Title: DEVIATIONS TO IRB APPROVED RESEARCH AND IRB SOPS

Version No.: 1.8

SOP No.: RR-407

Effective Date: January 20, 2026

1. Purpose

This policy defines protocol deviations and describes requirements for reporting, review, and management of deviations.

2. Policy

2.1 Definitions

Deviation: Any incident involving noncompliance with IRB approved research. Deviations typically do not have a significant effect on the rights, safety, or welfare of research participants or on the integrity of the resultant data. Deviations may be intentional or unintentional and they may be identified before or after they occur.

2.2 Policy

Except when necessary to eliminate apparent immediate hazards to the research participants [45 CFR 46.103(b)(4)(iii) and 21 CFR 56.108(a)(4)], federal regulations require IRB approval of modifications to IRB approved protocols prior to initiating a change to the IRB approved protocol.

A deviation that impacts the rights, safety, or welfare of research participants require submission to and review by the IRB in accordance with MSK IRB SOP RR-408 (Reporting of Serious Adverse Events), MSK IRB SOP RR-409 (Unanticipated Problems Involving Risks to Participants or Others) or MSK IRB SOP FO-309 (Noncompliance in Human Research).

Deviations to IRB approved protocols that involve participant eligibility, informed consent procedure change, and/or intervention/interaction/pharmacy alterations as defined in section 3.1 require prospective IRB approval prior to the change being carried out.

Deviations to IRB approved protocols that may affect the scientific validity of the study, may meet the criteria of serious or continuing noncompliance, or have the potential to result in increased risk or decreased benefit to participants must be reported to the HRPP Office as retrospective deviations. Deviations that occurred prior to 5/20/24 and have not been reported to the HRPP in PIMS must follow version 1.7 of this policy.

Occasionally, minor changes to the requirements of the IRB approved protocol are required for a single participant. These deviations do not adversely affect the rights, safety, or welfare of participants and do not result in a substantive impact/change to the conduct of the protocol and human subjects protection oversight. These deviations are considered non-reportable.

Department of Laboratory Medicine or Department of Pharmacy changes that impact protocol-required laboratory tests and/or medications do not require deviation reporting to the IRB, as they are considered an institutional change in clinical operations with appropriate notifications and approval. Department of Laboratory Medicine and Department of Pharmacy announcements of changes should be filed in the protocol regulatory binder, when applicable. If the Department of Laboratory Medicine or Department of Pharmacy changes impact a protocol participant's safety, the IRB must be notified as per Section 3 of this policy.

All prospective and retrospective deviations are required to be submitted via PIMS, unless otherwise instructed by the HRPP Office. All deviations must be saved in the regulatory binder.

Specific reporting requirements are described in Section 3 of this policy.

Sites relying on the MSK IRB must adhere to the requirements outlined in this SOP. The MSK study team responsible for working with the site must submit the deviation in PIMS if a site does not have access to the PIMS deviation submission module.

3. Specific Procedures

3.1 Prospective Deviations Reporting

Any event that impacts one of the below requires reporting and approval from the IRB in advance of the event occurring:

Deviation Type*	Examples
Eligibility**	• Participant does not meet eligibility criteria outlined in the protocol.
Informed Consent	• Deviation from recruitment plan indicated in protocol and/or informed consent procedures
Intervention/ Interaction /Pharmacy	• Dose modification that is not stipulated as an allowance in the protocol. • Provision of additional and/or different interventions/interactions not outlined in the current protocol. • Dispensing additional self-administered drug (e.g., oral meds) for participant to accommodate scheduling.

**Prospective Deviations are not allowed for NCI Network research protocols. Other external sponsors may not allow for this either; sponsor allowances overrule the MSK IRB SOP allowance.*

***Eligibility deviations are not allowed for MSK IND/IDE held or cross-referenced protocols unless an exception has been granted by the INDC Chair. If an exception is granted, the deviation will be sent to the IRB for review.*

Documentation (e.g., e-mail, memo, etc.) with sponsor acknowledgement and/or approval is required for all applicable protocols prior to submission to the IRB. For MSK held IND/IDE protocols, the INDC Chair/designee is required to approve/acknowledge prior to asking for IRB approval.

