



# Weill Cornell Medical College

Office of Research Integrity

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## **Office of Research Integrity & Assurance** **Human Research Protections Program (IRB, IBC, WCMC DSMB)** **Unexpected, Study-Related Adverse Events, Incidents, and Information Reporting Policy**

**Applicability:** This policy applies to all Principal Investigators and research staff conducting human research at WCMC.

Principal Investigators must report the following information to all applicable human research committees immediately, **within 7 calendar days, except where “within 24 hours” reporting is specified**. If the PI or any committee determines that the report requires an amendment to the protocol or consent, the PI has 3 weeks from the date of that determination to submit a protocol amendment to the IRB.

- **Institutional Review Board (IRB):** If the study is a human research study, then reporting to the IRB is required.
- **Institutional Biosafety Committee (IBC):** If the study is a human gene transfer study, or any other human research study approved by the IBC, then reporting to the IBC is required.
- **Weill Cornell Medical College Data Safety Monitoring Board (WCMC DSMB):** If the study uses the WCMC DSMB, then reporting to the WCMC DSMB is required.
- **Clinical and Translational Science Center (CTSC):** If the study uses the CTSC, then reporting to the CTSC is required.

### **How to Submit A Report:**

- All reports must contain a cover letter with PI name and signature, the IRB protocol number, title, and detailed information about the incident or information and its impact on the WCMC research and/or research subject(s).
  - **Exception:** In the case of adverse events or protocol deviations, use of the *Adverse Event Reporting Form* with current consent documents *or Protocol Deviation Reporting Form* with current consent documents is required. No cover letter is necessary.
- Submissions must be sent as a single bookmarked PDF document.
- The IRB submission can be CC'd to all applicable committees in lieu of creating a separate submission for each committee. For large documents, submit via <http://transfer.med.cornell.edu>:
  - IRB: [submit2irb@med.cornell.edu](mailto:submit2irb@med.cornell.edu)
  - IBC: [submit2ibc@med.cornell.edu](mailto:submit2ibc@med.cornell.edu)
  - WCMC DSMB: [submit2dsmb@med.cornell.edu](mailto:submit2dsmb@med.cornell.edu)
  - CTSC: [ctscrsa@med.cornell.edu](mailto:ctscrsa@med.cornell.edu)

**What to Report:** The following must be reported immediately, within 7 calendar days, except where “within 24 hours” reporting is specified:

a) Information that indicates a change to the risks or potential benefits of the human research. For example:

i) An interim analysis, safety monitoring report, 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.

ii) Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a human research protocol.

iii) Protocol deviation that harmed participants or others or that indicates participants or others might be at increased risk of harm. If the WCMC study site is the lead or coordinating site, then deviations *from all sites* must be reported within 7 calendar days of PI notification.

**Reporting Timeline Exception:** If the protocol deviation was made in order to eliminate an apparent immediate hazard to a participant, the PI must submit the information **within 24 hours**.

**Note:** Submission using the *Protocol Deviation Reporting Form* is required, with PI signature and the consent form attached. No cover letter is necessary.

iv) Complaint of a participant that indicates participants or others might be at increased risk of harm or at risk of a new harm.

b) Any harm (i.e., adverse event) experienced by a participant or other individual, whether occurring to a subject enrolled at WCMC or elsewhere, including Investigational New Drug (IND) reports and MedWatch reports, which is both unexpected **and** at least probably related to the human research procedure(s), intervention(s), and/or device(s).

i) A harm is “unexpected” when its specificity and severity are not accurately reflected in the consent document or Investigator’s Brochure.

ii) A harm is “at least probably related” if the research procedure(s), intervention(s), and/or device(s) more likely than not caused the harm.

**Reporting Timeline Exception:** If the unexpected and at least probably related harm is death of a research subject, the PI must report the information **within 24 hours**.

**Note:** Submission using the *Adverse Event Reporting Form* is required, with PI signature and the consent form attached. No cover letter is necessary.

c) Finding of Non-Compliance or Allegation of Non-Compliance.

d) Protocol Deviations: Failure to follow the protocol due to the action or inaction of the investigator or research staff. *If the WCMC site is a lead/coordinating site, then reports received from other sites must be sent to the WCMC IRB within 7 calendar days of PI notification.*

**Reporting Timeline Exception:** If the protocol deviation was taken in order to eliminate an apparent immediate hazard to a participant, the PI must report the information **within 24 hours**.

