Alliance Audit Regulatory Review

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Alliance Chicago Office

November 1, 2018

Presentation Objectives

- Identify the Regulatory Review Process and the Documents that will be reviewed

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Presentation Objectives

- Identify the Regulatory Review Process and the Documents that will be reviewed
  - Prior to the audit
    - Protocols approved through the utilization of a local IRB
    - Protocols approved through the utilization of the CIRB

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  - During the audit
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    - Protocols approved through the utilization of the CIRB

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    - Protocols approved through the utilization of the CIRB
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    - Protocols approved through the utilization of local IRB
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- Describe Common Regulatory Deficiencies found during an audit

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    - Protocols approved through the utilization of local IRB
    - Protocols approved through the utilization of the CIRB
- Describe Common Regulatory Deficiencies found during an audit
- How to Avoid Regulatory Deficiencies

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Regulatory Review

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Regulatory Review

- Regulatory review is the review of the foundation documents for conducting a particular study at your site.

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Regulatory Review

- Regulatory review is the review of the foundation documents for conducting a particular study at your site.
  - Two Step Process
    - Pre-review
    - At time of audit

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Regulatory Review

- Regulatory review is the review of the foundation documents for conducting a particular study at your site.
  - Two Step Process
    - Pre-review
    - At time of audit
  - Three Parts
    - IRB review
    - Informed Consent Content Review
    - Delegation Task Log (DTL) if applicable

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Regulatory Review

- Regulatory review is the review of the foundation documents for conducting a particular study at your site.
  - Two Step Process
    - Pre-review
    - At time of audit
  - Three Parts
    - IRB review
    - Informed Consent Content Review
    - Delegation Task Log (DTL) if applicable

  Note: A minimum of 4 studies will be selected for review

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Step I: Regulatory Pre-Review

- Per CTMB guidelines section 4.2, the list of protocols and patient cases selected will be supplied to the site at least 2 weeks (no more than 4) prior to the audit

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Step I: Regulatory Pre-Review

- For each protocol selected for audit and consent content compliance the site will forward the following regulatory documents to the Chicago Office prior to the audit date

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Step I: Regulatory Pre-Review

- For each protocol selected for audit and consent content compliance the site will forward the following regulatory documents to the Chicago Office prior to the audit date
  - Initial (Final) IRB Protocol Approval
  - Continuing / Annual Renewal Approvals
  - Required Amendment / Update Approvals
  - Selected Locally Utilized Informed Consent Form
  - Applicable Corresponding Model Consent

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Step I: Regulatory Pre-Review

- For each protocol selected for audit and consent content compliance the site will forward the following regulatory documents to the Chicago Office prior to the audit date
  - Trials reviewed under the CIRB
    - Approval letter from CIRB noting acceptance as IRB of record
    - Study specific worksheet with local context
    - Selected locally utilized informed consent form
    - Applicable corresponding model consent
  - All other CIRB approval documents will be reviewed at the time of audit

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Step I: Regulatory Pre-Review
Part I: IRB Review

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Step I: Regulatory Pre-Review
Part I: IRB Review

What are Auditors looking for?

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Step I: Regulatory Pre-Review
Part I: IRB Review

What are Auditors looking for?

- Documentation of IRB Approval

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Step I: Regulatory Pre-Review
Part I: IRB Review

What are Auditors looking for?

- Documentation of IRB Approval
- IRB Review Type

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Step I: Regulatory Pre-Review
Part I: IRB Review

What are Auditors looking for?

- Documentation of IRB Approval
- IRB Review Type
- Timing

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Part I: IRB Review

Initial IRB Protocol Approval

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Part I: IRB Review

Initial IRB Protocol Approval

What are we looking for?

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Part I: IRB Review

Initial IRB Protocol Approval

What are we looking for?

July 1, 2014

Project Number:	Alliance A011106
Project Title:	ALTernate Approaches for Clinical Stage II or III Estrogen Receptor Positive Breast Cancer NeoAdjuvant TrEatment (ALTERNATE) in Postmenopausal Women: A Phase III Study
Sponsor:	Alliance for Clinical Trials in Oncology
Primary Investigator:	
Meeting Date:	5/22/2014
IRB Approval Date:	6/26/2014
IRB Expiration Date:	5/21/2015
Type of Approval:	Full Committee Review

Dear Investigator:

This is to certify that your research proposal involving human subject participants has been reviewed and **approved** by the IRB. This approval is based upon the assurance that you will protect the rights and welfare of the research participants, employ approved methods of securing informed consent from these individuals, and not involve undue risk to the human subjects in light of potential benefits that can be derived from participation.

Approval of this research is contingent upon your agreement to:

(1) Adhere to all Policies and Procedures Relating to Human Subjects, as written in accordance with the Code of Federal Regulations (45 CFR 46).
(2) Maintain copies of all pertinent information related to the research study including, but not limited to, video and audio tapes, instruments, copies of written informed consent agreements, and any other supportive documents in accordance with the Research Records Retention Policy.
(3) Report potentially serious events to IRB by completing the "Adverse Event Report".
(4) Submit deviations from previously approved research activities which were immediately necessary to eliminate apparent and immediate dangers to the subjects.
(5) Submit Amendments to the IRB for any proposed changes from the previously approved project. Changes may not be initiated without prior IRB review and approval.
(6) Submit an Application for Continuing Review to the IRB before the expiration date. Federal regulations and policies require continuing review of research at intervals appropriate to the degree of risk, but not less than once per year.

If you have any questions regarding the human subject protection process, please do not hesitate to contact our office.

