WHAT WILL BE COVERED IN THIS PRESENTATION?

Definitions
Non-compliance
Protocol Deviations
Unanticipated Problems
  • SUSARs and SAEs
Sponsor requirements
Revised IRB process
IRB resources
Questions
DEFINITIONS

**Internal event:** event that occurred in participants enrolled at Emory or in a site under Emory IRB’s oversight (Emory S-I)

**External event:** events that occurred in participants who were not enrolled at Emory or at sites under Emory IRB’s oversight

**Promptly reportable:** reportable within 10 business days from when the study team learned about the issue

**Periodically reportable:** reportable at continuing review
NONCOMPLIANCE
NONCOMPLIANCE

Failure to follow the regulations, Emory P&Ps, or Emory IRB determinations, e.g.: IRB FB reconsent requirement was not followed

Information the IRB needs: How this happened (root cause analysis) and substantive plan to correct (if possible) and prevent in the future (CAPA plan)

Reporting time: Promptly (10 business days)
PROTOCOL DEVIATIONS
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Reportable protocol deviations are ones that are considered substantive and negatively affecting:

- Rights, safety or welfare of subjects
- Willingness to continue with study participation
- Integrity of research data

Information the IRB needs: We need to know why this deviation affects (or not) any of the above. For example, missing a lab may be not considered a safety matter because the drug may not affect the value, but the members may think otherwise without your input.

Reporting time: Promptly
UNANTICIPATED PROBLEMS
UNANTICIPATED PROBLEM

An UP is an event that is:
- Related to study participation
- Unanticipated (not described or not expected and/or observed previously)
- Poses an increased risk for participants or others (serious)

Information the IRB needs: similarly with PD, the IRB needs to know why the event was assessed as UP. More serious events than described (allergic reaction vs. anaphylaxis) may be reportable unless the same frequency, severity or duration of the event was described already.

Reporting time: Promptly
UNANTICIPATED PROBLEMS

Examples of UPs:

- New SAE in a subject (or subjects) that was unknown and that will be added to the ICF.
- SAE previously described in the ICF but that is occurring in a higher frequency, severity or duration
- An event that it is not an SAE but that increases risk. E.g., a stolen laptop containing subjects’ PHI
UP: SUSARS AND SAES

SUSARs: sponsor’s reports of Suspected Unexpected Serious Adverse Reactions. Probably reportable to the IRB unless PI assessment indicates otherwise.

SAEs: Not promptly reportable unless they are also UPs OR if they are a related, internal death

When to report SAEs that are not UPs:

<table>
<thead>
<tr>
<th>Event</th>
<th>At CR</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internal, expected SAEs</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Internal, unrelated deaths</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Unrelated events (even if internal)</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>External events (PI is not a S-I) that are not UPs (even if related death)</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>External events (PI is a S-I)</td>
<td>Should be seen as internal (so, if expected SAEs, at CR, if unrelated deaths, at CR).</td>
<td></td>
</tr>
</tbody>
</table>
Timing of Report of Protocol Deviations, Adverse events, Deaths and Non Compliance

**Protocol Deviations**
- Promptly: if substantive deviations from protocol and affect rights and welfare of subjects, safety of subjects, their willingness to continue in study or the integrity of the research data.
- Never: if they do not affect any of the above.

**Adverse Events**
- Promptly **: if unanticipated, related and involving risk to participant or others or if happening at increased frequency, duration or intensity that previously anticipated.
- Periodically ***: if related to study participation.
- Never: If not related to study participation.

**Deaths**
- Promptly **: if related to study participation.
- Periodically ***: If not related to study participation.

**Non-Compliance**
- Promptly **: The CoRe team will make a determination if it is possibly serious and/or continuing; if so, Committee Q will review.

(*) This applies to internal events, and external events from sites of Emory sponsor-investigator studies.
(**) Promptly: 10 business days from the date the PI first learn about the event
(***) Periodically: at continuing review
This guidance does not apply to VA studies.
SPONSOR REPORTING REQUIREMENTS
Sponsors want to receive reports of protocol deviations and SAEs, but that does not mean you need to report these to the IRB.

Sometimes sponsors want you to report an event to the IRB, even if it is not reportable

- What to do? Check your protocol and contract. If required, you have to report
- What would the IRB do? We will review it and acknowledge it for your records
REVISED IRB PROCEDURE
REVISED IRB PROCEDURE: FOR 2 OR MORE STUDIES USING SAME DRUG

When a RE is submitted, the IRB staff will run a report to check if any other submitted study is using the same drug. If the Full Board makes a determination of an UP, the PIs on these studies may be required to add the event to the ICF and reconsent subjects.

**Why is the IRB doing this?** Because an UP determination implies a new risk subjects should know about.

**How would this affect my study?** The majority of studies should have (or soon will receive) a report with the same information. This should not negatively affect study teams since they are required to submit potential UPs to the IRB.
IRB RESOURCES

Emory (Non-VA) Guidance and Forms

Start here:
Reporting Obligations for Investigators (ver. 2-14-14) - What you need to know about what to report and when, including:

- Internal and External Unanticipated Problems, Serious Adverse Events, and Deaths
- Protocol Deviations (only internal ones are reportable)
- Noncompliance with laws, regulations, Emory HRPP policies and procedures, or the requirements of the IRB

Timeframes for Reporting Adverse Events, Protocol Deviations, and UPs (ver. 2-14-14) - At-A-Glance one page chart. Note: Noncompliance is always promptly reportable, but feel free to check with the IRB if unsure whether your situation meets the definition of noncompliance

