WCG WEBINAR

FDA's Updated IND Safety Reporting Guidance

What Changed, What Didn't, and What to Do Now

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Meet Your Speakers

WCG IRB | Indiana University | National Institutes of Health

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Executive IRB Chair & VP of IBC Affairs, WCG

Leads the compliant, efficient operation of WCG's IRB and IBC. A certified IRB professional with a PhD in chemical engineering, she has been with WCG since 2014.

Purna Garimella, MS, CIP, RAC-US

Executive Director, Human Research Protection Program & IRB, Indiana University

Oversees the strategic direction of IU's HRPP across all campuses and affiliated hospitals, with 15+ years in IRB operations and regulatory affairs.

Nicole Grant, RN, BSN, MPH

Acting Director & Executive IRB Chair, Office of Human Subjects Research Protections, NIH

Leads OHSRP and chairs the NIH IRB and has led NIH's guidance to investigators on the updated FDA IND safety reporting expectations.

What the Updated Guidance Says

What Changed - and What Didn't

What Changed

Two final guidances, issued together

Separate documents for investigators and for sponsors, each setting out safety reporting responsibilities for its own audience.

A clearer map of the regulations

Shows how 21 CFR 312.32, 312.64, 312.66 and 56.108 intersect to determine who reports what.

Sharper IRB expectations

FDA states that information meeting the IND safety report criteria is an unanticipated problem, so those reports go to the IRB - on the window each IRB sets.

What Didn't Change

- The underlying regulations are untouched - 21 CFR 312.32, 312.64, 312.66 and 56.108 still govern
- Sponsors still notify FDA and all participating investigators within 15 calendar days when information meets 312.32(c)(1)(i)-(iv)
- Unexpected fatal or life-threatening suspected adverse reactions still carry the 7-day clock
- Investigators still report all serious adverse events to the sponsor immediately, whether or not drug related
- IRBs still set the submission window for prompt reporting in their written procedures under 56.108

Same obligations - clearer instructions for applying them

Four Terms, Four Distinct Obligations

Distinguishing the trigger from the report

Serious Adverse Event	SUSARs	IND Safety Report	Unanticipated Problem
WHAT IT IS Death, a life-threatening event, hospitalization or its prolongation, persistent incapacity, or a congenital anomaly. Seriousness is about outcome, not severity.	**WHAT IT IS** A suspected adverse reaction is an adverse event with evidence the drug caused it. A SUSAR is one that is both serious and unexpected.	**WHAT IT IS** The sponsor's expedited notice to FDA and all participating investigators. Often describes events at other sites or in other studies.	**WHAT IT IS** Unexpected, related to the research, and suggesting greater risk than previously known. An IRB concept under 21 CFR 56.108(b)(1)and 45 CFR 46.108(a)(4)(i).
WHO ACTS The investigator reports every serious adverse event to the sponsor immediately, whether or not the drug is the suspected cause.	**WHO ACTS** The sponsor assesses causality across the full data set. Expectedness is judged against the investigator brochure.	**WHEN** 15 calendar days after the sponsor determines it qualifies; 7 calendar days if unexpected and fatal or life-threatening.	**WHO ACTS** The investigator reports promptly to the IRB, following its written procedures. The IRB determines whether the event constitutes an unanticipated problem.

Who Reports What, to Whom, and by When

How 21 CFR 312.32, 312.64, 312.66 and 56.108 fit together

	Investigator*	Sponsor*	IRB	Regulation
Reports what	All serious adverse events, plus an assessment of whether there is a reasonable possibility the drug caused the event	Information meeting the IND safety report criteria in 312.32(c)(1)(i)-(iv)	Unanticipated problems involving risks to subjects or others, including qualifying IND safety reports, and any actions taken	312.64(b), 312.32(c), 56.108(b)
Reports to whom	Sponsor for serious adverse events; IRB for unanticipated problems	FDA and all participating investigators	Institutional officials and FDA	312.66, 56.108(b)
By when	Immediately to the sponsor; to the IRB within the window set in its written procedures	15 calendar days; 7 calendar days for unexpected fatal or life-threatening suspected adverse reactions	Per its written procedures for prompt reporting.	312.32(c)(1)-(2)

Source: FDA final guidances on sponsor and investigator safety reporting responsibilities, December 2025.
* In some cases the investigator and sponsor may be the same.