Very truly yours,

IRB Coordinator

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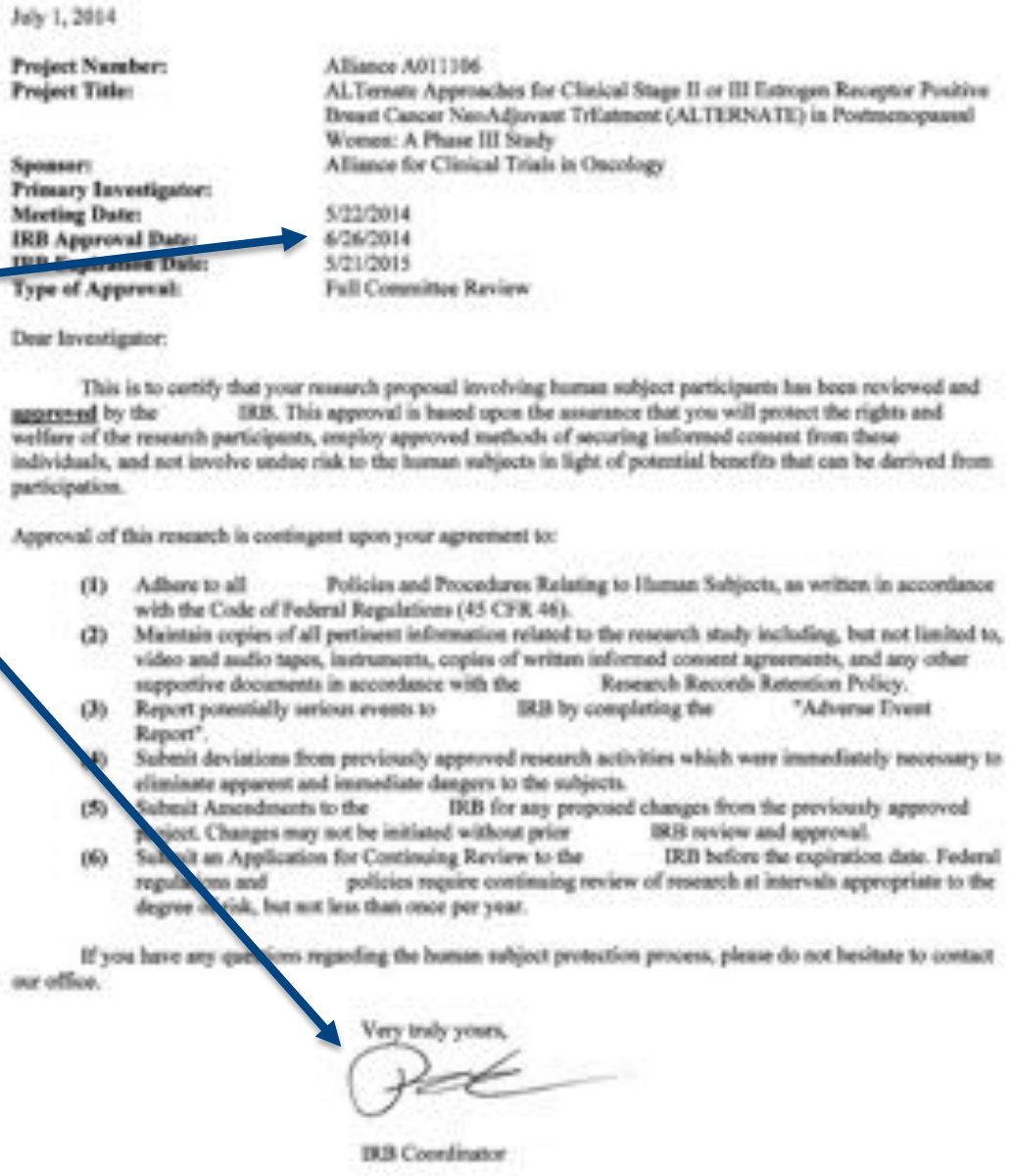
Part I: IRB Review

Initial IRB Protocol Approval

What are we looking for?

- Approval date and signature by the Chair (or designee)



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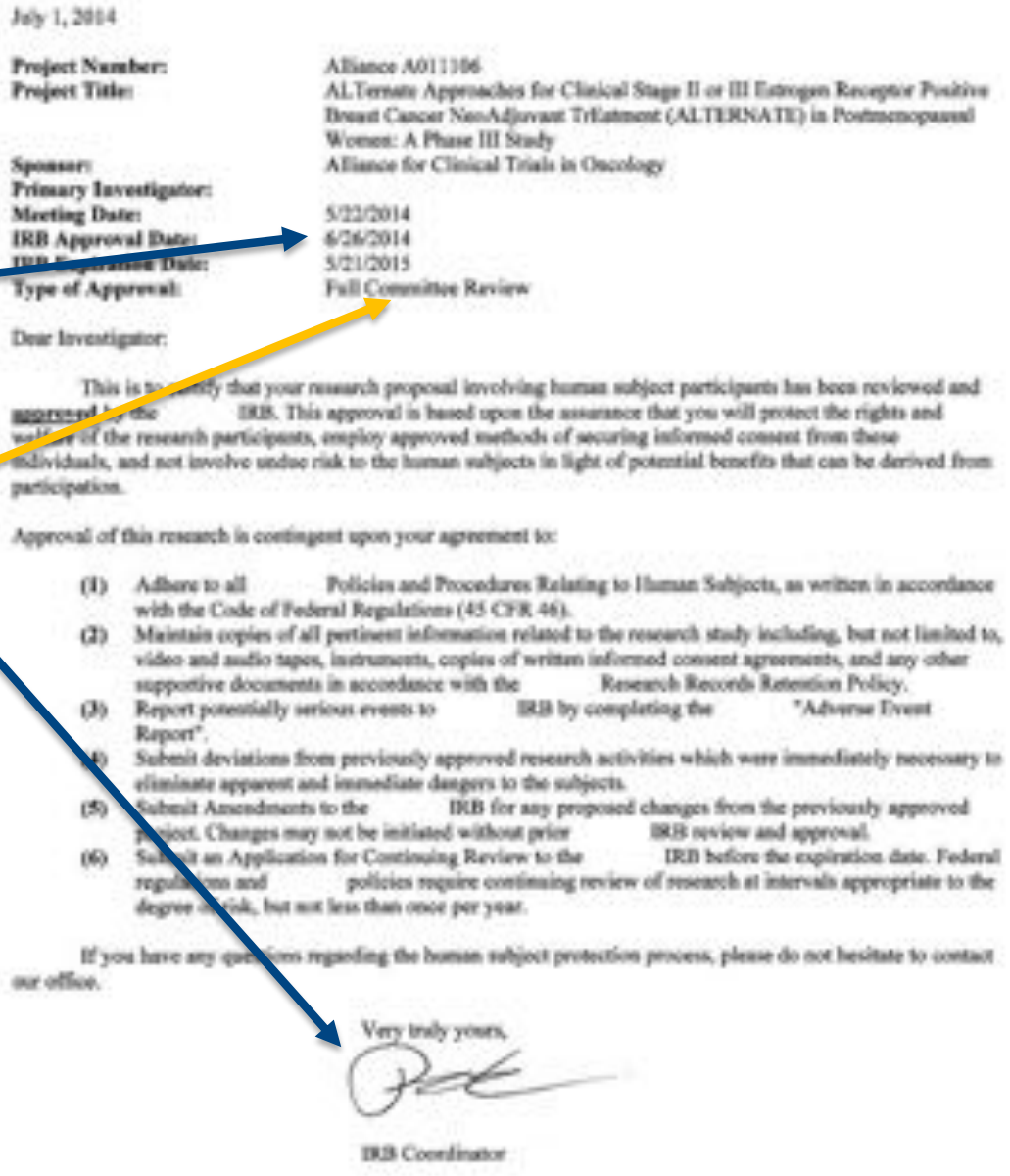

