Investigator Review of External Safety Reports

DF/HCC RESEARCH SUPPORT OFFICE HOURS

January 7, 2022

Submit questions using the Zoom Q&A function

On the agenda for today…

DF/HCC POLICY REQUIREMENTS

OVERVIEW AND RECENT UPDATES TO RCO-204

STRATEGIES FOR INVESTIGATORS

HANDLING UNNECESSARY / UNINFORMATIVE REPORTS

PANELIST Q&A

SUBMIT YOUR QUESTIONS VIA ZOOM Q&A

Why are we making changes to RCO-204 now?

Clarify the federal regulatory requirements for our investigators

Update language in response to sponsor and FDA feedback

Ensure consistent language and process for all phases of research

Allow more flexibility via delegation

RCO-204 – Key Updates/Clarifications

New Changes

- The requirements for PI review of safety reports is now consistent for all studies, regardless of phase
- The PI can delegate INDSR review to an appropriately qualified sub-investigator
- Documentation may occur per institutional practice (i.e., outside of sponsor systems).

Clarified Language

- The sponsor is responsible for analyzing new information, ensuring proper reporting to FDA and investigators, and providing sufficient information when such reports are distributed
- The PI, or designee, must look at each IND safety report to determine whether any action is required. Properly reported INDSRs received from the sponsor must be reviewed and acted on.

Sponsor Reporting Requirements

The sponsor must send safety reports to the FDA and all participating investigators within 15 calendar days.

Reporting is required for any suspected adverse reaction that meets the following criteria:

- Serious
- Unexpected
- There is evidence to suggest a causal relationship between the investigational drug and the adverse event

The FDA has stated that if the adverse even does not meet all three criteria, it should not be submitted as an IND safety report

21 CFR Part 312.32

Sponsor Reporting Requirements

The sponsor is required to include the following information in each IND safety report:

- ✓ A **brief narrative** describing the suspected adverse reaction and any other relevant information
- ✓ All **prior IND safety reports** submitted to FDA concerning **similar events**
- ✓ **Analysis** of the significance of the event in light of previous information

21 CFR Part 312.32

Investigator Requirements

Investigators are expected to review all IND safety reports as part of their ongoing commitment to protect the rights, safety, and welfare of subjects

This may be ***delegated*** to appropriately trained and qualified members of the study team, but the **PI retains ultimate responsibility**

Investigators also must report to the IRB all unanticipated problems involving risks to human subjects.

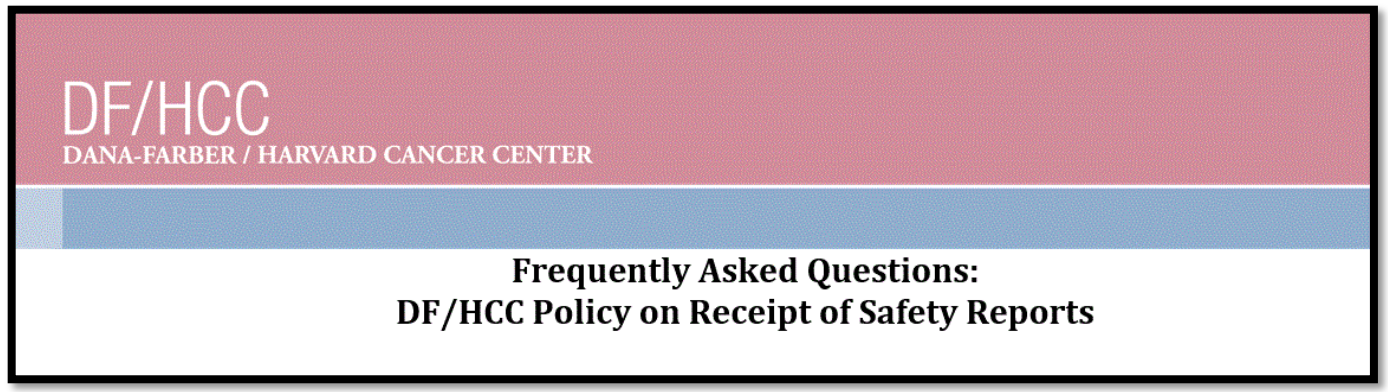
Guidance indicates this includes any incident, experience, or outcome that is unexpected, related to participation in the research, and suggests that research places subjects or others at a greater risk of harm than was previously known or recognized.

The FDA has stated that an event that meets the criteria for reporting in an IND safety report should generally be considered an "unanticipated problem".

When sponsors overreport, what options do our investigators have?

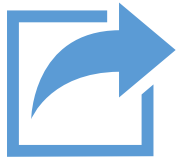
What can be shared with sponsors?

- You can send sponsors:
  - DF/HCC policy RCO-204
  - DF/HCC FAQ on IND safety reports



Provide this document to sponsors to clarify DF/HCC requirements and what is expected of them with regards to proper reporting of IND/IDE Safety Reports

Strategies for Handling Uninformative/Unnecessary Reports



If it's unclear why something was reported, ask! Share specific examples that do not appear to meet the FDA reporting criteria.

Discuss with the sponsor. The regulations require sponsors to make the assessment on whether new information is reportable. Ask sponsors to ensure the regulations are followed and INDSRs are clearly marked.

Maintain email/communications to document occurrence of reports not meeting criteria, and reason why they are not being signed or filed.

If a sponsor continues to send uninformative reports, and PI is unable to resolve issue directly with sponsor, escalate to DF/HCC leadership.

Additional Considerations – Delegation Logs

- **Updated: DF/HCC Key: Delegation of Tasks for Clinical Research** (used in accordance with the DF/HCC DOA Log Template)

Research Tasks	Physician	Physician Assistant (PA) / Nurse Practitioner (NP)	Research Nurse (RN)	Pharmacist	Coordinator [1]
Review of IND safety report from external sponsors	Yes, only when listed as a subinvestigator on the FDA Form 1572	Yes, only when listed as a subinvestigator on the FDA Form 1572	Yes, only when listed as a subinvestigator on the FDA Form 1572	No	Only initial triage and reviewing for expectedness in the Investigator Drug Brochure; requires confirmation by PI or sub-investigator
Final Determination of IND safety report requiring reporting to the IRB (DF/HCC subsite PIs should communicate with the Core Site. Only Core Site should make a single report to the IRB.)	Principal Investigator only	No	No	No	No

Updated as of January 2022

What about CTEP Studies using CTSU DTLs?

- Per CTSU, because the DTL master task list does not have this task (INDSR review) specified, teams do not need to take further action at this time.

Q&A

Please submit questions using the **Zoom Q&A** button!

Panelists:

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Brittney Delsesto (DFCI)

***Please do not submit questions in Chat.*