Clinical Trials Monitoring Branch (CTMB)

Auditor/Monitor Training Modules

1. Introductory Module
2. Regulatory Module
3. Pharmacy Module
4. Patient Case Module
5. SAP & TSDV Module
Welcome to the Auditor Training Modules sponsored by the Clinical Trials Monitoring Branch (CTMB) at the National Cancer Institute (NCI). These modules apply to auditors and audits conducted for the NCI National Clinical Trials Network (NCTN) and NCI Community Oncology Research Program (NCORP).
Purpose of the Auditor Training: These modules are not meant to be a remedial course; rather they are meant to: provide a refresher on the CTMB Audit Guidelines (the full title of which is *NCI Guidelines for Auditing Clinical Trials for the NCI National Clinical Trials Network (NCTN) Program Including NCI Community Oncology Research Program (NCORP) and NCORP Research Bases*) to ensure all auditors follow them as written; share the latest updates to the Audit Guidelines, effective September 6th, 2017; and deliver training on the new technology for audit preparation, conduct, and reporting.

Throughout, you may see a theme of efficiency, standardization where possible, and collaboration.
Training Information: All auditors must complete this training. This includes those who are employed by an NCTN Group or other entity performing audits of NCI-sponsored clinical trials, as well as those who are considered to be “volunteer” or “ad hoc” auditors. It also includes both those who have been auditing for the NCTN/NCORP for some time as well as those who are new in this role.

The training has been broken down into a series of five short modules, so that you have the choice of doing it all at once or over time. You will have a deadline for completion of this training; please check with your organization for more information about this.
Training Modules: As stated previously, this training currently comprises five separate modules.

This module serves as an introduction to the training and the CTMB audit program. The next three modules cover the three components of an audit, i.e., regulatory documentation review; pharmacy review; and patient case review. Please note that the material shared in these first four modules comes from the Audit Guidelines. Your Group or Research Base may have more stringent policies or procedures than what is included in the Audit Guidelines, but what is presented here is what is mandated by CTMB. Do follow your Organization’s procedures. The fifth module covers the Site Audit Portal (SAP) as well as the process of documenting Targeted Source Data Verification, or TSDV, in the Rave clinical data management application, a part of patient case review. The primary source for the content in the TSDV module is the Site Audit Reporting (SAR) – Auditors User Guide. The next screen will show the locations for these two resource documents.

It is possible that with time, additional modules will be added to this training program. If so, you will be notified by CTMB and/or your Group.
Primary Resources: As noted previously, the primary sources for the content of this auditor training are the CTMB Audit Guidelines and the Site Audit Reporting (SAR) – Auditors User Guide. The direct URLs for both of these documents are shown on the screen; both are publicly available.

References to these and other resource documents will be included as appropriate in the upcoming modules.

Now, let’s get started.

Cited links:

The goal of the CTMB audit program is to ensure the integrity of data submitted, the protection of human subjects, and investigator compliance with protocol and regulatory requirements. This is accomplished through the detection of problems such as error, fraud, and protocol compliance issues through the independent verification of study data with source documentation through onsite audits; appropriate action and follow-up on problems found; and education and training on Good Clinical Practice (GCP), CTMB procedures, and techniques successfully used at other sites.
Onsite Audits: Auditing and monitoring ensure compliance with Food and Drug Administration (FDA) and GCP requirements for Sponsor oversight of a clinical trial. Onsite auditing is like taking a “snapshot in time.” The purpose of an audit is to document the accuracy of data submitted to the Lead Protocol Organization (LPO) and to verify investigator compliance with protocol, GCP, regulatory, and Group/Research Base requirements. In addition, onsite audits provide an opportunity for the audit team to share feedback and best practices concerning data quality, protocol compliance, and other aspects of quality assurance with the site’s research staff.

The main objective of auditing is to verify study data that could affect the interpretation of the primary study endpoints. This is from Section 1.3 of the Audit Guidelines. Do notice the wording of “primary study endpoints.” Your Organization may audit differently, but there is no mandate from CTMB to verify 100% of data points for each audited patient case. This is the impetus for TSDV in the program.
TIMING OF AUDITS

• All institutions are required to be audited at least once every 36 months, although audits can take place more frequently.
  • The initial audit for a new Network Group Main Member (Tier 1) is due within 18 months of the first enrolled patient at that site.
  • If a re-audit is required due to an Unacceptable rating, it is to be conducted within one year or when sufficient patients have been accrued.

All institutions are required to be audited at least once every 36 months, although audits can take place more frequently.

The initial audit for a new Network Group Main Member (Tier 1) is due within 18 months of the first enrolled patient at that site.

If a re-audit is required due to an Unacceptable rating, it is to be conducted within one year or when sufficient patients have been accrued.
Types of Audits:
Routine audits are the ones conducted at least every 36 months, to determine the quality of the research at a site.

Re-audits are conducted in response to an Unacceptable rating at a routine audit.

Off-cycle audits are those that do not fit the above definitions, and include “for cause” and special audits. These are defined on the next screen.
“FOR CAUSE” AND SPECIAL AUDITS

• “For cause” audits are those conducted due to concerns or irregularities at a site.

• Special audits are requested if promising preliminary findings from a particular study warrant verification of the findings.

“For cause” audits are those conducted due to concerns or irregularities at a site.

Special audits are requested if promising preliminary findings from a particular study warrant verification of the findings.

In general, all audits, whether routine, for cause, or special audits, should be conducted in the same manner.
Composition of the Audit Team: Audits are typically conducted by a team of auditors representing the credited organization, although a small audit could be conducted by a single auditor. Most auditing organizations assign an individual to serve as the Lead Auditor on a given audit. The role of lead auditor can differ by Organization, and you should check with yours about what the role entails and how you can expect to interact with that individual (or what it means if you are the lead auditor). All auditors must have completed training in Human Subject Protection (HSP) and Good Clinical Practice (GCP). Auditors must also complete this training.

The audit team should be selected based on knowledge of the protocols to be reviewed and knowledge of the organization’s audit guidelines and procedures. The team must include a physician or other qualified individual to provide medical assessments, evaluate protocol compliance, and conduct an effective exit interview with the Clinical Investigator (CI) and institution staff.

CTMB staff, or an NCI designee, may be present during an audit and must be given full access to all documents and materials present for the audit. Furthermore, a Cancer Trials Support Unit, or CTSU auditor will likely attend all multi-group audits, and should also be provided the same access as Group audit team members.
AUDITOR REGISTRATION

All auditors, including Group/Research Base staff auditors and “volunteer” auditors, must register with Cancer Therapy Evaluation Program (CTEP) systems to obtain the necessary auditor role and privileges.

Procedure:

1. Obtain account with CTEP-IAM (Identity and Access Management)
   - For more information: https://ctep.cancer.gov/branches/pmb/associate_registration.htm
2. Register via the RCR (Registration & Credential Repository) at the Associate Plus Level
   - This level (or the Investigator level) is required to be on a Group’s auditor roster in CTMB-AIS (Audit Information System) and to obtain access to Rave
   - The following are required to attain and maintain Associate Plus status: Proof of GCP and HSP training, NCI Biosketch, and Financial Disclosure Form
   - For more information: https://www.ctsu.org/public/RegProced_IR-AR.aspx

Auditor Registration: A new CTMB requirement is for all auditors, including Group/Research Base staff auditors and volunteer auditors, to register with Cancer Therapy Evaluation Program (CTEP) systems to obtain the necessary role and privileges. This is the procedure to do so:

- First, obtain an account with CTEP-IAM (Identity and Access Management). Most auditors already have an account and can move on to the next step. If you don’t, the website URL is provided as a resource on the screen.
- Register via the RCR (Registration and Credential Repository) at the **Associate Plus** level (although auditors who are also CTEP-registered investigators can and should be registered at the Investigator level). This is required to be on a Group’s auditor roster in CTMB-AIS (Audit Information System), and to obtain access to Rave. To register at the Associate Plus level, you must provide proof of GCP and HSP training, an NCI Biosketch, and a financial disclosure form.

For more information about RCR registration, please visit the website listed on the screen.

Cited links:
https://ctep.cancer.gov/branches/pmb/associate_registration.htm
https://www.ctsu.org/public/RegProced_IR-AR.aspx
An audit consists of three main components:
- A regulatory documentation review, in which you assess documentation and conformance to IRB and informed consent content requirements, as well as delegation of tasks logs (DTLs);
- A pharmacy review, in which you assess pharmacy operations, procedures, and documentation on NCI-approved drug logs; and
- Patient case review, in which you assess compliance with the protocol and accuracy of the data submitted.

These will be addressed more thoroughly in the individual modules.
ASPECTS OF THE AUDIT

• Changes in the CTMB Audit Guidelines include reviewing a minimum of 4 protocols at a site, when applicable. Priority review: registration trials, IND trials, multi-modality trials, advanced imaging trials, and preventive/cancer control trials, as well as high accruing trials.

• Electronic Medical Record (EMR) use: You may be provided with hardcopies from the EMR, or given EMR access. If EMR access is provided, a site staff member must be present to assist with navigating the system.

• Certain documents related to pharmacy and regulatory review may be reviewed prior to the onsite audit. The audit report must state which items were reviewed offsite.

Aspects of the Audit: Changes in the CTMB Audit Guidelines include reviewing a minimum of four protocols at a site, when applicable. The previous requirement was three protocols. Priority should be given to the following types of trials: registration, IND, multi-modality, advanced imaging, and preventive or cancer control, as well as high-accruing trials.

If an electronic medical record system (EMR) is used by the site, they may print out hardcopies of source documentation for your review, or they may provide you with EMR access. If EMR access is provided, a site staff member must be present to assist with navigating the system.

Certain documents related to the pharmacy and regulatory components may, at the discretion of the auditing organization, be reviewed prior to the onsite audit. These may include drug accountability forms, current informed consent forms, and Investigational Review Board (IRB) approval documentation, among others. The audit report must state which items were reviewed offsite.
Audit Results: Component Ratings.

