MISSION POSSIBLE: Transform

The mission of the Clinical Trials Transformation Initiative (CTTI) is to identify practices that will increase the quality and efficiency of clinical trials. According to the organization, its first year was defined by great stakeholder enthusiasm, a strong organizational foundation, and rapid progress in a number of projects.

The public/private partnership began in November 2007 as a collaboration between the U.S. Food and Drug Administration and Duke University Medical Center to develop new standards and to identify new methods and technologies to improve safety, boost the quality of information derived from clinical trials, and to make the research process more efficient.

DR. JUDITH KRAMER *Duke University*

THE PURPOSE OF CTTI IS TO IDENTIFY PRACTICES THAT, IF BROADLY ADOPTED, WOULD IMPROVE THE QUALITY AS WELL AS THE EFFICIENCY OF CLINICAL TRIALS.

To date, 51 organizations have joined CTTI. Members represent all aspects of the industry — pharmaceutical, biotech, device, and clinical research organizations — the FDA and other government agencies, investigators, academia, and other stakeholders with expertise and interest in making improvements to the clinical-research enterprise. (For a full list of CTTI members, please see chart on following page.)

"The purpose of CTTI is to identify practices that, if broadly adopted, would improve the quality as well as the efficiency of clinical trials," says Judith Kramer, M.D., M.S., executive director of the CTTI and associate professor of medicine at Duke University.

Because drug development is a complex system of processes, identifying efficiencies and finding solutions to cost and quality challenges requires collaboration among all parties — clinical investigators, consumer and research participant representatives, government institutions, regulatory institutions, as well as research institutions, says Jay Siegel, M.D., group president, research and development, for biotechnology, immunology, and oncology at Johnson & Johnson. Dr. Siegel is also a member of the CTTI executive committee. (For a full list of CTTI executive committee members, please see box on following page.)

"One of the exciting things about the CTTI initiative is that it has brought together a broad range of perspectives and expertise, which I believe is a requisite to do this job appropriately," he says. "Our hypothesis is that by studying various approaches and best practices and working together with this broad-based group, including regulators and others in the clinical-trial enterprise, we stand the best chance of identifying solutions that can be implemented."

CTTI is an extension of the FDA's Critical Path Initiative, which is the agency's effort to modernize clinical trials.

"Even with significant advances to improve the productivity of clinical research, inefficiencies in the development process continue to delay patient access to important treatments," says Alberto Grignolo, Ph.D., corporate VP of Parexel Consulting and executive committee member of CTTI. "An additional consideration is that very often there is limited information on the appropriate use of approved products. Key challenges facing clinical trials today include slow start up,

the Clinical-Trial Process

INTERESTED STAKEHOLDERS ARE JOINING TOGETHER TO IDENTIFY BEST PRACTICES AND TO INCREASE THE QUALITY AND EFFICIENCY OF CLINICAL TRIALS.

paper-based execution, and high costs. Importantly, the outcomes of trials should be better able to answer critical questions with efficiency and relative certainty."

Melissa Robb, senior program management officer at the Office of Critical Path Programs, Office of the Commissioner, at the FDA, points out that the CTTI, as with the Critical Path Initiative, aims to use emerging technology and collaborative resources to increase the efficiency and quality of clinical studies.

"The goal is to answer more questions, more quickly, and in a more efficient manner so we can learn more about the products currently in use and in the pipeline," she says.

Glenn Gormley, M.D., Ph.D., president and CEO of Gemin X Pharmaceuticals, and a member of the executive board of CTTI, says the initiative has three areas of focus: improving the design of clinical trials so that they are appropriate and answer the right questions; improving the execution of clinical trials without compromising quality; and improving communications about clinical trials both within the scientific system and to the public.

THE INITIATIVE'S GOALS

CTTI oversees specific projects to identify existing issues related to current practices, designs models for improvement, and tests the new models and compares these with the existing system.

