



Central Office Update

Trini Ajazi
CALGB Group Meeting, Chicago

CRA Committee Meeting, June 26, 2008

For CALGB Participants Only

Presentation Objectives

- Update CRAs on Central Office (CO) Staffing Changes
- Provide Guidelines for CO Review of IRB Policies Re: External AE Reports and Unanticipated Events
- Provide Guidelines for CO Review of Model Consent Form Changes
- Discuss OHRP Guidelines in Clinical Trial Informed Consent Documents and Enrollment of New Participants

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Central Office Staffing Updates

- Protocol Coordinator: Kelly Colclasure (GI, PET Committees)
- Temporary Audit Coordinator: Chelsea Pearsall
- Audit Program Manager: Barbara Barrett
- Executive Officer: Cara Rosenbaum, MD (August 1, 2008 - Leukemia, LCS, Lymphoma, Transplant Committees)

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IRB Policies on Review of External Adverse Events

- IRB policies on external adverse event reports and unanticipated events.
 - IRB may choose not receive to external adverse event reports - OK.
 - IRB may require submission only as part of annual continuing review - OK.
 - IRB policy should include definitions and criteria for types of events reviewed and not reviewed.
 - Serious
 - Related
 - Unanticipated
 - External

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IRB Policies on Review of External Adverse Events

- Additional considerations for review of external adverse events.
 - Research staff should have process for review of external adverse events by investigators/physicians, regardless of IRB policy.
 - If no policy, submit external adverse events within 90 days of Group/CTSU distribution.
 - CALGB requires IRB acknowledgement of all action letters including action letters related to external adverse events.

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Central Office Review of IRB Policies on AE Reports

- Central Office Review and Processing
 - ✓ Policies may be sent to Trini Ajazi. Trini or Barbara Barrett may review the policies.
 - ✓ Check criteria for IRB review clearly stated; references regulations (CFR 21 and 45).
 - ✓ Check process for review by research personnel (SOPs may not be part of IRB policy).
 - ✓ Notify institution of approval and/or questions.
 - ✓ File in audit files.
 - ✓ Notify auditor prior to audit.
 - ✓ Auditors will audit based on effective dates of policy.

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Central Office Review of Changes to Model Consent

- Significant changes to model consent form
 - Changes to risks and benefits section.
 - Deletion of risks is not allowed.
 - Deletion of any section of the model consent.
 - Significant changes to wording of any section.
 - Minor clarifications and administrative changes per local IRB do not require Central Office review.

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Review of Changes to Model Consent cont.

- Limitations
 - Limitations in what Central Office can approve for CIRB approved model consent forms and deviations from NCI model consent form.
 - CALGB utilizes NCI model informed consent form which lists risks by regimen and not drug.
 - Specimen-related questions need to remain as they are. Tied to registration and used to track allowable use of specimens.
 - NCI is working on new model language including definition of "genetic."
 - Send request to Trini Ajazi. Review may be performed by Trini Ajazi, Kathy Karas, Barbara Barrett and/or Linda Bressler.

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OHRP Guidance Re: Changes in Risk-Benefit

- Letter from CTEP dated March 20, 2008
 - New or modified risk information requires an amendment.
 - Enrollment of new participants must stop until IRB approves amendment and revised informed consent form.
 - OHRP did not approve of verbal notification of new patients.
 - Based on CFR 45 Part 46.116(a)(2).

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Past Practice

- CTEP and Groups have suspended accrual due to **major** alteration in overall risk-benefit ratio for new participants.
- Suspension in effect until IRB approval of amendment and revised informed consent.
- Accrual not suspended for **minor** alteration in overall risk-benefit, including editorial changes.
- Documented verbal notification of new participants allowed. Reconsent upon approval of revised ICF by IRB.

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Change in Past Practice Per OHRP

- No change in practice with regard to **major** changes in overall risk-benefit ratio.
- Accrual suspended **locally** for **minor** changes in **overall** risk-benefit ratio.
 - CIRB approves changes prior to Group distribution.
 - Local IRB must approve amended protocol and consent prior to new patient enrollment.
 - IRB may approve amendment via **expedited review**.
 - If patient consented on or prior to date of suspension, patient may be enrolled.
- Key issue: Major vs. minor change in **overall risk-benefit ratio**.

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Implementation

- If new information changes overall risk-benefit for study participants, CALGB works closely with CTEP and CIRB to quickly generate a protocol amendment and revised informed consent form.
- CALGB to inform institutions on a study-by-study basis regarding requirements for accrual suspension and IRB approval.

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Stay Tuned

- Discussions between the Groups and CTEP ongoing regarding impact and implementation.
- Clarification expected regarding types of modifications not affected by policy.
- OHRP expected to issue a statement regarding the use of expedited review in these circumstances.

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What else can we do?

- Local IRBs can allow expedited review of amendments due to **minor** changes in risk-benefit ratio.
- Institutional IRBs with concerns can contact OHRP.
- CRAs can provide feedback to the Central Office regarding the local impact of the change in practice.

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Resources

- Trini Ajazi, Group Administrator
 - E-mail: tajazi@uchicago.edu
 - Phone: (773) 702-8672
 - Central Office Fax: (312) 345-0117
- Kathy Karas, Director, Protocol Operations
 - E-mail: kkaras@uchicago.edu
 - Phone: (773) 702-9674
- Linda Bressler, Director, Regulatory Affairs
 - E-mail: bressler@uic.edu
 - Phone: (773) 834-7973
- Barbara Barrett, Audit Program Manager
 - E-mail: bbarrett@calgb.org
 - Phone: (312) 206-8216
- OHRP: <http://www.hhs.gov/ohrp/>

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Summary

- IRB policies on external AE
 - - Include criteria for IRB review in policy
- CO review of changes to model consent form
 - Significant changes to model, including risks and benefits
- Minor changes to risk-benefit ratio
 - Requires protocol amendment and revised informed consent form
 - Local suspension of accrual as required until IRB approval obtained
 - Expedited IRB approval allowed by OHRP
- Major changes to risk-benefit
 - Study may be suspended centrally

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Questions

- Questions from Audience

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