

# Case Cancer Institutional Review Board Policy

## Protocol Deviations

### Purpose

To describe the IRB's process for reviewing unapproved changes in a research activity, which were not previously reviewed and approved by the IRB.

### Policy

During the conduct of the study, changes to an IRB-approved protocol may be proposed or unintentional changes in the conduct of the study may be discovered. Amendments are reviewed and approved by an IRB as federal regulations specifically require the Case Cancer IRB to review proposed changes in a research activity, and to ensure that such changes in approved research are not initiated without prospective IRB review and approval, except when necessary to eliminate apparent immediate hazards to the subject [45 CFR 46.103(b)(4)(iii) and 21 CFR 56.108(a)(4)].

### Definitions

Protocol Deviation—any change, divergence, or departure from the study design or procedures of an IRB-approved research protocol that is under the Principal Investigator's (PI) control and that has not been approved by the Case Cancer IRB. Upon discovery, the PI is responsible for reporting protocol deviations to the Case Cancer IRB using either the *Case Cancer IRB Major Protocol Deviation Report Form* or the *Case Cancer IRB Minor Protocol Deviations Log*.

Minor Protocol Deviations—any change, divergence, or departure from the study design or procedures of an IRB approved research protocol which does not have a major impact on the subjects' rights, safety or well-being, or the completeness, accuracy and reliability of the study data. Examples of minor protocol deviations include but are not limited to the following:

- Participant does not show up for scheduled research visit.
- Failure of participant to return study medications.
- Missing original signed and dated consent form (only a photocopy available).
- Missing pages from an executed consent form.
- A failure to follow the approved study procedure that, in the opinion of the PI, does not affect subject safety or data integrity:
  - Study procedure conducted out-of-sequence.
  - Omitting an IRB-approved research activity on a protocol (e.g., failure to mail out or collect quality of life surveys, failure to evaluate and document performance status).
  - Failure to perform a required lab test.
  - Missing lab results, tests and/or procedures.
  - Study visit conducted outside of required timeframe.
- Missed oral medications, not relating to treatment of toxicities, or a missed day of treatment with continuous therapy.

Major Protocol Deviations—a deviation from the IRB-approved protocol that may affect the subject’s rights, safety, or well-being and/or the completeness, accuracy and reliability of the study data. Examples of major protocol deviations include but are not limited to the following:

- A research subject received the wrong treatment or incorrect dose.
- Performance of a study procedure not approved by the IRB.
- A research subject met withdrawal criteria during the study but was not withdrawn.
- A research subject received an excluded, concomitant medication.
- Breaches of confidentiality.
- A research subject was enrolled, but does not meet the protocol’s eligibility inclusion/exclusion criteria.
- Failure to treat research subjects per protocol procedures that specifically relate to primary efficacy outcomes.
- Changing the protocol without prior IRB approval.
- Locally enrolling significantly more subjects than approved by the IRB (>10%).
- Inadvertent loss of samples or data.
- Missed oral medications, not relating to treatment of toxicities, or a missed day of treatment with continuous therapy.
- Failure to obtain informed consent prior to initiation of study-related procedures.
- Inadequate or improper informed consent procedures (e.g., participant signed expired consent document).
- Failure to report serious adverse events within required timeframe to the IRB and/or sponsor and FDA.
- Falsifying research or medical records.
- Performing tests or procedures beyond the individual’s professional scope or privilege status (credentialing).
- Enrollment of subjects after IRB-approval of a study has expired.
- Failure to submit continuing review application to the IRB before study expiration.

### **Reporting Requirements**

The PI is responsible for ensuring that research involving human participants is conducted in accordance with the IRB-approved protocol. Investigators must report within 14 calendar days any major protocol deviation using the *Case Cancer IRB Major Protocol Deviation Report Form*. Careful monitoring by the PI of the conduct of the protocol should readily identify such problems to ensure proper reporting. Deviations that are reported to the IRB in accordance with this policy are usually not considered non-compliance; however, non-reported deviations identified through quality improvement reviews, complaints, monitoring reports, or means other than the research team will be reviewed in accordance with the *Non-Compliance Policy*.

**Minor protocol deviations** need not be submitted to the IRB for prospective review. All minor protocol deviations should be documented using the *Case Cancer IRB Minor Protocol Deviations Log* and submitted to the IRB for review at the time of continuing review. In lieu of providing the *Case Cancer IRB Minor Protocol Deviations Log* at the time of continuing review, an investigator may provide a final report, resulting from a quality assurance or monitoring site visit conducted during the current review cycle for an IRB approved study. The quality assurance or monitoring site visit must have been conducted by a federal agency, study sponsor,

or a local institutional IRB. Minor deviations will be placed in the protocol file along with the continuing review report and reviewed by an IRB member during continuing reviews.

To report *major protocol deviations*, investigators should utilize the *Case Cancer IRB Major Protocol Deviation Report Form* and, if appropriate, the PI should provide a corrective action plan. If a change in the protocol is needed, an amendment request should be submitted in addition to the *Case Cancer IRB Major Protocol Deviation Report Form*. All major protocol deviations will be triaged initially by the Case Cancer IRB office. The IRB Chair and/or member designee will review and decide at that time whether to bring the major protocol deviation to the full Board. All deviations resulting in harm or significant risk of harm (both physical and non-physical) to participants must be reviewed by the full Board and the PI will receive a formal written response/acknowledgement from IRB following the review.

Study sponsors may have different reporting requirements than the IRB and it is the PI's responsibility to be knowledgeable about, and meet, the study reporting requirements of the Case Cancer IRB. Planned ongoing protocol changes (amendments) to an IRB-approved protocol must be submitted as a formal protocol amendment and not as a protocol deviation.