



Weill Cornell Medical College

Office of Research Integrity
1300 York Avenue, Box 89
New York, NY 10065

Human Research Protections Program Immediate Reporting Policy

Purpose

The purpose of this policy is to immediately identify and manage emergent risk and compliance information involving human subjects research. Such information may require protocol or informed consent amendments or compliance management.

Applicability

This policy applies to all Weill Cornell Medicine (“WCM”) Principal Investigators conducting human subjects research that falls under the purview of the WCM Institutional Review Board (“IRB”) and/or the following human subjects research committees, as applicable: (1) WCM Data and Safety Monitoring Committee (“WCM DSMC”); (2) WCM Institutional Biosafety Committee (“IBC”); (3) Translational Research Advisory Committee (“TRAC”). It spans five (5) categories: Adverse Events, Unexpected Adverse Device Effects, Other Risk Reporting; Protocol Deviation Reporting, and Other Compliance Reporting.

Principal Investigator Reporting Responsibilities

In order to immediately address emergent risks to research subjects, Principal Investigators must submit an Immediate Report of the following information to all applicable human research committees/boards **within 7 calendar days, except where “within 24 hours” reporting is specified** using the Reportable Events module in WRG-HS. The IRB will forward applicable submissions to the IBC and TRAC for review as needed. For review by the WCM DSMC, study teams must forward a PDF of the submission to dsmc@med.cornell.edu for review. If the PI or any committee/board determines that the Immediate Report requires an amendment to the protocol or consent, the PI has 30 days from the date of making the Immediate Report (or release of the sponsor amendment) to submit a protocol amendment to the IRB. If this requirement cannot be met, a request for an extension must be made.

IMPORTANT: In the event that a study is terminated due to emergent risk information, including but not limited to those involving mortality rates, the IRB requires that the PI and/or a medically qualified co-investigator, who has had contact with subjects in the past, contact subjects directly by phone and in writing.

I. Adverse Event Reporting

A. Immediately report any harm experienced by a participant or other individual, whether occurring to a subject enrolled at WCM or elsewhere, including Investigational New Drug (IND) reports and MedWatch reports, related to the human research procedure(s), intervention(s), and/or device(s) **when ALL of the following three (3) conditions are met:**

1. The harm is “unexpected” when its specificity and severity are not accurately reflected in the WCM consent document, Investigator’s Brochure (if applicable), or package insert (if applicable); **AND**
2. The harm is “related” or “possibly related”, where there is a reasonable possibility that the harm may have been caused by the research procedure(s), or intervention(s) **AND**

3. The harm suggests that the research places WCM subjects **at greater risk of harm** (including physical, psychological, economic or social harm) **than was previously known or recognized**.

If ALL of the three (3) conditions are met, submit the Immediate Report within 7 calendar days of PI awareness.

B. At the time of IRB Continuing Review, an Adverse Event & IND Safety Reporting Cumulative Table must be submitted listing adverse events from the WCM site that are **both expected and unexpected** and for which **ANY** of the following apply:

1. Severe or medically significant, but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care activities of daily living (Grade 3)*
2. Life-threatening consequences; urgent intervention indicated (Grade 4)
3. Death related AE (Grade 5)

C. If this is a multi-site study, the Adverse Event & IND Safety Reporting Cumulative Table must include individual adverse events from **all external sites** that meet all of the following criteria and must be submitted as an immediate report, as described in part A:

1. The harm is “unexpected” when its specificity and severity are not accurately reflected in the WCM consent document, Investigator’s Brochure (if applicable), or package insert (if applicable); **AND**
2. The harm is “related or possibly related”, where there is a reasonable possibility that the harm may have been caused by the research procedure(s), or intervention(s) **AND**
3. Necessitates changes in the conduct of the study, i.e., requires a significant, usually safety-related, change in the protocol. This may include, but are not limited to, revising the inclusion/exclusion criteria, monitoring requirements, informed consent form, or investigator’s brochure.

***Note:** If this is a Phase III or IV multicenter study that utilizes a Data and Safety Monitoring Board or a Phase I, II, III or IV study that is part of a cooperative group or consortium, the requirement to list Grade 3 adverse events in the cumulative table can be waived upon request. If either of these conditions applies, you will be permitted to provide a brief summary of the Grade 3 adverse events that have occurred for this study directly on the Adverse Event & IND Safety Reporting Cumulative Table.

Grade definitions adapted from page 2 of http://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03_2010-06-14_QuickReference_5x7.pdf

D. Humanitarian Device Exemption: As of July 25, 2011, an Immediate Report is required within 7 calendar days if a Humanitarian Use Device (HUD) **may have caused or contributed to a death of a patient at WCM OR if a HUD may have caused or contributed to a serious injury to a patient at WCM**.

