

The Predictive Safety Testing Consortium



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Specific Aims:

1. *To identify and cross-qualify new and improved pre-clinical and clinical safety testing methods through a collaboration of scientists from the pharmaceutical industry, FDA, EMEA (European Medicines Evaluation Agency), and academia.*
2. *To facilitate the development of new regulatory (FDA and EMEA) processes for approving such testing methods.*

The Predictive Safety Testing Consortium (PSTC) brings pharmaceutical companies together to share and qualify (i.e. validate) new and improved safety testing methods with US and European regulatory agencies as advisors.

The tests currently used to determine drug safety are decades old. Not surprisingly, many drugs that appear safe in laboratory tests may be found later to have side effects when large numbers of patients have taken the drug. Conversely, hundreds of promising drugs never see human use because of ambiguous results from these laboratory tests. While companies may develop safety testing methods based on new technology, these are not generally accepted by the FDA as proof of safety because the tests have not been evaluated by a third party. To change this, the Critical Path Institute (C-Path) created the PSTC to allow pharmaceutical companies to share and critically examine their internal experience and methods, pool data for more powerful analyses, and ultimately seek scientific consensus on the value and appropriate context of use of these new tests. Data and results from consortium activities will be submitted to the FDA and EMEA for their formal evaluation; ultimately, results are made broadly available in the public domain.

The Consortium was officially announced by the FDA on March 16, 2006, when Health and Human Services Secretary Michael Leavitt, FDA Commissioner Dr. Andrew von Eschenbach and FDA Deputy Commissioner Dr. Janet Woodcock announced the next phase for the FDA's Critical Path Initiative.

In three years the PSTC has grown from ten to seventeen members and gained international attention. The European equivalent of the FDA, the EMEA, has engaged with the Consortium, so that now 18 FDA and 8 EMEA scientists participate as advisors with the more than 250 industrial and academic scientists. C-Path serves as the "trusted third party" collecting and summarizing the data, and coordinating scientific efforts. Recently, the Japanese medical product regulatory body, the PMDA, also developed a biomarker qualification process and is piloting this for the first time with data submitted by the PSTC's kidney toxicity working group.

The PSTC is governed by a unique Consortium Agreement and organized in working groups addressing different areas of safety, currently kidney injury, liver injury, muscle injury, vascular injury and carcinogenicity. Through teleconferences and face to face meetings, the Consortium has made tangible progress. Grand Rounds and Workshops at the FDA have introduced agency scientists to preliminary biomarker data and helped prioritize important safety questions. Formal research plans describe cross-qualification of assays, based upon the data and samples shared among companies. The Carcinogenicity Working Group identified two promising genomic signatures predicting chemically-induced tumors from short-term studies, and is now in a final validation phase of determining the predictive value of a reduced number of genes on a TaqMan platform. The Liver Injury Working Group has identified four assays of liver injury where individual companies have extensive and promising internal experience. The Skeletal Muscle working group has similarly identified eight candidate assays and developed a large sample and data set compiled from member companies existing work.

The Kidney Injury Working Group has over 20 assays that have extensive data from three organizations, with 7 forming the basis of a submission to the FDA and EMEA on June 15, 2007.

A year later, in a dramatic first for trans-Atlantic cooperation, these agencies not only jointly approved the use of these biomarkers for laboratory evaluation of drug safety, but also used the experience to establish a process for biomarker review. This data is now being actively evaluated by the PMDA. To determine the utility of these new safety tests in human clinical studies, the PSTC's Kidney Working Group and Translational Team are coordinating clinical assay evaluation, clinical protocol designs, and synergistic partnerships to generate supporting data. All in all, the PSTC is providing new tools for safety assessment in drug development useful for pharmaceutical scientists, regulators, and clinicians.

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