Continuing Review Considerations

EMORY IRB WEBINAR

APRIL 9, 2015
Who needs to submit a continuing review?

- Yes, continuing to enroll subjects
- Yes, but no subjects have been enrolled to date
- No, enrollment is closed, but not all subjects have completed all research-related interventions
- No, the research is permanently closed to the enrollment of new subjects; all subjects have completed their research-related interventions
- No, the remaining research activities are limited to data analysis
- No, the study has been completed. (If checked, you will need to complete a close-out request.)
- Yes, ongoing retrospective chart review and/or study of existing data/specimens (existing when
- Yes, ongoing prospective chart review and/or study of data/specimens
Interventions/Interactions

- New subjects are still being sought
- On active study intervention
- Long-term follow-up

Identifiable data

- New charts/records are still being obtained for analysis
- Existing study dataset(s) contain identifiable data
About Long-Term Follow-Up

No Research-Related Interventions
- Long-Term Follow-Up ONLY
- Standard of care procedures OK
- Access of records/data OK
- Expeditable under 8(a)

Research-Related Interventions
- “Active” participants
- Procedures carried out on account of being in a study
- Not expeditable (unless already)
About Data Analysis Only

- No interventions
- No follow-up with subjects
- Identifiable data still held
- Expediteable under 8(c)
Key Information

- Number of subjects
- Data Safety and Monitoring reports
- Protocol Deviations and Adverse Events
Numbers of Subjects

- New enrollments
- Total enrollment
- Total "Active"
  - Actually took part/taking part in the study
Who is “enrolled?”

Anyone who signs a consent
Before all this:

Screening

Randomization

Am 1

Am 2

Am 3

Am 4

Am 2-1

Am 1-2

Am 4-3

Am 3-4

Non-Respondent

Respondent

Wash-Out

Combination Therapy

Evaluation

Dose Escalation

Follow-Up Studies

Follow-Up

Genetics Sub-Study
Data Safety and Monitoring
Who Needs Data and Safety Monitoring?

All greater than minimal risk studies:
Probability of greater harm/discomfort than found in the general population
Data and Safety Monitoring Board/Committee

- Panel of unconflicted experts
- Regular meeting schedule
  - Calendar based
  - End-point based
- Report from latest meeting must be provided

Data and Safety Monitoring Plan

- General plan to protect subjects and their data
- Recommended even for minimal risk studies
- Adherence to plan must be shown
What about monitoring reports?

- Do not send reports to the IRB
- Send to the Clinical Trials Audit and Compliance (CTAC) office
  - ctcompliance@emory.edu
Protocol Deviations & Adverse Events
Timing of Report of Protocol Deviations, Adverse events, Deaths and Non Compliance

**Protocol Deviations**
- Promptly: if substantive deviations from protocol and affect rights and welfare of subjects, safety of subjects, their willingness to continue in study or the integrity of the research data.
- Never: if they do not affect any of the above.

**Adverse Events**
- Promptly: if unanticipated, related and involving risk to participant or others or if happening at increased frequency, duration or intensity that previously anticipated.
- Periodically: if related to study participation.
- Never: If not related to study participation.

**Deaths**
- Promptly: if related to study participation.
- Periodically: if not related to study participation.

**Non-Compliance**
- Promptly: The CoRe team will make a determination if it is possibly serious and/or continuing; if so, Committee Q will review.

(*): This applies to internal events, and external events from sites of Emory sponsor-investigator studies.
(**): Promptly: 10 business days from the date the PI first learn about the event
(***) Periodically: at continuing review

This guidance does not apply to VA studies.
**Promptly?**

**Protocol Deviations**
- Affect subjects’ rights, welfare, safety, willingness to continue
- Affects integrity of data

**Adverse Events**
- Related to the research AND
  - Unanticipated – severity/frequency/duration OR
  - Places subjects at greater risk

**Deaths**
- Related to participation in the research
Periodically?

Protocol Deviations?
- None
- If reportable, then reportable promptly

Adverse Events & Deaths
- SUMMARY of expected internal events
- Deaths not related to participation
- Previously reported UPs
Reportable Events

