SOP#: PM-3	**Clinical Research Documentation**
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NCI Clinical Director Signature/ Effective Date:	James Gulley Digitally signed by James Gulley Date: 2023.10.27 09:33:26 -04'00'

POLICY

All encounters with patients/research participants by licensed practitioners must be documented in the legal medical record (i.e., CRIS) in accordance with applicable state practice acts. Encounters must be documented in a structured note within **24 hours** of any inpatient encounter and **3 calendar days** for outpatient encounters including phone calls/emails.

PURPOSE

To establish guidelines for clinical research documentation for various time points during a research participant's involvement in a clinical research protocol. Proper documentation ensures compliance with state practice acts, good clinical practices (GCP), AND allows for source documentation to be available at the time of data abstraction, monitoring visit, audit or inspection.

Note: Clinical Data Managers and Patient Care Coordinators under contract to the Center for Cancer Research (CCR) are not allowed to document in CRIS.

RESOURCES

- Code of Maryland Regulations (COMAR) Title 10
  - Subtitle 27 Board of Nursing, Chapter 07 *Practice of the Nurse Practitioner*
  - Subtitle 27 Board of Nursing, Chapter 09 *Standards of Practice for Registered Nurses*
  - Subtitle 32 Board of Physicians, Chapter 01 *General Licensure Regulations*
  - Subtitle 32 Board of Physicians, Chapter 03 *Delegation of Duties by a Licensed Physician – Physician Assistant*
  - Subtitle 32 Board of Physicians, Chapter 12 *Delegation of Acts by a Licensed Physician to an Assistant Not Otherwise Authorized under the Health Occupations Article or the Education Article*
- Center for Cancer Research Policies/Standard Operating Procedures webpage
- NIH Clinical Center (CC) Health Information Management Department (HIMD) Handbook
- NIH Medical Administrative Series (MAS) Policies
  - MAS M09-3 (rev.) *Communicating Protected Health Information via Electronic Mail (Email) at the NIH Clinical Center*
- FDA Compliance Program Bioresearch Monitoring: Clinical Investigators and Sponsor-Investigators

PROCEDURES

General Principles

- Documentation should be attributable, legible, contemporaneous, original, accurate and complete (ALCOA-C).
- Label structured CRIS Notes: Start a new document. In the left side panel, click on the "Document Info" tab and at the bottom is "Document Topic" box for the entry of a note title or label (e.g., Baseline, end of Cycle 2, Cycle 5 Day 15, Day 0, and Day 100 Post-transplant). Consistent labeling of documents allows for easier sorting, modification, and searching.

  NOTE*:* Document label should include protocol number. Free text progress notes do not have this option. Labeling a note is a feature for structured progress notes.
- Participant and/or family/guardian education should be documented in CRIS **each time** performed.
  - Patient education structured note is available.
- Conflicting, discrepant, or missing documentation requires a note to be written in CRIS. This note can be written by any licensed practitioner (MD, NP, PA, RN, etc.). Examples of notable events include:
  - Fellow note, dictated note, and/or nursing note have differing adverse event start dates
  - Tumor measurements/response per radiology report differs from CRIS note
  - Missing performance status
- For outside records, see CCR SOP PM-4 *Submitting Outside Records for Entry in CRIS.*
- All source documents must be maintained per GCP guidelines. Research source documents that cannot be placed in CRIS (e.g., PK flow sheets, participant diaries, surveys or other participant completed forms) must be maintained in a research record created by the team. The Research Coordinator is responsible for maintaining the research record on a secure network location, or if records are in paper form, in a locked cabinet with limited access.

Past Medical History/Prior Therapies

- Summarize past medical history and prior therapies on initial visit.

  NOTE*:* Documentation of past medical history including pathology as applicable and prior therapy can be information from outside providers or medical facilities which are filed in CRIS.
- If participant returns to NIH after receiving outside therapy, provide a summary of past history and other therapies that the participant received during that time period.