**Note:** Submission using the *Protocol Deviation Reporting Form* is required, with PI signature and the consent form attached. No cover letter is necessary.

e) Breach of confidentiality.

**Reporting Timeline Exception:** The PI must report the information **within 24 hours**.

f) Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a participant.

**Reporting Timeline Exception:** The PI must report the information **within 24 hours**.

**Note:** Submission using the *Protocol Deviation Reporting Form* is required, with PI signature and the consent form attached. No cover letter is necessary.

g) Incarceration of a participant in a protocol not approved to enroll prisoners.

h) Complaint of a participant that cannot be resolved by the research team.

i) Unanticipated adverse device effect (Any serious adverse effect on health or safety or any life threatening problem or death 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 application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of participants.)”

**Reporting Timeline Exception:** If the unexpected and at least probably related adverse device effect results in the death of a research subject, the PI must report the information **within 24 hours**.

**Note:** Submission using the *Adverse Event Reporting Form* is required, with PI signature and the consent form attached. No cover letter is necessary.

### 24 Hour Reporting Quick Guide

<b>Report Within 24 Hours</b>
Any protocol deviation that was made in order to eliminate an apparent immediate hazard to a participant.
Any death of a participant that is unexpected and at least probably related.
Breach of confidentiality

### **Unexpected, Study-Related Adverse Event, Incidents and Information Reporting FAQ**

1. Which adverse events need to be reported to the Division of Research Integrity within 7 calendar days?

If an adverse event (including those received as part of IND Reports or MedWatch reports) is unexpected *and* at least probably related to the research procedure(s), intervention(s), and/or device(s), then you must report it within 7 calendar days. *This includes both serious and non-serious adverse events that occur to a subject enrolled at WCMC or elsewhere.* For adverse events that occur to a subject enrolled elsewhere, the adverse event must be reported within 7 calendar days of PI notification.

**Exception:** *If the unexpected and at least probably related adverse event is the death of a research subject, then you must report it within 24 hours of notification.*

When reporting unexpected and at least probably related harms, fill out the Averse Event Reporting Form, available at [http://www.med.cornell.edu/research/for\\_pol/ins\\_rev.boa.html](http://www.med.cornell.edu/research/for_pol/ins_rev.boa.html). All relevant documentation (i.e. informed consent, Medwatch forms, etc.) must be included and submitted as a single PDF. Remember to CC the submission to **all applicable committees**, not just the IRB. If you are not sure which committees apply, contact our office.

2. Which incidents and information need to be reported to human research committees within 7 calendar days?

Please see the policy itself for which types of incidents and information must be immediately reported. In general, the human research committees are required to view any unexpected and at least probably related information that:

- May indicate a change in the risk or benefit of the research
- May adversely affect the rights and welfare of research participants
- May indicate that new or additional regulations apply (such as incarceration of a participant in a protocol not approved to enroll prisoners)

3. Which incidents and information need to be reported within 24 hours?

There are three items that need to be reported within 24 hours:

- Any protocol deviation that was made in order to eliminate an apparent immediate hazard to a participant.
- Any death of a participant that is unexpected and at least probably related
- Breach of confidentiality

4. When is a harm considered "unexpected"?

A given harm qualifies as unexpected if its specificity and severity are not accurately reflected in the consent document or Investigator's Brochure.

5. What if adverse event relatedness has been assessed differently by different individuals or agencies?

If there is a difference in opinion concerning an assessment or relatedness, always choose the assessment that assumes the most relatedness in determining what to report. You have an opportunity on the reporting form to discuss the impact that the adverse event, incident, or information may or may not have on the protocol.

6. What if an amendment is needed?

If the PI or any committee determines that the report requires an amendment to the protocol or consent, the PI has 3 weeks from the date of that determination to submit a protocol amendment to the IRB.

*If the reportable event involves the death of a research subject, do not wait until an amendment is created before submitting notice. Reporting within 24 hours is required.*

7. Which adverse events, incidents and information do *not* need to be reported within 7 calendar days?

Adverse events, incidents or information that are expected or that are, at best, only possibly related do not need to be reported. For example, a DSMB Report that simply states the protocol can continue without modification does not need to be immediately reported since it does not contain new information, a request for modification, or an indication that the risks or benefits of the research have changed.

