

Suicidal Ideation and Behavior: Risk Mitigation Guidance

Participants at risk of suicidal ideation and behavior are a vulnerable population group. Therefore, additional measures may be warranted to ensure their protection while they are enrolled in research studies. Researchers may not always be aware, in advance, of participants who may be at risk of suicidal behavior. However, when a research team is made aware of immediate suicide risk in a participant, there is an obligation and responsibility for timely and appropriate follow up to ensure participant safety. The intent of this document is to provide guidance on ensuring the safety of research participants who may be at risk of suicidal behavior.

Section A: Who is at-risk?

There is a higher standard to ensure the safety of participants who are known to be at risk for suicide. The following groups are noted to be at a higher risk for these behaviors:

- American Indians/Alaska Natives;
- Family members, friends, and others affected by the suicide of a loved one
- Individuals in justice (e.g., prisoners) and child welfare settings;
- Individuals who engage in non-suicidal self-injury (NSSI);
- Individuals who have attempted suicide;
- Individuals with certain medical conditions (e.g., cancer, degenerative diseases, traumatic injuries, etc.);
- Individuals with mental illness (e.g., depression) and/or substance use disorders;
- Members of the LGBTQ+ community;
- Members of the Armed Forces and veterans;
- Men in midlife; and
- Older men.

Additionally, participants in FDA-regulated clinical trials (including otherwise healthy volunteers) may also be at risk for suicidal ideation and behavior, when they are being administered:

- A drug being developed for any psychiatric indication,
- Any antiepileptic drug, and/or
- Other neurologic drugs with central nervous system (CNS) activity

Section B: When Should Screening and Assessment be Conducted?

The FDA recommends prospective suicidal ideation and behavior assessments be conducted in all clinical trials involving participants taking the above mentioned drug products.

Prospective screening and assessment may be appropriate to include in other types of research studies as well. An investigator should consider whether prospective screening and assessment is appropriate, if conducting research with one of the at-risk groups above. Additionally, many clinical and behavioral research studies utilize common

mental health measures for various purposes. Some of these commonly used measures include questions about suicide, including but not limited to:

- Beck Depression Inventory (BDI)
- Hamilton Rating Depression Scale
- Patient Health Questionnaire (PHQ)-9

Use of such scales in research indicates that the research team could receive information related to a participant's suicidal ideation and behavior. When mental health scales are used, the study team should assess the scale to determine if there are questions related to suicidal ideation and behavior. If the measure includes such items, the study team should develop a plan for handling disclosures of suicidal intent. This is especially important in mitigating harm when the research targets population groups who are at risk for suicidal ideation and behavior.

Section C: How Should Screening and Assessment be Conducted?

FDA-Regulated Clinical Investigations

The FDA document, *Suicidal Ideation and Behavior: Prospective Assessment of Occurrence in Clinical Trials*, provides guidance on actively questioning and assessing suicide risk in clinical trial participants.

The FDA recommends the use of the Columbia-Suicide Severity Rating Scale (C-SSRS). The instrument has high sensitivity and specificity as well as inter-rater reliability. However, the FDA notes that there may be appropriate alternatives. If an alternate instrument is used, the FDA recommends an instrument that directly classifies suicidal ideation and behavior into the 11 preferred categories:

A. Suicidal Ideation

1. Passive
2. Active: Nonspecific (no method, intent, or plan)
3. Active: Method, but no intent or plan
4. Active: Method and intent, but no plan
5. Active: Method, intent, and plan

B. Suicidal Behavior

1. Completed suicide
2. Suicide attempt
3. Interrupted attempt
4. Aborted attempt
5. Preparatory actions toward imminent suicidal behaviors

C. Self-Injurious Behavior, No Suicidal Intent

The FDA guidance also provides recommendations for specific trial considerations during study design. If an investigator is developing a protocol that administers one of

the drugs listed in Section A, the IRB strongly recommends the investigator review the FDA's guidance, which is linked in the Reference section.

