Guidance
Planned Protocol Exceptions

Notes and important reminders
Federal regulations require that all protocol modifications (any change from the approved protocol) must be submitted to the Institutional Review Board (IRB) for review, and receive approval prior to implementation unless the change is to eliminate an immediate harm to a research subject. When a Principal Investigator (PI) anticipates a one-time, intentional action or process that departs from the approved protocol and which the PI deems significant, he or she must request an exception be granted by the IRB prior to implementation.

What is a planned protocol exception?
A planned protocol exception is any **planned** or intended change or **deviation** from the IRB approved study **protocol**, consent document, recruitment process, or study materials. They are deviations that occur because an investigator, research staff or other party involved in the conduct of research intentionally decides to deviate from the approved protocol.

Like protocol amendments, deviations initiated by the clinical investigator must be reviewed and approved by the IRB and the sponsor prior to implementation, unless the change is necessary to eliminate apparent immediate hazards to the human subjects (21 CFR 312.66), or to protect the life or physical well-being of the subject (21 CFR 812.35(a)(2)).

The Office for Human Research Protections (OHRP) has not issued written guidance on protocol deviations. However, OHRP's unwritten position is that all intentional protocol deviations are changes in research that need prior IRB review and approval before implementation.

How is a planned protocol exception different from a protocol deviation?
The basic difference is that the departure from the approved protocol was not planned nor intentional, and/or it occurs without prior IRB approval.

The U.S. Department of Health and Human Services (HHS) and Food and Drug Administration (FDA) regulations are inconsistent in addressing protocol deviations. In addition, among the various FDA regulations and guidance there are inconsistencies. However, FDA and OHRP have each indicated in various formats that intentional protocol deviations are changes in research that need prior IRB review and approval.

https://www.hhs.gov/ohrp/sachrp-committee/recommendations/2012-march-30-letter-attachment-c/index.html

"Protocol deviation" is used to refer to any unplanned instance(s) of protocol noncompliance. For example, situations in which the investigator failed to perform tests or examinations as required by the protocol

or failures on the part of study subjects to complete scheduled visits as required by the protocol, would be considered protocol deviations.

If the IRB approves the exception prior to implementation, it is not considered noncompliance for deviating from what the IRB had previously approved. If IRB approval is not sought and granted, this is considered noncompliance that must be reported to the IRB as a reportable event with root cause analysis and an appropriate corrective and preventative action plan (CAPA).

When is it appropriate to request a planned protocol exception?
A planned protocol exception is a one time, temporary action or process that departs from the IRB-approved protocol, and is generally intended for one specific subject because of an unusual or specific circumstance.

It is intended to be limited to a particular subject or circumstance, without plans to make this a permanent change to the protocol.

For example, there may be specific, unique circumstances that prevent a subject from completing study activities within the protocol defined window. The investigator may request a one time, planned exception from the protocol defined window to accommodate a particular subject's unique situation at that time.

A planned protocol exception should not be used to enable implementation of a change PRIOR to approval of a pending amendment that would make the proposed change permanent. In these cases the PI should wait for the approval of the amendment. If the PI plans on the deviation being a permanent change for all subjects it should be submitted as a modification/amendment with all changes described and approved BEFORE implementation.

How do I request approval of a planned protocol exception?
When a protocol exception is anticipated, the PI should promptly assess the potential impact the exception may have on the rights, safety and welfare of subjects, as well as the integrity of resultant study data.

The PI should also consider whether obtaining and documenting consent from the affected subject to implement the planned exception is appropriate. Contact the Children's Wisconsin HRPP if needed to discuss if consent is appropriate.

Submit the request to the IRB as follows:

- Complete the Planned Protocol Exception Request form found in IRBNet under "Forms and Templates."

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- When appropriate, create a consent addendum for use in obtaining and documenting consent from the subject. A consent addendum template is available in IRBNet under "Forms and Templates."

- Submit the Planned Protocol Exception Request form and the consent addendum via IRBNet as an "other" package.

Other things to keep in mind

- When the same exception is requested more than once, the IRB may not grant the exception and request the investigator to submit a protocol amendment. Feel free to contact the Children's Wisconsin HRPP to discuss a particular scenario if uncertain.

- If a change is implemented without prior IRB approval, the event should be promptly reported to the IRB using the "Reportable Event" Form and include a root cause analysis and corrective and preventative action plan.

- If a change is implemented prior to IRB approval to eliminate an immediate harm to a research subject, the event must be promptly reported to the IRB using the "Reportable Event" Form as an Unanticipated Problem.