Regulatory Education and Action for Patients

• Seeking Common Ground

May 31, 2012

ELECTRONIC SUBMISSION VIA REGULATIONS.GOV

Dr. Margaret Hamburg, Commissioner
Food and Drug Administration
Division of Dockets Management (HFA–305)
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. FDA-2012-N-0170
Modernizing the Regulation of Clinical Trials and Approaches to Good Clinical Practice; Public Hearing; Request for Comments

Dear Dr. Hamburg:

The Regulatory Education and Action for Patients (REAP) appreciates the opportunity to submit comments to the docket on FDA's efforts to modernize its regulatory approach to the conduct and oversight of clinical trials for agency-regulated products.

REAP is an umbrella coalition comprised of 50 patient advocacy groups whose mission is to communicate to Federal and State policymakers the challenges patients face in accessing care. REAP's collective voice assures a wide range of patient concerns are considered in policy development to maximize care access and improved outcomes as well as minimize unintended consequences upon implementation. Through its member entities, REAP contributes information and perspectives regarding important health care decisions to a degree that has not been possible heretofore by health care advocacy groups in the regulatory arena.

As FDA noted in the Federal Register announcement of this initiative, "there have been dramatic changes in the clinical trial enterprise, including increased size and complexity of clinical trials, increases in the number of clinical trials performed globally, greater use of contract research organizations (CROs), participation of vulnerable populations, and numerous scientific and technological advances" over the past 25 years.[1] REAP believes that, in some cases, those changes have not ensured sufficient protections for patients. In addition, REAP feels that advances in science and technology, such as the validation of new biomarkers, should assist sponsors in getting novel and effective treatments to patients as quickly as possible. REAP will make six main points in these written comments.

[1] Modernizing the Regulation of Clinical Trials and Approaches to Good Clinical Practice; Public Hearing; Request for Comments, 77 Fed. Reg. 13,513, 13, 514 (March 7, 2012).

First, REAP believes that the informed consent process should be simplified for subjects participating in clinical trials. It may be possible to achieve this goal by having a template that would harmonize the process across domestic and international study sites. Using a single informed consent process for all subjects in a multicenter study would ensure that they all receive the same information and have access to the same educational resources. Informed consent also should be made more efficient and patient-friendly to ensure the proper education of subjects in such trials, using different types of tools to give patients information via different media. These tools could include a study subject bill of rights, a clear list of subject responsibilities, and informed consent videos that clearly explain the process and terminology.

Second, REAP urges FDA to require study results to be communicated to trial participants in an accessible way. Human subjects should not be treated as just another piece of the study "materials" – they have a vested interest in the outcome of the trial and getting effective treatments to patients who need them. Simply referring participants to the raw data results posted on ClinicalTrials.gov is not adequate, as the majority of patients would not be able to interpret those results and data. Sponsors should be required to send an explanatory letter to the subjects who participated in the trial after the trial is completed. The letters should let those subjects know – in accessible and plain language – the outcomes and the long-term impact of the study. For example, if the sponsor is seeking FDA approval for a new product based on that study, that information should be available to the participants of the study.

Third, REAP believes that clinical trials should be monitored using a risk-based approach to ensure the safety of human subjects. Trials that are low risk to subjects do not need the same level of monitoring, which would allow them to be completed more quickly. Human subject protection also should be promoted by having a single Institutional Review Board approve and oversee a multicenter trial, rather than one IRB for each participating trial site. That approach would avoid both duplicative efforts and a potential lack of communication about adverse events or protocol changes across involved IRBs. As FDA certainly knows, multicenter trials and complex late-stage clinical trials have become the norm in the research enterprise. A centralized IRB for reviewing and monitoring a multicenter trial reduces costs and logistical burdens, and also provides better oversight of the trial and greater protections for study subjects.

Fourth, REAP believes that clinical trial design during the early stages of drug development (such as when the Investigational New Drug Application or Investigational Device Exemption is submitted to FDA) should be more flexible and responsive to the technology being studied. For example, FDA should allow sponsors to incorporate new scientific advances as well as predictive biomarkers to select the best patient population for the trial. REAP also believes that FDA should work with sponsors to determine whether a rigid Phase I, II, III sequence is really necessary and whether it would be possible to get valid data on an investigational product with fewer participants and more targeted information. Further, FDA should establish with sponsors before the trial begins whether a predictive biomarker could be used to select patients who may be most responsive to the investigational product. Targeting the selection of trial subjects in this way also might reduce the adverse events seen during the study, because patients who are less responsive to an investigational product often disproportionately contribute to reported adverse events. Accordingly, this recommendation would both protect patients more effectively and provide the possibility of an alternative route to get novel medications to market more quickly. Integrating biomarkers into clinical trial design also would reduce study costs for sponsors.

Fifth, REAP urges FDA to require safety biomarkers to be integrated more consistently into the trial design to avoid patient harm. For example, tracking a biomarker during the course of a clinical study could provide a signal that a patient is developing early signs of kidney toxicity, thus allowing the investigational drug to be stopped before the patient has a more serious reaction to the drug. Using safety biomarkers would ensure that patients receive a high degree of safety monitoring during the trial and reduce the likelihood of serious harm.

Finally, pharmacodynamic biomarkers should be incorporated into clinical trial design as surrogates for clinical endpoints to allow sponsors to gain approval of a drug without necessarily collecting data on mortality or morbidity. This would get products to market more quickly and without inflicting unjustifiable harm to study subjects, both of which should be goals of a modern and streamlined clinical trial enterprise.

Thank you again for the opportunity to comment on this important issue. REAP and its members look forward to continuing to work collaboratively with FDA and other stakeholders to ensure that patient perspectives are considered during various regulatory reform efforts.

Sincerely,

Alliance for Aging Research
Alpha 1 Association
Alpha 1 Foundation
American Brain Tumor Association
C-Change
COPD Foundation
Friends of Cancer Research
Huntington's Disease Society of America
Hypertrophic Cardiomyopathy Association
Komen Advocacy Alliance
National Alliance on Mental Illness
National Patient Advocate Foundation
Ovarian Cancer National Alliance
Prevent Cancer Foundation
Sisters Network
Us TOO International Prostate Cancer Education and Support Network