Implementation Challenges and Solutions

IMPLEMENTATION CHALLENGES AND SOLUTIONS

Reconciling the FDA and OHRP Frameworks

OHRP'S THREE-PART FRAMEWORK

- Unexpected
- Related or possibly related
- Suggestive of greater risk

FDA'S DECEMBER 2025 POSITION

Information meeting the IND safety-reporting criteria is a UP and must be submitted to the IRB.

FOR SITES, SPECIFICALLY IRBS

IRBs may want to discuss their interpretation and proposed approach with appropriate institutional officials and, as applicable, legal counsel.

IMPLEMENTATION CHALLENGES AND SOLUTIONS

Local vs. External Reports: Who Submits to Which IRB?

FDA DOES NOT DISTINGUISH BETWEEN

- Events occurring at the investigator's site
- Events occurring at other sites or in other studies

Both must be submitted to the Reviewing IRB.

TWO SUBMISSION PATHWAYS

- **Investigator:** Submits the report to the Reviewing IRB.
- **Sponsor:** May submit on the investigator's behalf when the arrangement is documented and the investigator receives confirmation.

WHAT EACH SIDE CAN DO

- **Sponsors:** Identify qualifying reports and state whether they were submitted to the reviewing IRB.
- **Sites:** Know the reviewing IRB's requirements and retain confirmation of sponsor submission.

IMPLEMENTATION CHALLENGES AND SOLUTIONS

The Qualifying Determination

WHAT THE DETERMINATION IS

The sponsor decides whether information meets the IND safety reporting criteria in 21 CFR 312.32(c)(1)(i)-(iv). That determination, not the event on its own, is what makes a report an IND safety report and sends it to the IRB.

SPONSORS AND CROS

- State the 312.32(c) determination and the rationale in the report itself.
- Say plainly what changed in the protocol, consent, or investigator brochure, and what the site is expected to do.

SITES

- Request the determination and the rationale with the report rather than re-deriving it locally.
- Route on the sponsor's assessment so triage does not shift to the IRB by default.

IMPLEMENTATION CHALLENGES AND SOLUTIONS

Report Volume Across Multi-Site Studies

WHY ONE REPORT ARRIVES MANY TIMES

In multi-site studies a single IND safety report can reach the same reviewing IRB from every participating site, so review effort follows volume rather than risk.

SPONSORS AND CROS

- Tune distribution settings so duplicate copies of the same report are not sent to one reviewing IRB.
- Where the arrangement is documented, submit to the reviewing IRB on behalf of participating sites.