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Part I: IRB Review

Initial IRB Protocol Approval

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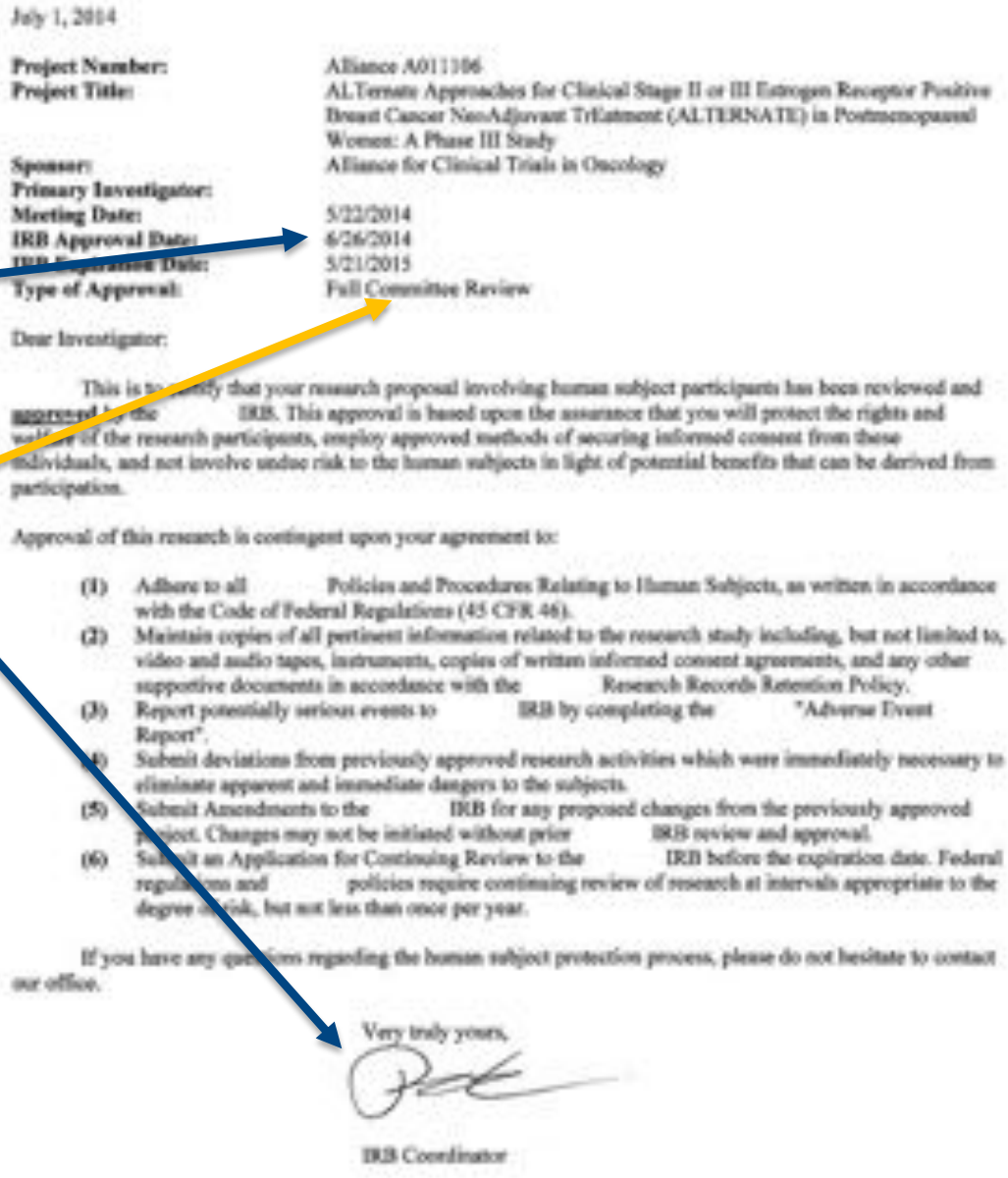
- Approval date and signature by the Chair (or designee)
- Full Board Review
- Approval was received prior to patient enrollment



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Part I: IRB Review

Continuing / Annual Reviews

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Part I: IRB Review

Continuing / Annual Reviews

What are we looking for?

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Part I: IRB Review

Continuing / Annual Reviews

What are we looking for?

DATE: April 20, 2015

TO: M.D.
FROM: Institutional Review Board

STUDY TITLE: [S64231-3] A041202 - A Randomized Phase III Study of Bendamustine Plus Rituximab Versus Ibrutinib Plus Rituximab Versus Ibrutinib Alone in Untreated Older Patients (>65 Years of Age) With Chronic Lymphocytic Leukemia (CLL)

IRB REFERENCE #:
SUBMISSION TYPE: Continuing Review/Progress Report

ACTION: APPROVED
APPROVAL DATE: April 2, 2015
EXPIRATION DATE: April 1, 2016
REVIEW TYPE: Full Board

- Continuing Review - IRB Submission Form
- Consent Form, Update 1, Dated 6/1/14 - (Addition of Physician Name - Submitting consent for renewal stamp)
- HIPAA Consent/Authorization (Only submitting for renewal stamp)
- Alliance Data and Safety Monitoring Board (DSMB) Report Dated 12/23/14

Thank you for your submission of the items as listed for the above research study. Institutional Review Board has approved the items as submitted at its regularly scheduled meeting.

Please remember that informed consent is a process beginning with a description of the study and insurance of participant understanding followed by a signed consent form. Informed consent must continue throughout the study via a dialogue between the researcher and research participant. Federal regulations require each participant receive a copy of the signed consent document.