Each component of an audit will be reviewed independently during the visit, and each will receive a rating. These ratings are derived from the number and types of deficiencies found during the audit visit, although the pharmacy component is a bit different, and is based on the number of non-compliant items, not deficiencies per se. Deficiencies are described a bit further on the next screen, and examples of deficiencies and non-compliant items are provided as appropriate in each of the individual component training modules.

During an audit, you and your audit team will assign each of the three components (Regulatory, Pharmacy, and Patient Case Review) a rating of Acceptable, Acceptable needs Follow-Up, or Unacceptable (although do note that the pharmacy review has a couple of additional rating options, those will be covered in the pharmacy review module). These ratings are to be based on findings at the time of the audit, and the definitions of these ratings are explained further in each component’s training module.
Audit Results: Deficiencies: As just stated, for two of the three audit components, the audit rating stems from the number and type of deficiencies discovered during the visit.

Critical Deficiencies are a new category, and they are also used within the European Union. They refer to any condition, practice, process, or pattern that adversely affect the rights, safety, or well-being of the patient/study participant and/or the quality and integrity of the data. This category includes, but is not limited to, manipulation and/or serious violation of safeguards in place to ensure safety of a patient/study participant and/or intentional misrepresentation of data. For more information about critical deficiencies, please see the document from the European Medicines Agency at the URL listed on the screen.

A major deficiency is defined as any variance from protocol-specified procedures that makes the resulting data questionable, while a lesser deficiency is any variance that is judged to not have a significant impact on the outcome or interpretation of the study data. An unacceptable frequency or quantity of lesser deficiencies should be treated as a major deficiency in determining the final assessment of a component or category.

Again, some examples of these different types of deficiencies will be provided in later modules.

Cited links:
POSSIBLE SCIENTIFIC MISCONDUCT

Data irregularities that raise any suspicion of intentional misrepresentation of data, and/or any disregard for regulatory safeguards in any component of an audit (or through any other quality control procedures), must immediately be reported to the CTMB by telephone at 240/276-6545 by the Group or Research Base.

Note that the irregularity, misrepresentation, or disregard does NOT need to be proven prior to reporting it; a reasonable level of suspicion suffices. Also follow your own organization’s procedures for this situation.

Any finding of scientific misconduct is considered a critical deficiency.

Data irregularities that raise any suspicion of intentional misrepresentation of data, and/or any disregard for regulatory safeguards in any component of an audit (or through any other quality control procedures), must immediately be reported to the CTMB by telephone at 240/276-6545 by the Group or Research Base.

Note that the irregularity, misrepresentation, or disregard does NOT need to be proven prior to reporting it; a reasonable level of suspicion suffices. Also follow your own organization’s procedures for this situation.

Any finding of scientific misconduct is considered a critical deficiency.
Audit Follow-Up: If a component is deemed Acceptable Needs Follow-Up or Unacceptable, the site must submit a written response and/or Corrective and Preventative Action Plan (CAPA) to the Group or Research Base, which along with CTMB will determine if the response or plan is satisfactory.

A re-audit will be mandatory if an audit component was Unacceptable, and it is to be conducted within one year from that audit, or when sufficient patients have been accrued (assuming the site continues to participate in Group or Research Base research).

In some circumstances, a re-audit may be designated for a component or components rated Acceptable Needs Follow-Up.
Conducting the Exit Interview: At the end of the audit, your team must conduct an onsite exit interview. The responsible CI and their designated research staff are expected to be present at this meeting, either in person or by phone if necessary.

Your audit team is to review preliminary findings, discuss the items reviewed offsite, and present recommendations. Do discuss any CAPAs needed, and the timeframe for submission, if applicable. Keep in mind that this meeting is an opportunity to educate the staff, have immediate dialogue about the findings, provide feedback, and give and receive clarification about potential findings.
Preliminary Report of Audit Findings: Ensure that you report all critical and major findings to your audit team lead in a timely manner, as the preliminary report of audit findings is due to CTMB within one business day of audit completion. Remember that CTMB should be contacted immediately for any suspicions of intentional misrepresentation of data.

A revised preliminary report may be submitted within 10 business days of the audit, if, for instance, a site is able to provide documentation that leads to the deletion of a major deficiency. Note that all deficiencies documented in the initial preliminary report must be included in the final audit report, and any revisions of that initial report would need to be explained in the final report.

A separate report will be needed for each audited institution, unless the audit was conducted “as a whole.”
Final Report Submission: The final audit report must be submitted in the CTMB-AIS within 70 calendar days of Day 1 of the audit. This institution-specific report should summarize: the items audited, the audit process — for instance, what was reviewed onsite and what was reviewed offsite - the findings at the time of the audit for each of the three components of the audit, plus the discussions at the Exit Interview. Recommendations from the Group or Research Base should be noted in the general comments or exit interview sections of the final audit report.

As with the preliminary report, a separate final audit report is required for each audited institution. However, if the audit was conducted as a combined audit ‘as a whole’ (e.g., a parent and their nonauditable institutions), just a single final audit report is required.

This concludes the introduction to the training and audit program. Please click the link to return back to the Learning Management System (LMS) page and record your completion of this module, then continue on to the other training modules.

[Provide link back to the LMS completion screen.]
Module Complete: You have completed the Introductory module. Please exit the module using the X in the upper right corner, and return to the course screen in the Learning Management System, where the module should now show as completed. You can always revisit this and other completed modules in your My Courses screen.

Note, this and the other training modules in this series were developed for the Clinical Trials Monitoring Branch of the Cancer Therapy Evaluation Program, Division of Cancer Treatment & Diagnosis, National Cancer Institute. For more information on the CTMB, visit the URL shown on the screen. This version of this individual module was produced in September 2018.

Cited links:
https://ctep.cancer.gov/branches/ctmb
Clinical Trials Monitoring Branch (or CTMB) Audit Guidelines, Regulatory Documentation Review. In this module, we will examine the three main categories of regulatory review, reveal differences for sites that utilize the National Cancer Institute Central Institutional Review Board (NCI CIRB), and provide some examples of critical, major and lesser deficiencies. New CTMB guidance will also be shared.
The goal of the regulatory documentation review is to assess the institution’s conformance to various regulatory requirements, and this is done by looking at three categories of documentation. This includes ensuring compliance with Institutional Review Board (IRB) requirements, which are assessed by reviewing initial approvals, amendment approvals, re-approvals, safety updates, etc.

It also includes confirming compliance with informed consent content (ICC) requirements, which are assessed by reviewing local consent forms, comparing them to the NCI model consent form, and ensuring that required elements are included.
GOAL OF THE REGULATORY DOCUMENTATION REVIEW

• Conformance to requirements related to the Delegation of Tasks Log (DTL), when applicable
  ▪ Review the DTLs and ensure they correspond with clinical site staff involved in the audited studies

Your Group or Research Base may conduct much of the regulatory review offsite, prior to the audit. In that case, the site(s) will submit documents such as IRB approvals and local informed consent templates for review as instructed in advance of the onsite visit.

Finally, it includes confirming compliance with requirements related to the use of delegation of tasks logs (DTLs) when required for a given study. This is done by reviewing the DTLs and ensuring they correspond with clinical site staff involved in the conduct of the study or studies in question. Review of DTLs is a new auditing task. Each of these areas will be reviewed in more detail as we proceed through this module.

By the way, your Group or Research Base may conduct much of the regulatory review offsite, prior to the audit. In that case, your organization will request, and the site or sites will submit, documents such as IRB approvals and local informed consent templates for review as instructed in advance of the onsite visit.
Classification of Deficiency Types: As you audit the regulatory component, keep these definitions of critical, major, and lesser deficiencies in mind:

Critical deficiencies are a new category. They refer to any condition, practice, process, or pattern that adversely affects the rights, safety, or well-being of the patient or study participant and/or the quality and integrity of the data. This category includes, but is not limited to, manipulation and/or serious violation of safeguards in place to ensure safety of a patient or study participant and/or intentional misrepresentation of data. Critical deficiencies must be reported to CTMB immediately.

When it comes to review of IRB documentation and ICC, any finding that fraudulent activity is observed would constitute a critical deficiency.
A major deficiency is defined as any variance from protocol-specified procedures that makes the resulting data questionable, while a lesser deficiency is any variance that is judged to not have a significant impact on the outcome or interpretation of the study data. An unacceptable frequency or quantity of lesser deficiencies should be treated as a major deficiency in determining the final assessment of a component or category.

Examples of findings that fit into these categories will be described as we go along.
Audit Tool for Regulatory Documentation Review: The CTMB provides a listing of lesser, major, and critical deficiencies to assist you during the regulatory documentation review.

You can find the Regulatory Documentation Review Worksheet posted as Appendix 1 of the CTMB Audit Guidelines, on the CTEP/CTMB website, along with the Audit Guidelines themselves, as well as directly at the link shown on the screen.

For those with access, this audit tool is also downloadable from a tab in the CTMB-AIS. It is helpful to keep a copy of this audit tool nearby, either in hardcopy or electronically, for reference during your regulatory reviews.

Cited link:
https://ctep.cancer.gov/branches/ctmb/clinicalTrials/docs/Appendix_1.pdf
Review of IRB Approvals When a Local IRB is the IRB of Record: Please note that when it comes to IRB-related documentation, there are some differences between sites using a local IRB versus those using the NCI CIRB as their IRB of record for a given study; the latter are described in a future screen.

For each protocol selected for audit, the following minimum IRB approval items will be reviewed: full IRB initial approval, full IRB annual re-approval, IRB approval for amendments that affect more than minimal risk, IRB approval or re-approval prior to patient registration, and appropriate use and conduct of expedited reviews.
Note Regarding Review of IRB Approvals: As you audit, keep this in mind about the review of IRB approvals:

The CTMB guidelines denote the minimum requirements for review. For instance, you are not mandated to audit IRB approval of editorial- or administrative-only amendments. Your Group or Research Base may, however, choose to do a more stringent review. Please note that any IRB-related finding before or during an audit that is suspected to indicate fraudulent activity is a critical deficiency, and must be reported immediately to CTMB.
Dates And Timing of IRB Approvals, when a Local IRB is the IRB of Record: Make note of the IRBs used by each site, including affiliates and components. Also note the dates and timing of each approval reviewed. Determine when the first patient was registered on that study at that site, and check that the initial IRB approval occurred prior to that date. If it did not, assign a major deficiency.

