# PharPoint Research Announces Target SAE System Initiative

## Response to FDA's Final Rule Amending IND Safety Reporting Requirements

On September 29, 2010, FDA published a Final Rule amending the IND safety reporting requirements under 21 CFR part 312. The new requirements clearly describe circumstances in which adverse event reports should be aggregated and compared to a control group in a systematic analysis. The effective date for the Final Rule has been extended to September 28, 2011.

The FDA noted that the new requirements should increase the likelihood that submitted information will be interpretable and will meaningfully contribute to the developing safety profile of investigational drugs and improve the overall quality of safety reporting.

The new requirements specify reporting certain adverse events in the aggregate rather than individual cases (as has been the practice) and FDA notes that it will be important for sponsors to have in place a systematic approach to safety surveillance during product development that includes a process for evaluating accumulating safety data.

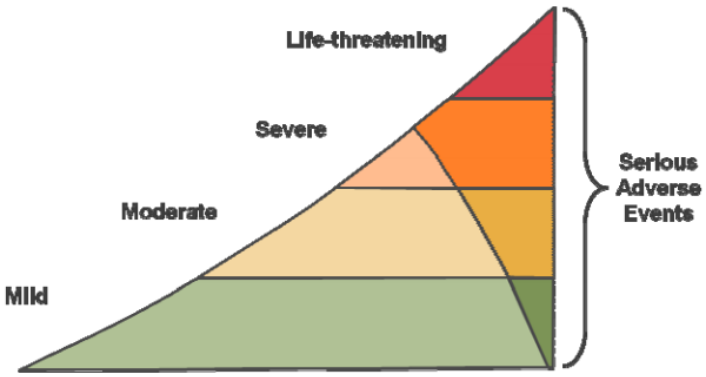
The Final Rule includes guidelines that aggregate analysis of specific events will occur [21 CFR 312.32 (c)(1)(i)(C)]. The Final Rule states: "At appropriate intervals, the numbers of such events in each arm of a controlled study should be compared and reported to FDA expeditiously as an IND safety report if there is an imbalance between arms suggesting there is a reasonable possibility that the drug caused the adverse event." Moreover, the guidance recommends that safety surveillance for ongoing clinical trials employ a systematic approach. "Such an approach should include a process for reviewing, evaluating and managing accumulating safety data from the entire clinical trial database at appropriate intervals."

## PharPoint's Rationale for the Creation of Target SAE System

PharPoint is a provider of data management and biostatistical services to a growing segment of the pharmaceutical industry – including smaller to medium-sized companies that have chosen to strategically out-source these key components of drug development. In this role, PharPoint routinely collects and analyzes non-serious adverse event data from clinical trials. Non-serious adverse event data are distinguished from serious adverse events (SAEs) in that prompt or expedited reporting of individual non-serious adverse events has not been required by FDA regulations.

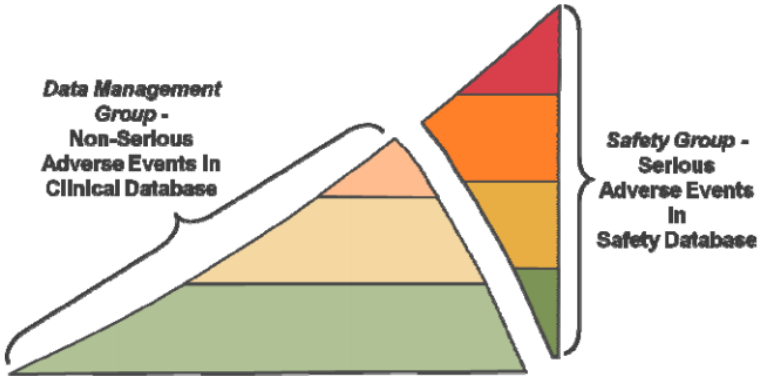
The continuum of clinical trial adverse events in any given clinical trial is depicted in Figure 1 below. Adverse events are categorized as to severity as mild, moderate, or severe. As illustrated, some adverse events are severe in intensity but do not meet regulatory criteria for serious adverse events, and some events of mild severity may, in fact, meet serious criteria as specified by 21 CFR 312.32.

**Figure 1. The Continuum of Adverse Events in a Clinical Trial**




Traditionally, PharPoint has provided data management services and creates databases for non-serious adverse events, but many sponsors have either relied on independent contractors or in-house personnel to receive reports of serious adverse events and populate a database for SAEs. This process results in separation of the complete safety data from a clinical trial as illustrated by Figure 2 below. The result is two separate and independent databases that are maintained by two different groups of personnel. Thus, the totality of the safety data may not be effectively reviewed until well after the clinical trial has ended. There could be a delay in identification of important safety signals that may emerge during a clinical trial.

**Figure 2. Separation of Non-Serious and Serious Adverse Event Databases**

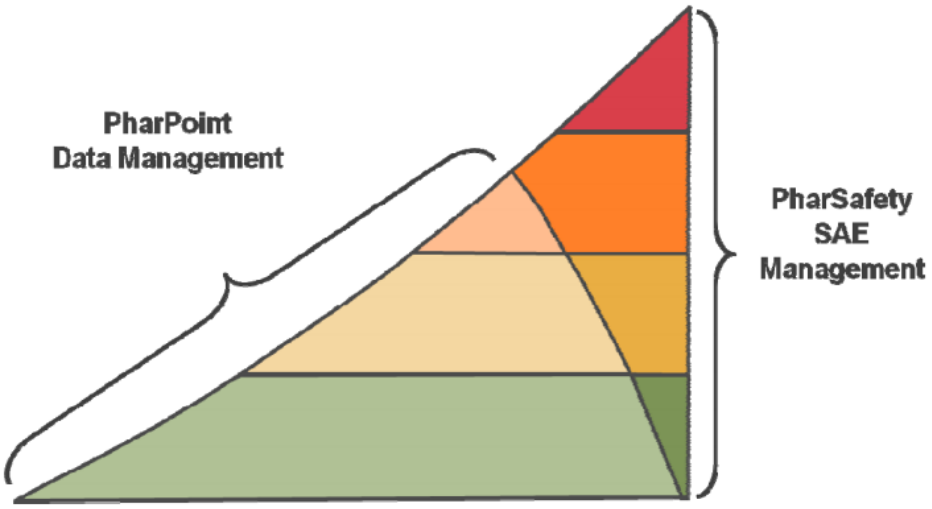



When separate safety databases are created by this process, it is difficult, if not impossible, for sponsors to comply with the FDA Final Rule requiring aggregate analysis of non-serious and serious adverse events at periodic intervals during conduct of a trial.

## The PharPoint Target SAE System Solution

PharPoint's response to the FDA Final Rule is to provide an integrated safety database to be known as Target SAE System that contains both non-serious and serious adverse events. The Target SAE System may be used to conduct periodic aggregate analysis of events to satisfy the requirements of the FDA Final Rule and to enable accurate safety event analyses for Investigator Brochure updates. Target SAE System is depicted in Figure 3 below.

**Figure 3. The PharPoint Target SAE System**




In summary, PharPoint's safety data management and analysis services now include:

- Analyses of frequency of events (both non-serious and serious events):
    - Periodically during conduct of a trial, i.e. 3-monthly
    - At conclusion of trial
- Identification of events which may justify Expedited Safety Reports on basis of frequency (by comparison among dose levels or with comparator drugs)
- Provision of safety data to Data Monitoring Boards and for preparation of Investigator Brochure revisions