Please note that any revision to previously approved materials must be approved by this office prior to initiation. Please use the appropriate revision forms for this procedure.

All SERIOUS and UNEXPECTED adverse events must be reported to this office. Please use the appropriate adverse event forms for this procedure. All FDA and sponsor reporting requirements should also be followed.

Please report all NON-COMPLIANCE issues or COMPLAINTS regarding this study to this office.

Please note that all research records must be retained for a minimum of three years.

Based on the risks, this project requires Continuing Review by this office on an annual basis. Please use the appropriate renewal forms for this procedure.

If you have any questions, please contact or Please include your study title and reference number in all correspondence with this office.

Chairperson

ALLIANCE
FOR CLINICAL TRIALS IN ONCOLOGY

Part I: IRB Review

Continuing / Annual Reviews

What are we looking for?

- Approval is ≤ 365 days from last review/initial approval

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ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

Part I: IRB Review

Continuing / Annual Reviews

What are we looking for?

- Approval is ≤ 365 days from last review/initial approval
- Full board reviewed for protocols w/ active recruitment or subjects on active treatment

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Part I: IRB Review

Required Amendments / Updates

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Part I: IRB Review

Required Amendments / Updates

What are we looking for?

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Part I: IRB Review

Required Amendments / Updates

What are we looking for?

- Approvals are obtained within 90 days of the group's notification date
  - Alliance broadcasts occur on the 1st and 15th of the month
  - CTSU broadcasts occur on the 8th and 22nd of the month

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FOR CLINICAL TRIALS IN ONCOLOGY

Part I: IRB Review

Required Amendments / Updates

What are we looking for?

- Approvals are obtained within 90 days of the group's notification date
  - Alliance broadcasts occur on the 1st and 15th of the month
  - CTSU broadcasts occur on the 8th and 22nd of the month
- The IRB review is appropriate to the requirement (i.e. full board vs. expedited)

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Part I: IRB Review

Required Amendments / Updates

Protocol Update #06
03/25/2015

ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

PROTOCOL UPDATE TO ALLIANCE A021202

PROSPECTIVE RANDOMIZED PHASE II TRIAL OF PAZOPANIB (NSC # 737754, IND 75648) VERSUS PLACEBO IN PATIENTS WITH PROGRESSIVE CARCINOID TUMORS

Pazopanib and matching placebo will be supplied by GlaxoSmithKline and distributed by CTEP

[X]	**Update:**	[ ]	**Status Change:**
[ ]	Eligibility changes	[ ]	Activation
[ ]	Therapy / Dose Modifications / Study Calendar changes	[ ]	Closure
[X]	Informed Consent changes	[ ]	Suspension / temporary closure
[ ]	Scientific / Statistical Considerations changes	[ ]	Reactivation
[ ]	Data Submission / Forms changes		
[ ]	Editorial / Administrative changes		
[X]	Other : Updated CAEPR		

The changes included in this update to A021202 have been made in response to the NCI Action Letter from Dr. Pamela Harris dated March 24, 2015. This Action Letter is posted on the A021202 Study Page on the Alliance web site. A revised CAEPR with the new risk has been added to the protocol. Therefore, the model consent form has been revised to incorporate this new risk consistent with the new NCI Model Template Instructions.

IRB approval (or disapproval) of this update is required within 90 days. Full Board review is recommended. Please follow your IRB of record's policies.

No new patients may be consented onto this protocol until IRB approval for this amendment has been obtained. Patients consented on or before March 25, 2015 may be enrolled onto this trial before local IRB approval of the revised protocol and informed consent form has been obtained.

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FOR CLINICAL TRIALS IN ONCOLOGY

Part I: IRB Review

Required Amendments / Updates

Protocol Update #06
03/25/2015

ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

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Common IRB Major Deficiencies

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Common IRB Major Deficiencies

- Local IRB Oversight

Major Deficiencies
Initial approval by expedited review instead of full-board review
Expedited reapproval for situations other than approved exceptions
Registration and/or treatment of patient prior to full IRB approval
Reapproval delayed greater than 30 days, but less than one year
Registration of patient on protocol during a period of delayed reapproval or during a temporary suspension (i.e., Request for Rapid Amendment)
Missing reapproval
Expired reapproval
Internal reportable adverse events reported late or not reported to the IRB
Lack of documentation of IRB approval of a protocol amendment that affects more than minimal risk or IRB approval is greater than 90 days after Network Group's notification; this includes a "Request for Rapid Amendment (RRA)" resulting from an Action Letter indicating temporary suspension of accrual with expedited review permitted
Failure to submit or submitted after 90 days, any reportable external safety report to the IRB that is considered an unanticipated problem as defined by OHRP, unless there is a local IRB policy that does not mandate reporting of external safety reports

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Common IRB Major Deficiencies

Update 3, broadcast on 3/1/17, was submitted to the IRB. A review of documents revealed the site over looked the submission of update 2, broadcast on 12/15/16. The site informed the IRB. The IRB acknowledged the changes for update 2 incorporated in update 3, therefore update 2 was approved with update 3 on 5/5/17.

Registration of patient on protocol during a period of delayed reapproval or during a temporary suspension (i.e., Request for Rapid Amendment)
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Internal reportable adverse events reported late or not reported to the IRB
Lack of documentation of IRB approval of a protocol amendment that affects more than minimal risk or IRB approval is greater than 90 days after Network Group's notification; this includes a "Request for Rapid Amendment (RRA)" resulting from an Action Letter indicating temporary suspension of accrual with expedited review permitted
Failure to submit or submitted after 90 days, any reportable external safety report to the IRB that is considered an unanticipated problem as defined by OHRP, unless there is a local IRB policy that does not mandate reporting of external safety reports