Concomitant Medications/Measures

- Participant's concomitant medications such as prescription medications, over-the-counter medications, herbals, supplements, and any complementary and alternative medications and measures (e.g., oxygen therapy) all need to be captured and include the following data:
  - Start date - document approximate month and year or the approximate number of years taken if participant unsure of exact dates.

- Reason/indication for use

  NOTE: This information is important due to off-labeled use of medications. Some medications are given for indications not approved by the FDA. Staff should NOT assume that the participant is taking the medication for the condition listed in the package insert.
- Dosage/Amount in unit of measure (i.e. 5 mg, one tab)
- Frequency (i.e. daily, one-time dose)

- Once on study, the exact date of new concomitant medications/measures must be documented, along with the information above.

Eligibility

- Teams must verify that all results (e.g., labs, pathology, protocol specific procedures) and clinical documentation (e.g., performance status, life expectancy, prior therapies) that are required to confirm eligibility are in CRIS. This information can be contained in outside records scanned into CRIS.
- If the patient is eligible, this must be specifically documented. If the patient is not eligible, document the discussion as to why the patient is ineligible including results from tests or procedures that may deem them ineligible.

Informed Consent Process

- Write a note using the CRIS structured "Documentation of Research Consent" template. See CCR SOP PM-2 *Obtaining and Documenting the Informed Consent Process (Adult and Pediatric).*

Baseline Symptoms

- Baseline symptoms including abnormal physical exam findings or laboratory values must be documented in CRIS. Include approximate start date (mm/yyyy), description and frequency of **each** symptom. At each visit, review them with the participant and update in CRIS as needed.

NOTE: For treatment trials, baseline signs and symptoms are those that are present when the patient starts protocol therapy (e.g., Cycle 1 Day 1 pre-dosing). These are not signs or symptoms that occurred and resolved between the time screening studies/exams/procedures are done and start of protocol therapy. The adverse events section of the protocol should define when to start collecting adverse events, this is the cut-off time for collecting baseline symptoms.

Scheduled Study Visit

- All protocol related visits, procedures, exams, etc. must be documented in CRIS. For intervention trials, this includes all visits that are part of active treatment, follow-up or any other clinically related problems.
- Date of visit, result or plan from the visit and any follow-up needed must be documented, including PI assessment or concurrence. This could include a separate note from PI or co-signature or a "discussed with [*insert PI name*]".

- Protocol-specific activities including biopsy obtained, surveys administered, diaries reviewed with participant must be documented in CRIS by the individual conducting the activity.
    - For protocol-specific activities that are carried out by the Clinical Center (CC) staff (e.g., PK or serial blood draws), ensure that these activities have been documented in CRIS.
    - For participant completed forms (e.g., surveys and diaries), a CRIS education note is required and needs to include that the participant was given instructions and understands how to use the forms.
    - For documentation of tumor measurements, see *Guidelines for Entering Tumor Measurements in CRIS* below this SOP on the CCR SOP website.
- Document any missed scheduled visit or study procedure/activity in CRIS and include the reason for the missed visit and any applicable follow-up that needs to occur (e.g., Day 8 labs missed by participant and arrangements made to be drawn on Day 10 instead).

Clinical Laboratory Review

- All laboratory results will be reviewed and noted if they are, or which results are clinically significant or not. This is for labs drawn at the NIH CC or from the outside. Clinically significant labs will include a plan for treatment, protocol changes and /or follow up.
    - Note: all outside lab results will be uploaded into CRIS

Study Drug Administration

- Most study drugs will be administered by the nurses in the CC Nursing and Patient Care Services. If administered by an NCI licensed practitioner, he/she must document in CRIS the following:
    - Date, time, amount, route
    - For IV medications, start and stop times
- Study drugs that are self-administered by the participant must have the following documented in CRIS:
    - Instructions for proper use/administration and storage of drug(s)
    - Date and amount dispensed/returned (to be done by the dispensing pharmacist and can be found in CRIS)
    - Participant's compliance with regimen including the amount of drug taken during a specified time period
    - If using a diary, include instructions on use of diary

  NOTE: Ensuring that participants are taking and storing their study drug appropriately is an ongoing process. All documentation related to teaching/reinforcement must be documented in CRIS. Refer to PM-8 *Conducting and Documenting Drug Accountability for Oral Investigational Products that are Self-Administered by Research Participants* for more information.

