

WASHINGTON REPORT

COLLABORATION AND
TRANSPARENCY KEY TO MORE
EFFECTIVE CLINICAL RESEARCH

Much of the credit for improving the quality and efficiency of clinical trials in recent years goes to joint reform initiatives and greater disclosure of regulatory decisions and study results. Bioresearch sponsors are listing more studies on the ClinicalTrials.gov website, although the record is weaker for timely disclosure of research results for newly approved medical products. Under pressure to share more research data to avoid repeated errors and waste, biopharma companies also are providing qualified experts with access to confidential studies. And some sponsors are pledging to publish new research reports only in open access journals.

Leaders of the biomedical research community support these and other changes promoted by the Clinical Trials Transformative Initiative (CTTI), including expanded use of registries, adoption of a "single IRB of record" for multicenter trials, a more effective informed consent process, and rational use of study monitors and data monitoring committees. The group also works to improve investigator training, encourage pediatric studies for antibacterial medicines, and promote effective patient engagement in clinical trial design and implementation.

These achievements were noted at a February meeting marking the 10th anniversary of the CTTI public-private partnership established by FDA and Duke University. The partners sought to modify the rules and practices that were making clinical trials increasingly expensive, complex, irrelevant, and unattrac-

ive to potential investigators. Robert Temple, deputy director of the Center for Drug Evaluation and Research (CDER), described progress in promoting a "quality by design" (QbD) approach to developing and launching clinical trials. This project encourages analyzing the purpose and requirements of a protocol to inform the choice of population, sample size, inclusion/exclusion criteria, data collection, procedures, assays, and endpoints.

A notable milestone is the recent use of FDA's Sentinel Initiative database to conduct a randomized controlled trial, in this case evaluating the benefits of increased use of anticoagulant medicines by thousands of patients with atrial fibrillation (IMPACT-AFib). This exercise raises expectations of even more dramatic change in the clinical research enterprise over the next five to 10 years, according to former FDA Commissioner Robert Califf, who was previously involved with CTTI at Duke. He envisioned how greater use of big data and the digital revolution will create the long-sought "learning healthcare system" that will transform treatment and biomedical innovation and lead to more data sharing and transparency in trials.

Seeking CRLs

Such developments fit the drive to reduce the secrecy surrounding prescription drug regulation, pricing, and research findings. A main transparency issue involves greater disclosure of the status of drug applications and FDA's decision-making process, particularly the complete response letters (CRLs) the agency sends sponsors. These essentially delay or reject an application and outline

what additional clinical/manufacturing information is needed to achieve approval. When FDA approves a new drug or biologic it currently posts summaries and some data. But current rules prevent agency disclosure of information on products that fail to pass muster, and drug companies prefer that approach.

FDA Commissioner Scott Gottlieb addressed these issues at a January forum to discuss a "Blueprint for Transparency at FDA" issued in March 2017 by a group of experts organized by the Johns Hopkins Bloomberg School of Public Health (view: <http://bit.ly/2EVoXpp>). Gottlieb unveiled a new pilot to test the impact of FDA posting more detailed data from clinical study reports (CSRs) of approved drugs, asking that sponsors of nine new products voluntarily provide CSR data, protocols, and statistical analysis plans for pivotal studies. FDA also aims to better track drug studies through the R&D process by adding the ClinicalTrials.gov identifier (NCT) number to all clinical data submitted to the agency.

However, Gottlieb hedged about publishing CRLs, proposing instead to further explore FDA's authority to disclose these documents, while evaluating the feasibility of redacting and releasing a subset of CRLs that raise important public health issues. While acknowledging that some information in CRLs might enhance the appropriate use of marketed products, Gottlieb noted that redacting proprietary data from these letters is burdensome and that much of the data may not be useful.

— Jill Wechsler



FDA NOTES

The FDA recently released the following industry guidance documents:

2/23/18: Q11 Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities)—Questions and Answers

2/15/18: Amyotrophic Lateral Sclerosis: Developing Drugs for Treatment

2/15/18: Duchenne Muscular Dystrophy and Related Dystrophinopathies: Developing Drugs for Treatment

2/15/18: Migraine: Developing Drugs for Acute Treatment

The following committee meetings are scheduled for March and April:

- Peripheral and Central Nervous System Drugs Advisory Committee **April 19**
- Pediatric Advisory Committee **March 23**
- Joint Meeting: The Blood Products Advisory Committee and the Microbiology Devices Panel of the Medical Devices Advisory Committee **March 21-22**

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