Preparing Your Audit Response: Corrective and Preventative Action Plans (CAPAs)

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Alliance Fall 2015 Group Meeting

Goals of CAPAs:

- Assess to measure
- Measure to correct
- Correct to prevent
- Prevent to achieve
  - *[SoCRA SOURCE – August 2012]*

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CAPAs and Good Clinical Practice

Preventing errors in the future:

1) Eliminates potential patient safety issues
2) Provides cleaner research data
3) Saves time for staff and lead group
4) Ultimately reduces costs

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Exit Interview Reminders

- Take notes throughout the audit and at the Exit Interview
- Make sure to understand the comments from the Exit Interview - don’t be afraid to ask questions

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The Final Audit Report (behind the scenes)

- Team Leader creates a draft audit report and resolves any outstanding issues with the site
- A second review is conducted to check for accuracy and consistency

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The Final Report (behind the scenes)

- The final version is submitted in the CTMB via the AIS (Audit Information System) electronic database
- An electronic version of the final audit report is emailed to the Principal Investigator and Lead CRP

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Audit Report Distribution to Affiliates and Components

- It is the Main Member's or NCORP's responsibility to share and review the audit report with affiliates/ components

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Understanding the Audit Report

Reminder of three audit components:

- IRB/ Consent Content
- Pharmacy
- Patient Case Review

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Understanding the Audit Report

Category ratings:

- *OK* (no deficiency is warranted)
- *Lesser Deficiency* (minor deficiency)
- *Major Deficiency* (significant error or omission)

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Understanding the Audit Report

Overall Category Assessment for IRB/ICC and PCR:

- *Acceptable* – No follow-up is needed
- *Acceptable Needs Follow-up* – corrective and preventative action plan required within 15 business days
- *Unacceptable* – As above and re-audit scheduled within 12 months required

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Clinical Trials Monitoring Branch Final Report

Run By: **Date:**

Audit Date: /2014 **Group :** ALLIANCE **Audit Category:** **Audit Type:**
Institution NCI Code: **Name:**
Audit Location:
Revision Number: **Revision Date:**

Date of Prior Audit: **Number of Cases Audited:** **Average Annual Accrual:** **Principal Investigator:**

Institution Details

Institution NCI Code	Institution Name	Role

Audit Outcome Summary

Component	Assessment	Follow up Required (Y/N)	Follow up Due Date	Reaudit Required (Y/N)	Reaudit Time (in months)
IRB and Informed Consent Content Review	Acceptable	No		No	
Accountability of Investigational Agents	Acceptable needs follow-up	Yes	11/13/2014	No	
Patient Case Review	Acceptable needs follow-up	Yes	11/13/2014	Yes	18 Months

Reaudit Timeline History

Component	Reaudit Time	Reaudit CTMB Comments
Patient Case Reaudit Time Line History	18 Months	

Institution Staff	Title	Affiliation

Audit Team	Title	Affiliation
Barrett, Barbara (MS, CCRP)		Alliance- Chicago Office
Sutton, Linda (MD)		Duke University Medical Center

If you receive an Unacceptable rating…

- Alliance Policy - An *Unacceptable* rating in any section of the audit is evaluated on a case-by-case basis and may warrant immediate suspension of registration privileges
- Should a suspension occur, it will be lifted when a response is submitted and found to be Acceptable