The C-SSRS and other validated alternatives are diagnostic tools normally administered by licensed mental health professionals. A brief screening such as the [4-item Ask Suicide-Screening Questions \(ASQ\) toolkit](#) may be a useful and appropriate tool for the research team.

Other Research

The appropriate method or instrument to assess risk of suicidal ideation and behavior in other types of research studies may depend on the following:

1. The risk of the research,
2. The likelihood of suicidal ideation and behavior being exhibited or disclosed in the study, and
3. Whether the research targets population groups who are at-risk for suicidal ideation and behavior.

The method or instrument should probe and ask open-ended questions to determine level of suicide risk to determine appropriate follow up. When the research targets participants in higher risk groups, the IRB recommends using a more sensitive instrument like the C-SSRS and other validated alternative diagnostic tools.

Section D: Who should Screen and Assess?

As noted above, clinical assessments such as the C-SSRS and other validated alternatives are diagnostic tools administered by trained and licensed mental health professionals. Therefore, the IRB recommends that these scales be completed by licensed mental health professionals with the appropriate expertise to assess responses. If the study team includes a mental health professional, this may be written into the trial plan.

If the study team does not include a licensed mental health professional, a plan for quick screening and subsequent clinical referral is appropriate. A brief screening tool such as the [4-item Ask Suicide-Screening Questions \(ASQ\) toolkit](#) or an alternative would be appropriate for the research team to utilize prior to referral to a licensed mental health professional.

Section E: What should the risk mitigation plan entail?

When a research participant is determined to be at-risk for suicidal ideation and behavior or such information is disclosed to the study team, a plan for timely screening, assessment, and follow-up care should be included in the research protocol or IRB application.

Risk-mitigation strategies may differ depending on the risk of both ideation and behavior as well as the risk of the research and whether the research targets at-risk

populations. It is important to note that the plan may also require additional training of research personnel involved in screening and following up actions with participants.

The research team should consider the following in developing a risk mitigation plan:

1. Timing
 - a. When will instruments with questions about suicide be administered?
 - b. Is there any delay between the time the questions are administered and when they will be reviewed by research personnel, if applicable?
 - c. When will a follow up screening be conducted if ideation or behavior is disclosed?
2. Personnel
 - a. Is research personnel involved in administering the instruments or do the participants complete them on their own?
 - b. Which research personnel are administering instruments or reviewing responses?
 - c. Is a licensed mental health professional need as part of the research team?
 - d. Do research personnel have the appropriate training to conduct screening and follow up actions?
3. Responding
 - a. Upon screening, how will risk of potential self-harm be responded to? Will this differ based on the risk of potential self-harm [e.g., providing a handout with resources (low risk), referral to a mental health professional for further evaluation, calling 911 immediately (high risk), etc.]?
 - b. How will reporting to the PI be conducted and within what timeline?
 - c. Does any other reporting need to be conducted (e.g., to the Sponsor, Monitor, DSMB, etc.)?
4. Resources and Support
 - a. What mental health resources will be provided to participants who disclose?
 - b. If a participant is unwilling to receive help, how will the research team ensure support for the participant?

Section F: Should suicidal ideation and behavior be reported to the IRB?

This will differ depending on the protocol design. Suicidal ideation and behavior may be a reportable event to the IRB if it is both: 1) an unexpected adverse event as outlined in study documents and 2) probably or definitely related to the study procedures.

References

- National Institute of Mental Health (NIMH). [Ask Suicide-Screening Questions \(ASQ\) Toolkit](#).
- Conducting Research with Participants at Elevated Risk for Suicide: [Considerations for Researchers](#)
- 2012 National Strategy for Suicide Prevention: Goals and Objectives for Action: A Report of the U.S. Surgeon General and of the National Action Alliance for Suicide Prevention. [Appendix D: Groups With Increased Suicide Risk](#)
- [FDA Guidance: Suicidal Ideation and Behavior- Prospective Assessment of Occurrence in Clinical Trials](#)