Children's Hospital LOS ANGELES®

TEA WITH THE IRB

NEW INFORMATION THAT REQUIRES PROMPT REPORTING

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Learning Objectives

- Understand the monitoring responsibilities of
  - Investigators and sponsors
  - IRB

- Understand what new information requires prompt reporting to the IRB

IRB Review and Oversight of Research

Initial Review

- Are the criteria for approval met?
- Of the criteria: Is there an adequate plan to monitoring the data to ensure subject safety?

New Information

- Are the criteria for approval still met?
- Has the risk to benefit assessment changed?
- Is the new information an unanticipated problem?
- Is the new information non-compliance?

Sources of New Information

- Reporting of new information from investigators and sponsors
- Changes in research resulting from review of data
- Auditing and monitoring of the conduct of research
- Annual review – study progress information
  - New safety, scientific information
  - Summary of events that do not require prompt reporting

Monitoring by Investigator and Sponsor

Responsibilities:

- Monitoring of safety for individual subjects
- Monitoring of the conduct of the research
- Monitoring of the data collected to ensure subject safety

Monitoring by the IRB

Responsibilities:

- §46.111 Criteria for IRB approval of research:
  - (a) In order to approve research…the IRB shall determine that all of the following requirements are satisfied: …
  - (6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

Monitoring by the IRB

Ensure the protocol includes:

- Procedures to ensure the safety of individual subjects
- A plan for monitoring the data collected to ensure the safety of subjects
  - Who reviews the data (local and study-wide)?
    - Investigator, medical monitor, internal committee, independent committee (DSMB)
  - What data are reviewed?
    - Safety data, e.g., unexpected events, AEs/SAEs, sponsor safety reports
    - Efficacy data

Plan for Monitoring the Data Collected

- A good plan for monitoring data will allow for prompt reporting of new information to the IRB
- It is the responsibility of the investigator/sponsor to notify the IRB of information that might affect the criteria for approval, e.g., risk to benefit assessment
  - IRBs need information to evaluate if the risk to benefit assessment has changed.
  - IRBs are not in a position to review individual events (data) except when events are unanticipated problems involving risk to subjects or others.

What Does the IRB Do with New Information?

- The IRB must assure criteria for approval continue to be met
  - Has the risk to benefit assessment changed?
  - What changes to the study need to happen to assure criteria for approval continue to be met?

- The IRB must also determine whether the information represents:
  - An unanticipated problem involving risks to subjects or others;
  - Non-compliance with the federal regulations or with the requirements or determinations of the IRB; and
  - Non-compliance that is serious or continuing.

What New Information?

- Information that indicates a new or increased risk, or a new safety issue

- Harm experienced by a subject or other individual, which in the opinion of the investigator are unexpected and probably related to the research procedures

- Non-compliance with the federal regulations governing human research, or with the requirements or determinations of the IRB, or an allegation of such non-compliance

CHLA - Former Reporting Requirements

- Former guidance focuses on the kinds of events to be reported

- Former criteria for reporting events places the IRB in position to review events (data) and not information about how the data impacts subject safety

Former Reporting Requirements

- Internal adverse events
  - Serious, unexpected and related
  - All deaths of subjects within 30 days of active research participation
  - Any AEs involving normal subjects

- Deviations
  - Report all deviations
  - Unless the deviation was a late visit, and
    - Visit occurred no later than twice the allotted window
    - Visit did not include any safety tests
    - Visit was due to a subject's scheduling problems

Former Reporting Requirements

- External adverse events
  - Serious, unexpected and related
    - Same study – report it
    - Different study, report if a change in research is required, or event results in hold/suspension

New Reporting Requirements

- Investigators and sponsors should review events according to the research plan to monitor data to ensure the safety of subjects
  - Multi-center: Events (data) are reviewed study-wide
  - Local events: Investigators review data and trends according to CHLA study monitoring plan

- After data analysis, is there any new information that indicates:
  - A new or increased risk, or a new safety issue?
  - Harm experienced by a subject or other individual, which in the opinion of the investigator are unexpected and probably related to the research procedures?
  - Non-compliance with the federal regulations governing human research, or with the requirements or determinations of the IRB, or an allegation of such non-compliance?

- If yes, the information requires prompt reporting

Reporting New Information

- The IRB needs the following information:
  - Description of the new information
  - How it impacts current and future subjects
  - Corrective action plan
    - Medical intervention/treatment when harm to subject
    - Change in research to assure risk-benefit ratio is maintained

Prompt Reporting of New Information

Information that indicates a new or increased risk, or a new safety issue

- Examples:
- New information (e.g., an interim analysis, safety monitoring report, publication in the literature, sponsor report, or investigator finding) indicates an increase in the frequency or magnitude of a previously known risk, or uncovers a new risk.
- Withdrawal, restriction, or modification of a marketed approval of a drug, device, or biologic used in a research protocol
- Protocol violation that harmed subjects or others or that indicates subjects or others might be at increased risk of harm
- Complaint of a subject that indicates subjects or others might be at increased risk of harm or at risk of a new harm
- Any changes significantly affecting the conduct of the research
- Unanticipated adverse device effect (any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device)

Prompt Reporting of New Information

Harm experienced by a subject or other individual, which in the opinion of the investigator are unexpected and probably related to the research procedures

- A harm is “unexpected” when its specificity or severity are inconsistent with risk information previously reviewed and approved by the IRB in terms of nature, severity, frequency, and characteristics of the study population.

- A harm is “probably or possibly related” to the research procedures if in the opinion of the investigator, the research procedures more likely than not caused the harm.

Prompt Reporting of New Information

Non-compliance with the federal regulations governing human research, or with the requirements or determinations of the IRB, or an allegation of such non-compliance

Examples:

- Audit, inspection, or inquiry by a federal agency and any resulting reports (e.g., FDA Form 483.)
- Written reports of study monitors that identify non-compliance with the approved protocol
- Failure to follow the protocol due to the action or inaction of the investigator or research staff
- Breach of confidentiality
- Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a subject
- Incarceration of a subject in a study not approved by the IRB to involve prisoners
- Complaint of a subject that cannot be resolved by the research team
- Premature suspension or termination of the protocol by the sponsor, investigator, or institution

Reporting of New Information

- Report new information that falls into one or more of the three categories to the CHLA IRB within 5 business days.

- Information that does not fall under any of the three categories does not require reporting to the IRB.

Things to Do

- A new face page for Reportable Events has been added to iStar
  - Face page is consistent with our SOPs – HRP-214 FORM New Information
  - Additional iStar programming is required to focus on information and not events that require prompt reporting
- Guidance will be posted on HSPP Website soon
  - Information requiring prompt reporting and what does not require reporting
  - FAQs for Reportable Events
- Continue with education sessions for investigators and research coordinators

Review of Draft Guidance Document