For Huds, in the case of any adverse event that is not immediately reportable under this policy, list the adverse event on the AE & IND Cumulative Table for submission at the time of IRB Continuing Review.

II. Adverse Event Reporting for Protocols Using Devices: Unanticipated Adverse Device Effect

- A. In addition to the above, immediately report (within 7 calendar days) any unanticipated adverse device effect (any serious adverse effect on health or safety or any life threatening problem or death) that is **EITHER**:
 - 1. Caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or IDE application (including a supplementary plan or application); **OR**
 - 2. Any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of participants.

- B. At the time of IRB Continuing Review, an Adverse Event & IND Safety Reporting Cumulative Table must be submitted listing adverse events from the WCM site that are **both expected and unexpected** and for which **ANY** of the following apply:
 - 1. Severe or medically significant, but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care activities of daily living (Grade 3)*
 - 2. Life-threatening consequences; urgent intervention indicated (Grade 4)
 - 3. Death related AE (Grade 5)

- C. If this is a multi-site study, the Adverse Event & IND Safety Reporting Cumulative Table must include individual adverse events from **all external sites** that meet all of the following criteria and must be submitted as an immediate report, as described in part A:
 - 1. The harm is “unexpected” when its specificity and severity are not accurately reflected in the WCM consent document, Investigator’s Brochure (if applicable), or package insert (if applicable); **AND**
 - 2. The harm is “related or possibly related”, where there is a reasonable possibility that the harm may have been caused by the research procedure(s), or intervention(s) **AND**
 - 3. Necessitates changes in the conduct of the study, i.e., requires a significant, usually safety-related, change in the protocol. This may include, but are not limited to, revising the inclusion/exclusion criteria, monitoring requirements, informed consent form, or investigator’s brochure.

***Note:** If this is a Phase III or IV multicenter study that utilizes a Data and Safety Monitoring Board or a Phase I, II, III or IV study that is part of a cooperative group or consortium, the requirement to list Grade 3 adverse events in the cumulative table can be waived upon request. If either of these conditions applies, you will be permitted to provide a brief summary of the Grade 3 adverse events that have occurred for this study directly on the Adverse Event & IND Safety Reporting Cumulative Table.

Grade definitions adapted from page 2 of http://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03_2010-06-14_QuickReference_5x7.pdf

III. Other Risk Reporting

Immediately report any information that indicates a change to the risks or potential benefits of the human research. For example:

- A. An interim analysis, safety monitoring report, finding from tests in laboratory animals, including reports of mutagenicity, teratogenicity or carcinogenicity, publication in the literature, or revised

Investigator Brochure that indicates an increase in the frequency or magnitude of a given harm, uncovers a new risk, or provides more information about the benefits of the human research.

- B. Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a human research protocol.
- C. Clinical Hold, Enrollment Hold (excluding planned holds for interim analysis), or Study Termination due to Emergent Risk Information.
- D. Complaint of a participant that indicates participants or others might be at increased risk of harm or at risk of a new harm.

IV. Protocol Deviation Reporting

Immediately report if **ANY** of the following conditions are met:

- A. Protocol deviation that was made in order to eliminate an apparent immediate hazard to participant(s). (**Submit an Immediate Report within 24 hours**) OR
- B. Breach of Confidentiality (**Submit within 24 hours**) OR
- C. Protocol deviation that represents a failure to follow the IRB approved protocol or IRB policies and determinations due to the action or inaction of the investigator or research staff (Exception: Rescheduling of research appointments due to holidays, vacations, accommodation of research subject), which meet **BOTH** of the following conditions:
 - a. The deviation has the potential to negatively impact subject safety or integrity of study data (ability to draw conclusions from the study data), or affect the subject's willingness to participate in the study **AND**
 - b. The deviation places WCM subjects **at greater risk of harm** (including physical, psychological, economic or social harm).

Deviations that do not meet the any of the above conditions must be recorded by the PI on a protocol-specific Deviation Log and submitted to the IRB at the time of continuing review. The Deviation Log should include all deviations, including those that are immediately reportable. A Deviation Log template and guidance document for reporting protocol deviations are available in the Researcher's Toolbox on the JCTO website (jcto.weill.cornell.edu)

It is the responsibility of the PI to determine whether a deviation from the IRB approved protocol is immediately reportable to the IRB as outlined above. The PI is responsible for reviewing the Deviation Log periodically to ensure timely and appropriate reporting to the IRB. If a deviation that is not immediately reportable occurs repeatedly, this pattern should be immediately reported to the IRB.

If the WCM site is a lead/coordinating site, then protocol deviation reports submitted from other sites must be sent to the WCM IRB and included on the protocol-specific Deviation Log.

V. Other Compliance Reporting

- A. Finding of noncompliance or allegation of noncompliance
- B. Complaint of a participant that cannot be resolved by the research team.
- C. Incarceration of a participant in a protocol not approved to enroll prisoners.