Category: Quality Assurance & Remote Monitoring and Auditing - Work in Progress

Implementation of an Audit Assessment Category Guidance System to Define Audit Deficiencies as Critical, Major, or Minor

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1. Background

Internal protocol audits conducted by MD Anderson's Clinical Research Audit Group consist of reviewing and evaluating the regulatory documents and the individual patient records for compliance with the study. All deficiencies are identified and recorded on a report during the audit review process and then discussed with the study principal investigator (PI) and research team. We define a deficiency as any incomplete, incorrect, or missing item that is not in keeping with the investigational plan, institutional requirements, or federal regulations. This definition is in line with the National Institute of Health (NIH) and National Cancer Institute (NCI) monitoring and auditing guidelines. While our audit process is very consistent, we were lacking a standardized method to categorize the severity of each audit deficiency.

2. Goals

Our primary goal was to come up with a systematic way to label and categorize each audit deficiency by degree of severity to be in line with industry and federal guidelines/processes. By developing an internal reference chart to define the severity of each deficiency, this would standardize the way that each auditor captures audit deficiencies. We believe these labeling categories provide a means of making the audit process more impactful for the principal investigator (PI) study team and our internal Data Safety Monitoring Committee (DSMC).

3. Solutions and Methods

An "Audit Assessment Category Guidance Process" was initiated in September 2021 to provide standardized categories that the auditors could use to grade the severity of each audit deficiency. The auditors now assess and label each audit deficiency as "critical," "major," or "minor" per a reference chart within the guidance document. The audit deficiencies are further broken down into the following categories: regulatory documents, informed consent, eligibility, protocol compliance, treatment administration, disease outcome, toxicity, and data quality. If critical or major deficiencies are noted in the audit, the PI may also be asked to complete and return a Corrective and Preventive Action Plan (CAPA).

4. Outcomes

The feedback has been positive on the initiation and usefulness of the audit deficiency categories. This has been a very effective method for both the auditor and the PI in understanding which audit deficiencies are more serious in nature. Since this process was initiated, CAPAs for major deficiencies have been requested and completed for 28 studies out of the 171 total protocol audits conducted representing approximately 16 percent of all audits conducted. For internal studies with DSMC oversight, the review categories have assisted the DSMC in determining the severity of the audit. Additionally, the PI and study team are now encouraged to take internal research topic educational courses for any repetitive audit deficiencies categorized as major or critical.

5. Lessons Learned and Future Direction

We plan to continue updating this process and the reference chart as more data and different audit situations arise. Over the last six months, we have started tracking additional audit metrics and trends

on the number of major and critical audit deficiencies. We plan to use this data to better identify PIs and departments who have repetitive major findings within the same audit categories. We will also share this information with our research education team so that they can assist with re-education needs as identified through the audit deficiencies.

Figure: Office of Protocol Support and Management Clinical Research Audit Group: Audit Assessment Category Guidance Process for Critical, Major and Minor Deficiencies

Audit Deficiencies Reference Chart

Regulatory Documents or Process	
Critical Deficiency	• Any finding identified before or during an audit that is suspected to be fraudulent activity
Major Deficiencies	• Failure to obtain IRB approval for the study or informed consent document (ICD) • Interruption or delay greater than 30 calendar days in the IRB continuing review approval of the study • Participant enrollment or study procedures conducted prior to study approval/activation by IRB or during a period of delayed reapproval or during a temporary hold or suspension • No 1572 (when applicable) or Investigator Agreement (when applicable) • 1572 (when applicable) signatures are missing • No Delegation of Authority Log (DoA) • Performing tasks not assigned for three or more study team members • Multiple cumulative effect of lesser DoA deficiencies • Multiple missing source documents • Required institutional training (GCP, HSPT, CRT) not complete for three or more study team member • Other (Explain)
Minor Deficiencies	• Minimal DoA Log findings; Failure to keep DoA current • Not all appropriate investigators are listed on the 1572 • Required institutional training (GCP, HSPT, CRT) not complete for one or two study team members • Other (Explain)
Informed Consent Document/Process	
Critical Deficiency	• Any finding identified before or during an audit that is suspected to be fraudulent activity
Major Deficiencies	• Missing ICD document • Failure to obtain appropriate signatures on the ICD