A list of all reported and approved prospective deviations will be reported to the IRB/PB at the time of continuing review.

3.2 Retrospective Deviations

A retrospective deviation is any deviation that has occurred and

- may affect the scientific validity of the study,
- may meet the criteria of serious or continuing noncompliance, and/or
- may have the potential to result in increased risk or decreased benefit to participants.

Retrospective deviations must be reported to the HRPP Office within 10 business days of identification by the MSK PI or study team.

Examples of retrospective deviations that must be reported to HRPP include but are not limited to:

- Enrollment of an ineligible participant without prior approval from the MSK IRB (prospective deviation) or any eligibility deviation that occurs on a study using an external IRB.
- Incorrect dose of study drug/treatment administered to a participant.
- Infusion timing error that resulted in an adverse event.

- Expired drug given to a participant.
- Consent not obtained:
  - Consent not obtained before the start of research activity,
  - Missing signature on consent before the start of research activity,
  - Short form, interpreter, and/or or witness not used for non-English speaking participants.
- Reconsent never obtained.
- Unnecessary and/or repeat research biopsy or other invasive test/procedure performed due to study team error.
- Privacy deviations that the Privacy Office determines to be a breach.

The HRPP Director and/or HRPP Office staff will review retrospective deviations submitted by or on behalf of PIs. The IRB Chairs delegate this responsibility to the HRPP staff.

These deviations will be reviewed and accepted by the HRPP staff and escalated in real-time to IRB Leadership, as appropriate. A list of all reported and accepted retrospective deviations will be reported to the IRB/PB at the time of continuing review.

Retrospective deviations that represent non-compliance, unanticipated problems involving risks to participants or others, or serious adverse events will be reviewed in accordance with their respective policies and procedures.

3.3 Non-Reportable Deviations

If a deviation does not meet retrospective or prospective reporting criteria as outlined in sections 3.1 and 3.2, it does not require reporting to the IRB or HRPP. Non-reportable deviations must be documented in the regulatory binder. Examples of non-reportable deviations include but are not limited to:

- Protocol-required tests/evaluations (non-eligibility) that were missed or performed outside of the protocol window.
- Treatment/intervention scheduling changes.
- Virtual physical conducted in place of an in-person physical, if the sponsor considers the virtual physical to be incomplete and/or missed.
- Missing responses in questionnaires/surveys or pill diaries.
- Consent documentation errors (e.g., missing date), with exception of above reportable events.

Missing or incomplete drug accountability forms, case report forms and/or other forms that were not corrected according to GCP requirements are not considered deviations.

The PI and study team are responsible for reviewing non-reportable deviations for trends that could constitute continued and/or serious non-compliance and report such findings per MSK IRB SOP FO-309.

3.4 Additional Reporting Requirements

- When MSK is not the IRB of record (IoR), deviations must also be reported to the IoR in accordance with the IoR's policy.

4.0 Applicable Regulations and References

- MSK IRB SOP FO-309
- MSK IRB SOP RR-408
- MSK IRB SOP RR-409
- Clinical Research SOP CR 1001

