Editor-in-Chief's Commentary: Collaborative Models for Drug Development, Evaluation, and Clinical Use

Stephen P. Spielberg, MD, PhD

As we enter a time of ever-increasing complexity in the prevention, diagnosis, and treatment of disease, the need for cross-disciplinary collaboration becomes not just desirable but essential. Efficient and effective drug discovery, development, regulation, and clinical use are truly a "team sport." In this issue, we have 2 papers (Stephenson et al and Woodcock and Rowzee) that describe new approaches to collaboration in one of the most complex arenas: disease of the central nervous system. Stephenson et al discuss collaborative, precompetitive efforts to advance the excellence and success of studies of medicines for Alzheimer and Parkinson diseases. Woodcock and Rowzee present perspectives on a new outcome assessment consortium for multiple sclerosis. Both address a broad-based approach from patients, physicians, investigators, drug companies, and regulators to develop methodologies to ensure that new therapeutic advances will be developed with the best, standardized, validated clinical and biomarker tools.

For drug development and regulation, the standardization of clinical assessment tools can speed the process, with industry and regulators confident that the information resulting from using validated methods will be meaningful and interpretable. Improved efficiency of, and confidence in, the development/regulatory process may well justify precompetitive investment by multiple companies (together with regulators, physicians, and patients) to ensure that studies will yield biologically and clinically meaningful data. Too often, when a new drug is being developed for any indication, an assessment of positive and negative effects will be undertaken with only partial understanding and validation of the outcomes. End points frequently vary among studies of different drugs, and each sponsor often develops and defines end points that are not standardized and validated for international regulatory and clinical use. It is often stated that many published papers (both industry and investigator sponsored) fail to be replicated in subsequent studies. Some of the failure may result from subtle differences in outcomes variables and how they are assessed. This also challenges the utility of meta-analyses across studies in which the assessment tools used, and the way in which they are

implemented, vary in ways often not presented in summarized data or presentations.

Similarly, after medicines have been approved, outcomes in the real world often do not quantitatively or qualitatively reflect data from clinical trials. While there are myriad reasons for such a "study/real-world" gap, one issue is that the assessments used in the studies may not reflect what physicians and patients are concerned about in clinical practice and that there is no consistency about the way in which patients are evaluated in different investigative and clinical settings.

The opportunities and challenges presented in the 2 papers in this issue of *TIRS* suggest a new pathway forward. Involvement of patients/patient advocacy groups and clinicians early in discussions along with the academic, industry, and regulatory communities provides the opportunity to define those outcomes, positive and negative, that are of most concern to patients. Just as validation and standardization are vital to the effectiveness and efficiency of drug development and regulation, the incorporation of end points that reflect real-world care of patients can lead to actionable information for clinical use. If the ultimate goal of drug development is to improve the lives of patients, information flow from the clinical trial and therapeutic worlds needs to flourish.

Given the complexity of the impact of chronic illness on patients, a new drug may have an impact on an aspect of a disease that is either not "valued" by or explained adequately to patients. Lack of adherence in the real world for such a compound is more likely than for one in which patients have had input from the beginning, and practicing physicians are provided the tools to help their patients better understand what to expect from a treatment. As is pointed out by Woodcock and Rowzee, using validated end points addressing a number of different aspects of concern to patients and their doctors may help "distinguish" different medicines for a condition that address different aspects of the condition, from changing disease progression and "curing" the disease to alleviating different aspects of suffering from the disease. Different medicines or combinations of medicines can then be "targeted" for the

greatest effectiveness to specific patient needs and concerns. For diseases such as Alzheimer disease, Parkinson disease, and multiple sclerosis, beyond absolute "cure" or prevention of the conditions, patients with these broad diagnostic labels may experience symptoms in a variety of spheres: movement, ability to manage tasks of daily living, cognitive impairment, and emotional and behavioral changes. Being able to objectively and consistently measure the impact in each of these spheres (in clinical trials and in therapeutic use), and understanding the roles of different medicines in ameliorating various symptoms, can help match drugs with patient needs in clinical use. The incorporation of such clinical thinking along with the use of molecular and other biomarkers can then lead to true individualized medicine. Information developed in clinical trials driven by advanced molecular understanding and clinically meaningful outcomes can then be used most effectively by patients and their doctors. Engaging in dialogue about these complex issues and developing validated tools in a precompetitive space with all who develop, prescribe, and take medicines hold the promise of better drug development, drug evaluation, and real-world therapeutics.

—Stephen P. Spielberg, MD, PhD
Editor-in-Chief