

OHSU Policy on Protocol Deviations in Recombinant DNA and Infectious Agent Research

Protocol Deviations

A. Definitions:

1. Protocol Deviation: A protocol deviation occurs when there is an inconsistency in a research study between the protocol that has been reviewed and approved by the Institutional Biosafety Committee (IBC) and the actual activities being done. Protocol deviations may be minor, moderate or major as defined below. Protocol deviations involving a human gene transfer study will be subject to both Institutional Review Board (IRB) and IBC deviation policies.

2. Minor Protocol Deviation

- The deviation has no substantive effect on the biosafety risks; and
- The deviation does not meet any of the criteria listed for Moderate or Major Protocol Deviations.

3. Moderate Protocol Deviation

- The deviation has posed a risk of minimal harm to the safety of personnel or human subjects; or
- The deviation resulted in the loss or improper collection or recording of some data but did not invalidate the entire data set for the study or;
- The deviation resulted in a regulatory violation that can be acceptably resolved; or
- There is a history of repeated minor protocol deviations from the same laboratory, site or research team; or
- There has been a failure to follow action ordered by the IBC to correct minor or moderate protocol deviations.

4. Major Protocol Deviation

- The deviation has harmed or posed a risk of substantive harm to the safety of personnel or human subjects; or
- The deviation resulted from willful or knowing misconduct on the part of the investigator(s); or
- The deviation involves serious or continuing noncompliance with federal, state or local research regulations; or
- The deviation resulted in a violation of the select agent regulations; or
- There have been repeated minor or moderate protocol deviations from the same investigator; or
- There has been a failure to follow action ordered by the IBC to correct minor or moderate protocol deviations; or
- There has been a failure to follow action ordered by the IBC in accordance with the emergency action section of this policy.

B. Reporting Requirements

1. Minor Protocol Deviations. Minor protocol deviations do not need to be reported to the IBC. However, the IBC Integrity Manager will review any minor protocol deviations that come to the attention of the IBC and may require that corrective action be taken.

2. Moderate Protocol Deviations. All moderate protocol deviations must be reported to the IBC as described below.

3. Major Protocol Deviations. All major protocol deviations must be reported to the IBC as described below.

- A direct substantive harm or risk of substantive harm is a major protocol deviation and must be reported to the OHSU IBC (and IRB if human subjects are involved) within 24 hours of discovery of the deviation.
- All other major or moderate protocol deviations must be reported within 10 working days of discovery of the deviation.

C. Process

1. Principal Investigators (PI) must report moderate and major protocol deviations to the IBC via e-mail within the timeframes specified above. This report must contain a description of the deviation, the date of the deviation and a plan for preventing future similar deviations.
2. An inquiry will be conducted by the IBC chair with the assistance of the IBC Integrity Manager and Biosafety officer for the appropriate campus (IBC admin group).
3. The IBC admin group will collect and assess all information related to the protocol deviation and contrast the deviation with the approved protocol. The IBC admin group will discuss the matter with the PI and give the PI a meaningful opportunity to provide information. The IBC admin group will then make a preliminary conclusion as to whether or not a protocol deviation appears to have occurred and, if so, whether any apparent protocol deviation is major, moderate or minor. Consultation with experts in the particular area of research may be obtained as needed.
4. The matter will be dismissed if the IBC admin group determines that no deviation occurred. The matter will be handled as a minor protocol deviation if the IBC admin group determines that the deviation meets that definition.