	• ICD not signed and dated by the patient/study participant (or parent/legally authorized representative, if applicable) or not signed prior to study procedures performed • Incorrect version of the ICD was used • Failure to obtain re-consent as required within the timeframe, if applicable • The informed consent process is not documented in the medical record • English consent signed/dated by a non-English speaking patient/study participant • Non- physician consented patients on a treatment study per MD Anderson policy requirements • Multiple cumulative effect of lesser informed consent deficiencies • Other (Explain)
Minor Deficiencies	• Consent dated incorrectly, or signatures in the wrong location • The person obtaining consent signed the ICD on a different date than the participant with no documentation explaining the date difference • The signature on the ICD for the person obtaining consent is not legible and missing other identifiers so not able to identify who consented the patient • Documentation not present in IC process to state that the person who signed consent explained the study to the patient or LAR • Other (Explain)
Eligibility	
Critical Deficiency	• Any finding identified before or during an audit that is suspected to be fraudulent activity
Major Deficiencies	• Unable to verify multiple eligibility criteria due to missing documentation • Participant not eligible for study • Tests and/or study required procedures to determine eligibility not completed prior to enrollment or not completed within the timeline specified in the protocol. • Patients received previous therapy or has a current treatment not allowed for study enrollment per the study I a • Other (Explain)
Minor Deficiencies	• Source documentation confirming some of the eligibility criteria was not found. The criteria may have been met/done correctly and patient eligible, but was not clearly documented in medical records • Other (Explain)
Compliance with Study Plan	

Critical Deficiency	• Any finding identified before or during an audit that is suspected to be fraudulent activity
Major Deficiencies	• Excessive study documentation missing • Recurrent missed study evaluations • Excessive failure to follow investigational plan • Recurrent collection of research blood or tissue sample at the incorrect timepoint or on a participant who did not elect to have them collected. • Excessive (more than 5) missing questionnaires on a non-treatment-based questionnaire study. • Other (Explain)
Minor Deficiencies	• A minimal number of missing study specific tests/assessments or required lab tests • Research related blood or tissue sample was collected but the total amount differed from amount specified in study or was collected at wrong time point • Minimal number (5 or less) patient questionnaires missing on a treatment or non-treatment based study. • Assessment completed but not in compliance with the description/timeline in the study • Patients were removed from study, but source documentation of study removal was not found • Other (Explain)
Treatment Administration	
Critical Deficiency	• Any finding identified before or during an audit that is suspected to be fraudulent activity
Major Deficiencies	• Incorrect administration or dosing of study agent. • Additional agent/treatment intervention used which is not permitted by the study • Dose calculated incorrectly (error greater than +/- 10%) • Treatment/intervention incorrect, not administered correctly, or not adequately documented • Timing and sequencing of treatment/intervention not per study. • Unjustified delays in treatment/intervention • Incorrect dosing modification due to an ongoing AE. • Inappropriate administration of non-study anticancer treatment (additional drugs, radiation, etc.) • Repetitive or systemic errors in dosing • Failure to return unused investigational drug by multiple patients and/or time points if specified in the study • Excessive (more than 5) missing patient self-dosing records for oral study medications.

	• Other (Explain)
Minor Deficiencies	• Minimal (5 or less) missing patient self-dosing records for oral study medications. • Discrepancy between oral drug return listed in study notes or on pill diary vs. what amount should have been returned • The study gives guidelines in how the oral med is to be self-administered (i.e. on an empty stomach) and there is no documentation stating this. • Other (Explain)
Disease Outcome/Response	
Critical Deficiency	• Any finding identified before or during an audit that is suspected to be fraudulent activity
Major Deficiencies	• Multiple restaging scans not completed per study requirements • Documentation of tumor measurements and/or tumor response was not provided for multiple patients and/or study time points • Other (Explain)
Minor Deficiencies	• Minimal missing documentation of tumor measurements and/or tumor response • Tumor measurements completed but scans not done within the time frame specified in the study • Other (Explain)
Toxicity	
Critical Deficiency	• Any finding identified before or during an audit that is suspected to be fraudulent activity
Major Deficiencies	• Failure to report an Unanticipated problem or SAE appropriately or in a timely manner (per study specifics to sponsor and/or IRB) • Excessive (more than 5) unreported AEs, or the grade/date associated with multiple AEs is missing or deemed inaccurate • Recurrent or repetitive issues with proper characterization or grading of adverse events • Other (Explain)
Minor Deficiencies	• Minimal (5 or less) incomplete or missing assessments (documentation of grade/duration/attribution) for adverse events (AE's) noted in the medical record • AEs attribution not signed off on by the treating physician. • Other (Explain)
Data Quality	

Critical Deficiency	• Any finding identified before or during an audit that is suspected to be fraudulent activity
Major Deficiencies	• Excessive delinquent data entry in database • Recurrent documentation errors and/or frequent inaccuracies of documentation into the database • The study specifies that data will be entered into a database, but no data has been entered in any database • Excessive (more than 5) source documents not found for date entered into the database. • Excessive number (more than 5) of research documents/notes not dictated within 14 days per institutional standard/policy • Other (Explain)
Minor Deficiencies	• Source documents missing authentication with the signature/date of the person performing the assessments • A small number (5 or less) of research documents/notes were not dictated within 14 days per institutional standard/policy • A minimal number of source documents (5 or less) were not found for some data entered into the database or data entered differs from source documentation • Hard copy source documents or questionnaires are missing patient identification and/or study number • Other (Explain)

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