If continuing review re-approval was delayed up to 30 days, assign a lesser deficiency; if re-approval was delayed more than 30 days or completely expired, it is a major deficiency.

IRB approval of greater-than-minimal-risk amendments more than 90 days after notification would also constitute a major deficiency.

Any finding that fraudulent activity is observed would be a critical deficiency.

The Regulatory Documentation Review Worksheet provides a more comprehensive list of deficiencies related to the IRB approvals category.
Safety Reports/Unanticipated Problems When a Local IRB is the IRB of Record: While performing the IRB section of the regulatory assessment, review a random sample of at least 10% of the unanticipated external safety reports for each protocol selected for the audit. If submission is not required by the site’s IRB, you need to see documentation of that policy. If reporting is required, submission to the IRB must be within 90 days of notification. (Note dates.)

You must also review local unanticipated problems, and it is a major deficiency if internal reportable adverse events were reported late or not reported to the IRB.
IRB Approval for Sites Using the NCI CIRB: There are some differences in the IRB part of the regulatory review for sites that are using the NCI CIRB as their IRB of record for a particular study. These are the minimum items to look for when auditing such a site:

Look for the approval letter from the CIRB to the site clinical investigator for the site’s Study-Specific Worksheet (SSW); this is the primary indicator that the CIRB has approved the site to conduct the study and that it is now the IRB of record for the study. This approval must be obtained prior to the site enrolling any patients to the study. It is a lesser deficiency if this document cannot be accessed or located.

Barring any changes to their local context considerations (as noted and approved in the SSW), a site does not need to take any direct action with the CIRB to approve protocol amendments.

With respect to safety reports, sites do not have to submit unanticipated external safety reports to the CIRB, as they will already have been submitted by the Lead Protocol Organization, or LPO. However, unanticipated local problems do need to be reported to the CIRB, as do reports of serious non-compliance and/or continuing non-compliance (as defined by the Office for Human Research Protections, or OHRP). Some examples of these types of reportable problems could include, but are not limited to, enrollment of ineligible participants, as well as incorrect dosing of participants. Per the CIRB Administrator, deficiencies related to these types of issues are common. Failure to report issues such as these, or unanticipated local problems, is a major deficiency.
Any finding that fraudulent activity is observed with respect to CIRB approval is a critical deficiency.

The Regulatory Documentation Review Worksheet provides a more comprehensive list of deficiencies related to the CIRB approvals category.
Review of Informed Consent Content (ICC) for All Sites: The second main area within the regulatory review component of an audit is the review of informed consent content, or ICC. This involves:

Reviewing the content of current, local informed consent documents for at least four variable-type protocols (if four or more protocols will be audited). [Note that section 5.2.4 of the CTMB Audit Guidelines calls for at least three protocols to be reviewed for ICC, but this is incorrect and will be updated shortly via an addendum.]; ensuring that the federally-required elements of informed consent are present, as listed in the Regulatory Documentation Review Worksheet (any missing category would be considered a major deficiency); and confirming that the risks and side effects language matches the NCI-approved model informed consent.
REVIEW OF INFORMED CONSENT CONTENT (ICC) – ALL SITES

- Check that any revisions to the consent per an amendment or in response to an NCI Action Letter have been made.
- Make certain that any changes made to the consent document were approved by the IRB of record.

Your Group or Research Base may have additional rules regarding informed consent requirements and language.

Reviewing ICC also involves: checking that any revisions to the consent per an amendment or in response to an NCI Action Letter have been made; and making certain that any changes made to the consent document were approved by the IRB of record.

Auditors should recognize that their Group or Research Base may have additional rules regarding consent requirements and language; please check with them to find out about those. Also, there are some items to note with respect to ICC when auditing sites using the NCI CIRB; they are on the next screen.

Please look over the list of required elements of informed consent listed in the Regulatory Documentation Review Worksheet.
Review of ICC for Sites using the CIRB: As noted previously, there are a couple of items to note when it comes to auditing ICC for sites using the NCI CIRB as their IRB of record.

First, review the CIRB approval of local context information, which is part of the SSW, and ensure that the only changes to the site’s consent (from the CIRB-approved consent) are those included on the SSW. According to the CIRB, changes beyond what is included in the SSW are a common finding.

Second, note when any amendment-driven changes to the informed consent were implemented, and recognize that failure to have the informed consent document revised when needed (after CIRB amendment approval) and locally implemented within 30 days of notification (i.e., posting on the CTSU website) is a lesser deficiency.
Delegation of Tasks Logs: A new category within the regulatory documentation component is review of Delegation of Tasks Logs, or DTLs.

Due to the nature and complexity of conducting clinical research, a clinical investigator may delegate activities or duties associated with the clinical trial to his or her staff. These duties should be allocated based on training, education, and experience.

To document the roles and responsibilities of the individuals contributing efforts to certain clinical trials, a DTL must be maintained by site and by protocol, and must be signed by the clinical investigator. CTMB and/or your organization will let you know which protocols require DTLs.
How to access DTLs:

How to access DTLs: Auditors can request that site staff access and then print out DTLs. Alternatively, any Group or Research Base audit staff member who is on the CTSU administrative roster with an affiliation with their organization can go into the Site DTL Browser screens on the CTSU website (under the Delegation Log tab) and view/print DTLs for their member sites that are:

- Participating on their own trials, and
- Participating on other organizations’ trials on which the auditing organization is an official participant (e.g., as needed for cross-Group auditing).

In most cases this means that a Lead Auditor for an organization can access and provide DTLs for the audit team.
REVIEW OF DELEGATION OF TASKS LOGS (DTL)

When applicable, the auditor will request the DTLs for the protocols being audited (for one or more sites).

- The DTL should list anyone who contributes significant trial-related duties, and must be kept current.
- Review the enrollment information for the enroller, Rave for the data coordinator, and source documents for healthcare professionals working with the trial. Compare to staff listed on the log.
- Examples of major deficiencies: Trial-related duties being performed by individual not listed on the DTL; or staff performing duties not assigned to that individual. (See the DTL list of deficiencies in the Regulatory Documentation Review Worksheet for a full list.)

Review of Delegation of Tasks Logs, DTLs. Your role as the auditor is to review the logs to ensure appropriate implementation and maintenance.

The DTL should list anyone who contributes significant trial-related duties, and must be kept current with any staff changes. To audit this category, review the enrollment information for the name of the enroller; review Rave for the data coordinator’s name; and source documentation for the names of healthcare professionals working with this trial and patient. Compare these names to the entries on the DTL.

Examples of major deficiencies are: a finding that trial-related duties are being performed by an individual not listed on the DTL, or staff performing duties not assigned to that individual. See the DTL list of deficiencies in the Regulatory Documentation Review Worksheet for a full list.
Assessing the Regulatory Review: The auditing organization will assess the regulatory review based on the number of lesser, major, and critical deficiencies identified during the visit.

An Acceptable rating may be assessed if the auditor identified: No deficiencies and no follow-up requested; few lesser deficiencies; or a major deficiency that was addressed and corrected prior to being notified of the audit (with a written and dated Corrective and Preventative Action Plan [CAPA]) and no further action is required. (Check with CTMB if the deficiency is associated with a safety concern.)
A rating of Acceptable Needs Follow-up must be assessed if the auditor identified: any major deficiency that was not corrected and/or addressed prior to the audit; or multiple lesser deficiencies.

A rating of Unacceptable must be assessed if the auditor identified: a single critical deficiency; multiple major deficiencies; or multiple lesser deficiencies of a recurring nature found in most of the protocols or informed consent documents reviewed.
Module Complete: You have completed the Regulatory Review module. Please exit the module using the X in the upper right corner, and return to the course screen in the Learning Management System, where the module should now show as completed. You can always revisit this and other completed modules in your My Courses screen.

Note, this and the other training modules in this series were developed for the Clinical Trials Monitoring Branch of the Cancer Therapy Evaluation Program, Division of Cancer Treatment & Diagnosis, National Cancer Institute. For more information on the CTMB, visit the URL shown on the screen. This version of this individual module was produced in September 2018.

Cited link: https://ctep.cancer.gov/branches/ctmb
Clinical Trials Monitoring Branch (or CTMB) Audit Guidelines, Pharmacy Review. This module covers the pharmacy review component of a site audit. It provides expectations and reminders related to the Guidelines, as they pertain to your role as an auditor.
The goal of the pharmacy review is to assess the institution’s accountability of study-supplied agents and pharmacy operations. Note that a pharmacy audit may not be required if no study-supplied agent was in stock or used during the timeframe being reviewed or audited.
Your Group or Research Base may conduct part of the pharmacy review in advance of the audit, by requesting and then reviewing National Cancer Institute (NCI) Drug Accountability Record Forms (DARFs) and other documentation.

- Even when documentation is reviewed in advance of an audit visit, the pharmacy (or pharmacies) must still be visited during the audit.
Review of Accountability of Study-Supplied Agents and Pharmacy Operations: While conducting a pharmacy review, you will need to assess the following: Drug accountability (which includes documentation of receipt, dispensation, and transfer/return/destruction of study-supplied agents; transfer to/from satellite sites; and while onsite, comparison of balance on log to amount in stock). You will also need to assess the proper use of NCI DARFs.
REVIEW OF ACCOUNTABILITY OF STUDY-SUPPLIED AGENTS AND PHARMACY OPERATIONS

Also assess the following:

• Compliance with required procedures
• Appropriate storage and security of study-supplied agents
• Authorized prescriptions
• Imaging agents may be stored at the imaging department instead of pharmacy.

You must also review the following: Compliance with required procedures; appropriate storage and security of study-supplied agents; and the use of authorized prescriptions. Cancer control or prevention and imaging study-supplied agents must also be assessed. Note that imaging study-supplied agents will usually be sent directly to the imaging department or center, as opposed to the pharmacy itself.
Types of Pharmacies: A given site might utilize two levels of onsite pharmacy, and both need to be included in the pharmacy review component of an audit. [Please note that these are different from an affiliate pharmacy, which is covered in a later screen.]

