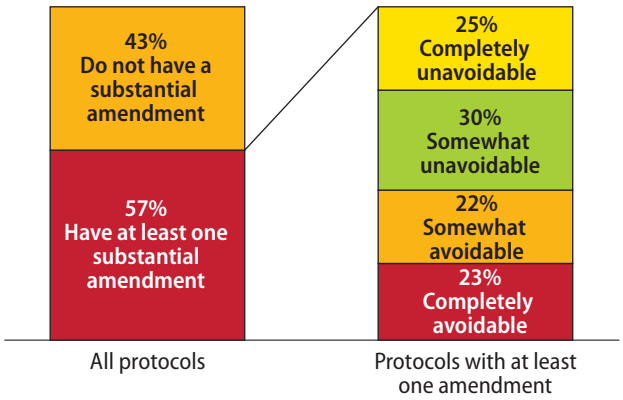
Facing protocol amendments head-on

Cycle time and cost impact shining light on avoidable amendments

The unplanned costs and delays associated with protocol amendments have prompted many sponsor companies to identify new approaches to simplify protocol designs and reduce the frequency of protocol amendments over the course of the past few years. Yet a new Tufts Center for the Study of Drug Development (CSDD) analysis found that the majority of protocols still require substantial amendments, which led to significantly longer clinical trial cycle times and higher costs.

Prevalence and avoidability of amendments



Source: Tufts CSDD, 2016 <csdd.tufts.edu>

The new analysis builds on a 2010 Tufts CSDD study that, for the first time, quantified the prevalence and causes of protocol amendments. It found that 57% of protocols had at least one substantial amendment and nearly half (45%) of these amendments could have been avoided, compared to 33% in 2010. About one in four (23%) amendments were implemented before the first patient was dosed.

On average, clinical trials with at least one substantial protocol amendment took three months longer to complete than those without an amendment. Overall, the Tufts CSDD estimates protocol amendments cost the industry a total of $20 billion a year in direct and indirect costs.

"It's a call to action," said Rob DiCicco, Pharm.D., vice president of Clinical Innovation and Digital Platforms at GlaxoSmithKline (GSK). "It may be that different initiatives that companies started a few years ago aren't reflected in the data or that the problem is getting worse because of a variety of factors, including protocol complexity. Either way, there is a massive opportunity for improvement."

The peer-reviewed study findings, published in the journal *Therapeutic Innovation & Regulatory Science*, link protocol amendments to performance measures for the first time and offer opportunities for companies to better understand the impact of major changes to finalized protocols.

In the following, CenterWatch looks at highlights from the new Tufts CSDD study and initiatives at forward-looking companies—including Amgen, Pfizer, GSK, Eli Lilly and Parexel—that are designed to improve the quality of study design, reduce the frequency of protocol amendments and better inform the decision-making processes.

Amendments impact performance and cost

The 2015 Tufts CSDD study, which was based on data from 836 protocols provided by 15 large and mid-sized pharmaceutical and biotechnology companies and CROs, found small signs of improvement in reducing protocol amendments compared to the 2010 study, but the frequency of substantial amendments remained high. The study defined "substantial amendment" as any change to a protocol on a global level requiring approval both internally and from a review board or regulatory authority.

The incidence of amendments in the 2015 study (57%) was below that observed in the Tufts CSDD 2010