REPORTING OF ADVERSE EVENTS AND UNANTICIPATED PROBLEMS INVOL VING RISK TO SUBJECTS OR OTHERS

WHAT IS AN UNANTICIP ATED PROBLEM INVOLVING RISK TO SUBJECTS OR OTHERS?

An unanticipated problem involving risk to subjects or others is any incident, experience, or outcome that meets **all** the following criteria:

1. The event is unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
2. The event is related or possibly related to participation in the research (*possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
3. The event 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.

WHAT IS AN ADVERSE EVENT?

An adverse event is any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research.

Adverse events encompass both physical and psychological harms. They occur most commonly in the context of biomedical research, although on occasion, they can occur in the context of social and behavioral research. [For the definition of a serious adverse event, see next section.]

WHAT NEEDS TO BE REP ORTED TO THE IRB?

Unanticipated problems involving risk to subjects or others, in other words events that meet the three criteria in the definition presented above, always need to be reported to the IRB. Adverse events do not necessarily need to be reported. Adverse events are only reported if they meet the definition an unanticipated problem involving risk to subjects or others; that is, if the event is unexpected, related to or possible related to participation in the research, and increases risk beyond what was previously known or recognized.

For example, if a participant with a serious medical condition experiences symptoms of or even natural deterioration of the condition after enrollment in a research this does not need to be reported to the IRB; this is an adverse event but does not meet the criteria for being unexpected or related to the research. However, if the same participant experiences a deterioration in medical condition as a result of study procedures and this was unanticipated (not specified in the IRB protocol, consent form, or other study documents) this would need to be reported.

The vast majority of adverse events occurring in the context of research are *expected* in light of (1) the known toxicities and side effects of the research procedures; (2) the expected natural progression of subjects' underlying diseases, disorders, and conditions; and (3) subjects' predisposing risk factor profiles for the adverse events. Thus, most individual adverse events do not meet the first criterion for an unanticipated problem and do not need to be reported under the HHS regulations 45 CFR part 46.103(a) and 46.103(b)(5)

Please note, however, that adverse events that meet the criteria for an unanticipated problem involving risk to subjects or others and meet the following criteria are considered a serious adverse event. OHRP defines ***serious adverse event*** as any adverse event that:

