elements (e.g. risks, benefits, etc.)
- Not updated with new findings from protocol updates
- Specimen banking/other correlative questions missing if required to be offered to patient
- Specimen banking/other correlative questions worded substantially different from model

Recommendations

- Implement a secondary review process to ensure consent forms are complete after modifications are made (e.g. risks inadvertently deleted during copy and paste)
- When the informed consent document is revised, the IRB should have a system that identifies the revised consent document to preclude the use of the older version (i.e. version date, date approved, etc.)

REVIEW OF SIGNED CONSENT FORMS IN THE PATIENT CHARTS

Verification of the Following Items:

- Signed and dated by the patient prior to registration
- Contains all required signatures
- Specimen banking responses reported correctly at time of registration
- Patient informed of new findings (updated risks, etc.) in a timely manner (per sponsor requirements)
- HIPAA authorization signed that allows release of PHI to SWOG or CTSU representative for the life of the study

Examples of Patient Consent Deficiencies

- Most current version of the consent not used (updated consents should be implemented within 7 days of IRB approval)
- Responses to specimen questions reported incorrectly at time of registration
- Patient not informed of new findings (i.e. new risks, early study closure) in a timely manner
- Updated responses not reported to the sponsor if patient changes responses to specimen questions at any time after initial consent
- Improper editing techniques (e.g. incorrect date scratched through)
- Missing required signatures
- Missing and/or incorrect dates, date of witness or person obtaining consent signature different from patient signature, date of investigator signature > 14 days after date of patient signature
- Patient's signature dated by research personnel

Recommendations

- Implement a system to ensure you use the most current version of the consent when consenting new patients
- Document the consent process in the research record including any unusual circumstances (e.g. consent signed by patient at home so date of staff signature [witness, person obtaining consent, etc.] is different from date of patient signature)
- If there is a substantial delay from the time the patient signs consent and is enrolled in a study (> 30 days), it is recommended that the information contained in the consent form be reviewed with the subject prior to initiating any research procedures with the subject and the discussion documented in the research record. The patient must be reconsented if there have been any significant updates to the consent (new study design, added risk, etc.). Reconsent is not required if there are no changes or only minor changes to the consent.
- When significant new findings develop during the course of the research that may relate to a subject's willingness to continue participation (i.e. Action Letters), this information must be provided to subjects. There is no requirement to wait for IRB review and approval of such information before it is provided to already enrolled subjects. New risk information must be communicated promptly (as directed by the SWOG/CTSU cover memo)
- Implement procedures for informing research staff about changes that require patients to be informed of new findings and/or reconsented including the timeframe for informing patients
- If the patient is informed verbally of new findings, this action MUST be documented in the research record.