The control pharmacy is the main or primary dispensing area or pharmacy at the site, and is the one identified as the shipping address receiving the study-supplied agent from the supplier. The control pharmacy is responsible for direct receipt of study-supplied agents from the supplier, appropriate storage and security of agents, dispensing of agents to study participants as prescribed by CTEP-registered investigators and dictated by each protocol, overall inventory control (including provision of agents to and oversight of satellite dispensing areas, and dissemination of agent stock recovery information), and final disposition of study-supplied agents (that is, returns, transfers, and authorized local destructions).
Satellite Pharmacy: A satellite dispensing area or pharmacy is at a different location from the control pharmacy at the same site, for example, within an infusion center, or connected to a patient care unit. During an audit, the auditor must ensure that as with the control pharmacy, any satellite pharmacies are compliant with federal and NCI requirements, and also that study-supplied agent can be accurately tracked between the different locations.

A satellite pharmacy is under the direct responsibility of the control pharmacy, and is responsible for receiving study-supplied agents from the control pharmacy via in-house personnel, appropriately storing, securing, and accounting for study agents, dispensing agents to study participants, and returning agents to the control pharmacy for further or final disposition. They may also physically destroy patient-returned study-supplied agents, if their policies and procedures allow for that. Do note that a drug accountability log is required at the satellite pharmacy if study drug is stored there for more than one day.
Pharmacy Module Screen 8

Review of Affiliate Pharmacies: Pharmacies at affiliate institutions function administratively under a parent site but do receive study-supplied agents directly from the supplier.

Review options per the CTMB Audit Guidelines:
• For routine pharmacy audits, Groups can now use their own discretion to determine if/when an on-site audit should be conducted.
• If audited offsite, required documents can be sent to the audit location or to the Group/Research Base prior to the audit.

Re-audit needed for storage or security non-compliance? Conduct onsite within 12 months.

Review of Affiliate Pharmacies: Pharmacies at affiliate institutions function administratively under a parent site, and dispense study-supplied agent to study participants at their locations. These pharmacies do receive study-supplied agents directly from the supplier.

Review options per the CTMB Audit Guidelines: For routine pharmacy audits, Groups and Research Bases can now use their own discretion to determine if and when an onsite audit of an affiliate pharmacy should be conducted. This is new in the Guidelines. If audited offsite, required documents can be sent to the audit location or to the Group/Research Base prior to the audit.

If a pharmacy (affiliate or main) requires a re-audit due to storage or security non-compliance, the re-audit must be conducted onsite, within 12 months.
Audit Tool for Pharmacy Review: The CTMB provides a listing of items to review for compliance to assist you during the pharmacy review. The Pharmacy Review Worksheet is divided into nine sections, with the first page being the overall rating for each of the eight categories assessed. Subsequent pages list the individual items to be evaluated within each category and checked as compliant or not compliant, and whether they meet criteria for critical non-compliance.

You can find the Pharmacy Review Worksheet posted as Appendix 2 of the CTMB Audit Guidelines, on the CTEP/CTMB website, along with the Audit Guidelines themselves, as well as directly at the link shown on the screen. For those with access, this audit tool is also downloadable from a tab in the CTMB-AIS. It is helpful to keep a copy of this audit tool nearby, either in hardcopy or electronically, for reference during your pharmacy review.

Cited link:
https://ctep.cancer.gov/branches/ctmb/clinicalTrials/docs/Appendix_2.pdf
Here are some reminders regarding the conduct of the pharmacy audit: 1) Any electronic drug accountability logs used must be able to produce a paper printout that is identical to the NCI DARF. 2) Satellite DARFs must be used if study-supplied agent is stored in a satellite pharmacy for more than one day. Cross-check these with the control pharmacy DARFs to confirm documentation of transfers between the pharmacies. 3) Cross-check DARFs with the dates and doses on the case report forms (CRFs) for patients selected for case review to ensure that they match. 4) Review all DARFs, shipping receipts and return, transfer, or destruction forms to ensure that all agents coming into and going out of the applicable pharmacies are accounted for.

<table>
<thead>
<tr>
<th>REMINDERS</th>
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<tr>
<td><strong>1. Use of electronic drug accountability logs</strong></td>
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<tr>
<td>• Electronic logs must produce a paper printout that is identical to the NCI DARF</td>
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<tr>
<td><strong>2. Use of satellite drug accountability logs</strong></td>
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<tr>
<td>• Must be used if study-supplied agent stored in satellite pharmacy for &gt; 1 day</td>
</tr>
<tr>
<td>• Cross-check with control pharmacy DARFs to confirm documentation of transfers</td>
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<tr>
<td><strong>3. Confirmation of dates/doses for patient cases selected</strong></td>
</tr>
<tr>
<td>• Cross-check DARFs with dates and doses on patient-specific CRFs</td>
</tr>
<tr>
<td><strong>4. Documents to review/cross-check</strong></td>
</tr>
<tr>
<td>• Review DARFs, shipping receipts, and return, transfer, or destruction forms</td>
</tr>
<tr>
<td>• Ensure that all agents coming into and going out of the applicable pharmacies are accounted for.</td>
</tr>
</tbody>
</table>
 MORE REMINDERS

5. Confirmation of physical quantities of study-supplied agents
   • Physical quantities in the pharmacies must match what is on the DARFs

6. Adequacy of storage and security
   • Check temperature logs, ensure agents are stored properly
   • Ensure physical security of the pharmacy itself

7. Procedure for verifying prescriber’s authority
   • Must be documented procedure to ensure prescriptions signed by active
     CTEP-registered investigators

More reminders regarding the conduct of the pharmacy audit: 5) Ensure that the physical quantities of study-supplied agents in all covered pharmacies match what is on the associated DARFs. 6) Check temperature logs to ensure that equipment is functioning properly and that agents are stored according to requirements, and confirm that appropriate safeguards are in place to guarantee proper physical security of the agents within the pharmacy itself. 7) Make sure that the institution has a documented procedure for ensuring that prescriptions have been signed by an active, CTEP-registered investigator.
Assessing Compliance: The pharmacy review is a bit different from the regulatory and patient case review components in that it is based upon a system of compliance and non-compliance, not different levels of deficiencies.

When conducting a pharmacy audit, the auditor will review the different categories and assign each category one of the following ratings: Critical-Non-Compliant, Non-Compliant, Compliant, or Not Reviewed. The next screen will provide more information on what critical non-compliance means.
Critical-Non-Compliance: A Critical-Non-Compliance finding is one that potentially affects patient or study participant safety, rights, and/or well-being, and/or the quality and integrity of the data, and/or a finding suggestive of intentional misrepresentation of data. It includes serious violation of safeguards in place to ensure a patient’s safety. Due to the severity of a Critical-Non-Compliant rating it is important to immediately communicate such a finding to CTMB by telephone at 240-276-6545.
ASSESSING THE PHARMACY REVIEW

The auditing organization will assess the pharmacy review based on the presence of non-compliant items identified during the visit.

• A rating of **Acceptable** may be assessed if the auditor identified:
  • No non-compliant categories during the audit; or
  • Non-compliant items that were addressed prior to notification of the audit (with a written and dated Corrective and Preventative Action Plan [CAPA], and no further action required).

Assessing the Pharmacy review: The auditing organization will assess the pharmacy review based on the presence of non-compliant items identified during the visit.

To attain an Acceptable rating, the site must be compliant in all categories or have addressed and corrected any non-compliant items prior to notification of the audit (with a written and dated Corrective and Preventative Action Plan [CAPA], and no further action required). Note the requirement that correction of non-compliant items must have been accomplished prior to notification of the audit; this is a new timing requirement from CTMB.
ASSESSING THE PHARMACY REVIEW

• A rating of Acceptable Needs Follow-up must be assessed if the auditor identified:
  • Any non-compliant category during the audit.

• A rating of Unacceptable must be assessed if the auditor identified:
  • An inability to track the chain of custody of study-supplied agents;
  • A critical non-compliance; or
  • Multiple non-compliant categories.

If a category is found non-compliant during the audit, the rating must be Acceptable Needs Follow-up.

If an audit reveals that there is an inability to track the chain of custody of study-supplied agents, a critical non-compliance was identified, and/or there are multiple non-compliant categories, the rating must be Unacceptable.

Two additional assessment or rating options for the pharmacy review are covered on the next screen.
Two additional options are available for rating the pharmacy review component. They both apply to onsite pharmacy audits only.

**No Assessment Required:**
- No study agent was in stock or in use during timeframe of review and the only items reviewed consist of security, storage areas, and pharmacy procedures.
- All reviewed categories were found to be compliant.

No Assessment Required is used when no study agent was in stock or in use during the timeframe being reviewed, and the only items reviewed consist of security, storage areas, and pharmacy procedures. The reviewed categories must be found to be compliant to receive this assessment.
Limited Review Needs Follow-up is a new rating option for the pharmacy component. It is used when any non-compliance was identified during a limited review of security, storage areas, and pharmacy procedures, and a CAPA plan or follow-up response is requested.
Resources to Review: Please review the Pharmacy Review Worksheet, or audit tool, for a detailed listing of non-compliant items; you can find this at the URL shown on the screen.

Additionally, the Pharmaceutical Management Branch (PMB) has developed a series of investigational drug accountability training videos on the expectations for pharmacy operations and accountability. While these short videos are primarily intended for site staff, they provide valuable information for auditors as well. Please review all of the videos if you have not seen them before. They can be found at the second URL shown on the screen.

Cited links:
https://ctep.cancer.gov/branches/ctmb/clinicalTrials/docs/Appendix_2.pdf
Module Complete: You have completed the Pharmacy Review module. Please exit the module using the X in the upper right corner, and return to the course screen in the Learning Management System, where the module should now show as completed. You can always revisit this and other completed modules in your My Courses screen.

