



Safety Monitoring and Evaluation in Late Phase Clinical Development

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Regulatory agencies have shown increasing concern about potential, specific (usually rare) safety signals during clinical drug development. Entire classes of drugs have been placed on clinical hold because of such concerns, with regulators requiring safety monitoring rules for reducing patient risk in ongoing development programs as a pre-condition for lifting the clinical hold. Multiplicity issues arise naturally in this context, both from the repeated looks into accumulating, unblinded data, but also due to the various studies included in a program. From a regulatory perspective, the associated false positive rate is less of a concern, but from the sponsor point-of-view it can make investing in the development program unfeasible. This talk will describe the experience of developing a safety alert rule in a late phase clinical development program, presenting different alternatives considered and their respective operating characteristics at the trial and program levels. More generally, the issue of safety signal detection vs. demonstrating lack of a clinically relevant safety signal will be discussed in the context of safety monitoring strategies to achieve a balance between protecting patients and keeping drug development economically viable.

Keywords: Adverse events, detection of safety signal, false positive, safety alert rules.