

Rules and reasons

By Samuel Finlayson, M.D.

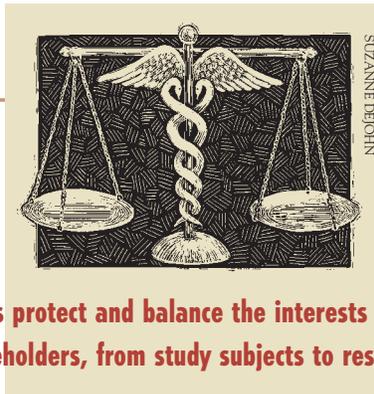
Now more than ever, clinical research is conducted in the context of extensive regulation. Investigators may lament the administrative and regulatory hurdles they face, but most would agree that regulation, while sometimes onerous, serves an important purpose. Regulators—at government agencies, research institutions, and professional associations—protect and balance the interests of a variety of stakeholders, from study subjects and the public to researchers and health-care institutions.

The effects of regulation are incredibly complex, for better and for worse. On the one hand, regulations, policies, and guidelines protect those involved in research and can even benefit investigators and institutions. On the other hand, regulations can limit the scope of research, create piles of paperwork, run up the cost of research, and foster a culture of administrative timidity.

Beneficial: Regulations can be beneficial to clinical investigators in several ways. First, they can help identify possible problems with a study early on. For example, the requirements of internal review boards (IRBs), institutional committees that oversee biomedical research, force investigators to thoroughly consider all potential risks of their proposed research before the project is initiated. Second, investigators benefit from the protection that internal review and data safety monitoring provides. If something untoward occurs, investigators have some degree of assurance that they were not alone in having failed to anticipate such an outcome. Third, regulations provide clear guidance on such matters as privacy and conflicts of interest.

Institutions can also benefit from regulations. In a competitive research environment, uniform standards level the playing field, removing the temptation to take shortcuts or to allow research to proceed less thoughtfully (and perhaps less ethically) than it should. When a research institution complies with guidelines and protocols, it is better able to ensure the proper conduct of clinical research within its walls, and it is better protected from allegations of inadequate oversight—which could threaten its ability to attract funding, hire faculty, or forge research collaborations.

Lamented: The negative effects of regulation are easily identified, too, and commonly lamented by clinical investigators. The most obvious downside is the frustration that accompanies the tangle of administrative hoops through which investigators must jump. The number of reviews, approvals, and signatures required can be demoralizing and can significantly delay a clinical research project. Once underway, a study that involves human subjects faces ongoing regulatory requirements, including IRB reviews and approvals for even minuscule



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changes in a protocol. To some degree, the regulatory environment suffers from a one-size-fits-all mentality, wherein controls and safeguards are implemented with the same rigor for benign interventions as they are for potentially harmful interventions.

Regulations also add to the expense of clinical research. In addition to high IRB fees—payments that cover the cost to the institution of running IRBs—clinical investigators must pay for additional administrative support to process approvals, maintain records in accordance with specific requirements, and communicate with institutional regulatory offices and external funding organizations. The amount of administrative work involved in conducting clinical research has spawned a third-party for-profit industry focused on navigating these daunting regulatory, legal, and administrative seas. This further increases the costs of conducting clinical research. Because health-care research dollars are limited, higher per-project costs result in fewer projects being funded.

In addition to these quantifiable problems, regulations have several intangible negative effects. Strict regulatory requirements can make investigators reluctant to pursue certain questions. Regulations can also make institutional administrators reluctant to act (or not act) for fear of censure from regulatory agencies.

Confusion: Ironically, tight regulatory control can engender confusion between what is ethical and what is legal, which can translate into intolerance of harmless mistakes but a willingness to overlook ethical missteps that do not violate a specific rule. When one is swamped in regulations, there is a natural tendency to forget that the rules are intended to approximate moral conduct, not define moral conduct, and that something may be permissible but still wrong. Even when detailed regulations and protocols are in place, there are always discretionary decisions—judgment calls, such as the inclusion or exclusion of a subject—that can be nudged by the investigator in one direction or the other. Sometimes a focus on just following the rules can result in a distraction from the greater moral obligation to produce results reflective of scientific truth.

In summary, regulation of clinical research involves a complex interplay of public opinion, government, research institutions, professional organizations, and individual investigators. The resulting regulatory environment safeguards research subjects and provides important benefits to other stakeholders as well. However, it also creates barriers to the timely and efficient conduct of clinical research, giving rise to fears that such research in coming years will increasingly be exported to countries that do not provide a high level of oversight. Clearly, our challenge is to unburden the U.S. research apparatus by streamlining regulatory controls, while maintaining effective safeguards for researchers, institutions, patients, and the public. ■

The Grand Rounds essay offers insight or opinion from a member of the DMS faculty. Finlayson is an associate professor of surgery and of community and family medicine.