Note, this and the other training modules in this series were developed for the Clinical Trials Monitoring Branch of the Cancer Therapy Evaluation Program, Division of Cancer Treatment & Diagnosis, National Cancer Institute. For more information on the CTMB, visit the URL shown on the screen. This version of this individual module was produced in September 2018.

Cited link:
https://ctep.cancer.gov/branches/ctmb
Clinical Trials Monitoring Branch (CTMB) Audit Guidelines, Patient Case Review. In this module, we will examine the six main categories of patient case review and delineate between the different levels of deficiencies. Of note, the process for recording your Targeted Source Data Verification (TSDV) in Rave as part of patient case review is presented in a separate module.
The goal of the patient case review, per the CTMB Audit Guidelines, is to determine whether the evaluated trial-related activities were conducted according to protocol and the evaluated data were verified and accurately reported.

Per the CTMB Audit Guidelines, the major objective of the audit program is to verify study data that could affect the interpretation of primary study endpoints. Thus, it is not mandatory to review 100% of the data points for each patient case selected, but instead to focus on those that are related to the primary study endpoints. Groups or Research Bases may, of course, have more stringent criteria, so you should check with your organization about any additional expectations.
What is assessed during a patient case review: While auditing patient cases, you will need to review six categories: patient-specific informed consent, eligibility, treatment, disease outcome/tumor response, adverse events (or AEs) related to treatment, and general data quality. These will each be discussed in more detail as we proceed through this module.
Special notes about the patient case review: It should be noted that the majority of patient cases selected for an audit will be announced to the site two to four weeks in advance of the visit, and auditors should review all six of these categories for those announced cases.

That being said, many audit visits also feature one or possibly two unannounced cases, which are disclosed to the site one business day prior to, or on the day of, the audit. These unannounced cases may have a more limited audit, consisting of, at a minimum, review of the informed consent and eligibility categories.
All patient cases, whether they undergo full or limited review, must be documented in the final audit report. If a category is not reviewed for any reason, e.g., it was an unannounced case, or the patient never received treatment, or the auditor ran out of time, it should be found Not Reviewed and explained in the audit report.
CLASSIFICATION OF DEFICIENCIES

- **Critical Deficiency**: any condition, practice, process or pattern that adversely affect the rights, safety or well-being of the patient/study participant and/or the quality and integrity of the data; includes manipulation and/or serious violation of safeguards in place to ensure safety of a patient/study participant and/or intentional misrepresentation of data. Report to CTMB immediately.

- **Major Deficiency**: a variance from a protocol-specified procedure that makes the resulting data questionable.

- **Lesser Deficiency**: a finding that is judged to not have a significant impact on the outcome or interpretation of the study and is not described above as a major deficiency. An unacceptable frequency or quantity of lesser deficiencies should be treated as a major deficiency.

Classification of Deficiencies: Auditors will assess the patient case review category based on the number of critical, major, and lesser deficiencies identified during the audit. As you audit the patient cases, keep these definitions in mind:

Critical deficiencies are a new category. They refer to any condition, practice, process, or pattern that adversely affect the rights, safety, or well-being of the patient/study participant and/or the quality and integrity of the data. This category includes, but is not limited to, manipulation and/or serious violation of safeguards in place to ensure safety of a patient/study participant and/or intentional misrepresentation of data. Critical deficiencies must be reported to the CTMB immediately.

In all six categories of the patient case review, any finding that fraudulent activity is observed constitutes a critical deficiency. However, a few categories (namely, patient-specific informed consent and treatment) have additional findings that are considered to be critical; they are referenced in later slides.

A major deficiency is defined as any variance from protocol-specified procedures that makes the resulting data questionable, while a lesser deficiency is any variance that is judged to not have a significant impact on the outcome or interpretation of the study data. An unacceptable frequency or quantity of lesser deficiencies should be treated as a major deficiency in determining the final assessment of a component or category.
POSSIBLE SCIENTIFIC MISCONDUCT

Data irregularities that raise any suspicion of intentional misrepresentation of data, and/or any disregard for regulatory safeguards in any component of an audit (or through any other quality control procedures), must immediately be reported to the CTMB by telephone at 240/276-6545 by the member’s Group.

Note that the irregularity/misrepresentation/disregard does not need to be proven prior to reporting it; a reasonable level of suspicion suffices. Also follow your own organization’s procedures for this situation.

Any finding of scientific misconduct is considered a critical deficiency.

Possible scientific misconduct: This content on possible scientific misconduct was initially presented in the introductory module, but is repeated here because it comes up most often (although not always) in the patient case review portion of an audit.

Data irregularities that raise any suspicion of intentional misrepresentation of data, and/or any disregard for regulatory safeguards in any component of an audit (or through any other quality control procedures), must immediately be reported to the CTMB by telephone at 240/276-6545 by the Group or Research Base. Note that the irregularity, misrepresentation, or disregard does not need to be proven prior to reporting it; a reasonable level of suspicion suffices. Also follow your own organization’s procedures for this situation.

Any finding of scientific misconduct is considered a critical deficiency.
Audit tool for patient case review: The CTMB provides a listing of critical and major deficiencies in each of the categories to assist you during the patient case review. You can find the Patient Case Review Worksheet posted as Appendix 3 of the CTMB Audit Guidelines, on the CTEP/CTMB website, along with the Audit Guidelines themselves, as well as directly at the link shown on the screen.

For those with access, this audit tool is also downloadable from a tab in the CTMB-AIS. It is helpful to keep a copy of this audit tool nearby, either in hardcopy or electronically, for reference during your patient case reviews.

Now let’s go over each of the six categories included in the patient case review, starting with informed consent on the next screen.

Cited link:
INFORMED CONSENT

Confirm that:

• The informed consent process was documented in the patient’s chart, and the consent form document is available
• The patient signed and dated the consent document prior to study registration/enrollment
• The correct version of the investigational review board (IRB)-approved consent document was used, and the consent form does not contain any changes not approved by the CIRB/IRB.

Informed consent: These are some of the items to confirm while reviewing a patient-specific signed informed consent. Deviations from these would be considered major deficiencies.

Ensure that the informed consent process was documented in the patient’s chart, and that the consent form document is available. Check to make sure that the patient signed and dated the consent document prior to study registration/enrollment. Confirm that the correct version of the institutional review board (IRB)-approved consent document was used, and that the consent form does not contain any changes not approved by the CIRB/IRB.

Items to review for patient-specific informed consent continue on the next screen.
Also confirm that:

- The translated consent or short form was available and signed and dated by non-English-speaking patient
- The consent form includes updates or information required by the IRB (e.g., initials, witness)
- All required signatures are present
- Consent for ancillary/advanced imaging studies were executed properly
- Any required re-consents have been obtained and documented

During your review of patient-specific informed consent, also ensure that in the case of a non-English-speaking patient, the translated consent, short form, or other form of translation was available and signed and dated by the patient. For all patients, confirm that the consent form includes updates or information required by the IRB. This may include things like requiring patient initials on every page of the consent form, or the presence/signature of a witness. Make certain that all required signatures are present, and that consents for ancillary and/or advanced imaging studies were executed properly. Finally, confirm that any required re-consents have been obtained and documented. As stated earlier, deviations from these items constitute major deficiencies.

The informed consent category also includes some specific findings that can lead to critical deficiencies; these are covered on the next screen.
Informed consent – Critical deficiencies: These are the newly-designated critical deficiencies for patient-specific informed consent: any finding that fraudulent activity may have taken place; the discovery that a consent form document was not signed and dated by the patient or their legally authorized representative; a finding that the patient’s signature cannot be corroborated; or, a consent form that is not protocol-specific.

Please recall that critical deficiencies must be reported to the CTMB immediately.

As a reminder, the Patient Case Review Worksheet provides a list of deficiencies, both critical and major, related to the informed consent category.
Eligibility: As you audit a patient case for eligibility, ensure the following; any inability to do so should lead to major deficiencies.

Source documentation reflects that all eligibility criteria have been met as specified by the protocol; this includes all eligibility requirements being obtained within the specified timelines. All required tests to confirm eligibility must have been performed prior to registration.

Note that the focus here is on “eligibility-related tests,” not “all screening or baseline tests.” For instance, if a PT/PTT and INR are required at screening and were done out-of-window, but the results are not connected to any determination of eligibility, this would NOT be a major deficiency under the eligibility category. It would be considered a lesser deficiency under the general data management quality category, or under adverse events if applicable.
All documentation must be available and is able to confirm eligibility. If any source documentation is missing, request that the site find and provide it to you within 10 business days of the audit in order to avoid a major deficiency. It is a major deficiency if eligibility criteria were not met, or if eligibility cannot be confirmed.

A critical finding for this category would be any finding of fraudulent activity.

The Patient Case Review Worksheet provides a list of deficiencies, both critical and major, related to the eligibility category.
TREATMENT

Evaluate whether:

• The correct protocol treatment was given in the correct dose, correct order, with the correct timing, and is supported by documentation. (Dose deviation or calculation error >10% is a major deficiency; Using the incorrect agent, treatment, or intervention is a critical deficiency)

• Cycles started on time; there were no unjustified delays in treatment

• Dose modifications were done in accordance with the protocol and correctly calculated

• Any additional agents/treatments/interventions disallowed by the protocol were used

• There is any finding of fraudulent activity (a critical deficiency)

Treatment: It is worth noting that the treatment category, along with the general data management quality category, contributes the majority of deficiencies in a patient case review. Auditors should take care to ensure that the treatment requirements of a study have been met.

As you audit the treatment category of a patient case, consider the following: Evaluate whether the patient received the correct treatment, in the right dose, in the right order, and with the right timing. This must all be supported by documentation. Of note, a dose deviation or calculation error of greater than 10% would be a major deficiency, but not if less than 10%. Importantly, if a patient was given the INCORRECT agent, treatment, or intervention, you must assign a critical deficiency.

Did cycles start on time? An unjustified delay could be a major deficiency.

If the source documents reveal AEs that mandate a dose modification, was the dose modification applied per protocol? Or conversely, if a dose modification is noted, is there a documented rationale for that, e.g., toxicity, in the source documentation and case report forms (CRFs)? Improperly handled dose modifications constitute a major deficiency.

