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SANTA BARBARA • SANTA CRUZ

OFFICE OF THE VICE PRESIDENT – RESEARCH AND INNOVATION

OFFICE OF THE PRESIDENT
1111 Franklin Street, 11th Floor
Oakland, California 94607-5200

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April 3, 2026

Dockets Management
Food and Drug Administration
5630 Fishers Lane, Rm 1061
Rockville, MD 20852

RE: UC Comments on FDA Guidance Document: Investigator Responsibilities – Safety Reporting for Investigational Drugs and Devices (FDA-2021-D-0368)

To Whom It May Concern:

On behalf of the University of California (UC) system, we appreciate the opportunity to comment on the FDA's guidance entitled Investigator Responsibilities – Safety Reporting for Investigational Drugs and Devices issued on December 15, 2025.

The UC system is comprised of ten campuses, six academic health centers, an Agriculture and Natural Resources division, and three affiliated U.S. Department of Energy national laboratories. Our locations conduct a broad portfolio of clinical investigations, including studies conducted under an Investigational New Drug application (IND), Investigational Device Exemption (IDE), and bioavailability/bioequivalence (BA/BE) studies.

We write to seek clarification and recommend revisions to Section VI. of the FDA guidance, particularly on investigator responsibilities for reporting IND safety information to IRBs.

1. **Confusion on Equating an IND safety report or a BA/BE SAE as an Unanticipated Problem Needing to be Reported to the IRB**

The FDA guidance on page 9 states that:

> "[t]he investigator must submit IND safety reports to the IRB (§ 312.66) because FDA considers safety information that meets the IND safety reporting criteria under § 312.32(c) to be an unanticipated problem involving risk to human participants or others."

The FDA guidance further states that:

> "FDA considers the occurrence of any SAE in an IND-exempt BA/BE study to be an unanticipated problem involving risk to human participants or others that must be reported to the IRB (§ 56.108(b)(1))."

As written, this language suggests that all IND safety reports meeting the criteria under § 312.32(c) are unanticipated problems that must be reported to IRBs. As the guidance continues, FDA seems to consider any serious adverse event (SAE) in an IND-exempt BA/BE study to be an unanticipated problem that must be reported to the IRB.

This approach appears to depart from prior FDA guidance, which distinguished between Suspected Unexpected Serious Adverse Reactions (SUSARs) and unanticipated problems requiring IRB reporting. Under the prior framework, not all SUSARs were considered unanticipated problems. Instead, a determination was made as to whether the event met all of the following criteria in order to be considered an unanticipated problem:

- Was unexpected,
- Was related or possibly related to participation in the research, and
- Suggested an increased risk of harm requiring a change in the protocol, informed consent document, or other risk mitigation measures.

This distinction enabled a risk-based filtering approach, ensuring that IRBs received safety information that was actionable and relevant to participant protection.

2. Implications of FDA Departure from Prior Guidance

In practice, investigators receive a high volume of IND safety reports from sponsors. Many of these reports describe events that do not meet the criteria of an unanticipated problem. Requiring investigators to submit all IND Safety Reports to the IRB, including those that do not involve an unanticipated problem, would shift responsibility to investigators to transmit large volumes of safety information that may not meaningfully contribute to IRB oversight or participant protection.

From the IRB perspective, this apparent requirement raises significant implementation challenges. IRBs receive and review IND safety reports and focus on events that necessitate changes to the protocol, informed consent, or other risk management measures. If all IND Safety Reports must be submitted, IRBs will face a dramatic increase in reporting volume, which may:

- Strain administrative and reviewer capacity,
- Reduce the ability to identify truly significant safety signals, and
- Undermine the effectiveness of IRB review.

3. Request for Clarification and Revisions

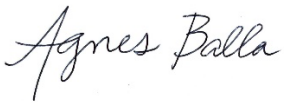
We respectfully request that FDA clarify that investigators do not need to submit **all** IND safety reports to the IRB, but rather only those that truly meet the criteria of an unanticipated problem. We also request that FDA continue to support a risk-based determination, in which only those safety reports that meet the criteria of an unanticipated problem are submitted to IRBs.

To promote clarity and effective oversight, we strongly recommend that FDA:

- Restore or incorporate language from prior guidance that distinguishes between suspected unexpected serious adverse reactions and unanticipated problems, and
- Explicitly state that not all IND safety reports require submission to IRBs, but only those that meet the criteria for unanticipated problems.

We appreciate your consideration of these comments and welcome further engagement on this topic. If you have any questions regarding these comments or would like additional information, please contact Agnes Balla, Director, Research Policy Analysis and Coordination, at Agnes.Balla@ucop.edu.

Sincerely,



Agnes Balla
Director
Research Policy Analysis & Coordination
University of California Office of the President