Reporting to the IRB
How to Report the Essentials and Improve the Protection of Human Subjects
April 10, 2013

Presented by:
James MacFarlane
Director of Board Operations
About the Webinar

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Established in 1983
US and Canadian boards fully accredited by the Association for the Accreditation of Human Research Protection Programs (AAHRPP)
Superior audit history with FDA—five consecutive audits with no findings.
21 CFR Part 11 compliant electronic systems
Compliant with FDA and OHRP requirements
About Schulman Associates IRB

- Full board meetings **five days a week**
- Dedicated **daily expedited review** of qualifying minimal risk protocols
- **Phase I Board** with streamlined processes tailored to Phase I timelines
- **Oncology Review Board** for all phases of oncology research
- Customized services for **institutions and AMCs**
- Experienced primary points of contact for sponsors, CROs, institutions and sites
About Today’s Presenter

James MacFarlane, BS, CIP
Director of Board Services

- BS in History of Science and Medicine from Northern Kentucky University
- With Schulman since 2008
- Responsible for direct support of board operations, including IRB liaison for informed consent development, safety reporting, and study change management
- Member of PRIM&R and Mensa
In this presentation, we’ll discuss:

- Why we’re required to report to the IRB
- What should be reported to the IRB
- The definitions of Serious or Continuing Noncompliance and Unanticipated Problems
- How to determine whether an event is reportable
Why Report to the IRB?

- CFR 21 and Common Rule requirements
- A different perspective
- The IRB is your partner in human subjects protection
  - The sharing of information allows for a relationship between investigators and the IRB that protects the rights and welfare of subjects, and ensures the integrity of the study data.
What Happens After I Submit to the IRB?

- Each IRB has its own reporting requirements and different processes for reviewing submissions.
- At Schulman, all reports of a potential noncompliance event or Unanticipated Problem are routed and processed by a dedicated team.
- If the event appears to create risk for the subject or others, it is forwarded for review by the full Board.
- As required by 21 CFR 56.108 and the Common Rule, the Board will report any events determined to be serious/continuing noncompliance or an Unanticipated Problem to the appropriate regulatory authority.
Reporting to the IRB: the Impact of Under & Over Reporting

**Under-reporting**
- Safety impact
- Regulatory trouble
- Quality impact

**Over-reporting**
- Impedes subject safety (needle in a haystack)
- Negatively impacts turnaround time
Why Not Report Everything?

Noncompliance Case Study

• A central IRB receives 50,000 deviations in a given year.
• Of these, 103 are found to be serious or continuing.
• Thus, .002% were reported by the IRB to the appropriate regulatory agency.
• Did the other 99.998% of the deviations reported that year help or hinder the protection of human subjects?
Why Not Report Everything?

- Adverse Events
  - The IRB does not have the full aggregate data available to the sponsor.
  - Per 2009 FDA Guidance:
    - Only events that meet the criteria for an Unanticipated problem Involving Risks to Human Subject or Others must be reported to the IRB.
What to Report

- Unanticipated Problems Involving Risks to Human Subject or Others (UP)
  - May include:
    - SAR (suspected adverse reaction)
    - UAE (unexpected adverse event)
    - USAR (unexpected suspected adverse reaction)
    - SAE (serious adverse event)
    - SSAR (suspected serious adverse event)
    - SUSAR (serious unexpected suspected adverse reaction)
    - Miscellaneous (Stolen laptop, etc.)
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<th>FDA</th>
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| • Unexpected  
• Serious  
• Would have implications for the conduct of the study (revision to protocol, IC, IB). | • Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;  
• Related or possibly related to participation in the research (in this guidance document, possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and  
• Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized. |
A subject develops Reversible Posterior Leukoencephalopathy Syndrome (RPLS) while participating in a lupus study. RPLS is not noted in the IB, IC, or protocol. The subject had no known signs or symptoms of RPLS before study participation.
Unanticipated Problems
Example: Reportable Event?

Criteria for Unanticipated Problem:
• Unexpected
• Serious
• Would have implications for the conduct of the study

A subject becomes hypertensive immediately following IV study drug dosing, and is hospitalized. The PI suggests that the reaction is directly related to the infusion. Hypertension is noted as a potential side affect in the IB.
80% of the subjects at site X become hypertensive immediately following IV study drug infusion, and are hospitalized. The PI suggests that the reaction is directly related to the infusion. Hypertension is noted in the IB with an occurrence rate of 7%.
What to Report

- Serious or Continuing Noncompliance
  - Not defined in CFR
  - As defined by Schulman:
    - **Serious Noncompliance** — An event that has a severe, negative affect on subject safety or study integrity that occurs as a result of negligence, misconduct, or violation of the protocol, GCP, or Board requirements.
    - **Continuing Noncompliance** — A pattern of events that affect the safety of the study subjects or study integrity, likely to continue without intervention.
Serious and Continuing Noncompliance: Example of a Reportable Event?

A study coordinator manipulates data in order to avoid exclusion criteria and enroll subjects who should not be included in the research.

Criteria for Serious or Continuing Noncompliance:

**Serious Noncompliance** – Severe, negative affect on subject safety or study integrity that occurs as a result of negligence, misconduct, or violation of the protocol, GCP, or Board requirements.

**Continuing Noncompliance** – A pattern of events that affect the safety of the study subjects or study integrity, likely to continue without intervention.
Serious and Continuing Noncompliance: Example of a Reportable Event?

Over the course of 18 months, a site reports 15 instances of subject mis-dosing.

Criteria for Serious or Continuing Noncompliance:

**Serious Noncompliance** – Severe, negative affect on subject safety or study integrity that occurs as a result of negligence, misconduct, or violation of the protocol, GCP, or Board requirements.

**Continuing Noncompliance** – A pattern of events that affect the safety of the study subjects or study integrity, likely to continue without intervention.
A man goes to his Primary Care Physician for a flu shot, and the staff inadvertently give him an injection of study drug.
Conclusion

- Responsible, thoughtful reporting allows for more meaningful IRB oversight and improved human subject protections.
- A clear understanding of regulatory guidance regarding UPs and Serious/Continuing Noncompliance is necessary to help investigators make meaningful decisions when reporting events to the IRB.
- It’s the investigators responsibility to determine whether something should be reported—they’re the ones best suited to make this decision.
- Over-reporting can overwhelm an IRB’s resources to properly oversee human subject protections.
- Under-reporting leads to regulatory trouble and can negatively impact human subject protections and study data.
To submit your questions, please use the in-webinar chat tool or email webinar@sairb.com
Thank You!

- We hope you found today’s webinar informative and useful.
- Please complete our survey to provide feedback on this session.
- In the survey, you can also request a certificate of attendance for this event.
- Stay tuned for more information on our next webinar: IRB Considerations in Phase I Research
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