Use of protocol-forbidden agents/treatments/interventions also constitutes a major deficiency.

In addition to the critical deficiency noted above, any finding that suggests treatment-related fraudulent activity also constitutes a critical deficiency.

The Patient Case Review Worksheet provides a list of deficiencies, both critical and major, related to the treatment category.
Disease outcome/response: Disease outcome or response is a primary endpoint of phase 2 and phase 3 studies, and thus should be reviewed carefully. As you review the disease outcome/response category, ask the following questions:

Has there been accurate documentation of the initial sites of involvement? Were any areas of involvement left out without reason? Has re-evaluation of disease status been performed per protocol? Has the response been documented in the CRFs using the protocol-mandated response criteria? On this point, do not go merely by the investigator’s mention of response in the clinic notes, as that may be a clinical assessment as opposed to a protocol-directed response assessment. Carefully review the claimed response (e.g., partial response or complete response). Is it correct? If the participant is on a cancer prevention study and cancer occurred, was it reported? If the participant is on a treatment study and cancer progressed, was that reported? Any issues with these examples would be major deficiencies.

A critical deficiency for this category is any finding of fraudulent activity.

The Patient Case Review Worksheet provides a list of deficiencies related to the disease outcome/response category.
Adverse events related to treatment: The fifth category of patient case review is adverse events (or AEs) related to treatment. (Note the “related to treatment” aspect of this category. While AEs not related to treatment do not need to be reviewed during an audit per the Guidelines, your organization may have more stringent requirements.)

As you audit this category, confirm that there was no failure or delay in reporting AEs that require filing an expedited AE report or reporting to the Group or Research Base. It must also be confirmed that AEs were assessed by the investigator in a timely manner. Ensure that the grades, types, and dates/durations of serious adverse events (or SAEs) were accurately recorded, and that all AEs can be substantiated.
ADVERSE EVENTS RELATED TO TREATMENT

Confirm that:

• Follow-up studies necessary to assess AEs were performed
• There was not recurrent under- or over-reporting of AEs
• There is no finding of fraudulent activity (a critical deficiency)

Confirm that any follow-up studies necessary to assess AEs were performed, and that there was no recurrent under- or over-reporting of AEs. Failures in any of these areas would be considered major deficiencies.

A critical deficiency for this category is any finding of fraudulent activity.

The Patient Case Review Worksheet provides a list of deficiencies related to the adverse event category.
General data management quality: As stated earlier, general data management quality issues and treatment errors compose the majority of deficiencies in patient case reviews.

During the review of general data management quality, you should review the patient case in its entirety. Ensure that documentation is complete; there should not be recurrent missing documentation. Confirm that protocol-specified laboratory tests and diagnostic studies (including baseline assessments) were performed, reported, and documented. Likewise, check to see that protocol-specified research and advanced imaging studies were also done and submitted properly. Check to make sure that there aren’t frequent data inaccuracies or errors in submitted data, and also that data submission has been timely (data more than 6 months delinquent is a major deficiency, while 3-6 months delinquent is a lesser deficiency).

A critical deficiency for this category is any finding of fraudulent activity.

The Patient Case Review Worksheet provides a list of critical and major deficiencies related to the general data management quality category.
Assessing the patient case review: The auditing organization will assess a patient case review based on the number of lesser, major, and critical deficiencies identified during the visit.

An Acceptable rating may be assessed if the auditor identified: no deficiencies and no follow-up requested; few lesser deficiencies, with no follow-up requested; or a major deficiency that was addressed and corrected prior to being notified of the audit (with a written and dated CAPA) and no further action is required (check with CTMB if the deficiency is associated with a safety concern).
ASSESSING THE PATIENT CASE REVIEW

• A rating of **Acceptable Needs Follow-up** must be assessed if the auditor identified:
  - Any major deficiency that was not corrected and/or addressed prior to the audit; or
  - Multiple lesser deficiencies.

• A rating of **Unacceptable** must be assessed if the auditor identified:
  - A single critical deficiency;
  - Multiple major deficiencies; or
  - Multiple lesser deficiencies of a recurring nature found in the majority of patient cases reviewed.

A rating of **Acceptable Needs Follow-up** must be assessed if the auditor identified: any major deficiency that was not corrected and/or addressed prior to the audit; or multiple lesser deficiencies.

A rating of **Unacceptable** must be assessed if the auditor identified: a single critical deficiency; multiple major deficiencies; or multiple lesser deficiencies of a recurring nature found in the majority of patient cases reviewed.
Module complete: You have completed the Patient Case Review module. Please exit the module using the X in the upper right corner, and return to the course screen in the Learning Management System, where the module should now show as completed. You can always revisit this and other completed modules in your My Courses screen.

Note, this and the other training modules in this series were developed for the Clinical Trials Monitoring Branch of the Cancer Therapy Evaluation Program, Division of Cancer Treatment & Diagnosis, National Cancer Institute. For more information on the CTMB, visit the URL shown on the screen. This version of this individual module was produced in September 2018.

Cited link:
https://ctep.cancer.gov/branches/ctmb
The Site Audit Portal and Targeted Source Data Verification in Rave: This module provides an overview of the Site Audit Portal (SAP), and provides step-by-step instruction in using the SAP, and documenting your patient case review in Rave using the targeted source data verification (TSDV) method.
As part of a site audit’s patient case review, source data verification (SDV) is required to be electronically captured directly in Medidata Rave for certain studies. This is accomplished through a number of integrations between existing National Cancer Institute (NCI) systems, including:

- Clinical Trials Monitoring Branch Audit Information System (CTMB-AIS), where Lead Protocol Organization (LPO) staff set up and manage audits
- Medidata Rave, where site staff enter and manage patient data, and where auditors conduct and capture TSDV
- The SAP on the Cancer Trials Support Unit (CTSU) website (https://www.ctsu.org)

www.CTSU.org
Introduction to the SAP: The SAP serves as a front end for you to view information for audits with which you are associated, manage auditor roles and activity, and directly access patient data in Rave. It provides a single platform that records TSDV activity and helps to manage all steps in the audit process, including set-up and close-out. Through all that, it helps to ensure consistency in processes across the Groups.
Introduction to auditing via the TSDV method: The SAP supports the TSDV method of auditing. At a basic level, TSDV is the review of all source documents for protocol adherence, as usual; but the verification of only the data points in Rave that have been specified by the LPO as being the most important. The chosen data points will be obvious in Rave as will be described in later screens.
How to View Audit Information in the SAP: Go to the CTSU website at [www.CTSU.org](http://www.CTSU.org), and log in to the members’ side of the website. Click on the dropdown list for the “Auditing & Monitoring” tab, and choose “Site Auditing.”
Sample SAP Screen: This screen shows what the SAP itself looks like. Once you have clicked on Auditing & Monitoring, then Site Auditing, you will be in the SAP. Choose Ongoing Audits from the second dropdown box. Here you will see the current audits in a table that shows the name or site code of the audit site, the start date for the audit, the auditing LPO, the audit status of Ongoing, the names of the auditors for that audit, and the studies and patient cases to be reviewed.

Some notes regarding this Ongoing Audits page are circled in red: For the entry for STROGER, do you see the notation next to the NRG study listed? It says TSDV but is in red ink, with a red line through the letters. This lets you know that this particular study has not been configured for documenting TSDV review in Rave. Instead, you will need to use the old paper-based method for doing SDV for this study.

Going along with that, you will see that the auditor for that visit, Caroline Porter, has a small red x just before her name. That shows that she has not been given TSDV rights in Rave for this study. That is okay because the study is not set up for TSDV documentation, so that type of access is not needed. The other auditors, for other studies that are set up for TSDV, do have those rights, as you can see.
For the entry for the organization named Cora, under “Audit Site,” you will see a question mark symbol, with a “0/2” in parentheses next to it. This lets you know that for this site’s audit, two queries have been created thus far, and neither of them have been resolved and closed. This is here so that after the site has a chance to resolve the queries post-audit, you can click on the question mark and be taken directly to the list of queries needing to be closed (and from that page, directly to the queries themselves).

Also in that entry, under the “Patients” column, you can see the study and patient to be audited. The letters TSDV are next to the study number, in blue, showing you that this study is configured for TSDV in Rave. The patient number is a clickable link that will bring you straight to their data in Rave.

By the way, see the icon we have circled next to one of the patient numbers listed for the second entry, site NY167? That icon lets you know that this was an unannounced patient case. Your Group may review different items for unannounced cases, and this icon alerts you to the possibility for this patient.

We will come back to this screen later in this module.
Pre-TSDV Activity: These are the main steps involving the SAP, CTMB-AIS, and Rave that take place prior to an audit that involves TSDV.

The Credited Group (or CG, that is, the Group conducting the audit) notifies the site of the need for an audit and agrees on dates. The CG then initiates the process in CTMB-AIS. The Group documents the site and dates, then selects the auditors, protocols, and patients for the audit based on the CTMB Audit Guidelines. CTMB-AIS interfaces with Rave, so for studies that will be utilizing the TSDV method, the selected patients will be made available in Rave’s TSDV module and auditors will be provided access to those patients’ data in Rave in an automated fashion.

See the next screens for more information about auditor roles and access to Rave.
Auditor Roles Within the System: The CTMB-AIS will assign you a role of either “LPO Auditor” or “Site Auditor” for each patient case chosen for an audit. Your role for a specific patient case will be called “LPO Auditor” if you audit for the LPO of the study that patient is on; in other words, you are employed by the LPO. For instance, you are a SWOG employee and auditor and you are auditing a patient on a SWOG protocol.

Your role for a specific patient case will be called “Site Auditor” if you are a volunteer auditor or if the Group being credited for that patient’s enrollment is not the LPO of that study, and you are auditing it for the credited Group (the latter is also called a cross-Network auditor). Think of it as being a “guest” auditor, gaining temporary rights to see that patient’s data. An example would be if you work for SWOG and are auditing a case from an Alliance protocol where the enrollment was credited to SWOG.