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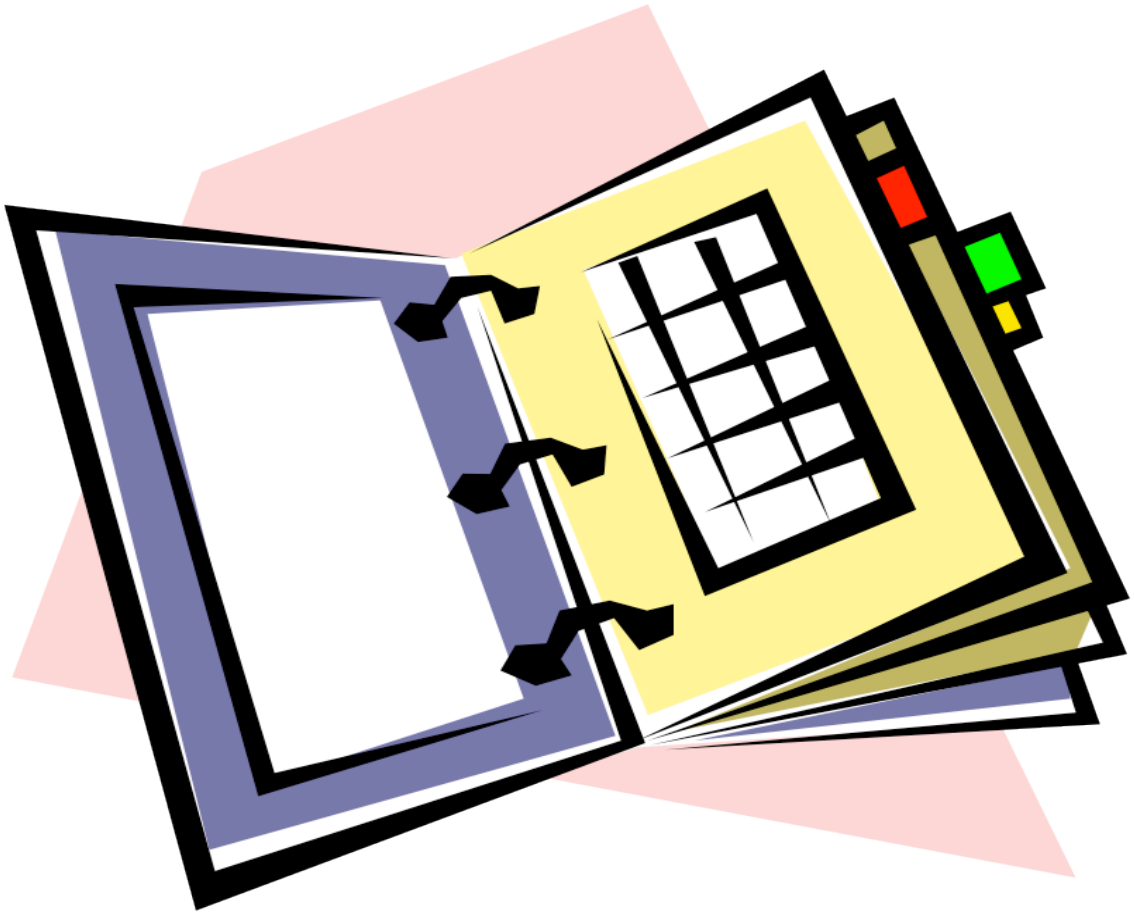
Sample Audit Reports



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Audit Report Cover Letter

Summarizes the three ratings:

- *The IRB/Consent Content review was rated **Acceptable Needs Follow-up**. The deficiencies include…... Pharmacy review was rated **Acceptable**. The Patient Case review was rated **Unacceptable**. The deficiencies include…….*

Provides a date the CAPA is due:

- *A written corrective and preventative action plan addressing the deficiencies in these areas must be submitted by **Tuesday, December 15, 2015.***

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Patient Case Review

Protocol#	Patient#	Informed Consent	Eligibility	Treatment	Disease Outcome / Response	Adverse Event	General Data Management Quality
		OK	OK	OK	OK	OK	Major
		OK	OK	OK	OK	OK	Major
		OK	OK	Not Reviewed	Not Reviewed	Not Reviewed	Not Reviewed
		OK	OK	OK	OK	OK	Major

Total # of Patient cases: 4 **Total # of Major deficiencies:** 3 **Total # of Lesser deficiencies:** 0 **Total # of items Not Reviewed:** 4

Patient Case Review Assessment

Patient Case Review Assessment: Acceptable needs follow-up
Follow-up required for Informed Consent: No
Follow-up required for Eligibility: No
Follow-up required for Treatment: No
Follow-up required for Disease Outcome/Response: No
Follow-up required for Adverse Event: No
Follow-up required for General Data Management Quality: Yes COMMENTS: A corrective and preventative action plan is required so that all data is submitted according to protocol guidelines.
Reaudit required: Yes
Reaudit Reason: Data delinquency was found in all three cases that were reviewed in full. Returning in 18 months provides the next audit to assess data submission compliance.
Reaudit required (in months): 18 Months

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Audit Procedures: This first Alliance audit for was conducted on-site and followed the Alliance procedures.

The IRB and ICC section of the audit is rated Acceptable. The site was commended for compliant regulatory processes and well organized documentation.

The Drug Accountability and Pharmacy review section is rated as Acceptable Needs Follow-up. The NCI DARF was not completed in full.

The Patient Case Review section is rated Acceptable Needs Follow-up. Three cases were audited in full. One unannounced case received limited review. Three major deficiencies were found for data delinquency. All study required research specimens were submitted and found acceptable.

