

Best Practices for SWOG Studies

The purpose of these guidelines is to provide information related to expectations for protocol compliance, documentation practices and consenting issues for SWOG studies to assist sites in avoiding deficiencies during a SWOG audit.

PROTOCOL COMPLIANCE

To provide clarification and bring consistency among protocols, the following standard procedures have been developed. In the absence of protocol specific guidance, the following procedures should be followed. All timeframes are based on calendar days.

Eligibility

All eligibility criteria must be verified and supporting eligibility forms (e.g., Local Pathology Review Form) signed prior to registration. The registering investigator/advanced practice provider (APP) or designate must also sign the Eligibility Checklist or affirmation of eligibility on the Registration Worksheet prior to registration. Electronic signatures are acceptable. The SWOG Statistics and Data Management Center will make no exceptions to the eligibility criteria in the protocol. No one in the Group is authorized to make an exception to eligibility criteria. Registration of an ineligible patient based upon an exception granted by the Study Chair will result in a major eligibility deficiency during an audit.

If a patient is deemed ineligible after registration, the patient should be treated and followed per protocol unless directed by the Study Chair to remove the patient from treatment.

Toxicity assessments

- Pre-study tests, observations and laboratory studies completed within 14 days prior to the first day of treatment need not be repeated prior to start of treatment unless otherwise required by the protocol.
- Dose or schedule modifications must be based on toxicity observed during the preceding cycle and on Day 1 of the current cycle. Labs required on Day 1 of a cycle may be obtained up to 2 days prior to treatment unless otherwise indicated, and results must be available prior to treatment. Dose modifications must be based on the toxicity requiring the greatest modification. Abnormal lab values, including those considered not clinically significant, noted during laboratory studies performed prior to start of a new cycle must be reported as adverse events for the previous cycle unless otherwise directed in the protocol.

Protocol Windows

These guidelines are for use when the protocol does NOT provide windows and is not intended to replace what is in a protocol.

a. Treatment administration and toxicity assessment on treatment, any disease assessment (on or off)

Treatment/Visit/ Assessment Interval	7 day interval	14 day to 28 day interval	6 week to 3 month interval	6 month interval	12 month interval
Allowed Window	+/- 1 day	+/- 3 days	+/- 7 days	+/-14 days	+/-28 days

Notes:

1. Disease assessment timing is to be based on calendar timing counted as weeks after study registration, not based on cycles or drug administration. Disease assessments are to be performed per protocol regardless of treatment delays until disease progression and discontinuation of protocol treatment or otherwise noted in the protocol.

2. When scheduled assessments are adjusted for a cycle using the allowed windows provided, all efforts should be made to return to the original schedule for subsequent assessments as noted in the study calendar.

b. Post treatment follow-up

Follow-up interval	Q 1 month	Q 2-3 months	Q 6 months	Q 12 months
Allowed window	+/- 7 days	+/- 14 days	+/- 21 days	+/- 28 days

c. Specimens (blood/urine/stool) collection:

- Baseline – prior to treatment on Cycle 1 Day 1; for observation within 10 days of registration
- Post baseline
 - Specimens linked to cycles: within 7 days prior to treatment for the cycle
 - Specimens at a specific timepoint (e.g., Day 30 after surgery, 6 months after registration) use table below.

Time of specimen from designated point of time (e.g., registration, off treatment, surgery)	1–7 days	1–30 days	31–90 days	91–120 days	>120 days
Allowed window	+/- 1 day	+/- 3 days	+/- 7 days	+/- 14 days	+/- 21 days

- Off treatment/progression – within 14 days of notification of off/progression

NOTES: Specimen collection

- If there is a requirement to seek additional patient consent for the future use of specimens, failure to include the specimen questions in the consent form will be considered a major informed consent content deficiency.
- Availability of specimens that are required for eligibility (i.e., for central pathology review or for correlatives that are an integral part of the study objectives) must be verified prior to registering the patient. Failure to submit adequate specimens required for eligibility will result in a major eligibility deficiency.
- If a patient consents to the future use of optional specimens, it becomes a requirement to collect and submit the specimens per protocol requirements. Failure to collect and submit specimens for which the patient provided consent will be considered a major data quality deficiency during an audit. To avoid a deficiency, inability to collect specimens (e.g., difficulty in drawing blood, patient refuses on the day of the blood draw, etc.) must be documented in the research record and noted in Specimen Tracking on the SWOG CRA Workbench.

NOTES: Specimen Submission

Unless indicated otherwise in Section 15 of the protocol, specimens should be submitted per the following guidelines:

- All specimens must be logged into the SWOG online Specimen Tracking system.
- Baseline tissue specimens must be shipped within 30 days after registration or within 30 days after surgery performed after registration unless otherwise stated in the protocol.
- Ambient temperature blood specimens must be shipped within one day of collection.
- Frozen blood and urine specimens must be shipped within 15 days of collection.
- If batch shipping of frozen specimens is allowed per protocol, they must be shipped at intervals no longer than every 3 months unless otherwise specified in the protocol. Batch shipments should include specimens for no more than 5 patients and no more than 50 individual specimens.

- Shipment of specimens greater than 3 months after the due date will result in a major data quality deficiency during an audit.
- d. **PRO instruments for therapeutic trials** (based on days from registration; may not be tied to actual treatment)
- Baseline: +/- 7 days of registration, prior to initiation of protocol treatment.
 - Follow-up (on or off treatment): +/- 28 days of the target assessment date based on the study registration date.