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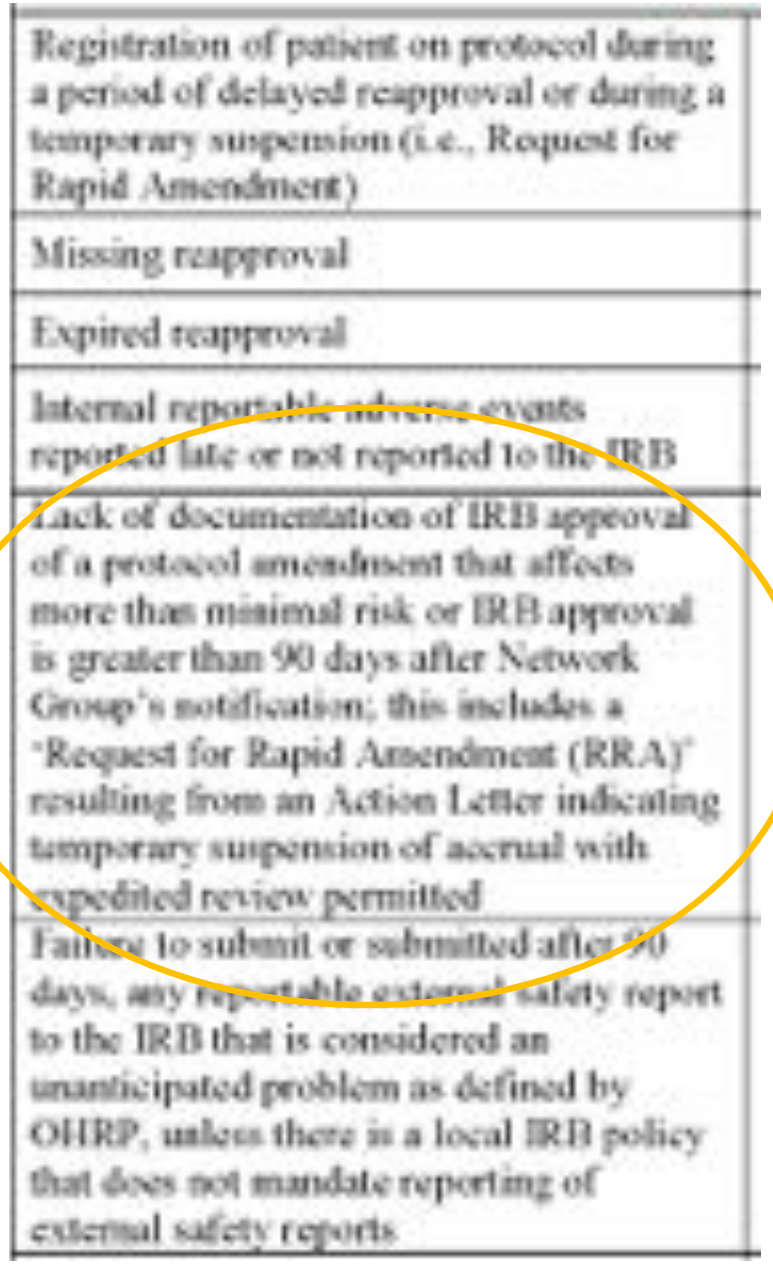
Common IRB Major Deficiencies

Update 3, broadcast on 3/1/17, was submitted to the IRB. A review of documents revealed the site over looked the submission of update 2, broadcast on 12/15/16. The site informed the IRB. The IRB acknowledged the changes for update 2 incorporated in update 3, therefore update 2 was approved with update 3 on 5/5/17.



Registration of patient on protocol during a period of delayed reapproval or during a temporary suspension (i.e., Request for Rapid Amendment)
Missing reapproval
Expired reapproval
Internal reportable adverse events reported late or not reported to the IRB
Lack of documentation of IRB approval of a protocol amendment that affects more than minimal risk or IRB approval is greater than 90 days after Network Group's notification; this includes a "Request for Rapid Amendment (RRA)" resulting from an Action Letter indicating temporary suspension of accrual with expedited review permitted
Failure to submit or submitted after 90 days, any reportable external safety report to the IRB that is considered an unanticipated problem as defined by OHRP, unless there is a local IRB policy that does not mandate reporting of external safety reports

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Common IRB Major Deficiencies

A study was submitted to the IRB for continuing review that would expire on 9/16/16. On 9/6/16 the site received contingent approval. The IRB required study clarifications. The study received full continuing review approval on 11/6/16.

Major Deficiencies
Initial approval by expedited review instead of full-board review
Expedited reapproval for situations other than approved exceptions
Registration and/or treatment of patient prior to full IRB approval
Reapproval delayed greater than 30 days, but less than one year

ALLIANCE
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Common IRB Major Deficiencies

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Reapproval delayed greater than 30 days, but less than one year

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Common IRB Major Deficiencies

Local IRB Oversight

- Amendment approvals obtained **greater than 90 days** post group's notification
- Continuing review approved by **expedited review** when full board review is needed
- Expired continuing reviews **greater than 30 days** late

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Common IRB Major Deficiencies

- CIRB Oversight

Major Deficiencies
Unanticipated problems, Serious Non-Compliance and/or Continuing Non-Compliance (per OHRP) problems not reported
Institution enrolls under an incorrect CTEP site code and the institution or institution CTEP site code is not covered by the CIRB

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Common IRB Major Deficiencies

Participant 987654 is enrolled to Alliance protocol A011106 for site US123. During the audit, the auditors note the participant was consented and enrolled at sub-affiliate/ component US124.

Major Deficiencies
Unanticipated problems, Serious Non-Compliance and/or Continuing Non-Compliance (per OHRP) problems not reported
Institution enrolls under an incorrect CTEP site code and the institution or institution CTEP site code is not covered by the CIRB
Other (explain)

