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In an effort to modernize drug development, the Predictive Safety Testing Consortium enables companies to share and validate safety biomarkers.

By Adam Istas

To address the issues surrounding a decade-long decrease in the number of new drug approvals, the [U.S. Food and Drug Administration](#) (FDA) in 2004 published a report titled [Challenge and Opportunity on the Critical Path to New Medical Products](#). This seminal paper—the cornerstone of the Critical Path Initiative—analyzed the pipeline problem of modern-day drug development and provided a framework for a more efficient development process. Subsequently, the [Critical Path Opportunities List](#) was published in 2006 and included 76 specific projects in priority areas such as creating better evaluation tools and streamlining clinical trials to help increase efficiency, predictability and productivity in the development of new medical products. One of the first projects initiated was the [Predictive Safety Testing Consortium](#) (PSTC), a collaborative effort among 16 pharmaceutical manufacturers and the [C-Path Institute](#), an independent non-profit facilitator of Critical Path projects. Charged with providing strategic and scientific input to validate genomic biomarkers of toxicity, the PSTC highlights the ways in which multiple stakeholder cooperation advances the science behind new drug development.

Although scientific advances have led to an explosion in the amount of biomarkers being developed, biomarkers are not incorporated into drug development as quickly as they should because they are not qualified through a process specifically developed for this goal, says Federico Manuel Goodsaid, Ph.D., senior staff scientist in the genomics group at the FDA's [office of clinical pharmacology](#), in Silver Spring, Md., USA. “The goal of the PSTC is to accelerate the pace of biomarker development and qualification and ultimately reduce the number of drug failures.” Predictive biomarkers improve the ability to assess drug failures early in the development process, and bridging biomarkers may contribute to a reduction of failures in the clinic, he says.

The FDA is acting in an advisory role to the PSTC. Although the agency still is an active stakeholder in the consortium, researchers from the participating pharmaceutical companies conduct the scientific work. In this capacity, the FDA is afforded a clear view of what is being developed, Goodsaid says. “The evaluation work will be easier when the agency starts getting multiple submissions and data,” he says. “Then we can start looking at the effectiveness of safety biomarkers in all compounds across all companies.” The FDA plays a fairly limited role as advisor, the “axis of the wheel“ is the C-Path Institute, Goodsaid says.

Early Focus

The Institute brings pharmaceutical companies together to share and validate their internally developed pre-clinical safety biomarkers in four workgroups: liver, kidney, vascular injury and carcinogenicity. As one of the Critical Path Initiative’s earliest projects, the creation of the PSTC underscores the importance of pre-clinical work in the drug development process.

The PSTC’s initial focus on pre-clinical research came about for two reasons, says Bill Mattes, Ph.D., director of toxicology at the C-Path Institute, in Rockville, Md., USA. The first reason is the overall impact that pre-clinical toxicology has on the development process. “Every time you make a mistake—whether it’s a decision to drop a drug that might actually have promise, or moving forward a drug that doesn’t have promise—it’s expensive,” he says. “Not just for drug companies, but sooner or later there’s not a viable medicine for people.” Secondly, pre-clinical work affords researchers the ability to answer questions that aren’t practical to discern through human research, Mattes says. It is the combination of these factors that has led pharmaceutical companies to join the consortium and share their internal data, he says.

The involvement of the FDA is one of the key drivers of the PSTC, Mattes says. Companies know that regulators want to see more data on biomarker qualification, and the thrust of the PSTC is to pool the data and resources of multiple companies, while at the same time to quantify safety biomarkers with guidance from the FDA, he says. “Put together like that, everything starts to fall into place.” Another reason for the success of the PSTC is the wealth of scientific knowledge available from each of the participating companies. “With 16 scientists sitting around a table, the intellectual resources that are shared on this are phenomenal,” Mattes says.

Although the PSTC initially is focused on the validation and qualification of pre-clinical biomarkers, the plan is to transition into clinical work, Mattes says. But thoroughly evaluating and qualifying pre-clinical biomarkers is “a necessary first step before considering clinical research,” he says. The kidney group will submit data to the FDA’s biomarker qualification process as early as July 2007, Mattes says.

The [European Medicines Agency](#) (EMA) also has been very active in the consortium’s efforts, Mattes says. “The EMA is very interested, and has been incredibly participatory in the process so far,” he says. “The more people that buy into the process, the better it is for everybody.”