5. If it appears that a moderate protocol deviation has occurred, the IBC chair will choose one of the following methods of review:
 - an expedited review process in which the IBC chair may make a determination and resolve the matter on his/her own;
 - a facilitated review, in which the IBC chair direct a meeting with the PI and appropriate others to seek resolution of the matter; or
 - a meeting with the convened IBC (the PI and/or co-investigators may or may not be required to attend).
6. If it appears that a major protocol deviation has occurred, the IBC chair will choose one of the following methods of review: a meeting with the convened IBC (the PI may or may not be required to attend) or a meeting with the PI and a hearing committee which may consist of:
 - IBC chair
 - IBC Integrity Manager
 - OHSU Biosafety Officer(s)
 - Additional IBC representatives, if needed
 - OHSU Chief Integrity Officer
 - Two or more representatives from the PI's department or discipline including the department chair
 - Veterans Affairs Medical Center (VAMC) or OHSU IRB, Institutional Animal Care & Use Committee (IACUC), or VAMC Research Safety Committee representatives if applicable*
 - Others, as selected by the IBC chair
7. The PI will be provided with notice of the charges against the PI and a meaningful opportunity to be heard by the IBC admin group, IBC convened committee or hearing committee. The IBC or hearing committee shall consider all the information submitted to it and conclude whether a major protocol deviation, a moderate protocol deviation, a minor protocol deviation or no protocol deviation has occurred. The IBC or hearing committee shall also submit recommended sanctions to the IBC Chair for any moderate or major protocol deviation, if appropriate. Recommended sanctions may include, but are not limited to, termination of the study, suspension of the study until corrective action is taken, increased reporting requirements for the study or the investigator, mandatory compliance education and/or additional oversight or reassignment of some or all of the PI's duties to another person. A written summary of the committee conclusions will be forwarded to the PI, his/her department chair and dean/director, and the Vice President for Research Development and Administration and a copy will be retained in the IBC study file.
8. Depending on the nature and seriousness of the deviation, the IBC or hearing committee may elect to recommend that the IBC chair audit all studies for which the investigator in question serves as PI. The IBC chair may delegate this duty.
9. If it appears to the IBC chair that academic misconduct (plagiarism, falsification, fabrication) has also occurred (OHSU Policy 04-15-005 through -035), the matter will be referred to the chair of the Scientific Integrity Committee (SIC) along with pertinent information collected by the IBC or hearing committee.
10. If the committee concludes that no protocol deviation has occurred, the matter will be dismissed and the PI will be so notified by the IBC chair.
11. If a hearing, as described in section 3-F is required, the process, charge to the committee, and rules for the hearing shall be established and conducted according to guidance provided by the OHSU Legal Counsel. A summary of the issue, process, recommendations and any action taken will be presented at the next scheduled meeting of the IBC.

Investigator's Right to Appeal the Committee's Decision

If an investigator disagrees with the findings and/or requirements arising from a protocol deviation, the PI may appeal the decision to the Vice President for Research (VPR). The IBC chair will forward all information gathered by the inquiry and/or hearing process to the VPR who will consider it along with any additional information the investigator provides. The VPR may not reverse a decision by the IBC to terminate a protocol but may direct a new hearing if the VPR determines that there was a failure to follow process, procedural error, or substantial evidence was not considered. The VPR will either uphold the decision or refer the matter back to the IBC chair for further review by the IBC or the hearing committee.

Emergency action by the IBC chair.

The IBC chair has the authority to take emergency corrective action to temporarily stop research activities if, in the IBC chair's assessment, it appears that research subjects or laboratory workers may be at risk of substantive harm due to the reported protocol deviation. Further review following the above procedures will occur as soon as is possible if the emergency action taken is to suspend the protocol or if it appears a major protocol deviation has occurred.

Reporting to Outside Agencies

In the event that approval of a protocol is suspended or terminated due to unanticipated problems involving substantive risks to subjects, laboratory workers or others or serious or continuing noncompliance with research regulations or the requirements of the IBC, the IBC Integrity Manager will promptly report this action to the NIH as required by the NIH Guidelines for Research Involving rDNA Molecules.

*When studies are conducted at both OHSU and the VAMC, the process of investigating and resolving protocol deviations will be coordinated between the chairs of the representative committees of the two institutions. Either chair may initiate an investigation and/or suspend approval of a study when warranted. Similarly, for human gene transfer studies or animal projects, the process will be coordinated between the IBC and IRB or IACUC if necessary.