The auditors appreciated the site's preparedness and assistance throughout the audit.

A written corrective and preventative action plan addressing the deficiencies for delinquent data is due to the Chicago Central Office by Friday, October 17.

General Comments: The regulatory documentation of approvals and local ICF review for consent content was conducted off-site prior to the audit by Ms. Jean Wittlief.

The next audit will be scheduled within 18 months to evaluate the effectiveness of the required corrective and preventative plan for data delinquency.

Exit Interview Comments: An exit interview was conducted with Dr. and his research staff listed on page 1 and 2 of this report.

The auditors recommended that one staff CRA be responsible for data submission compliance. In addition, the auditors recommended the site send someone to the Alliance Fall Group meeting to attend the Audit Preparation Workshop.

Prepared By **Date** **Approved By** **Date**

Submission of CAPAs

CAPAs must include:

- ***Corrective*** measures taken for deficiencies, including a root cause analysis (e.g., submission of outstanding data, correction and submission of data errors, or IRB submission of missed protocol updates)
- Measures for ***prevention*** of deficiencies in the future (e.g., revision of P&Ps, additional training, double check system)
- ****Happy to review draft CAPAs****

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Submission of CAPAs

- Author(s) of CAPA should be identified
- CAPA MUST be submitted on letterhead and signed by the PI, plus any other author(s)
- Attach any pertinent support documentation (submit amended CRFs to the data center, not to us)
- No need to attach copy of your audit report
- Submit CAPAs via email (audit@AllianceNCTN.org) or fax (312-345-0117)

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CAPA Review

- The audit program director (APD) reviews the corrective and preventative action plan to determine if the response is Acceptable. If the CAPA is not Acceptable, clarification of additional information will be requested.
- The CAPA will be submitted to the CTMB.
- If the CTMB requires additional information, they will contact the Alliance and we will contact you.

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Writing a Satisfactory CAPA

Address each issue listed in audit report as needing follow-up.

Address 3 questions:

- *Why did this deficiency occur?* (Conduct root cause analysis, i.e. why did the issue occur?)
- *Has the specific problem been corrected?* (i.e. has the outstanding data in question been submitted? Or has patient been re-consented with the updated consent form?)
- *What plan has been implemented to ensure this type of deficiency will not occur in the future?*

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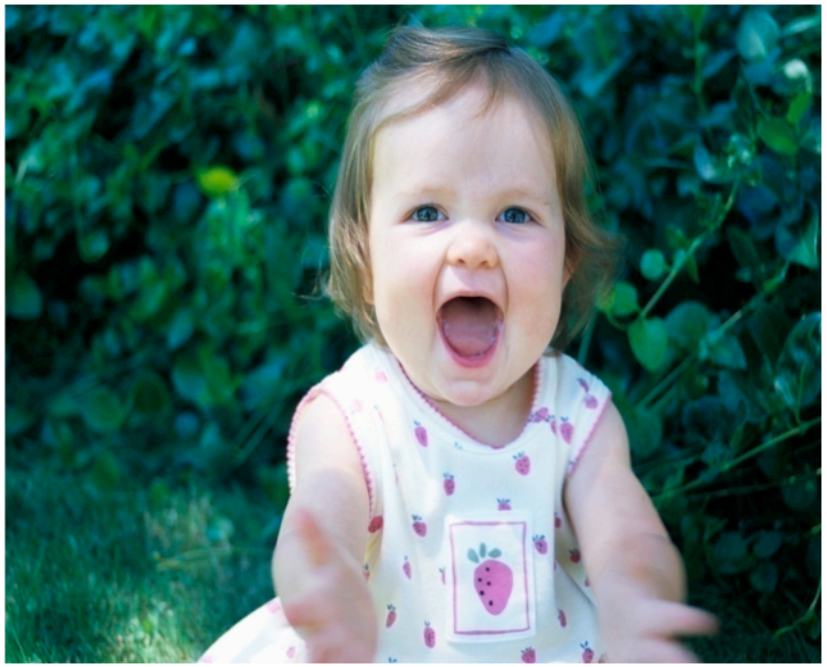
Samples of Acceptable/ Unacceptable Corrective Action Plans



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IRB Deficiency

Major Deficiency	Partially Acceptable CAPA
Update #6 posted on 02/15/14 has not been submitted to the IRB.	As updates are identified, they will be entered on the Outlook calendar to submit and track.

