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The Tranquil World of IND Safety Reports

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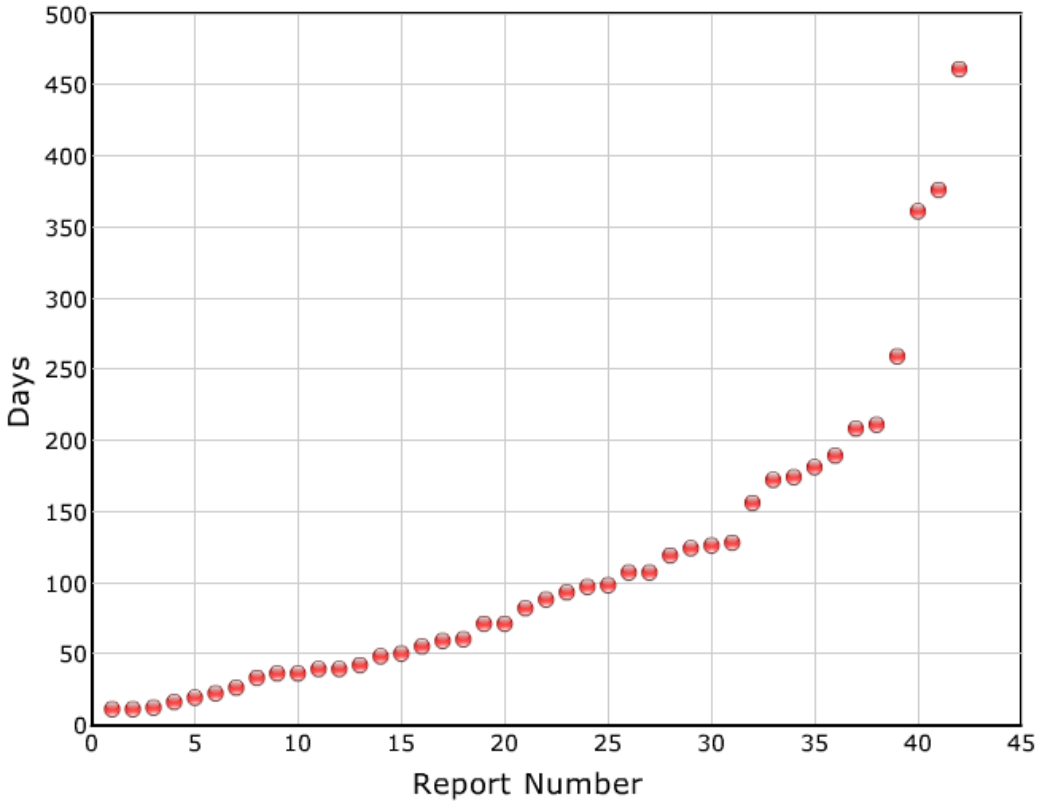
Federal regulations (21 CFR §312.32) require clinical trial sponsors to "notify FDA and all participating investigators in a written IND safety report of… any adverse experience [event] associated with the use of the [study] drug that is both serious and unexpected." If the experience is (a) unexpected and (b) fatal or life-threatening, the regulations require notification of the FDA "as soon as possible but in no event later than 7 calendar days after sponsor's initial receipt of the information." Although the regulations do not require sending IND safety reports to institutional review boards (IRBs), IRBs require that reporting from the sponsor or the investigator.

The regulations do not set forth a time period for reporting serious and unexpected adverse events to investigators. Nor do they set forth a time period for reporting less serious adverse events. Nevertheless, if the information is worth reporting at all, some level of timeliness is appropriate.

An independent (central) IRB provided data on a sample of 42 initial IND safety reports that it received in 2006-2007. Ten sponsors of 20 Phase II and Phase III drug studies generated the safety reports. No single study generated a significant number of the reports. Sponsors normally send IND safety reports directly to independent study IRBs, as well as to the investigators. IND safety reports to local (institutional) IRBs are normally relayed through the investigators.

Figure 1. IND Safety Report Time from Event to IRB Receipt



In these 42 reports, the median time period from adverse event to IRB receipt was 85 days, with a range from 11 to 461 days. It is hoped that any reports of unexpected fatal or life-threatening events were among the seven (17%) received within one month of the event. Figure 1 shows the timing distribution.

Distracted turtles could deliver some of these reports more quickly than evidenced by these data. If we expect IRBs to take seriously their responsibility to review and evaluate IND safety reports, we need to take seriously our responsibility to deliver them in a timely manner.

Notes

This article does not analyze how long it takes reports to travel from investigator to sponsor, from sponsor to investigator (and/or IRB), and (if necessary) from investigator to IRB. Nor does it consider the trivial significance or vast number of often redundant reports that ooze like sludge through the "system." Nor does it consider what the recipients actually do with the reports, if anything.

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