"CTTI projects evaluate methods or strategies to improve the design and operations of clinical trials, assess current practices, and develop recommendations for best practices, as well as develop models for improvement," Dr. Grignolo says. "On an ongoing basis, CTTI will promote the adoption of specific recommendations throughout the clinical-research enterprise, not only in the United States but also around the world where appropriate. Progress, activities, and innovations deriving from CTTI will be communicated to interested parties and the public."

While CTTI is not a policy-making initiative, Dr. Kramer believes that by bringing to the table people from across the clinical-trials enterprise, development processes can be improved.

"We hope to have an impact on the way in which sponsors decide to conduct research in

ABOUT CTTI

The goal of the Clinical Trials Transformation Initiative (CTTI) is to modernize the clinical trial system. The CTTI will oversee specific projects to identify existing issues related to current practice, design models for improvement, and test the new models and compare them with the existing system.

CTTI began in November 2007 as a collaboration between the U.S. Food and Drug Administration and Duke University Medical Center to develop new standards and identify new methods and technologies that improve safety, boost the quality of information derived from clinical trials, and make the research process more efficient.

Fifty-one organizations joined CTTI in 2008. Each organization is represented on the CTTI Steering Committee. The active involvement of its leaders, members, and government partners helped CTTI launch two cornerstone projects.

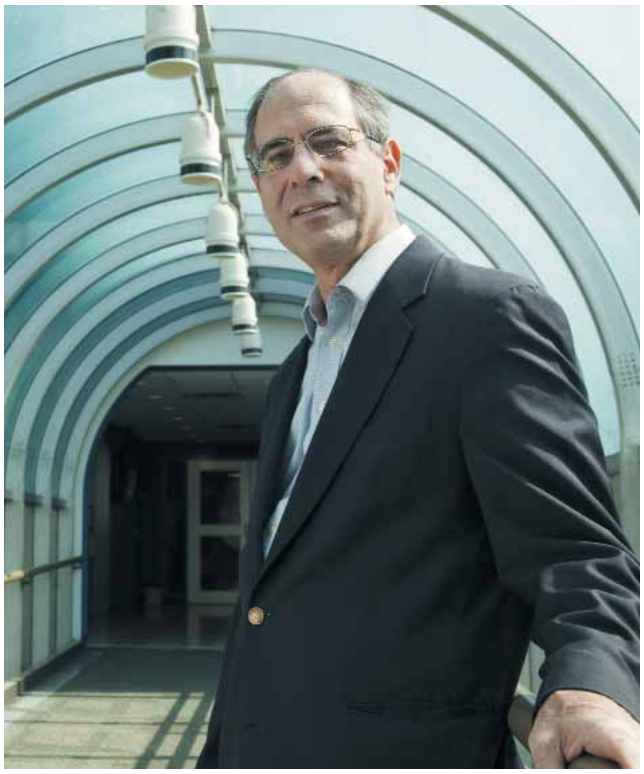
One of CTTI's first projects, Effective and Efficient Monitoring as a Component of Quality Assurance in the Conduct of Clinical Trials, is designed to assess a variety of clinical monitoring approaches to provide information that will assist medical products researchers in selecting the most appropriate monitoring methods for clinical trials.

The second project, Interpreting and Communicating Clinical Data in the Public Domain, aims to bring together stakeholders who are engaged in the collection, reporting, and interpretation of clinical data in the public domain to develop consensus on principles to analyze and report such data.

OTHER IDEAS THE INITIATIVE WILL EXPLORE INCLUDE:

- Establishing national standards for a wide range of research functions to streamline the current approaches to initiating and conducting clinical trials.
- Exploring alternative models for institutional review boards to minimize duplication of effort in multi-site clinical trials and identifying strategies to enhance the process of obtaining informed consent from clinical-trial participants.
- Establishing accreditation programs for both clinical investigators and research sites.
- Extending the use of technology to improve data management.

