

# REGULATORY REVIEW PROCESS

Elaine Armstrong, M.S.  
Quality Assurance Manager

## INITIAL REVIEW

Each IRB must follow procedures for:

- Conducting initial and continuing review of research and for reporting its findings and actions to the investigator and the institution
- For ensuring prompt reporting to the IRB of changes in research activity
- For ensuring that changes in approved research may not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the human subjects

## IRB PROCEDURES

Each IRB must follow procedures for:

- **Conducting initial** and continuing **review** of research and for reporting its findings and actions to the investigator and the institution
- For ensuring prompt reporting to the IRB of changes in research activity
- For ensuring that changes in approved research may not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the human subjects

## INITIAL REVIEW

Initial review of research must be conducted by full board review unless:

- Research activities present no more than minimal risk to human subjects
- Not conducted under an investigational new drug application
- Examples:
  - Behavioral studies
  - Quality of life studies
  - Some specimen submission studies

## CONTINUING REVIEW

Each IRB must follow procedures for:

- **Conducting** initial and **continuing review** of research and for reporting its findings and actions to the investigator and the institution
- For ensuring prompt reporting to the IRB of changes in research activity
- For ensuring that changes in approved research may not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the human subjects

## CONTINUING REVIEW

- At intervals appropriate to the degree of risk but not less than once per year.
- Full board unless one of the following applies:
  - Initial review qualified for expedited review
  - No subjects have been enrolled and no additional risks have been identified
  - Research is permanently closed and all subjects have completed treatment
  - The remaining research activities are limited to data analysis

## CONTINUING REVIEW

Continuing review of long term follow-up where the research is permanently closed and all subjects have completed treatment

- OHRP allows a single umbrella protocol to simplify and streamline continuing review for multiple protocols
- S9808, "Long Term Follow-Up Protocol: An Administrative Tool"
- List of applicable protocols available on the CRA Workbench

## REPORTING CHANGES

Each IRB must follow procedures for:

- Conducting initial and continuing review of research and for reporting its findings and actions to the investigator and the institution
- For ensuring *prompt reporting to the IRB of changes in research activity*
- For ensuring that changes in approved research may not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the human subjects

## REPORTING CHANGES

Changes in research activity distributed via:

- Amendments
- Revisions
- Memos
- Safety reports
- Closure notices

Note: Other group's terminology includes addendum, updates, etc.

## REPORTING CHANGES

Amendment: A change to the protocol that directly affects patient care or treatment and may substantively increase the patient's risk/benefit ratio (Full board required).

Revision: An administrative or editorial change that does not affect patient care or treatment, or a scientific or medical change that does not substantively increase the patient's risk/benefit ratio (Expedited review allowed).

## REPORTING CHANGES

Memorandum: Explanation of a study concept or other information about the study that do not change the study itself (Expedited review allowed / no review required).

Memorandum/Safety Reports (Expedited review allowed).

Permanent/Temporary Closure Notice: Planned and unplanned end to accrual (Full board required / expedited review allowed).

## IRB REVIEW OF CHANGES

Each IRB must follow procedures for:

- Conducting initial and continuing review of research and for reporting its findings and actions to the investigator and the institution
- For ensuring prompt reporting to the IRB of changes in research activity
- For *ensuring that changes in approved research may not be initiated without IRB review and approval* except where necessary to eliminate apparent immediate hazards to the human subjects

## **IRB REVIEW OF CHANGES**

Changes may not be initiated without IRB review and approval

- When a proposed change is not minor (e.g. procedures involving increased risk or discomfort are to be added), then the change must receive full board review
- Expedited review allowed for minor changes in ongoing previously approved research
- Some editorial or administrative changes need no review

## **IRB REVIEW OF CHANGES**

- When the protocol changes require revision of the informed consent document, the IRB should have a system that identifies the revised consent document to preclude the use of the older version.
- An IRB stamp is not required.
- A system that correlates to IRB review dates or amendment dates is recommended.

## **FULL BOARD REVIEW**

- Increased risk (e.g. new risk information, changes to eligibility to allow a higher risk population)
- Complete study redesign
- Addition of specimen submission requirements

## **EXPEDITED REVIEW**

- Minor changes in previously reviewed research
- Safety reports
- New or modified risk information that represents a minor alteration in the overall risk-benefit for new participants in order to minimize the suspension of accrual

## **NO IRB REVIEW**

- Minor editorial or administrative changes
- Memos (e.g. drug distribution, holiday hours, protocol clarifications, etc.)
- Form changes

## **ELIMINATING HAZARDS**

Each IRB must follow procedures for:

- Conducting initial and continuing review of research and for reporting its findings and actions to the investigator and the institution
- For ensuring prompt reporting to the IRB of changes in research activity
- For ensuring that changes in approved research may not be initiated without IRB review and approval *except where necessary to eliminate apparent immediate hazards to the human subjects*

## ELIMINATING HAZARDS

- Significant new findings developed during the course of the research that may relate to a subject's willingness to continue participation must be provided to subjects (i.e. Action Letters)
- There is no requirement for IRB review and approval of such information before it is provided to already enrolled subjects

## ELIMINATING HAZARDS

- New risk information must be communicated promptly (at the next scheduled visit) to already enrolled subjects
- Documentation of such communication must be made in the research record
- The IRB must be provided with a copy of significant new findings provided to subjects

## SAFETY REPORTS

[OHRP Guidance on AE Reporting, Jan. 15, 2007](#)

[FDA Guidance on AE Reporting, January 2009](#)

FDA and OHRP guidance on adverse event reporting to IRBs state that *unanticipated problems* involving risks to human subjects must be reported

- Related or possibly related
- Unexpected
- Places subjects or others at greater risk of harm than was previously known

## SAFETY REPORTS

- NCI requires that we forward all safety reports that they send to us
- NCI requires safety reports be submitted within 90 days unless the local IRB policy does not mandate reporting of external safety reports
- SWOG encourages sites to implement an alternate policy for reporting of safety reports to the IRB

## FAQs

**Q:** Who determines IRB review requirements?

**A:** Review requirements are determined by the protocol coordinator with input from QA based upon SWOG policies and OHRP guidance.

**Q:** What is the timeframe for review?

**A:** All protocol updates requiring review whether full board or expedited must be reviewed and approved within 90 days.

## FAQs

**Q:** What if the local IRB overrules the SWOG requirement for full board or expedited review?

**A:** Local IRB policy may differ with SWOG's interpretation of required review. If your local IRB has different written SOPs or provides a rationale at the time of the review, that is acceptable.

## FAQs

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**Q:** When does CTEP require suspension of enrollment?

**A:** In the past, CTEP allowed enrollment of new patients to continue after verbal communication of new risk information, after IRB notification but prior to official IRB review and approval of this information. OHRP recently informed CTEP this is not in compliance with OHRP regulations and that new patients cannot be enrolled until an amended protocol and informed consent have been reviewed and approved.

## FAQs

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However, if the changes to the protocol and informed consent represent no more than a minor alteration in the overall risk-benefit for patients, the amendment can undergo expedited review at the discretion of the Chair of the designated IRB.

Note: Suspension of accrual until the protocol update and consent have been approved will be monitored as part of the audit process