Improving the System of Reporting and Interpreting Unexpected Serious Adverse Events to Investigators Conducting Research Under an IND

A project of the Clinical Trials Transformation Initiative
Background

- Investigators conducting research under an IND have voiced concerns over current approaches to notifying them of unexpected and serious adverse events (SAE)
- Current regulations* (21 CFR 312.32) require IND sponsors to notify investigators of all unexpected SAEs associated with the drug
- Common practice is to provide all unexpected (per investigators’ brochure) SAEs as individual expedited reports
  - Contextualizing unexpected SAE difficult across indications and regimens

* Prior to new premarket safety regulations effective March 2011
Background (continued)

- Result: significant investigator investment of time for little-to-no gain in understanding risk-benefit of investigational product
  - Process can distract investigators from direct care of study participants and more meaningful communication of safety data
- FDA Guidance addresses similar issue for IRBs, but no corresponding guidance exists for investigators’ safety notifications
Goals

- Generate empirical evidence about the current U.S. system for reporting unexpected serious adverse events to investigators conducting research under an investigational new drug application

- Consider potential modifications of the current system to more efficiently and effectively inform investigators of these events
Specific Objectives

1. Document the current range of practices for safety monitoring and reporting of unexpected SAEs to investigators (Workstream 1)

2. Quantify resources required to manage individual expedited safety reports and assess investigators’ perceptions regarding the value of this information (Workstream 2)

3. Compare current practice of submitting individual unexpected SAEs with an alternative approach based on the European Commission's guidance (Workstream 3)
Specific Objectives

4. Explore patients' expectations for how investigators should monitor and communicate information about product safety during the conduct of a clinical trial, and explore current practice on how safety monitoring efforts are being conveyed to research participants in the informed consent document (Workstream 4)

5. Integrate results of all workstreams and recommend ways to optimize reporting of SAEs to investigators while ensuring human subjects protection (Workstream 5)
Organization of Project

Project Managers

Cheri Janning
Sr Clinical Project Manager
Duke University

Greg Nadzan
Project Manager
Amgen, Inc.

Jose Vega
Amgen Co Team Leader

Kathleen Uhl
FDA Co Team Leader

Susan Ellenberg
Univ. of Pennsylvania Co Team Leader

Sundeep Sethi
Amgen Workstream 1 Lead

Howard Greenberg
ACCP/Clinilabs Workstream 2 Lead

Lynda Szczech
Duke Clinical Research Institute Workstream 3 Lead

Kevin Weinfurt
Duke Clinical Research Institute Workstream 4 Lead

Robert Califf
Duke Translational Medicine Institute Workstream 5 Lead

Workstream 1 Team

Workstream 2 Team

Workstream 3 Team

Workstream 4 Team

Workstream 5 Team
## Workstream 1 Team

- Philippe Bishop (Roche)
- Dorothy DiChristofano (Sanofi-Aventis)
- Leann Fieldstad (Roche)
- Suzanne Gagnon (ICON Clinical Research)
- Greg Hockel (PharmaNet)
- Anne Meeker-O’Connell (FDA)
- Greg Nadzan (Amgen)
- Diane Ryan (Pfizer)
- Sundeep Sethi – **Workstream Lead** (Amgen)
- Jennifer Sorgen (Pfizer)
- Jose Vega (Amgen)
Workstream 2 Team

- Susan Ellenberg (UPenn)
- Howard Greenberg – Workstream Lead (ACCP / Clinilabs)
- Greg Hockel (PharmaNet)
- Kevin Jones (Accurate Clinical Trials)
- Greg Nadzan (Amgen)
- Janet Norden (FDA)
- Diane Ryan (Pfizer)
- Miklos Salgo (Roche)
- Sundeep Sethi (Amgen)
- Lynda Szczech (Duke)
- David Vock (Duke)
Workstream 3 Team

- Suzanne Gagnon  (ICON Clinical Research)
- Heather Macy  (Pfizer)
- Rachpal Malhotra  (Bristol-Myers Squibb)
- Margaret McLaughlin  (Pfizer)
- Greg Nadzan  (Amgen)
- Leonard Sacks  (FDA)
- Sundeep Sethi  (Amgen)
- Lynda Szczech – Workstream Lead  (Duke)
- Jose Vega  (Amgen)
Workstream 4 Team

- Kathryn Flynn (Duke)
- Kevin Weinfurt – Workstream Lead (Duke)
Workstream 5 Team

- Robert Califf (Workstream Lead)
- Susan Ellenberg
- Howard Greenberg
- Judith Kramer
- Janet Norden
- Sundeep Sethi
- Kathleen Uhl
- Jose Vega
Objectives of October 3\textsuperscript{rd}/4\textsuperscript{th} meeting (see Agenda)

- Discuss and integrate empirical findings from all components of this project
- Consider implications of the US FDA’s new premarket safety regulations
- Develop a set of recommendations for optimal reporting of unexpected serious adverse events to investigators that will improve human subjects’ protection