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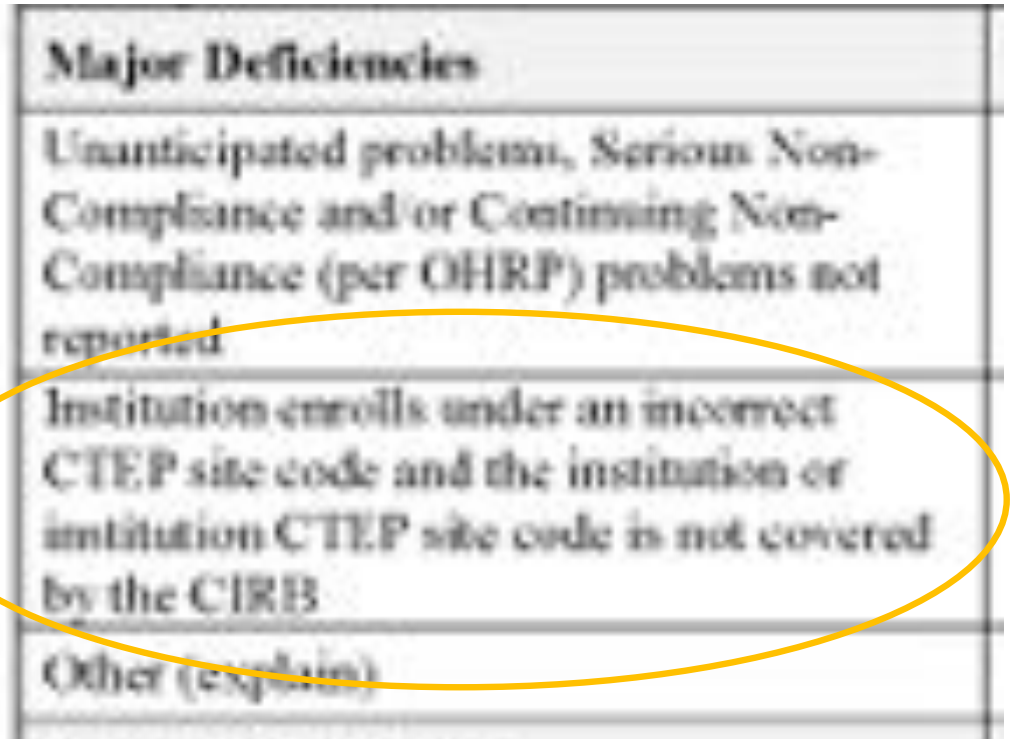
Common IRB Major Deficiencies

Participant 987654 is enrolled to Alliance protocol A011106 for site US123. During the audit, the auditors note the participant was consented and enrolled at sub-affiliate/ component US124.



Major Deficiencies
Unanticipated problems, Serious Non-Compliance and/or Continuing Non-Compliance (per OHRP) problems not reported
Institution enrolls under an incorrect CTEP site code and the institution or institution CTEP site code is not covered by the CIRB
Other (explain)

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Step I: Regulatory Pre-Review
Part II: Informed Consent Content

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Step I: Regulatory Pre-Review
Part II: Informed Consent Content

- A minimum of 4 consents will be selected for review

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Step I: Regulatory Pre-Review
Part II: Informed Consent Content

- A minimum of 4 consents will be selected for review
- For each consent selected the site will forward the following to the Chicago Office prior to the audit date (including CIRB reviewed studies)

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Step I: Regulatory Pre-Review
Part II: Informed Consent Content

- A minimum of 4 consents will be selected for review
- For each consent selected the site will forward the following to the Chicago Office prior to the audit date (including CIRB reviewed studies)
  - Current approved locally utilized informed consent form
  - Applicable model consent

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Part II: Informed Consent Content

ALLIANCE MODEL CONSENT FORM

RANDOMIZED PHASE II STUDY COMPARING CABOZANTINIB (NSC #761968 AND IND #116059) WITH COMMERCIALLY SUPPLIED SUNITINIB IN PATIENTS WITH PREVIOUSLY UNTREATED LOCALLY ADVANCED OR METASTATIC RENAL CELL CARCINOMA

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation.

You are being asked to take part in this study because you have advanced or metastatic kidney cancer

Why is this study being done?

The purpose of this study is to find out what effects, good and/or bad, two study drugs called sunitinib and cabozantinib have on you and on advanced or metastatic kidney cancer. Sunitinib has been approved by the FDA and cabozantinib is an investigational drug. Both medications target special proteins that are on the surface of the kidney cancer cell and both drugs are taken by mouth.

How many people will take part in the study?

About 150 people will take part in this study.

Site Name/Logo Here

Consent Form

Title of Protocol

Randomized Phase II Study Comparing Cabozantinib (NSC#761968 and IND#116059) with Commercially Supplied Sunitinib in Patients with Previously Untreated Locally Advanced or Metastatic Renal Cell Carcinoma

Who is conducting this study?

Principal Investigator:

Sub-Investigators:

Sponsor: Alliance for Clinical Trials in Oncology (Alliance)

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation.

Why have I been asked to take part in this research study?

You have been asked to take part in this study because you have advanced or metastatic kidney cancer.

Why is this study being conducted?

The purpose of this study is to find out what effects, good and/or bad, two study drugs called sunitinib and cabozantinib have on you and on advanced or metastatic kidney cancer. Sunitinib has been approved by the FDA and cabozantinib is an investigational drug. Both medications

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Step I: Regulatory Pre-Review
Part II: Informed Consent Content

What are we looking for?

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Part II: Informed Consent Content

- Informed Consent Forms are reviewed for the 8 basic required elements of a consent (21CFR50.25)
  - Study involves research
  - Description of foreseeable risks
  - Description of benefits
  - Disclosure of alternatives
  - Description describing confidentiality maintenance
  - Compensation / treatment in the case of injury
  - Contact information for questions regarding research/rights
  - Participation is voluntary

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Part II: Informed Consent Content

- Informed Consent Forms are reviewed for additional elements (21CFR50.25)
  - Treatment may involve risks
  - Anticipated circumstances in which subject's participation may be terminated
  - Additional costs to the subject
  - Consequences for subject's decision to withdraw
  - Subject will be informed of significant new findings
  - Approximate number of subjects
  - A copy of this form will be given to the subject
  - http://www.ClinicalTrials.gov website listed per U.S. law

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Part II: Informed Consent Content

CIRB Trials

Yes the informed consent form is reviewed!

Because CIRB is the **IRB of record** your locally utilized consent must be a **word for word** match with the model consent with the exception of what is approved **by the CIRB** on the study specific worksheet with local context

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Informed Consent Content
Common Major Deficiencies

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Informed Consent Content Common Major Deficiencies

- ICF missing any of the 8 required elements
  - Study involves research
  - Description of foreseeable risks
  - Description of benefits
  - Disclosure of alternatives
  - Description describing confidentiality maintenance
  - Compensation / treatment in the case of injury
  - Contact information for questions regarding research/rights
  - Participation is voluntary

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Informed Consent Content Common Major Deficiencies

- ICF missing language from the additional elements
  - Treatment may involve risks
  - Anticipated circumstances in which subject's participation may be terminated
  - Additional costs to the subject
  - Consequences for subject's decision to withdraw
  - Subject will be informed of significant new findings
  - Approximate number of subjects
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  - http://www.ClinicalTrials.gov website listed per U.S. law

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Informed Consent Content Common Major Deficiencies

When reviewing a site's ICF for an Alliance trial studying the effects of Cabozantinib in patients with Renal Cell Carcinoma, the auditor noted the addition of the risks Abdominal, oral, extremity, muscle and chest pain which were not listed in the model consent.