If you are a volunteer auditor, your role is “Site Auditor” no matter who the patient case is credited to. Otherwise, please note that you may be considered an LPO Auditor for one patient case and a Site Auditor for another patient’s case! It really only affects the amount of time you have access to their data, as you’ll see on the next screen.
Auditor Access to Patient Data in Rave: If you are an LPO Auditor, you will be assigned to your own Group’s studies in Rave by Group staff. This is a manual process, and once assigned, an LPO Auditor will be able to view patient data at all sites conducting the assigned studies. However, they will only be able to carry out certain audit-related tasks (e.g., verifying data in Rave) for a set amount of time around each audit.

If you are a volunteer auditor, or a cross-network auditor for a patient case, your role in Rave for that case will be called “Site Auditor.” Site Auditors with Rave credentials will be granted access to their announced patients’ data in Rave three business days prior to the audit start date for National Clinical Trials Network (NCTN) audits. You will be granted access in Rave to unannounced patients one business day prior to the audit start date. Again, this is for non-LPO Auditors; LPO Auditors will have access to their Group’s patient cases for all audits unless access is revoked.

Note that if the “Rave Access” option for someone with the Site Auditor role has not been set up in the CTMB-AIS, no Rave access can be granted until that is changed. This is something that is handled by your Group. If you don’t seem to have access to Rave but believe you should, please contact your Group.
TSDV Activities Overview: Details of the activities that compose the TSDV method are dependent on whether an auditor has access to Rave. At a very high level: An auditor (whether an LPO or Site Auditor) with access to Rave will review all source documentation at the site, then compare source documents with the data selected to be verified in Rave. The auditor will then record the results of that review directly in Rave.
An auditor with no access to Rave will need to use a “Pre-SDV Workbook” created for them to record their patient case findings. This workbook is an Excel file that contains all data points that must be verified using the TSDV method, and can be used in hard copy or electronically.

Your Group will provide the Pre-SDV Workbook. Once an auditor documents findings from the TSDV in the workbook, the Lead Auditor or designee will then have to manually enter that auditor’s findings and activity into Rave after the audit.

It should be noted that use of the Pre-SDV Workbook is highly discouraged, and should be used only for auditors who have not been granted access to Rave.
TSDV activities include capturing documentation of the patient case review in Rave. This is accomplished via the use of:

- “Verify” checkboxes for TSDV data found to be accurate
- Comments
- Queries for potentially inaccurate data

Summary of TSDV activities: Specific data points to be verified will have been decided on by the LPO for that protocol, and configured in Rave. The data points chosen will generally be those that could affect the interpretation of the primary study endpoints.

TSDV activities will include capturing documentation of your patient case review in Rave via the use of “Verify” checkboxes for TSDV data found to be accurate; creation of any comments needed; and creation of queries for potentially inaccurate data.
TSDV INSTRUCTIONS

• Reminder: These capabilities are only available in studies that have been configured for TSDV in Rave. Other studies will require the prior paper-based process.


• Still need help? Contact the CTSU Helpdesk at 888/823-5923 or CTSUContact@Westat.com.

TSDV instructions: This section of the module will focus on step-by-step instructions for using the SAP and Rave for performing TSDV of patient cases. As a reminder, these capabilities are only available in studies that have been configured for TSDV in Rave. Other studies will require the prior paper-based process.

The resource for instructions on how to document TSDV in Rave is the Site Audit Reporting (SAR) – Auditors User Guide, available on the CTSU website at the URL included on the screen, and from your Group. If you still need help, contact the CTSU Helpdesk at 888 823 5923; or CTSUcontact@Westat.com.

TSDV IF NO ACCESS TO RAVE

- Auditors that don’t have access to Rave must use the Pre-SDV Workbook to conduct and document TSDV
  - Provided by Group staff in Excel
  - Must be filled out by the auditor and then entered into Rave by the Lead Auditor or designee following the audit

*Reminder: This method is labor-intensive and should be avoided if possible.*

TSDV if No Access to Rave: As stated previously, if a protocol has been set up for TSDV in Rave, but you as an auditor do not have access to Rave, you will need to audit using the Pre-SDV Workbook, either electronically in Excel or in hardcopy. Note that this method is labor intensive, both for you and for the Lead Auditor. The Lead Auditor or their designee will need to configure the Pre-SDV Workbook for your use and email it to you, and they will also need to enter all your verifications, comments, queries, and deficiencies found into Rave after the audit. Therefore, this method should only be used when absolutely necessary. Only the basics of this method will be discussed here; for more details, please see the SAR Auditors User Guide.
Shown on this screen is an example of the Index tab from the Pre-SDV Workbook Excel file. It shows the study name, site code, patient ID, visit name such as Baseline, Cycle 1 Day 1, etc., form name such as Eligibility Checklist, Treatment, etc., and worksheet name (which corresponds to tabs at the bottom of the sheet). The only forms listed will be those requiring review using the TSDV method, and clicking on a form name will bring you to the tab for that individual form. Once reviewed, come back to this index and record in the columns on the right whether you completed the TSDV needed for that form, if there were any queries for the form, your name, and the audit date.
When you click on a form name in the index tab of the Pre-SDV Workbook, you will see a page like this. It will include the form and visit name, the questions (or fields) and responses (or data) from that form needing to be reviewed, and places for you to document your verification and/or comments. Standard questions or forms are those in portrait format, and log questions or forms are those in landscape format.

This is important: only call a data point “verified” if you first reviewed the source documents and the electronic case report form (eCRF) entry is correct. Otherwise, record a comment or query regarding the discrepancy. Once finished with this form, click on “Back to Index” at the top right of the page to document your review there, including queries that need to be addressed.

Again, use this method only if you have no possible access to Rave. The Lead Auditor or their designee will have to take these completed worksheets after the audit and enter the information, i.e., the comments, the queries, and the “Verify” checkmarks, into Rave manually for you.

Next we will review elements of the process for auditors who will be conducting the TSDV method directly in Rave, beginning with how to gain access to Rave.
Auditor Invitations to Rave: To document TSDV directly in Rave during an audit, an auditor must first be invited to Rave and accept the invitation (or invitations). These invitations arrive via email from Medidata, to the email address associated with the auditor’s CTEP-IAM account. It is important to note that if a particular audit will involve multiple TSDV studies, the auditor will receive multiple invitations, and must address and accept all of them.
The scope of these invitations differs depending on whether an auditor is an LPO Auditor or a Site Auditor. (Remember, some auditors may be both during a single audit.) LPO Auditors will receive invitations from Medidata whenever they are first assigned to one of their LPO’s studies, so this may occur well before an actual audit.

The assignment and invitation will cover a given study at all possible sites, and will be good until the assignment is revoked by the auditor’s Group. This means that an LPO Auditor will not receive a study-specific invitation for every study prior to each separate audit, but instead, just the first time they are assigned to a given study.

Site Auditors (that is, volunteer auditors and cross-network auditors) with Rave access will receive invitations from Medidata for each study and site involved in a given audit, and the invitation will only be good for that audit. A Site Auditor will receive separate sets of invitations for each audit they conduct, as each audit will involve different study and site combinations.

The next screen shows a sample invitation email.
This screen shows a sample invitation email. Remember that you will receive multiple emails if there are multiple studies being audited. You must address each email and accept all of the invitations.

The email will come from Medidata, and the subject line will inform you that you have been invited to join iMedidata. The body of the email includes a reference to the study you are being invited to join, and there is a link that reads “Take me to iMedidata.” By clicking on that link and signing into iMedidata, you will be able to accept the invitation.

Remember, you must accept the invitation to gain access to the needed data in Rave for the audit and study in question. Please do this prior to the audit, to ensure a smooth auditing experience.
Required training in Rave: The first time an auditor accesses Rave to audit, they will be required to complete an eLearning module within iMedidata, regardless of whether they are an LPO Auditor or a Site Auditor. This eLearning is separate from the module you are currently viewing. All LPOs require the Rave EDC Essentials for Monitor eLearning; this module takes about 50 minutes to complete, and only needs to be completed one time (even if auditing different LPOs’ studies). LPOs may also elect to require the Query Management eLearning, but at this time, it is optional for all LPOs.
At the audit: You have been “invited” by Medidata to the studies needing TSDV in Rave, you have accepted the invitations, and you are now at the audit. What now?

Remember seeing this SAP screen earlier? You will start the TSDV process from here. To get to it, log in to the CTSU website, click on the Auditing & Monitoring tab, then Site Auditing, then Ongoing Audits.

Let’s say that you are auditing at NY167. Under the “Patients” column, you can see the study and patients to be audited. The letters TSDV are next to the study number, in blue, showing you that this study is configured for TSDV in Rave. The patient IDs are located below the study number.

Now that you understand the information on this page, you can click on the patient’s ID number in the Patients column to access the selected patient’s data in Rave and see which data fields need to be verified. The SAP acts as a gateway to Rave and provides this “deep link” to each patient assigned to the audit in Rave. This patient’s data in Rave will open in a new window.
TSDV process using Rave: The first step in TSDV is always review of a patient’s source documentation for protocol compliance, safety, and effectiveness. Then, from the screen we just showed you of the Ongoing Audit information in the SAP, you will click on that patient’s ID number.

This will bring up Rave in a separate window. When you are ready to check the source against the data to be verified in Rave, look at the Subject Level Rave page for that patient. That is the view that automatically appears when you click on the patient ID; part of that view is shown on the screen here. On the page you will see the Task Summary for the subject, and under “Requiring Verification” there will be a list of the eCRFs that have data fields requiring auditor review. In the example shown on the screen, there are only four forms you need to look at for this patient, and they are listed. You click on a form name, such as Cycle 1 Adverse Events, to go to that form.
Recording TSDV Results in Rave: How to Create a Comment: Hopefully, when you are in the eCRFs, you will mostly be verifying that the targeted data is correct. But it’s important to first create any comments or queries, so let’s learn that first.