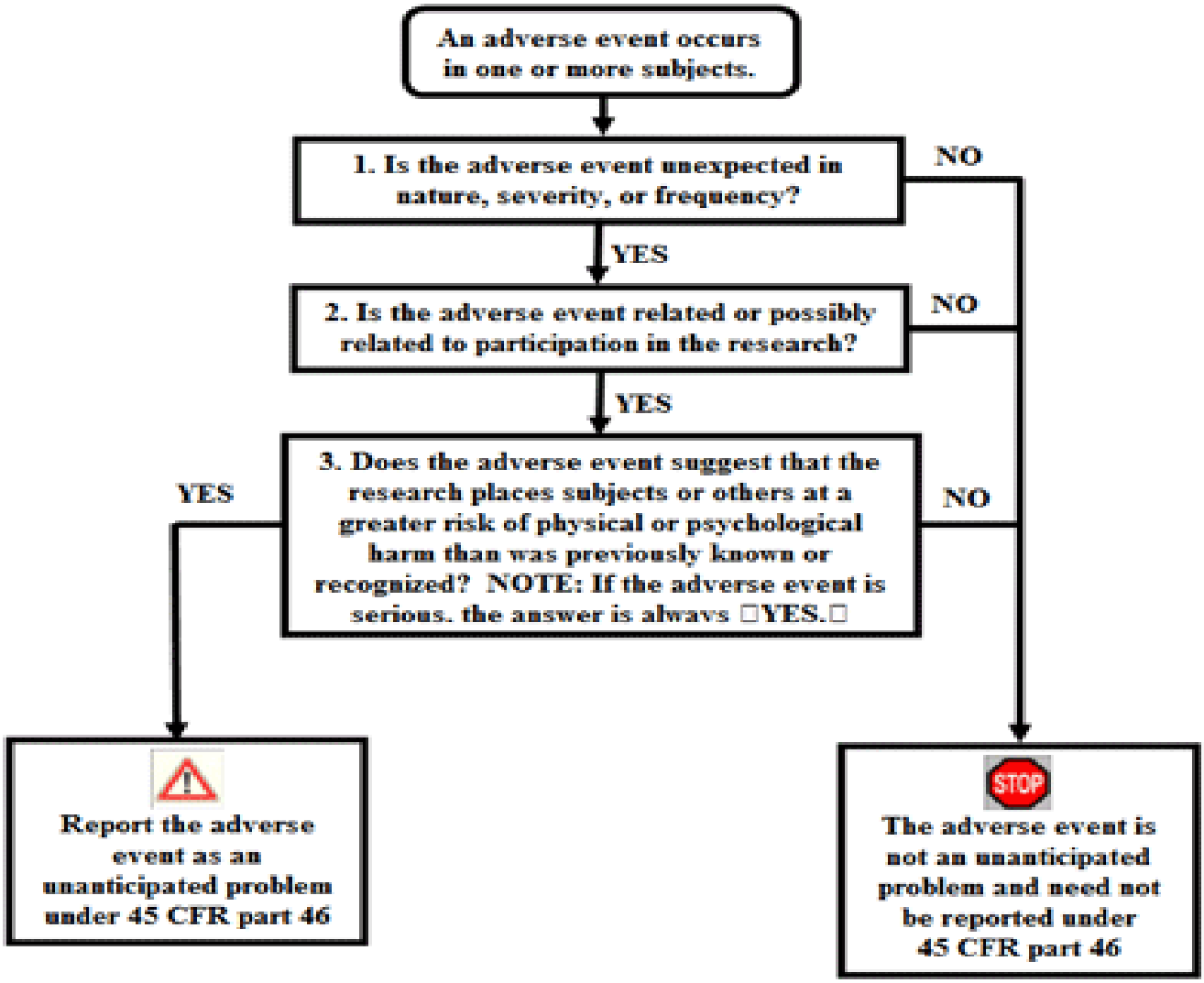
1. results in death;
2. is life-threatening (places the subject at immediate risk of death from the event as it occurred);
3. results in inpatient hospitalization or prolongation of existing hospitalization;
4. results in a persistent or significant disability/incapacity;
5. results in a congenital anomaly/birth defect; or
6. based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse).

Serious adverse events must always be reported.

Note that, regardless of whether the internal adverse event is determined to be an unanticipated problem, the investigator also must ensure that the adverse event is reported to a monitoring entity (e.g., the research sponsor, a coordinating or statistical center, an independent medical monitor, or a DSMB/DMC) *if required under the monitoring provisions described in the IRB-approved protocol or by the sponsor*.

Additionally, if an investigator determines that an adverse event is not an unanticipated problem but is later notified by a monitoring entity that they have determined the event to be an unanticipated problem, the investigator must report the event to the IRB.

The flow chart below provides an algorithm for determining whether an adverse event represents an unanticipated problem that needs to be reported under HHS regulations at 45 CFR part 46.



REPORTING PROCESS AND POSSIBLE OUTCOMES OF A RE PORT

If the investigator determines that the incident, experience, or outcome represents an unanticipated problem, the investigator must report it promptly to the IRB. Events not meeting the definition of a serious adverse event must be reported within 5 business days. Events meeting the definition of a serious adverse event must be reported within 24 hours. All reports should be made to the IRB Chair and Vice-Chair, by emailing the Unanticipated Problem/Adverse Event Reporting Form [Appendix XX, available through IRBnet] to the IRB Chair and Vice-Chair.

When the IRB Chairs receive a report they have the option of reviewing the report or brining the report to a convened meeting. This determination will be made on the basis of required expertise of review and whether the events suggest that immediate action is required.

The first step in any review will be to determine whether the incident meets the criteria for a reportable event. When reviewing a incident, experience, or outcome reported as an unanticipated problem by the investigator, the reviewing body (the IRB Chairs or the Full Board) may determine that the incident, experience, or outcome does not meet all three criteria for an unanticipated problem. In such cases, the case will be closed and the investigators will be notified.