8. What should I do with adverse events that do not need to be reported within 7 calendar days?

Principal Investigators must keep detailed records of all adverse events that occur during the course of their research. All adverse events that **are not** unexpected and at least probably related to the research procedure(s), drug(s) and/or device(s) must be listed on the Adverse Event & IND Safety Report Cumulative Table for submission to the IRB at the time of Continuing Review.

*If your study is using the WCMC DSMB and has more than one study arm, each study arm must have its own Adverse Event & IND Safety Report Cumulative Table, which you will be asked to provide at the time of WCMC DSMB Periodic Review. (Specific interventions in various arms need not be revealed in these reports for blinded studies.) You will also be required to provide the DSMB with (1) all IND Safety Reports; and (2) narratives for each serious adverse event and other medically significant adverse events that have occurred at each site since your last periodic review. See question (12) of this FAQ for further information.*

9. What if an unexpected adverse event occurs and its causality is unknown?

Unexpected adverse events for which causality is unknown or not yet determined do not need to be reported within 7 calendar days. If an unexpected adverse event is later determined to be related or probably related to participation in the research, then it must be reported within 7 calendar days of that determination (or within 7 calendar days of PI notification of that determination).

**Exception:** *If the unexpected and at least probably related adverse event is the death of a research subject, then reporting to all applicable committees within 24 hours is required.*

10. What if the study sponsor requires that all IND Safety Reports be submitted to the IRB, even if they do not meet the two criteria of unexpected and at least probably related?

Such reports may be submitted to the IRB as a single PDF file at the time of IRB Continuing Review. The bulk submission will be stamped "IRB Received" and returned to you for your records. These bulk submissions will not be reviewed by the IRB and must not contain any unexpected and at least probably related adverse events, which are immediately reportable within 7 calendar days.

***The following questions explain what other adverse events, incidents and information***

***you will need to provide to each committee in the Division of Research Integrity (IRB, WCMC DSMB, IBC) as part of post-approval monitoring.***

11. What other adverse events, incidents and information will I need to report to the IRB for Continuing Review?

In addition to providing an Adverse Event & IND Safety Report Cumulative Table, you will be asked to answer general questions about the incidence of adverse events in your study. You will also be asked to consider the risk/benefit ratio of your study. Refer to the IRB Continuing Review form, available at [http://www.med.cornell.edu/research/for\\_pol/ins\\_rev.boa.html](http://www.med.cornell.edu/research/for_pol/ins_rev.boa.html), or email [irb@med.cornell.edu](mailto:irb@med.cornell.edu).

12. What other adverse events, incidents and information will I need to report to the WCMC DSMB for Periodic Review?

If using the WCMC DSMB, you will be asked to submit an Adverse Event & IND Safety Report Cumulative Table for each study arm. You will also be asked to provide narratives for all serious adverse events and significant medical events under the Adverse Event Narrative Reporting Requirement. Refer to the WCMC DSMB Periodic Review Form, available at [http://www.med.cornell.edu/research/for\\_pol/ins\\_rev.boa.html](http://www.med.cornell.edu/research/for_pol/ins_rev.boa.html), or email [dsmb@med.cornell.edu](mailto:dsmb@med.cornell.edu).

13. What other adverse events, incidents and information will I need to report to the WCMC IBC for the Annual Human Gene Transfer Reporting Requirement?

If your study is a human gene transfer study, you will be required to submit to the IBC your last annual report to *NIH-OBA* (refer to the *NIH Guidelines for Use of Recombinant DNA Molecules*, Appendix M-I-C-3: [http://www4.od.nih.gov/oba/rac/guidelines\\_02/APPENDIX\\_M.htm#\\_Appendix\\_M-I-C-3\\_Annual](http://www4.od.nih.gov/oba/rac/guidelines_02/APPENDIX_M.htm#_Appendix_M-I-C-3_Annual)) under the IBC's Human Gene Transfer Annual Reporting Requirement at the time of IRB Continuing Review. For additional information, refer to the IBC website at <http://intranet.med.cornell.edu/research/ibc.html>, or email [ibc@med.cornell.edu](mailto:ibc@med.cornell.edu).