

HAC Policies and Procedures for HAC Members and OHRP Staff

Unanticipated Problems, Adverse Events and Serious Adverse Events

What is the Process for Reviewing Unanticipated Problems that Involve No More Than Minimal Risk to Self or Others?

The following documents are reviewed by the OHRP Director and the HAC Chairperson or designee reviews the following information:

- HAC Reviewers' Checklist
- OHRP Evaluation of Unanticipated Problems Form
- HAC Form 113 with support documentation such as:
 - Revised informed consent documents/childrens assent documents
 - Summary of Changes
 - Clean version for stamping
 - Changes noted copy
 - Revised protocol
 - Summary of Changes
 - Site added or removed information
 - Copies of reports:
 - Unanticipated problem
 - Data safety and monitoring board report
 - Audit report
 - Other
 - Summary of Changes
 - HAC requested information with copy of email/letter/report from the HAC
 - Revised FDA Form 1572
 - Summary of Changes
 - Changes noted copy
 - Revised Investigational Drug Brochure/Revised Package Insert
 - Summary of Changes
 - Research Team Personnel Changes

What is an Unanticipated Problem Involving Risks to Subjects or Others?

According to DHHS OHRP guidance, an unanticipated problem is any incident, experience, or outcome that meets all of the following criteria:

1. Unexpected (in terms of nature, severity, or frequency) given:
 - (a) the research procedures that are described in the protocol and related documents, such as the HAC approved Description of Research Proposal, the protocol and the informed consent documents; and
 - (b) the characteristics of the subject population being studied.
2. Related or possible related to a subject's participation in the research
3. Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

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Are Unexpected Problems Only Related To Physical Events?

No. For example, an unexpected event may be any of the following:

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

- A. An interim analysis or safety monitoring report that frequency or magnitude of harms or benefits may be different than initially presented to the IRB.
- B. A paper is published from another study that shows that the risks or potential benefits of your research may be different than initially presented to the HAC.

- Subjects being incoming incarcerated during their participation in the research which was not approved for a prisoner population
- Breaches of confidentiality such as a stolen laptop with protected health information on it, a digital camera or memory stick stolen with photographs or identifiable data of subjects or violation of policies related to confidentiality
- Increased time off from work resulting in less pay to subjects or parents
- Increased time out of school resulting in lower grades
- Suspected child or domestic abuse
- Errors made by pharmacy technician that gives a research subject several times the amount of the investigational drug which resulted in increased risk of toxicity to the participant, but no actual harm.
- Complaint of a research subject when the complaint indicates unexpected risks or cannot be resolved by the research team.
- Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.
- Change to protocol taken without prior IRB review to eliminate an apparent immediate hazard to a research subject.
- Event that requires prompt reporting to the sponsor.
- Sponsor imposed suspension of research or enrollment.

Each of these examples is unexpected in nature, related to participation in the research, and resulted in new circumstances that increased the risk of harm to subjects.

How Are These Unanticipated Problems Reported to the HAC?

The principal investigator is responsible for reporting these events to the HAC via the HAC Form 113.

What Is The Deadline For Reporting These Events?

The deadline for reporting these events is within 72 hours of any member of the research team becoming aware of the event.

Who Reviews These Reports?

The reports are reviewed by the HAC Chairperson or designee. If they feel that the event is an unanticipated problem, then the report is forwarded to the convened HAC for information. Additional information may be requested at that time. Institutional officials, DHHS OHRP or FDA may be notified in compliance with the institutional policy on reporting.

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How Do They Review These Reports?

The OHRP staff, when necessary in conjunction with the HAC Chairperson or designee, review reports and determines which reports are either (1) foreseen or (2) do not indicate that subjects or others are at increased risk of harm. If no to either, the event is not considered to be an unanticipated problem involving risks to participants or others and will be filed in the HAC hard copy file. All other problem reports are referred to the HAC Chairperson or designee and the convened HAC ,who is responsible for making the final determination. These will be posted on the provided to HAC members for review prior to the meeting for HAC member review prior to the meeting and made available at the meeting for additional scrutiny, if necessary.

If these pre-review processes are unable to determine that the event report is not an unanticipated problem involving risks to subjects or others, then additional information is requested from the principal investigator. The HAC will then review the event report and the additional information to determine if the event was an unanticipated problem involving risks to subjects or others. If the event was an unanticipated problem involving risks to subjects or others, then actions are discussed and conferred upon at the convened meeting. If the event is not an unanticipated problem involving risks to subjects or others, then the event is filed in the HAC hard copy file. If the event is determined to be non-compliance, then additional follow-up will be requested of the OHRP auditing and compliance program.

What Kind Of Actions May Be Taken By The Convened HAC When The Unanticipated Problem Does Involve Risks To Subjects Or Others?

The convened HAC considers the following actions:

- Modification of the protocol
- Modification of the information disclosed during the consent process
- Providing additional information to past subjects
- Notification of current participants when such information might relate to subjects' willingness to continue to take part in the research
- Requirement that current subjects re-consent to participation in the study
- Modification of the continuing review schedule
- Monitoring of the research by OHRP
- Monitoring of the consent process by OHRP
- Suspension of the research
- Termination of the research
- Referral to other organizational entities
- Reported to regulatory authorities and institutional officials.

How Are These Reported to Regulatory Authorities and Institutional Officials?

The HAC Chairperson, along with the OHRP Director, will report the unanticipated problem to Regulatory Agencies and Institutional Officials as outlined on page 15 of the

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MCG Human Research Protection Program
(<http://www.mcg.edu/research/ohrp/docs/hrpp.pdf>)

What Documents do the HAC Members Receive for Unanticipated Problems that Involve More Than Minimal Risk to Self or Others?

The following documents are scanned and placed on a common computer drive for review. HAC members that do not have access to the common computer drive receive the following information in their submission packets:

- HAC Reviewers' Checklist
- OHRP Evaluation of Unanticipated Problems Form
- HAC Form 113 with support documentation such as:
 - Revised informed consent documents/childrens assent documents
 - Summary of Changes
 - Clean version for stamping
 - Changes noted copy
 - Revised protocol
 - Summary of Changes
 - Site added or removed information
 - Copies of reports:
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 - Summary of Changes
 - Research Team Personnel Changes

What Documents do the HAC Members Receive for Adverse Events?

The following documents are reviewed by the HAC Vice-Chairperson via the expedited procedure and are reported to the HAC Members, Alternates, Advisors and Institutional Officials via the HAC Meeting Agenda and HAC Meeting Minutes:

- HAC Form 110 with support documentation such as:
 - Revised informed consent documents/childrens assent documents
 - Summary of Changes
 - Clean version for stamping
 - Changes noted copy
 - Copies of reports:
 - Other
 - HAC requested information with copy of email/letter/report from the HAC

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What Documents do the HAC Members Receive for Serious Adverse Events?

The following documents are reviewed by the HAC Vice-Chairperson. They are scanned and placed on a common computer drive for review. HAC members that do not have access to the common computer drive receive the following information in their submission packets:

- HAC Form 110 with support documentation such as:
 - Revised informed consent documents/childrens assent documents
 - Summary of Changes
 - Clean version for stamping
 - Changes noted copy
 - Copies of reports:
 - Other
 - HAC requested information with copy of email/letter/report from the HAC