Adverse Events

For all AEs, the following must be documented in CRIS in single note or a series of progress notes from multiple providers:

- Date AE started

  NOTE: May also need to document the time of the AE (e.g., allergic drug reaction, transfusion reactions).
- Description of AE so that a severity rating using CTCAE can be determined for data management purposes

  NOTE: Please make sure for subjective AEs that there is a description and not just a grade level.
- How AE was treated, if applicable

  NOTE: This includes interruption or discontinuation of protocol therapy.
- Causality of AE – Each AE must have a causality determined, either to the research or to some other reason (e.g., progression of disease, concomitant medication, comorbidity). A causality of the AE is needed for participant clinical care and data management. See Appendix A for examples.
- Date AE stopped

  NOTE: An AE must be followed until it has resolved or, for an adverse event that might not ever resolve (e.g., neuropathy, alopecia), until it has stabilized.
- Outcome of AE – This would include if the participant died, was hospitalized, required intensive care to avoid death, recovered, or stabilized.
- PI assessment or concurrence with AE documentation. This could include a separate note from PI or co-signature or a "discussed with [insert PI name]".

Unscheduled Visits

- Unscheduled protocol visits usually occur as a result of a participant's complaint or adverse event. All unscheduled study visits, procedures, exams, etc. must be documented in CRIS including reason for visit/procedure, any follow-up and PI assessment.

Off Treatment

- Enter a note in CRIS when a participant is taken off active treatment. The note should include:
  - Reason off treatment
  - Off treatment date which is the date the PI or designee decides no further protocol therapy will be given

    NOTE: This may be the same as the date of a scan or the last dose of drug, but not always. This is not the same date as holding the protocol therapy to wait for resolution of an AE.
  - Participant education related to follow-up that needs to occur per protocol
  - Drug accountability (i.e., return of drug, diary), if applicable

Follow-up

- Review and document all protocol-specific activities that occur in the follow-up period as defined in the protocol. This may include survival alone or in combination with adverse events (new and/or ongoing), concomitant medications or measures, tests/procedures conducted, disease/response and/or research labs. Please specify for which protocol the follow-up activity is conducted.
- Document **all attempts** to contact/locate the participant, including but not limited to:
    - Phone call and/or secure e-mail
    - Contact referring physician
    - Contact participant's emergency contact as identified in CRIS
    - Send certified, return receipt letter
    - Search public records (e.g., newspaper obituaries and Ancestry.com)

Off study

- When the participant is taken off-study, a note must be entered in CRIS including why the participant was removed from the study and the date. For participants who are lost to follow-up before they can come off study, every attempt should be made to locate the individual as noted above.

  Note: If a participant dies while on study, the date of death is the date off study, regardless of when the team learns about the death.

Telephone Calls/Emails

- **All** telephone calls/emails with participant, family, referring doctor, etc. must be documented and summarized in CRIS including the reason for call (e.g. adverse event, general question, test result, etc.). Emails containing participant information must be sent via secure email process.

  Note: For email correspondence with participants, see MAS Policy M09-3 *Communicating Protected Health Information via Electronic Mail (Email) at the NIH Clinical Center*
- Document outcome of call/email (e.g. instructed to have blood drawn the next day, how adverse event to be treated, etc.)
    - Telephone contact structured note is available for use

Appendix A

Adverse Event Attributions

Dichotomized Approach		5 Option Approach	
Attribution	**Definition**	**Attribution**	**Definition**
Related	Reasonable causal relationship between the AE and the intervention/research.	Definite	AE clearly related to the intervention/research.
		Probable	Likely related to the intervention/research.
		Possible	May be related to the intervention/research.
Unrelated	No reasonable causal relationship between the AE and the intervention/research.	Unlikely	Doubtfully related to the intervention/research.
		Unrelated	Clearly not related to the intervention/research.