Tools for helping to document and assess events and deviations:
Assessment Form for Events (Internal/External) (ver. 7-18-14)
Assessment Form for Non-Emory Sites Under Emory Sponsor Oversight (ver. 4-28-15)
Assessment Form for Protocol Deviations (ver. 11-3-11)
Root Cause Analysis Worksheet (ver. 11-23-10)
Continuing Review - A Sample Summary of Events (ver. 8-7-2015)

Other Guidance:
Guidance for Submitting Multiple Events at One Time (ver. 11-14-14)
Guidance on How IRB Makes Determinations of Serious or Continuing Noncompliance and UPs (ver. 1-20-15)
CONTACT THE QA AND EDUCATION TEAM

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QUESTIONS TO REVIEW
YOUR QUESTIONS?
SOP Updates

Tatiana Kurilo, MPH, CCRC
Quality Management and Education
Outline

• **SOP 2.1** Obtaining Informed Consent for Greater than Minimal Risk Interventional Clinical Trials
  * Change to Reconsent section
• **SOP 7.6** Study Calendars and Case Report Forms
• **Change to REMS** Procedure for Prescriber/Non-Prescriber Responsibilities

Effective September 24, 2015!

• Change to Pregnancy test verification
  Now in effect
2.1 Obtaining Informed Consent for Greater than Minimal Risk Interventional Clinical Trials

- The investigator or sub-investigator on DOA and when required on the 1572 **will have the initial discussion** about the study, answer questions, and **document** this discussion in the record.

- The investigator may obtain consent or **may delegate obtaining informed consent** to another designated licensed professional who delegated this task **on DOA log**.

- The physician-investigator or consenting licensed professional shall complete and sign the Informed Consent Documentation.
2.1 Obtaining Informed Consent for Greater than Minimal Risk Interventional Clinical Trials

**RECONSENT ONLY**

- The investigator or sub-investigator on DOA and when required on the 1572 will have the initial discussion about the study, answer questions, and document this discussion in the record **OR**

- If the changes to the trial **DO NOT change the risk**, then reconsent can be obtained by a designated licensed professional such as, NP, PA, CRN, RN, LCSW, or a physician-investigator. Individuals who obtain consent will be delegated this task on the DOA log and, when required, listed on the investigator agreement or Form FDA 1572

- The consenting licensed professional shall complete and sign the Informed Consent Documentation
2.1 Obtaining Informed Consent for Greater than Minimal Risk Interventional Clinical Trials

The investigator may delegate obtaining informed consent to another designated licensed professional who is delegated this task on DOA log:

- Medical Doctor (MD)
- Pharmacy Doctor (PharmD)
- Nurse Practitioner (NP)
- Physician’s Assistant (PA)
- Clinical Research Nurse (CRN)
- Registered Nurse (RN)
- Licensed Clinical Social Worker (LCSW)
7.6 Study Calendars and Case Report Forms

• **Purpose:** To define the process for creating and releasing case report forms (CRFs) and study calendars

**Scope:** All investigators and staff involved in conducting Winship clinical trials using OnCore®-based Case Report Forms (CRFs)
7.6 Study Calendars and Case Report Forms. Cont.

- The PI or Team Lead will email IT Analyst to notify them if they want a calendar for the study.
- CRFs will be designed during protocol development.
- IT Analyst will create and review with CRC/CRN the calendar and CRFs in the OnCore® test environment.
- CRC/CRN will test the calendar and CRFs in the test environment.
- CRC/CRN will review the calendar and CRFs with the sponsor/S-I, Biostatistician (if applicable) and Team Lead.
7.6 Study Calendars and Case Report Forms. Cont.

- If revisions are needed, the CRC/CRN will discuss and review the changes needed with IT Analyst.
- IT Analyst will meet with the study team at the activation meeting and sign-offs will be completed by the CRC/CRN, Biostatistician (if applicable) and sponsor/S-I via OnCore®.
- The calendar and CRFs are then released.
- Official and approved CRFs will be available to all staff in Oncore® and Oncore® will be the designated document storage site.
REMS Procedure

• POMALYST® (pomalidomide) was added to REMS procedure and forms

• **General Information:** To avoid embryo-fetal exposure, Risk Evaluation and Mitigation Strategy (REMS) programs are mandatory for the Celgene products REVLIMID® (lenalidomide) and POMALYST® (pomalidomide)

• Only certified prescribers can prescribe Revlimid and Pomalist

• Only certified pharmacies can dispense Revlimid and Pomalist in the REMS program

• In order to receive Revlimid and/or Pomalist, all subjects must be enrolled in the REMS program and agree to comply with the requirements of the REMS program
Pregnancy Test verification for Research Orders

Only **Licensed** medical professionals are allowed to sign off the pregnancy test verification

- Medical Doctor (MD)
- Clinical Research Nurse (CRN)
- Registered Nurse (RN)
- Advanced Practice Providers (APP), such as, Nurse Practitioner (NP) or Physician's Assistant (PA)

Is patient of child bearing potential? Yes☐ No☐

If yes, pregnancy test deemed to be negative Yes☐ No☐

Confirmed by MD/RN/APP Initial __________Date________
Important Reminders

• All SOPs are available:
  – In the CTO
  – At each Winship site
  – On the **Winship intranet under Clinical Trials**
    https://apps.winship.emory.edu/intranet/clinicaltrials/index.php

• The Monthly Protocol Card is now available on the Winship intranet under Clinical Trials
Questions?