Source: Clinical Trials Transformation Initiative (CTTI). For more information, visit trialstransformation.org.



■ DR. SUSAN ALPERT *Medtronic*

COMPANIES RECOGNIZE THAT BECAUSE MEDICAL DEVICES HAVE BECOME MORE SOPHISTICATED, THEY WILL BE SUBJECT TO CLINICAL TRIALS, NOW AND IN THE FUTURE, SO THE CTTI IS DOING VERY IMPORTANT WORK.

the future," she says. "We're focusing on those processes that can help determine whether reliable results are being generated from the research being done."

Susan Alpert, M.D., Ph.D., senior VP and chief regulatory officer at Medtronic, and a member of the CTTI executive committee, says the initiative benefits from having a critical mass of people who have different expertise and who represent a wide range of stakeholders.

■ DR. JAY SIEGEL
Johnson & Johnson

WE HAVE A BURNING PLATFORM; EVERYBODY IS AWARE OF THE INEFFICIENCIES IN THE CLINICAL-TRIAL SYSTEM AND OF THE TREMENDOUS OPPORTUNITY TO MAKE MEDICAL AND SCIENTIFIC ADVANCES THROUGH EFFECTIVE CLINICAL RESEARCH.

"The initiative can achieve much more than any one company could do by itself," she says. "The agency and the industry benefit by having a good, clear, well-founded understanding of what clinical trials should be and how they should be conducted."

THE PROJECTS

Two CTTI projects are now under way, and two more are under consideration by the executive committee. The design and timing of the two approved projects are intended to permit the collection of empirical data and the publication of findings and recommendations in the 2009-2010 timeframe.

CTTI MEMBER ORGANIZATIONS

- Academy of Pharmaceutical Physicians and Investigators
- American College of Cardiology
- American College of Clinical Pharmacology
- American College of Neuropsychopharmacology
- Amgen Inc.
- Association of Clinical Research Organizations
- bioMerieux Inc.
- Biotechnology Industry Organization
- Biotronik Inc.
- Black Hills Clinical Research Center
- Bristol-Myers Squibb Co.
- C.R. Bard Inc.
- Centers for Medicare and Medicaid Services
- Duke University
- Eli Lilly and Company
- Gemin X Pharmaceuticals
- Genentech
- GlaxoSmithKline
- Hoffmann-La Roche Inc.
- Human Genome Sciences Inc.
- Icon Clinical Research
- Johnson & Johnson Medical Devices & Diagnostics
- Johnson & Johnson Pharmaceutical Research & Development
- King & Spalding LLP
- MedAvante Inc.
- National Institutes of Health
- Novartis Pharmaceuticals
- Palo Alto Investors Inc.
- Parexel International
- Pfizer Inc.
- PharmaNet Development Group Inc.
- Pharmaceutical Research and Manufacturers of America
- Piedmont Medical Group
- Quintiles
- Rx Trials Inc.
- Society for Clinical Data Management
- St. Jude Medical
- Target Health Inc.
- The Medicines Company
- University of California - Davis
- University of Missouri
- University of Oxford
- University of Pennsylvania
- University of Wisconsin
- U.S. Food and Drug Administration
- Wright Medical

DR. ALBERTO GRIGNOLO *Parexel Consulting*

WHILE CTTI IS INITIALLY CONCENTRATING ON CLINICAL RESEARCH CONDUCTED IN THE UNITED STATES, IT SEEKS TO IDENTIFY PRACTICE IMPROVEMENTS THAT CAN BE APPLIED WORLDWIDE.

One of CTTI's first projects, Effective and Efficient Monitoring as a Component of Quality Assurance in the Conduct of Clinical Trials, is designed to assess a variety of clinical monitoring approaches. This information can assist medical product researchers in selecting the most appropriate monitoring methods for their particular clinical trial.

"We are planning to evaluate all of the different monitoring processes in the various development areas," Ms. Robb says. "We will also evaluate the goals associated with clinical monitoring, and based upon this information, we will identify best practices to consider when developing monitoring programs."