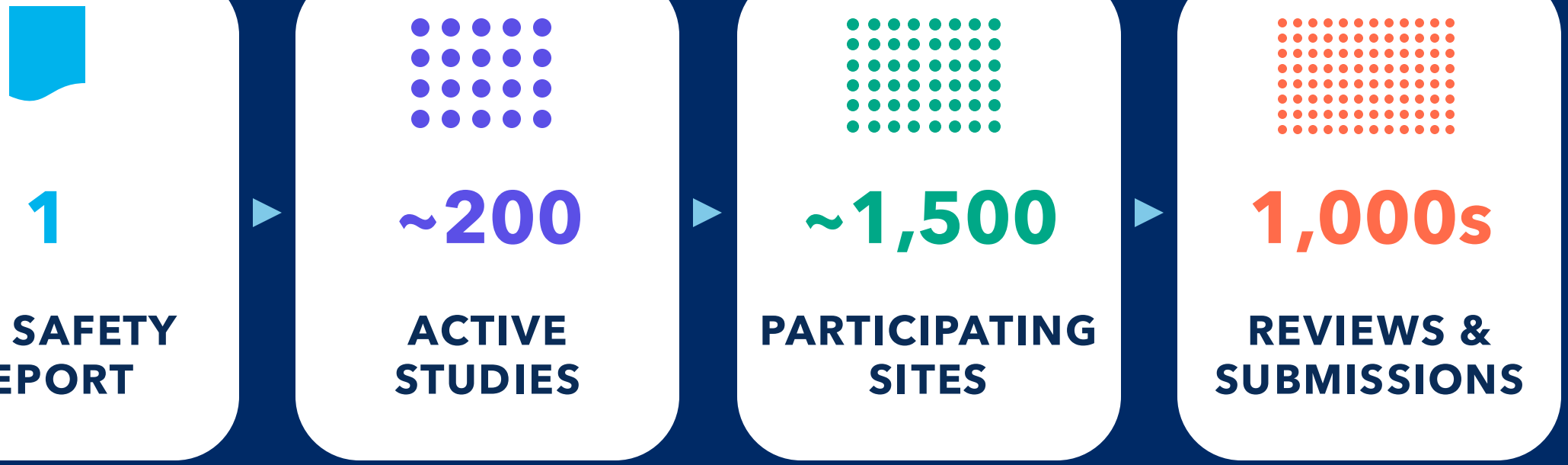
SITES

- Confirm with the sponsor who submits to the reviewing IRB for each study.
- Track what the IRB has already received so the same report is not submitted again.

IMPLEMENTATION CHALLENGES AND SOLUTIONS

One Report. Thousands of Reviews.

What a single IND safety report can set in motion - illustrative scale for a well-known oncology drug.



One determination cascades into thousands of separate site-level submissions and IRB reviews.

IMPLEMENTATION CHALLENGES AND SOLUTIONS

How Do IRBs Review Them?

IRB CONSIDERATION

Written procedures should define triage, review, documentation, and escalation pathways.

IRBS CAN DISTINGUISH AMONG:

RECEIPT

Confirm it is an IND safety report.

ASSESSMENT

Whether the information affects the locally approved research.

ACTION

Decide whether formal IRB review, study changes, or further reporting is needed.

IMPLEMENTATION CHALLENGES AND SOLUTIONS

Further Reporting Obligations

THE OBLIGATION, AND THE PRACTICAL CHALLENGE

IRBs are required to report unanticipated problems to FDA. If reported to FDA by the IND sponsor, an IRB can verify that and does not have to duplicate the report to the FDA. However, there is a practical challenge.

- Verification? Or
- Reporting?

Different operational processes for industry-sponsored studies and investigator-initiated studies.

SPONSORS AND CROS

- Identify the report as qualifying under § 312.32(c) and confirm FDA submission.

SITES

- Obtain and retain the sponsor's confirmation.
- IRBs: Define acceptable documentation and when additional FDA reporting is necessary.

What to Do Now

Practical moves

Sites can

01 Ask the sponsor before you forward

Request the qualifying determination and the rationale with the report, and ask what action the sponsor expects from the site.

02 Know each IRB's clock

The window is set by each IRB, not by FDA - five calendar days at WCG. Confirm it for every IRB of record and publish it internally.

03 Track the effort it takes

Log determination dates alongside event dates, so the added regulatory workload is visible when timelines and resourcing are discussed.

Sponsors and CROs can

01 Assess before distributing

Identify which reports meet the 312.32(c) criteria rather than passing that judgment downstream to every site.

02 Communicate proactively

State plainly what qualifies, what changed in the protocol, consent, or brochure, and what the site is expected to do.

03 Make the path easy to follow

Tune distribution settings, remove duplicates, and submit to the IRB on behalf of sites where documentation allows.

AUDIENCE POLL

Would you like to be contacted by a member of our IRB customer engagement team to discuss working with WCG IRB on an upcoming study?

YES

NO

Select your response in the poll panel.

Audience Q&A

Thank you!

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