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IRB Deficiency

Major Deficiency	Acceptable CAPA
Update #4 posted on 07/1/14 was IRB approved 3/16/14, which is > 90 days.	A 2 person team is now responsible for reviewing update broadcasts, ensuring updates are submitted to IRB and approved w/n 90 days.

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IRB Consent Content Deficiency

Major Deficiency	Partially Acceptable CAPA
The local ICF does not include sample submission question #1 from page 2 of the model consent. This study is still open to new enrollment.	A revision has been submitted to the IRB that includes all model consent questions. The site will now use the consent content checklist and review local consents compared to model consents.

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Pharmacy Deficiency

Major Deficiency	Acceptable or Unacceptable Plan?
The new ORAL DARF is not in use as per the PMB required date of September 1, 2014 for two studies.	Two new sections have been added to our Pharmacy policy (see attached). One is mandating use of Oral DARF and the other is to include the CTMB Guidelines section 5.3. Pharmacy staff have been re-educated.

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Pharmacy Deficiency

Major Deficiency	Acceptable or Unacceptable Plan?
DARF entries not in chronological order. Distribution of drug entered before date drug was received.	IND SOPs updated. Double checks will occur as drug is received, counted, and entered on DARF in real time. In-house audits will occur monthly and will include DARF reviews and shelf counts for accuracy.

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Eligibility Deficiency

Major Deficiency	Acceptable or Unacceptable Plan?
The patient had prior ketoconazole treatment which is not allowed per Eligibility criteria section 5.2b.	The CRP is now required to review the inclusion and exclusion criteria and be sure the past medical history is taken into account.

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Treatment Deficiency

Major Deficiency	Acceptable or Unacceptable Plan?
Dose modification error for Cycle 4. A 25% dose adjustment was warranted due to AE, but the patient received a 40% dose reduction. This is greater than 10% margin of error.	"In reviewing these, I believe she did a very good job overall, but there were some confusing items which were misinterpreted. I believe that with her experience now, the next case would be much better."

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Disease Response Deficiency

Major Deficiency	Acceptable or Unacceptable Plan?
Section 6.1.2 requires all measurable lesions w/ max of 2 per organs and 5 in total to be identified as baseline tumor measurements.	The measurement forms have been amended and re-submitted. The study team will now review all scans with the radiologist, attending, and CRP at baseline and follow-up time-points.

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Disease Response Deficiency

Major Deficiency	Acceptable or Unacceptable Plan?
The claimed response of PD on 7/4/2014 could not be verified.	The error is correct and was human error. The CRA will be reminded to refer to the protocol section about accurate reporting of target lesions.

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Adverse Event Deficiency

Major Deficiency	Acceptable or Unacceptable Plan?
Patient was ATH 3/26/15 and died 3/28/15 while still on study treatment. Sect 10.4 requires AER submitted w/n 24 hours of learning of death. AERs was submitted 6/20/15.	The oncology fellow who admitted the patient did not contact the CT office of the admission and death. She has been reminded of the need for this.

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Data Quality Deficiency

Major Deficiency	Acceptable or Unacceptable Plan?
Per the Alliance Pathology Coordinating Office, the study required blood samples and blocks were not submitted.	"The CRA has been re-educated. This was an isolated event and we do not feel it will occur again."

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Data Quality Deficiency

Major Deficiency	Acceptable or Unacceptable Plan?
Data forms for treatment, AE and disease response have not been submitted since cycle #7 (11/19/14). Patient had progressive disease on 11/26/2014.	All forms have been submitted. The cancer center has hired an additional experienced CRP. Monthly staff meetings will cover data submission schedules. A quarterly review of data will be performed by the office manager.

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Two Consecutive Unacceptable Ratings
(In the same component)

CTMB section 6.3.2: **Probation of Participating Institutions**

- The institution will be placed on probation
- The Group may assign a mentor
- A “site improvement plan” must be developed to “address key infrastructural issues contributing to poor performance”

(ALL of this in addition to a required corrective and preventative action plan.)

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Example of Acceptable Site Improvement Plan for IRB

- The local IRB policies were revised in response to the audit findings.
- The main member network will cover the costs of the site's CRP to attend the Audit Workshop at the next Alliance group meeting.
- The Lead CRP will perform two IRB audits of the affiliate over the next year.

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Questions?

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Thank you!

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2015 Fall Group Meeting

November 5 – 8 / Chicago, IL