Deficiencies

- Involves research, purpose, duration of participation
- Description of foreseeable / unforeseeable risks
- Description of any benefits
- Disclosure of alternative procedures/treatments
- Description of the extent of confidentiality of records
- Explanation of compensation/ treatments available if injured

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Informed Consent Content Common Major Deficiencies

When reviewing a site's ICF for an Alliance trial studying the effects of Cabozantinib in patients with Renal Cell Carcinoma, the auditor noted the addition of the risks Abdominal, oral, extremity, muscle and chest pain which were not listed in the model consent.

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- Explanation of compensation/ treatments available if injured

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Informed Consent Content Common Major Deficiencies

When reviewing the site's ICF for a trial studying Lenalidomide in Multiple Myeloma, receiving CIRB Oversight, the auditor noted additional language throughout the consent form not found in the model or approved Boiler Plate Language.

Deficiencies

- Failure to revise the ICF in response to an NCI Action Letter regarding risks
- Significant or substantial changes to the consent form document deviating from the CIRB-approved Boiler
- ICF contains changes not approved by the IRB, including changes to questions.

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Informed Consent Content Common Major Deficiencies

When reviewing the site's ICF for a trial studying Lenalidomide in Multiple Myeloma, receiving CIRB Oversight, the auditor noted additional language throughout the consent form not found in the model or approved Boiler Plate Language.

Deficiencies

- Failure to revise the ICF in response to an NCI Action Letter regarding risks
- Significant or substantial changes to the consent form document deviating from the CIRB-approved Boiler Plate language
- ICF contains changes not approved by the IRB, including changes to questions.

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Informed Consent Content Common Major Deficiencies

- **Omission** of one or more risks
- **Omission** of one or more of the required informed consent elements
- **Changes** to the following without Alliance approval
  - Additions to the risks
  - Additions / Omissions to the list of alternative options
  - Changes to the translational research section (including the questions)
- **Changes** to the ICF without the IRB of record approval

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Step II: Regulatory Review at Time of Audit

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Step II: Regulatory Review at Time of Audit

- Review of regulatory approval documents for any unannounced protocols

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Step II: Regulatory Review at Time of Audit

- Review of regulatory approval documents for any unannounced protocols
- Review submission of unanticipated / IND reports per your IRB policy

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Step II: Regulatory Review at Time of Audit

- CIRB reviewed trials
  - Ensure amendments that included ICF changes are implemented at your site within 30 days of CTSU posting

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Step II: Regulatory Review at Time of Audit

Part III: Delegation Task Log

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Part III: Delegation Task Log

- Review Delegation of Task Log (for applicable registration trials)

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Part III: Delegation Task Log

- Review Delegation of Task Log (for applicable registration trials)
  - To evaluate the roles and responsibilities of the individuals contributing efforts to a clinical trial a DTL must be maintained

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Part III: Delegation Task Log

What are Auditors looking for?

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Part III: Delegation Task Log

What are Auditors looking for?

- Ensure all research staff and roles are identified

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Part III: Delegation Task Log

What are Auditors looking for?

- Ensure all research staff and roles are identified
- Utilize the DTL during the patient case review to ensure tasks performed during the clinical trial correlate with the DTL

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Delegation Task Log
Major Deficiencies

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Delegation Task Log
Major Deficiencies

Major Deficiencies
Performing tasks not assigned to individual
Failure to keep DTL current
Individual not listed on DTL

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Delegation Task Log Major Deficiencies

While reviewing a patient case for Alliance registration trial A031203 the auditor noted documentation that the Data Coordinator conducted the consenting process with the participant. The consenting process is not a task listed for this staff member on the DTL.

Major Deficiencies
Performing tasks not assigned to individual
Failure to keep DTL current
Individual not listed on DTL

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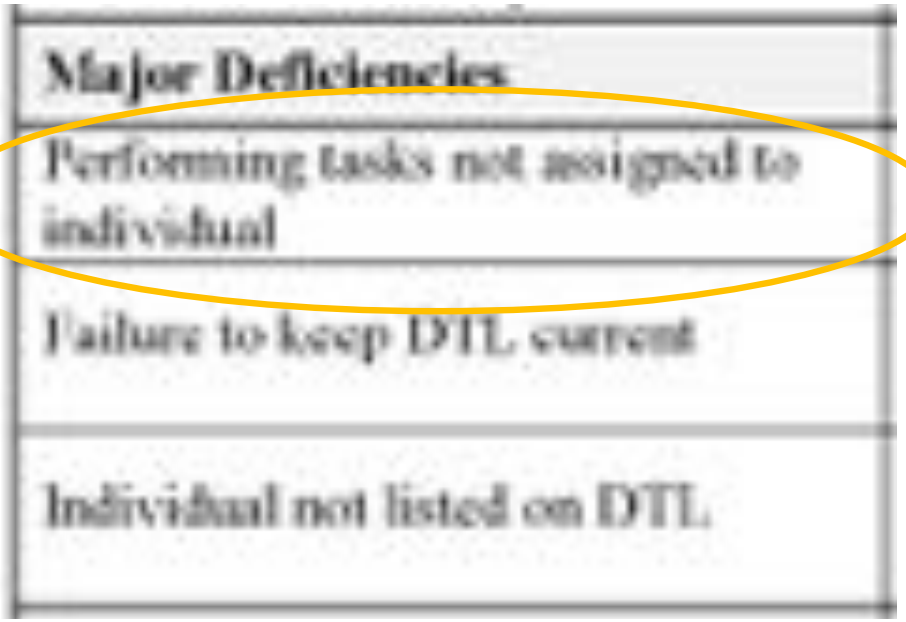
Delegation Task Log Major Deficiencies

While reviewing a patient case for Alliance registration trial A031203 the auditor noted documentation that the Data Coordinator conducted the consenting process with the participant. The consenting process is not a task listed for this staff member on the DTL.