Emory Guidance and Forms

- Assessment Form for Events (Internal/External) (ver. 7-18-14)
- Assessment Form for Protocol Deviations (ver. 11-3-11)
- Continuing Review - A Sample Summary of Events (ver. 5-2-13)
- Guidance for Submitting Multiple Events at One Time (ver. 11-14-14)
- Guidance for Serious or Continuing Noncompliance and UPs (ver. 1-20-15)
- Reporting Obligations for Investigators (ver. 2-14-14)
- Root Cause Analysis Worksheet (ver. 11-23-10)
- Timeframes for Reporting Adverse Events, Protocol Deviations, and UPs (ver. 2-14-14)
Non-substantive Protocol Deviations

If protocol deviations occur, but are not “substantive,” they do not require a Reportable Event, but would be a “Yes” for Question 3.

In this situation, log a comment to explain the lack of REs in study history.
Other Information

- When to submit a CR
- Changing documents and staff
- 30-Day Rule
- Sponsor-Investigators
When to Submit?

30-60 Days before the study expiration
Early submissions

- Studies submitted >60 days before their expiration may:
  - Not be reviewed until closer to the expiration
  - Sent back to the study team (esp. clinical trials)

- An early renewal means the expiration date of the study WILL change
  - Log a comment acknowledging this
If other groups need to review...

- Grady ROC, VA R&D, Sponsor, Coordinating Site, etc.
- Allow for extra time (submit closer to 60 days)
- Alert IRB analyst that further review will be needed
CRs are a good time to update to the latest consent templates

- Emory Biomedical Consent/HIPAA Template (ver. 9-29-14)
- Emory Expanded Access (IND/IDE)/HIPAA Template (ver. 1-16-15)
- CHOA Consent/HIPAA Template (ver. 9-29-14)
- Grady Consent/HIPAA Template (ver. 9-29-14)
- St. Joseph Consent/HIPAA Template (ver. 9-29-14)
Changing Documents

Did any events require a change to protocol related documents?
If yes, please upload:

- For reference only
- Changing documents must be done through an amendment
What about staff changes?

The majority of staff changes may go through the online tool.

Study Staff Change Request

All other staff changes require an amendment.
What about expired CITI?

- Staff with expired CITI certifications will prevent study renewal
- These individuals can be removed administratively by the IRB
- A logged comment from the study team listing the staff to be removed is required
The 30-Day Rule

- IRB approvals can be no longer than 1 year minus 1 day
- If a study is renewed within 30 days of its expiration date, the previous date may be kept

Ex: A study expires on 7/21/2015. It is reapproved by the IRB on 7/1/2015

- Without the 30-day rule: New expiration date is 6/30/2016
- With the 30-day rule: New expiration date is 7/21/2016
Consents and the 30-Day Rule

7/1/2015
IRB Approval

Use Previously Approved Consents

7/21/2015
Approval goes into effect

Use Renewed Consents

7/21/2016
New Expiration Date

Do Not Use Renewed Consents
Where are the consents?

- New Consents are under the documents tab
- Old consents may be
  - Deleted
  - Archived under “miscellaneous documents”
- Study teams should keep a copy of the previously approved consents to use until the new approval period comes into effect
ALL sites are considered “internal” for Emory Sponsor-Investigators.

S-I also need to complete for each CR:
- Annual Report
- Responsibility Form

Send these forms to the Office of Research Compliance (ORC)
- orc@emory.edu

Allow time for ORC to review and notify the IRB of completeness.
So your study has lapsed...
DON'T PANIC
Lapsed Studies

- Immediately cease all study activities
  - Including analysis of identifiable data
- Submit the CR to the IRB as soon as possible
- Include a statement as to whether any study activities occurred during the lapse
**Study Activities During a Lapse**

**Did Not Occur**
- Log comment noting this with the CR

**Did Occur**
- Log comment noting this with the CR
- Submit a RE detailing the nature of the activities
Lapsed FDA Studies

- FDA regulated studies that lapse MUST submit a RE regardless of activities
  - No study activities = RE
  - Study Activities = RE
Thank you for your time.

Questions?
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