If the incident meets the criteria for a reportable event the reviewing body will then determine whether the affected research protocol still satisfies the requirements for IRB approval under 45 CFR 46.111. In particular, the reviewing body will consider whether risks to subjects are still minimized and reasonable in relation to the anticipated benefits, if any, to the subjects and the importance of the knowledge that may reasonably be expected to result. Based on this assessment, the IRB may require action ranging from continued monitoring by the investigatory team up to and including termination of all study procedures. Examples of actions that will be considered are:

- suspension or termination of the research
- requiring notification and re-consenting of current participants, when such information might be related to their willingness to continue to take part in the study
- requiring modifications to the protocol and/or consent documents
- increase in frequency of continuing review
- imposition of additional monitoring requirements
- requiring additional training of some or all members of the research team

All determinations and any/all requirements for continuing the research will be reported to the primary investigator in writing.

All incidents, experiences, or outcomes determined to unanticipated problems involving risk to subjects or others will be reported to the Senior Vice President for the Division of Research Innovation, and Economic Development within 1 month. The Senior Vice President for the Division of Research Innovation, and Economic Development is responsible for the reporting of events, incidents, or outcomes to OHRP and, if applicable, the supporting HHS agency head (or designee). For multicenter trials only events occurring at the UTRGV site will be reported by the Senior Vice President for the Division of Research Innovation, and Economic Development and only if a central monitoring agency has not been designated for this purpose.

UTRGV	**The University of Texas Rio Grande Valley** **Institutional Review Board for the Protection of Human Subjects in Research** **Unanticipated Problem/Adverse Event Reporting Form**

Note that only events that are (1) unexpected in nature, severity or frequency AND, (2) related or possibly related to the research, AND (3) suggests that the research places the subjects or others at greater risk of psychological or physical harm was previously known or recognized need to be reported. Please see IRB handbook for additional guidance if needed.

Principal Investigator:		Phone:	
Department:		E-mail	
Title of Research Project:			
IRB Study No.:		IRB Approval Expiration Date	
The study is (check one):	☐ Currently in progress (open to enrollment) No. of subjects enrolled: No. of subjects still in treatment: ☐ Closed to enrollment (participants in follow-up)		
Date of Event: Date of awareness of event:			
Was this an internal or an external event	☐ Internal ☐ External (took place at another site in the context of a multicenter study or trial)		

☐ Serious Adverse Event ☐ Other Unanticipated Problem	OHRP defines serious adverse event as any adverse event that: 1. results in death; 2. is life-threatening (places the subject at immediate risk of death from the event as it occurred); 3. results in inpatient hospitalization or prolongation of existing hospitalization; 4. results in a persistent or significant disability/incapacity; 5. results in a congenital anomaly/birth defect; or 6. based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse).
Description of Event (give enough detail here to determine the rationale for study-or-treatment relatedness and determination of unexpected nature of event):	

Description of any and all steps and actions taken in response to the incident or to resolve the issue:
Number of similar experiences in this protocol:
Was the event reported within policy time frames (Events not meeting the definition of a serious adverse event must be reported within 5 business days. Events meeting the definition of a serious adverse event must be reported within 24 hours.)? If not, explain:
What was subject's participation level after the event? ☐ Subject stopped research participation ☐ Subject had already completed research ☐ Subject continued research participation ☐ Subject withdrew from further participation ☐ Subject continued participation/follow-up only ☐ Investigator withdrew subject from participation ☐ Other (describe):

Effect on Research – In your judgment, should the research

☐ **continue as planned** with no changes to the research protocol or consent process. Explain why:

☐ **continue with changes** to the research protocol or consent process;

Attach proposed changes for IRB review and approval using a modification form.

☐ **suspend new subject enrollment** until the event is further examined;

☐ **be terminated** (stopped completely), with all subjects removed from research.

Have other agencies or sponsors been notified of this event?

☐ Yes (list agencies/sponsors notified including dates and methods used)

☐ No (describe steps to be taken to notify appropriate parties)

Does this study have a Data Safety Monitoring Board (DSMB)? ☐ Yes ☐ No

If yes, has the DSMB been notified? ☐ Yes ☐ No

Investigator Assurance(s):

I have reviewed the contents of this form and hereby assure that the information provided is complete and accurate to the best of my knowledge.

_____ ☐ person filing report

Signature of Principal Investigator Date

_____ ☐ person filing report

Study Coordinator Date