Revision History

Revision	Effective Date	Reason for Change
1.0	7/11/16	• Formerly part of IRB SOP RR-402 Continuing Review – Ongoing • No longer using the term "violation" • Change to reporting requirements.
1.1	4/25/18	• 3.2 Clarified items that do not qualify for the +/- 5 day window • 3.2 Clarified that outside of window PK tests are reportable per cycle • 3.3 Clarified non-reportable deviations • 3.3 Clarified that this policy is not approval for dosing within the additional +/- 2 day window
1.2	5/11/20	• 3.1 Replaced NCTN and other NCI sponsored protocols with NCI Network research protocols
1.3	11/23/20	• 2.2 Added the following: When MSK is the data coordinating center (DCC), deviations at non relying participating sites do not require submission to the MSK IRB/HRPP. Non-relying participating site deviations should be reported to the Multicenter Trials (MCT) Office according to IRB SOP RI-802 • 3.1 Removed requirement for prospective deviation approval to ship drug to another center or participant's home • 3.2 Updated to note that the IRB chairs delegate the responsibility of retrospective deviation review to the HRPP Director and/or HRPP Office staff • 3.2, 3.3 Removed the word "delay" from deviation examples • 3.4 Added deviation reporting to MSK is not required if an event is not reportable according to this policy but is reportable to the outside IoR
1.4	5/10/21	• Removed reference to Clinical Research Portal throughout • 3.1 For eligibility deviations on MSK IND/IDE held or cross-referenced protocols, updated to note that they are allowed if an exception has been granted by the INDC Chair and approved by the IRB. • 3.3 Added virtual physical conducted in place of an in-person physical, if the sponsor considers the virtual physical to be incomplete and/or missed.
1.5	1/31/22	• 2.2 and 3.3 Added that source documentation that is missing, incomplete, or erroneous is not considered an IRB deviation and does not need to be reported to HRPP • 2.2 Updated the policy statement to clarify that sites relying on the MSK IRB must adhere to this policy. • 3.1 Table updated to remove examples that no longer require a prospective deviation request (e.g., using a short form to enroll a participant onto a protocol were the English consent has required questions about specimen future use). • 3.2 Removed PK tests performed outside of window as a reportable deviation

		• 3.3 Non-reportable deviation list was updated to include PK tests and pre/post treatment EKGs performed outside of the protocol specified window.
1.6	1/23/23	• 2.2, 3.3 Removed language added to version 1.5 regarding source documentation • 3.2 Clarified that all accepted retrospective deviations will be reported to the IRB/PB at the time of continuing review; removed "Protocol scheduling change involving protocol specific tests/evaluations occurring +/- 5 days outside the protocol specified window as this allowance has been added to section 3.3 as a non-reportable deviation • 3.3 Removed "Protocol scheduling outside of the allowed window due to a holiday (e.g., New Year's, Thanksgiving, etc.), inclement weather or other natural event. This does not include missed visits, which are reportable deviations." • 3.3 Added "Missing responses in questionnaires/surveys" as a non-reportable deviation; clarified that missing or incomplete drug accountability forms, case report forms and/or other forms that were not corrected according to GCP requirements are not IRB deviations.
1.7	5/20/24	• 2.2 Updated to indicate that deviations to IRB approved research that may affect the scientific validity of the study, may meet the criteria of serious or continuing noncompliance, and/or have the potential to result in increased risk or decreased benefit to participants must be reported to the HRPP as retrospective deviations. Deviations that occurred prior to 5/20/24 (version date 1.7) and have not yet been reported to HRPP in PIMS must follow the current version of this policy; Deviations that do not adversely affect the rights, safety, or welfare of participants and do not result in a substantive impact/change to the conduct of the protocol and human subjects protection oversight are considered non-reportable; • 3.1 Updated to note that a list of all reported and approved prospective deviations will be reported to the IRB/PB at the time of continuing review. • 3.2 Updated to reflect policy statement; updated list of retrospective deviation examples. • 3.3 Updated to reflect policy statement; updated list of non-reportable deviation example; revised the requirement to document non-reportable deviations in the medical record to documenting in the regulatory binder; added a statement noting that the PI and study team are responsible for reviewing non-reportable deviations for trends that could constitute continued and/or serious non-compliance and report such findings per MSK IRB SOP FO-309. • 3.4 Removed statement indicating that all sponsor reporting requirements must be followed as this is outside of the scope of this SOP; removed statement about reporting deviations to IRB at the time of continuing review as this requirement is outlined in sections 3.1 and 3.2; Clarified that when MSK is not the IRB of record (IoR), deviations must also be reported to the IoR in accordance with the IoR's policy.
1.8	1/20/26	• 2.2 Added statement about requirements associated with institutional changes, i.e., changes in the Department of Laboratory Medicine or the Department of Pharmacy that impact protocol-required laboratory tests and/or medications.