IND Safety Reporting: final results and best practices from the Clinical Trials Transformation Initiative IND Safety Advancement Project

BACKGROUND

The US FDA published a “final rule,” clarifying the reporting requirements for serious and unexpected adverse drug reactions. The Clinical Trials Transformation Initiative (CTTI) formed a work group to address the challenges associated with safety reporting. The first project developed recommendations that outlined an approach to transforming safety reporting practice and stressed the importance of understanding the context of safety reporting. The next phase involved testing the model through interviews and surveys to understand the current environment and the challenges sponsors face implementing the final rule. The CTTI IND Safety and Safety Advancement Project teams have conducted in-depth interviews and surveys of sponsors and investigators to understand the impact of the final rule and gather best practices. The CTTI websites contains detailed reports from these efforts. These groups are the first to study safety reporting and to identify tools and materials for the benefit of the industry.

RESULTS

Sponsor respondents were large and small companies, with diverse, active portfolios (median 30 current trials, 31-50 in the last 5 years). Interviews included both companies and investigator studies. The interviews focused on understanding how sponsors managed safety reporting in Phase 1-4, including regulatory considerations, concerns about public disclosure, and fear of regulatory repercussions, which results in a “conservative” approach to reporting. Results show that most companies believe the rule is reasonable and can reduce the number of reports. In a similar vein, investigators still make many reports causally related and sponsors may not agree. Investigator views differ by site and sometimes substantially. More popular safety systems can route reports based on reporting rules to recognize the most common event combinations.

METHODS

Gathering data:

– 68 respondents, 32 in-depth (1:1 interviews) and 36 online surveys-
– 32 of 54 respondents offered a survey respondent ID number, but not many by sponsor (i.e., may be interpreted as the sponsor “hiding” events)
– Additional direct interaction with the FDA to clarify nuances of the final rule
– Initial results from a 4-month pilot project to test a new system for reporting adverse drug reactions

Figure 5. Impact on the marketplace perception of uninformative safety reports

Perceived over the last year in Phase 3/4 of active IND trials

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<th>PHASE OF TRIAL</th>
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<th>LESS USEFUL</th>
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Figure 6. Summary of Expressions Perceptions

- Benefits of the final rule: more useful reporting in Phase 3/4 of active IND trials
- Challenges of the final rule: increased numbers of Medical Safety Review physicians, organized into review teams
- Impact of the final rule: increased numbers of Medical Safety Review physicians, organized into review teams
- Conclusion: the final rule is reasonable and can reduce the number of reports.