Major Deficiencies
Performing tasks not assigned to individual
Failure to keep DTL current
Individual not listed on DTL

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Step II: Regulatory Review at Time of Audit

- Resolve any regulatory and consent discrepancies found during the pre-review / time of audit

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Step II: Regulatory Review at Time of Audit

- Resolve any regulatory and consent discrepancies found during the pre-review / time of audit
- Assess any regulatory findings

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Step II: Regulatory Review at Time of Audit

- Assess any regulatory findings
  - **Critical** Deficiency

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Step II: Regulatory Review at Time of Audit

- Assess any regulatory findings
  - **Critical** Deficiency
  - Major Deficiency

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Step II: Regulatory Review at Time of Audit

- Assess any regulatory findings
  - **Critical** Deficiency
  - Major Deficiency
  - Lesser Deficiency

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Step II: Regulatory Review at Time of Audit

- Assess any regulatory findings
  - **Critical** Deficiency: Any finding identified before or during an audit that is suspected to be fraudulent activity (CTMB guidelines 5.1)

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Step II: Regulatory Review at Time of Audit

- Assess any regulatory findings
  - Critical Deficiency: Any finding identified before or during an audit that is suspected to be fraudulent activity (CTMB guidelines 5.1)
  - Major Deficiency: A variance from the protocol-specified procedures or practices that makes the resulting data questionable

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Step II: Regulatory Review at Time of Audit

- Assess any regulatory findings
  - Critical Deficiency: Any finding identified before or during an audit that is suspected to be fraudulent activity (CTMB guidelines 5.1)
  - Major Deficiency: A variance from the protocol-specified procedures or practices that makes the resulting data questionable
  - Lesser Deficiency: Findings do not have a significant impact on the outcome or interpretation of the study

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Step II: Regulatory Review at Time of Audit

- Assess any regulatory findings
  - Acceptable

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Step II: Regulatory Review at Time of Audit

- Assess any regulatory findings
  - Acceptable
  - Acceptable, Needs Follow-up

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Step II: Regulatory Review at Time of Audit

- Assess any regulatory findings
  - Acceptable
  - Acceptable, Needs Follow-up
  - Unacceptable

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Step II: Regulatory Review at Time of Audit

- Assess any regulatory findings
  - Acceptable
    - No deficiencies identified
    - Few Lesser deficiencies identified

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Step II: Regulatory Review at Time of Audit

- Assess any regulatory findings
  - Acceptable
    - No deficiencies identified
    - Few Lesser deficiencies identified
  - Acceptable, Needs Follow-up
    - Any Major deficiencies identified
    - Multiple Lesser deficiencies identified

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Step II: Regulatory Review at Time of Audit

- Resolve any regulatory and consent discrepancies found during the pre-review / time of audit
- Assess any regulatory findings
  - Acceptable
    - No deficiencies identified
    - Few Lesser deficiencies identified
  - Acceptable, Needs Follow-up
    - Any Major deficiencies identified
    - Multiple Lesser deficiencies identified
  - Unacceptable
    - A single Critical deficiency
    - Multiple Major deficiencies identified
    - Multiple Lesser deficiencies of a recurring nature

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How to Avoid Regulatory Deficiencies

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How to Avoid IRB Deficiencies

Get Organized!

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How to Avoid IRB Deficiencies

Get Organized!

- Create a separate chronological regulatory file for each protocol and each document type
  - Initial Final Approval
  - Continuing Reviews
  - Required Amendments

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How to Avoid IRB Deficiencies

Get Organized!

- Create a separate chronological regulatory file for each protocol and each document type
  - Initial Final Approval
  - Continuing Reviews
  - Required Amendments
- Print, Flag and File approval documents ASAP!

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How to Avoid IRB Deficiencies

Get Organized!

- Create a separate chronological regulatory file for each protocol and each document type
  - Initial Final Approval
  - Continuing Reviews
  - Required Amendments
- Print, Flag and File approval documents ASAP!
- Create a calendar for tracking regulatory deadlines
  - Deadlines for protocol submissions to IRB
  - Reminders to check email/sponsor website on broadcast dates

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How to Avoid ICC Deficiencies

- Utilize the model consent as your local informed consent form!
  - Copy the model **word for word**
  - Insert local language where appropriate
  - Have a double check system of review

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How to Avoid ICC Deficiencies

- Utilize the model consent as your local informed consent form!
  - Copy the model **word for word**
  - Insert local language where appropriate
  - Have a double check system of review
- The content of certain ICC sections should **NEVER** change
  - Risk List
  - Alternative procedures / treatment
  - Translational research section (wording/order of the questions)

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How to Avoid ICC Deficiencies

- Contact the **Alliance** for approval for ICC changes
  - Risk List
  - Alternative procedures / treatment
  - Translational research section
  - Changes that may alter the intent/methodology of the study

- See **Alliance** Policy & Procedure section 2.8.7.2.2

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How to Avoid DTL Deficiencies

- Create a study specific DTL at the time of study activation

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How to Avoid DTL Deficiencies

- Create a study specific DTL at the time of study activation
  - List all pertinent research staff and assigned roles
  - Ensure PI signs and dates

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How to Avoid DTL Deficiencies

- Create a study specific DTL at the time of study activation
  - List all pertinent research staff and assigned roles
  - Ensure PI signs and dates
- Ensure the research staff is aware of their study specific tasks
- Keep the DTL up-to-date with research staff/role changes

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Conclusion: Regulatory Review

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Conclusion: Regulatory Review

- Regulatory review is a two step process
  - Pre-review (prior to the audit date)
  - Items reviewed at the time of the audit

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Conclusion: Regulatory Review

- Regulatory review is a two step process
  - Pre-review (prior to the audit date)
  - Items reviewed at the time of the audit
- Regulatory review occurs in three parts
  - IRB review
  - Informed Consent Content review
  - DTL review (for applicable registration trials)

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Conclusion: Regulatory Review

- Regulatory review is a two step process
  - Pre-review (prior to the audit date)
  - Items reviewed at the time of the audit
- Regulatory review occurs in three parts
  - IRB review
  - Informed Consent Content review
  - DTL review (for applicable registration trials)
- Common Major Deficiencies
  - IRB review
  - Informed Consent Content review
  - Delegation Task Log review
  - How to Avoid Deficiencies

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Website Resources

The Alliance for Clinical Trials in Oncology

www.allianceforclinicaltrialsinoncology.org

FDA Code of Federal Regulations

https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm

Cancer Therapy Evaluation Program (CTEP)

http://ctep.cancer.gov/branches/ctmb/clinicalTrials/docs/ctmb_audit_guidelines.pdf

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THANK YOU!
Questions from Audience
Answers from Presenter