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## The Predictive Safety Testing Consortium

### Specific Aims:

- 1 *To identify and cross-qualify new and improved pre-clinical safety testing methods through a collaboration of scientists from the pharmaceutical industry, FDA (US Food and Drug Administration), EMA (European Medicines Evaluation Agency), PMDA (Japanese Pharmaceuticals and Medical Devices Agency), and academia.*
- 2 *To facilitate the development of new regulatory (FDA, EMA and PMDA) 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, 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, EMA, and PMDA 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.

To date, the PSTC has sixteen corporate members and gained international attention. The European equivalent of the FDA, the EMA, has engaged with the Consortium, so that now 28 FDA and 10 EMA 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 for the first time, qualified biomarkers 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, skeletal muscle injury, vascular injury, cardiac hypertrophy, 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.

In a dramatic first for trans-Atlantic cooperation, the FDA and EMA not only jointly approved the use of seven kidney biomarkers for laboratory evaluation of drug safety, but also used the experience to establish a process for biomarker review. This data was also evaluated and approved 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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