The second CTTI project, Interpreting and Communicating Clinical Data in the Public Domain, aims to bring together stakeholders who are engaged in the collection, reporting, and interpretation of publicly available clinical data. The goal is to develop principles and general guidance, based on a consensus, to analyze and report such data.

"One of the consequences of increased transparency is that there are a lot of clinical-trial data entering the public domain in different forms," Dr. Gormley says. "There are many ways in which the the public can gain access to information about studies without tapping into traditional peer-reviewed literature."

The public can benefit from a process that allows for the evaluation and analysis of clinical data in a standardized format.

"The information that is available now in various formats may not have been collected in the same way," Dr. Gormley says. "Without knowing how data were put into the public domain, there is the risk that information could be generated that confuses more than clarifies."

Dr. Gormley says this CTTI project is designed to develop some general guidance for investigators on how to work with data in the public domain, which may not necessarily have gone through the review system.

EXECUTIVE COMMITTEE MEMBERS

- Rachel E. Behrman, M.D., MPH (Co-Chair)
  Associate Commissioner for Clinical Programs
  U.S. Food and Drug Administration (FDA)
- Robert M. Califf, M.D., MACC (Co-Chair)
  Vice Chancellor for Clinical Research
  Director, Duke Translational Medicine Institute, Duke University
- Susan Alpert, M.D., Ph.D.
  Senior VP, Chief Quality and Regulatory Officer
  Medtronic
- David L. DeMets, Ph.D.
  Professor and Chair, Department of Biostatistics & Medical Informatics
  University of Wisconsin
- Hans-Georg Eichler, M.D., M.Sc. (Non-US Regulary Liaison)
  Senior Medical Officer
  European Medicines Agency (EMEA)
- James J. Ferguson III, M.D. (CTTI Steering Committee Co-chairperson, Ex Officio Member)
  VP, Global Medical Surgical and Critical Care
  The Medicines Company
- Kenneth A. Getz, MBA (At-Large Member)
  Senior Research Fellow
  Tufts Center for the Study of Drug Development
- Glenn Gormley, M.D., Ph.D.
  President and CEO
  Gemin X Pharmaceuticals
- Alberto Grignolo, Ph.D.
  Corporate VP, Global Strategy and Services
  Parexel Consulting
- Briggs Morrison, M.D. (CTTI Steering Committee Co-chairperson, Ex Officio Member)
  Senior VP, Worldwide Development
  Pfizer Inc.
- Amy Patterson, M.D. (National Institutes of Health (NIH) Liaison)
  Acting Director, Office of Science Policy
  National Institutes of Health
- Nancy Roach (Patient Advocate)
  Colorectal Cancer Coalition
- Jay P. Siegel, M.D.
  Group President, Research & Development, Biotechnology, Immunology, and Oncology
  Johnson & Johnson
- Robert Temple, M.D.
  Associate Director for Medical Policy, Center for Drug Evaluation and Research (CDER)
  U.S. Food and Drug Administration
- Bram Zuckerman, M.D.
  Director, Division of Cardiovascular Devices, Center for Devices and Radiological Health
  U.S. Food and Drug Administration (FDA)

DR. GLENN GORMLEY
Gemin X Pharmaceuticals

CTTI IS BROADLY REPRESENTED BY PATIENT GROUPS, REGULATORY AGENCIES, TRADE ORGANIZATIONS, THE GOVERNMENT, INDUSTRY SPONSORS, AND ACADEMIA. THE ORGANIZATION PROVIDES A NEUTRAL FORUM FOR DEBATE AND DISCUSSION ON HOW TO IMPROVE THE CLINICAL-TRIAL SYSTEM, WHICH WE ARE ALL DEPENDENT ON, MOST IMPORTANTLY THE PATIENTS.

Priority projects CTTI has identified include adverse event reporting and study start-up.