Data Submission

- Delinquent data greater than 3 months after the due date for baseline and on treatment forms and greater than 6 months after the due date for follow-up data will result in a major data quality deficiency during an audit.
- Data on all registered participants, including ineligible patients and patients who were never treated, are used in most analyses. If we pick and choose which patients are included in an analysis we open ourselves up to potentially biasing the study which could result in misleading conclusions. For this reason, we ask that all data be submitted for every patient, even if they are not eligible, so that we can protect ourselves from having biased studies.

DOCUMENTATION REQUIREMENTS

General documentation: All data reported in Rave must have supporting source documentation. Printed copies of the Case Report Forms may be used as source documentation as long as they are signed and dated. All source documents uploaded into Rave must include the SWOG patient ID.

Documenting the history and physical (H & P):

The baseline H & P must be performed within 28 days of registration unless indicated otherwise in the protocol. The H & P should include height and weight, vital signs, review of symptoms, performance status and past medical history performed by a physician or other qualified health professional. The medical history should include the following:

- Details of the malignancy including date of diagnosis, primary tumor characteristics (histology, grade, staging, size and hormonal receptor status);
- Relevant prior surgical procedures;
- Prior chemotherapy and/or radiotherapy (including start and stop dates, number of cycles and doses) for the current malignancy;
- Concomitant medications;
- History of hypertension, hyperglycemia, hypercholesterolemia, or relevant medical disorders and whether the subject has ever taken medications for these conditions;
- History of treatment for a prior malignancy;
- Menstrual, sexual and contraceptive use history;
- Social and Family history.

A focused, treatment-related exam may be done during follow-up at the discretion of the investigator. At a minimum, the exam should include weight, performance status, vital signs, concomitant medications and adverse event assessment.

Documenting performance status:

A numeric value using the Zubrod/ECOG scale is required to be documented to reflect the patient's functional status pre-treatment. This is usually part of the eligibility criteria. Subsequent evaluations during a study must also have a numeric representation of patient's performance status.

Documenting treatment administration:

- The rationale for a dose modification or a delay in treatment beyond the timeframe allowed in the protocol must be documented in the medical record. If the patient refuses treatment or for any

reason is unable to begin treatment, the rationale must be documented in the medical record and the patient must continue to be followed per protocol.

- Drug orders or a prescription indicating drug, dose, route, frequency, and duration of administration frequency must be on file as well as documentation of treatment administration.
- Infusions: Start and stop times must be documented to support the proper sequencing and timing of drug administration. Administration of any required supportive medication(s) must also be documented.
- Oral medication: Adherence to oral medications must be documented through the use of the Intake Calendar provided by SWOG, pill diaries or progress notes.

CONSENT ISSUES

Informing patients of new risk information:

- Per OHRP, new risk information typically described in CTEP Action Letters may be considered to represent significant new findings developed during the course of research that may relate to a subject's willingness to continue participation. There is no requirement for IRB review and approval of such statements before they are provided to subjects; therefore, CTEP may advise investigators to communicate such new risk information promptly to already enrolled subjects.
- Per SWOG policy, patients are required to be informed of new risk information no later than their next scheduled visit. If the responsible IRB requires that patients be re-consented, verbal communication of new risks to the patient must take place in the interim until the consent document is amended if necessary to meet notification requirements and the process documented in the research record.
- For sites using the CIRB, consent addendums provided as a tool for patient notification have already been approved by the CIRB and may be provided to the patient at the next visit without local approval.
- For sites using a local IRB, consent addendums may be approved by expedited review while waiting for approval of the associated revision.

Withdrawal of consent

- Unless a patient withdraws consent for all follow-up, patients must be followed as indicated in the protocol and SWOG Policy #30. If unable to contact the patient, information from the local EMR may be used to report follow-up status or public records, such as those establishing survival status (e.g., Social Security Index), may be consulted for reporting death or survival status.
- Withdrawal of consent occurs when the patient refuses to participate further in the research study and does not wish for future medical information to be collected or used for the purpose of research.
- Per SWOG Policy #30, if the patient withdraws consent after registration, the institution must determine with the patient whether 1) they no longer wish to be treated per protocol; 2) they no longer wish to be followed per protocol or 3) both. The subject may be willing to allow the investigator to continue other research activities (e.g., follow-up assessments, specimen collection, questionnaires, survival status, etc.). The distinction must be documented in the research record and on the Off Treatment Notice or Follow Up Form as appropriate.
- Withdrawal of consent from all components of the research study or just the primary intervention must be documented via:
 - A letter from the patient
 - A note in the research record by the investigator clearly reporting the patient's wishes for the study intervention (if on protocol treatment) and for study follow-up and participation.
- If complete consent withdrawal status is established, all research activities involving the subject's participation in the study (direct intervention, collecting PHI from outside sources such as other departments accessible through the EMR, etc.) must be discontinued.
- Data forms must be submitted, queries addressed, etc. for the timeframe prior to the time of withdrawal.
- When a subject withdraws from a study, the data collected on the subject to the point of withdrawal remains part of the study database and may not be removed and is subject to audit or FDA inspection.

See the SWOG Regulatory Audit Guidance for additional information related to the consent process. This document along with other Quality Assurance resources can be found under the Clinical Trials section of the SWOG website (in the Additional Resources section on the Quality Assurance & Audits page). For comments or questions, please contact the Quality Assurance Manager at the SWOG Operations Office at (210) 614-8808 or qamail@swog.org.