

DEPARTMENT: Yale University Human Investigation Committee  
POLICY NUMBER:  
SECTION: Unanticipated Problems Involving Risks to Subjects or Others  
REVIEW RESPONSIBILITY: IRB Leadership Committee and HIC Policy Review  
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## **Yale University School of Medicine HIC Policy Regarding: Reporting of Unanticipated Problems Involving Risks to Subjects or Others to the Human Investigation Committee**

**I. Purpose:** The purpose of this policy is to describe how and when researchers should report Unanticipated Problems Involving Risks to Subjects or Others to the Human Investigation Committee (HIC) and other university research oversight bodies.

### **II. Policy Summary**

#### **Unanticipated Problems Involving Risks to Subjects or Others**

Investigators must report to the HIC any Unanticipated Problems that fit the following criteria within 48 hours of discovery:

1. Any incident, experience or outcome that
  - a. Is unexpected (in terms of nature, severity, or frequency) given the research procedures and protections described in the protocol and the characteristics of the subject population; and
  - b. Suggests that the research participation places the subject(s) or others at greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized; and
  - c. Is related or possibly related to the subject's participation in the research

Unanticipated Problems Involving Risks to Subjects or Others must be submitted in writing using the HIC Protocol Deviation or Unanticipated Problems Report form found at:

<http://info.med.yale.edu/hic/forms/index.html>

In submitting the report, investigators must consider what types of corrective measures should be taken, if any, to prevent future occurrences. Investigators must also consider whether changes are required to the protocol or procedures in order to minimize risks. Investigators must also determine whether changes are required in the information shared with current and potential subjects (as reflected in the consent form) or whether currently or previously enrolled subjects should receive notice of the Unanticipated Problem (and the potential for possible risk). If a change or notice is required, an amendment addressing the issue must be submitted promptly to the HIC.

The HIC is responsible for evaluating the reported event and making a final determination as to whether further corrective action(s) or notice to subjects is required.

### **III. Guidance**

Unanticipated problems involving risks to subjects or others are those incidents, experiences, or outcomes which, in the opinion of the investigator, may adversely affect the rights, safety or welfare of the subjects or others involved in the research, or which significantly impact the integrity of the research data. For example, occurrences of breaches of confidentiality or

accidental destruction or loss of study records are Unanticipated Problems that must be reported to the HIC.

Unanticipated Problems can include incidents such as:

- A. A stolen laptop containing subject data and identifiers  
<http://www.yale.edu/its/forms/LostStolenForm.doc>
- B. A processing error resulting in a subject receiving a dose of study medication 10 times higher than the dose dictated by the IRB approved protocol but that produces no detectable adverse effect
- C. Subjects receiving an investigational product which was obtained from donors who were not appropriately screened and tested for viral contaminants
- D. Subjects receiving the wrong medication and experiencing AEs that are not reportable under the AE reporting policy  
<http://info.med.yale.edu/hic/policy/AdverseEventPolicy.pdf>

These incidents represent Unanticipated Problems that require reporting to the HIC because they are unexpected in nature, related to participation in the research and result in new circumstances that increase the risk of harm to subjects or others.

#### **IV. Background**

The rationale for reporting Unanticipated Problems to the IRB is to enable the IRB to fulfill its role of oversight for protection of human subjects. Per federal regulation (21 CFR 56.108(b)(1) (FDA) and 45 CFR 46.103.b.5 (HHS)), the IRB is required to follow written procedures for insuring prompt reporting to the IRB of any Unanticipated Problems involving risks to subjects or others. By reviewing reports of certain types of Unanticipated Problems that may impact the subjects' welfare, the IRB can require investigators to think about and implement subject protections. Consideration should involve assessing whether there has been a change to the risk/benefit ratio, assessing whether changes are required to the protocol or procedures in order to minimize risks, and deciding whether changes are required in the information shared with current and potential subjects (as reflected in the consent form) or whether currently or previously enrolled subjects should be notified of this new potential risk.

Principal investigators and sponsors have additional reporting responsibilities (e.g., FDA, OHRP), as stated in federal regulations and contractual agreements. This policy does not affect those responsibilities.

#### References

FDA regulations: 21CFR56.108.b and 113

DHHS regulations: 45CFR46.103.b.5

#### Links:

<http://info.med.yale.edu/hic/policy/dsmp.pdf>

[http://info.med.yale.edu/hic/policy/protocol\\_deviations.pdf](http://info.med.yale.edu/hic/policy/protocol_deviations.pdf)

<http://www.hhs.gov/ohrp/policy/AdvEvtGuid.htm>