"A near-term focus for CTTI is improving the system of reporting and interpreting adverse events, which will enable investigators, IRBs, biopharmaceutical companies, and the FDA to identify and communicate this information in a more efficient and informative manner," Dr. Grignolo says. "The CTTI Executive Committee will consider proposals for future projects based on a set of criteria, including alignment with the mission of CTTI, if the project addresses a priority area, if the objectives are achievable and practical, as well as if there is a clear course of action to improve the efficiency and quality of clinical trials."

Many of the practices and regulations regarding clinical trials were drawn up in an era when clinical trials involved smaller patient populations and were conducted at a smaller number of medical sites, Dr. Siegel says.

"Now, clinical trials frequently rely on dozens or hundreds of centers involving hundreds or thousands of patients around the world," he says. "Often, depending on the specifics of the regulations involved and how they are interpreted, an adverse event experienced by a single patient is reported to all investigators in the study and related studies as an isolated event, even though the study may involve hundreds of investigators and none have access to the aggregate data needed to assess its implications. The significance of this event may be impossible to evaluate in isolation but the workload in attempting to do so can be enormous. Investigators need a better way to monitor what's happening across the entire trial on a global scale. An improved process would allow them to pick up important safety signals earlier and in such a way that would take less effort and yield much better results."

Dr. Alpert says the questions that need to be

MELISSA ROBB
The Food and Drug Administration

THE GOAL IS TO HAVE A BETTER CLINICAL-TRIAL ENTERPRISE SO THAT WE CAN GET THE ANSWERS TO THE QUESTIONS WE NEED AND PROVIDE THIS INFORMATION TO PATIENTS AND HEALTHCARE PROVIDERS.

THE SENTINEL INITIATIVE

Another offshoot from the FDA's Critical Path Initiative is the Sentinel Initiative, which is a long-term effort by the agency to create a national electronic system for monitoring medical product safety. This program will strengthen the FDA's ability to track how drugs and other medical products perform once they reach the market and, ultimately, facilitate the development of tools to strengthen the agency's ability to communicate safety information to the public. The Sentinel Initiative, which is still in its early stages, will include the development of a new electronic system, called the Sentinel System, which will enable the FDA to gather information about medical products by posing targeted queries — consistent with strict privacy and security safeguards — of patient registry data, insurance claims data, and other large healthcare information databases.

Once the Sentinel System is up and running, the FDA will have the tools to query specific adverse event data in large databases, such as the Medicare database and in claims data and electronic health information maintained by private and federal entities that volunteer to participate in the Sentinel System. Creating an advanced surveillance system was one of the recommendations made by the Institute of Medicine in its 2006 report on ways to improve the safe use of drugs.

The FDA and CMS, with the help of the Assistant Secretary for Planning and Evaluation (ASPE), have launched a pilot program using Medicare data to better understand the safety of FDA-regulated products after they go on the market.

The project's goal is to help the initiative explore medical product performance, safety, and other clinical results among elderly patients.

Another example of a project that is contributing to Sentinel is the Observational Medical Outcomes Partnership (OMOP). The FDA, PhRMA, and the Foundation for the National Institutes of Health established a public/private partnership, which is governed by a multi-stakeholder executive board and designed to to protect human health by improving the monitoring of drugs for safety and effectiveness.

Source: The Food and Drug Administration. For more information, visit fda.gov.

addressed are similar for both devices and drugs.

"Those questions include: how to identify the best practices for developing clinical trials for regulated products and what are the best practices for working with clinical sites," she says. "Medical devices have changed a great deal in the past few decades. They've gone from being simply handheld tools that a surgeon used to being both a diagnostic and therapeutic product. Companies recognize that because medical devices have become more sophisticated, they will be subject to clinical trials, now and in the future, so the CTTI is doing very important work." ✦

PharmaVOICE welcomes comments about this article. E-mail us at feedback@pharmavoice.com.

Experts on this topic

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