Let’s say that you are auditing this patient and that from the Task Summary you have clicked on the Patient and Disease Description eCRF that needs verification. The form appears. First, identify the Verify checkboxes; these are the left-most empty checkboxes, and are circled on the screen. You’ll know which data points need to be reviewed by looking for the Verify checkboxes that are boldly outlined and enabled for checking. Data points that do not need to be reviewed will have Verify checkboxes that have been grayed out and inactivated. In this sample form, there are four data points, and three of them need to be reviewed. The checkbox for Height is grayed-out, and non-actionable.
Moving on to data that must be verified, the site has recorded 150 kilograms for the patient’s weight, but let’s say you were unable to decipher what the weight was in the source document and you want to create a comment. Here’s how: Click on the icon that is just to the right of the data that was entered. In the example on the screen, we have circled that icon next to the 150 kilogram entry. It will bring up a comment field in which you can state: “Source doc not legible.” Click Submit, next to the comment. That comment will now show on the form. (It is shown on the screen, under “Weight.”) Please note that we will show you more about where and how to enter a comment on the next screen.
Let’s say that the other two fields needing to be reviewed, Performance Status and Date Current Staging Assessment Completed, have data that agree with your review of the source documentation. After you have created and submitted the comment for the Weight field, click on the “Verify” checkbox (the left-most empty checkbox) for each of the correct data points and click “Save” in the bottom right corner. Checkmarks will show in those boxes, and the Comment should show under “Weight.” You are done with this form and can click on the Subject ID tab to go back to the list of forms needing verification. That Subject ID tab is not shown in this partial screenshot, but is located in the upper left section of the eCRF.

Please note: Create any comments and click Submit, and create any queries and click Save, prior to checking any Verify boxes and clicking Save. Otherwise you will lose some of your entries! Also, only check a Verify box if you have determined that the data entered is in agreement with what you found in source documentation. Otherwise enter a comment or a query instead.
Sample Comment Screen: We want you to understand what the Comments screen looks like. On the eCRF, once you click on the icon next to the data on which you want to comment – in this case, the 150cm height – this new screen will appear. It mostly shows the history of entries for that eCRF. However, at the bottom you will see a free-text field. This is where you would enter your comment, then click Submit. The comment will now show on the eCRF.
Recording TSDV results in Rave: How to Create a Query: Let’s say that you are auditing this patient and that from the Task Summary you have clicked on this form’s name. Again, you’ll know which data points need to be checked by looking for the boldly outlined Verify checkboxes. The Verify checkboxes are the left-most empty checkboxes. In this sample form, there are four data points, and two of them need to be reviewed, Weight and Date Current Staging Assessment Completed. The other Verify checkboxes are grayed-out, and non-actionable. The site has recorded 54 kilograms for the weight, but you found different results in the source document and you want to create a query. Here’s how to do it:
Click on the icon just to the left of the Verify checkbox for that field. In the example shown, we have circled that icon. Clicking there will bring up a query field in which you can click on the dropdown box above it if needed, so that it says “Site from Site Auditor,” or “Site from LPO Auditor.” Then enter something like: “Dr. Jones’ note from that date states 64 kilograms; should this entry say 64?” Click Save, in the bottom right corner of the eCRF. That query will now show on the form.

Tip for queries: If you state in the query what you believe the correct answer should be, it will be much easier to resolve and close the query later, when you might not have access to source documentation. Note that for data you query, you would not click on the Verify checkbox for that field, because you are not in agreement with the data entered.

Remember to go back to any queries later, once the site has responded to them, to close them out and verify the fields. The goal is to have accurate data reported!

For this form, there is one other data point to check – the date the current staging assessment was completed. If you agree with the data entered in that field, check the Verify checkbox for that field, then click Save at the bottom right of the form. Now you can click the patient ID number at the top left of the form to go back to the subject-level list. Note that you cannot see the Save button nor the Patient ID number in this example as we are providing just a partial screenshot of the form on the screen.
Recording TSDV Results in Rave. How to Document that all Reviewed Data on a Form are Correct: Let’s say that you are reviewing an eCRF and all the fields needing to be checked have data that agree with your review of the source documentation. This is the result that you always hope for!

Click on the “Verify” checkbox, that is, the left-most empty checkbox that is at the top of the form, but do not check any other boxes. That box is circled on the screen. Then click “Save” in the bottom right corner. Checkmarks will then show in all of the “Verify” checkboxes for fields that needed review.

You can choose, instead, to check each “Verify” box manually and then click Save, but utilizing just the top-most Verify checkbox is a convenient shortcut when you agree with all the data reviewed on that eCRF. You are done with this form and can click on the Subject ID tab at the top left of the form to go back to the list of forms needing verification.
Tips for Documenting TSDV in Rave: Here are some reminders as you go through this process. First, start at the source, meaning, begin your patient case by reviewing the source documentation for protocol compliance, safety, and efficacy, before looking at the data fields needing review on an eCRF.

If there are any comments or queries needed on a form, create those first. Create any comments, then click Submit. Create any queries needed on that form, then click Save. If you do not click Submit or Save after each of these items, you will lose some of your entries.

Once you have created any needed comments and queries on that eCRF, click the “Verify” checkboxes for the other reviewed items, but only if you have determined that the data entered is in agreement with what you found in source documentation. Then click Save.

You should see that for the data items needing review (that is, ones with highlighted Verify checkboxes), you have either a query or a checked Verify box; but not both. If all the items to be reviewed on a form are correct, you can click just the top-most Verify checkbox (and then click Save) as a shortcut for confirming that all reviewed data on that form was correct.

Finally, record deficiencies found per your Group’s preferred method. Please note that in the future, some Groups may use a form to document deficiencies directly in Rave, but for the time being, follow your Group’s regular procedure.
Post-TSDV-related activities include preparation and submission of reports. All TSDV documentation becomes a Post-TSDV report that is generated from Rave by the audit team. This report, along with the preliminary audit report, is submitted by the Lead Auditor or designee to CTMB via the CTMB-AIS.

Upon submission of the preliminary audit report, volunteer auditors will lose access to Rave for the patients that had been selected for audit. Any remaining open queries that had been created by the volunteer auditors will need to be addressed by LPO or cross-network auditors at that point.
LPO auditors and cross-network auditors will retain auditing access for a while so that they can handle queries and/or comments.

The audit team will submit the Final Audit Report via CTMB-AIS per their normal procedure. Cross-network auditors will then lose access to Rave for the patients that had been selected for audit. LPO auditors will lose access at that point to the Verify checkboxes for the audited patients. (They will still be able to open or close queries.)

Finally, let’s address review of answered queries.
How to Review and or Close Out Queries in Rave: The short answer is that you will get to the queries from the Task Summary list at the Subject Level in Rave. This is the same area that you clicked in Rave to see the forms with data points requiring verification for a specific patient. If you’re not well-versed in Rave, here’s a reminder of how to get there from the SAP:

Go to the CTSU website (www.CTSU.org), and sign in. Click on the tab named “Auditing & Monitoring,” then choose “Site Auditing” from the dropdown list. Choose “Ongoing Audits” from the second dropdown box.

Find the row for the Site that was audited, then click on a patient you audited. The “deep-link” will take you into the Subject Level in Rave, and show you the Task Summary. One of the sections in the Task Summary will be “Answered Queries,” and you can click on forms with answered queries from there. Another way is to click on the Question Mark link on the SAP. Either way will work.

See the next screen for a screenshot of the Task Summary list in Rave.
At the Subject level in Rave, the Task Summary will show the forms with Answered Queries. Click on a form to see the query or queries on that eCRF.
How to review an answered query: The query you created will be in the pink highlighted area, with the site’s response and the current data. In the example here, the site answered the query by saying that they had provided an updated source document, and it agrees with the data reported. If you are not satisfied by their response, open the dropdown box, click on Re-Query, and re-state your concern about the data. Remember to then click Save at the bottom of the eCRF. If, instead, you see their response and agree with it, click on Close Query in the dropdown box, then click Save at the bottom of the eCRF.

If you close the query, remember to then click the Verify box to signal that you agree with the data point, and again click Save. If there were other queries on the same eCRF, you can address them now. Otherwise, click on the patient ID number at the top of the eCRF to go back and see the remaining list of forms with Answered Queries.
How to cancel a query not yet addressed by the site: Say that you created a query, such as the one about the patient’s weight, shown above. During the audit, you find source documentation that supports the data the site had entered; and the site had not yet addressed this query. You can delete the query easily, by clicking on “Cancel” right next to the query; then click Save. And now that you agree with the data entered by the site for that field, click on the Verify checkbox for that field and again click Save at the bottom right of the eCRF.
How to delete or edit a comment: Let’s say that you have added a comment for weight for this patient, saying that the source documentation was not legible. You can see it on the screen shot, circled. Now let’s say that later on, the study coordinator shows you another place the weight for that day was written in source, and you can read that just fine. How do you delete, or edit that comment?

It’s quite easy. On the eCRF where the comment appears, click on the icon next to it which says “Inactivate or Edit,” then indicate what you want to do. Remember to click Save at the bottom of the eCRF. Also ensure that the Verify box gets checked and saved, if not yet done. By the way, site staff will not be able to delete or edit the comments.
This is a reminder of resources for documenting your TSDV, whether in Rave or (if necessary) using the Pre-SDV Workbook.

Your main resource is the Site Audit Reporting (SAR) Auditors User Guide, which is available on the CTSU members’ website at [www.CTSU.org](http://www.CTSU.org), and from your Group. You may want to keep it close at hand at first.

If you still need help after reviewing the User Guide, contact the CTSU Helpdesk at 888/823-5923 or email [CTSUcontact@Westat.com](mailto:CTSUcontact@Westat.com). If you are on a Multi-Group Audit with a CTSU Audit Facilitator present, they should also be able to answer your questions.
Module Complete: You have completed the SAP/TSDV module. Please exit the module using the X in the upper right corner, and return to the course screen in the Learning Management System, where the module should now show as completed. You can always revisit this and other completed modules in your My Courses screen.

Note, this and the other training modules in this series were developed for the Clinical Trials Monitoring Branch of the Cancer Therapy Evaluation Program, Division of Cancer Treatment & Diagnosis, National Cancer Institute. For more information on the CTMB, visit the URL shown on the screen. This version of this individual module was produced in September 2018.

Cited link:
https://ctep.cancer.gov/branches/ctmb