Procedure for Reporting of Protocol Deviations, Violations and Exception Requests

A. Background

The Human Research Protection Program recognizes that there will be situations where research activities deviate from the approved research protocol due to scheduling conflicts, patient non-compliance, emergency situations, or errors by research staff. This document strives to ensure accurate reporting to the UToledo IRB while making reporting as efficient as possible.

B. Definitions and Examples

A protocol deviation, violation, or participant non-compliance occurs when there is a departure from the approved research study protocol. In most cases, these are either 1) research activities that take place in a manner different from what the approved protocol states will occur, 2) failure to complete all research activities described in the approved protocol, or 3) research activities that are not included in the approved protocol.

Classification of a departure from the approved protocol as a deviation (minor departure) or a violation (major departure) will depend upon the extent of the departure as well as potential or actual consequences of the departure on

participant non-compliance that increase risk to the participant and/or result (or may result) in a negative consequence must be reported in a timely manner to the UToledo IRB. Other instances should be tracked and submitted to the IRB at the time of continuing review.

3) A principal Investigator can request that the UToledo IRB (and sponsor if one exists) review and approve in writing a waiver for minor protocol departures prior to their occurrence by completing the **Single Subject Exception Request** form. If this written pre-approval occurs, these deviations do not need to be reported afterward to the UToledo IRB *unless* an unanticipated adverse event results from the variance. In such an instance, an adverse event report form must be filed along with the protocol/deviation form, and the UToledo IRB and all other required agency(ies) must be notified in compliance with government regulations.

4) A **violation** is a departure from the approved protocol, without previous IRB-approval, that has the potential to cause harm or increase risk to participants, has the potential to affect the scientific integrity of the research, and/or impacts a subject's safety, rights, or welfare.

Examples of a violation include failure to properly obtain informed consent, or using an unapproved consent form, enrollment of ineligible subjects, or performing a research procedure not included in the approved protocol or changing an approved study procedure such as using different dosing or infusion rates. In all cases, willful misconduct by investigators is classified as a protocol violation.

In some cases, a protocol violation may occur as a result of the investigator's decision to deviate from the approved protocol in an attempt to avoid an increase in risk to the subject in an emergency situation. An example may include withholding the study drug in response to a serious adverse event that has occurred or the expectation that one may occur if the drug is administered as scheduled. In such emergency situations, the departure from protocol may proceed and the IRB must be notified.

C. The Procedure for Reporting Protocol Deviations, Violations and Exception Requests

To determine when a

as soon as possible, but in no event later than 5 working days after the emergency occurred (21 CFR 812.150(a)(4)).

2) If the decision to depart from the approved protocol ***is not*** under the control of the PI (for example, if there is an unavoidable scheduling conflict, the subject fails to complete all necessary steps/tasks required of them, or a member of the research staff makes an error), the PI should submit a Protocol Deviation/Violation form to the IRB within 10 working days ***only*** in the event that the departure from the protocol will or could possibly adversely affect the subject's rights, safety or welfare ***or*** if the departure has or will impact the science of the study. If neither of these impacts will occur, the departure should be tracked and reported at the time of continuing review.

The PI (and sponsor, if applicable) should review protocol deviations/violations to determine whether a protocol amendment is necessary to reduce the number of deviations. Such amendments might include adding a plus/minus window to study days to allow for more flexible scheduling, so long as subject safety would not be adversely affected.