CRITICAL PATH INSTITUTE

Improving the Path for Innovative Therapies

2007 Annual Report
The Critical Path Institute, founded in 2005 in Tucson, Arizona, is an independent, non-profit organization dedicated to bringing scientists from the FDA, industry and academia together to improve the path for innovative new drugs, diagnostic tests and devices to reach patients in need.

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Dear Friends and Supporters:

The Critical Path Institute completed its second full year of operations with many successes of which we can all be proud. A few highlights include:

Our $2.1 million grant from Science Foundation Arizona to partner with Ventana Medical Systems on “Diagnostics for Targeted Therapy.” The project is expected to bring new business and prestige to Arizona by establishing an Arizona-based national laboratory for validation of diagnostic tests.

The Predictive Safety Testing Consortium (PSTC) has now grown to 190 scientists from 16 major pharmaceutical companies, the FDA and the EMEA (Europe’s FDA counterpart). On June 15, 2007, the PSTC submitted the first ever formal submission of a biomarker qualification package to the FDA and EMEA for approval of tests to better predict drug-induced kidney damage.

Our successful renewal of a $4.0 million, four-year grant from the Agency for Healthcare Research and Quality (AHRQ) for the continued support of the Arizona Center for Education and Research on Therapeutics (ArizonaCERT). This award includes a $1.6 million subcontract to The University of Arizona College of Pharmacy. ArizonaCERT’s goals are to prevent adverse drug reactions, with a focus on those that harm women.

Governor Napolitano presented us with an Arizona Innovation Award, recognizing the unique contribution the Critical Path Institute has brought to the state.

Since our beginning, the financial and professional support from the Tucson region has been exceptional and this past year was no different. Our donors and supporters continue to provide the core funding that enables the Critical Path Institute to be a neutral party bringing together federal regulators and pharmaceutical scientists.

Please review this annual report and let us know what you think. We truly value your comments and suggestions.

Sincerely,

Raymond L. Woosley, MD, PhD
President and CEO

Governor Janet Napolitano presented an Arizona Innovation Award to Dr. Raymond Woosley who accepted on behalf of the Critical Path Institute in October 2007.

Photo courtesy of Daniel Snyder Photography
Faster, Safer, Smarter

What We Do and Why We Do It
The Critical Path Institute works as a neutral third party with scientists from government, industry and academia to create and foster transparent, efficient partnerships that support the U.S. Food and Drug Administration’s (FDA) efforts to identify methods that will better serve the industry in the rapid development of safe medical products. The Critical Path Institute, with its in-house scientific and medical experts, evaluates the tools of medical product development and focuses on improving the process by forming cross-industry consortia to test and validate the methods.

The urgent need for this work was outlined in 2004 by the FDA in a white paper, and is referred to as the Critical Path Initiative. In this paper, the FDA called attention to the alarming decline in the number of new medical products submitted to them for approval, and cited the need for innovative new methods in drug development. This decline in submissions continues and is reflected in the fact that only 16 new medicines were approved in 2007, one of the lowest numbers in over two decades.

The Institute’s Role as a Neutral Third Party
The Critical Path Institute’s mission from the beginning has been to serve as a “trusted third party” to enable innovative collaborations between government regulators, the academic community and regulated businesses to come together to improve the process of developing new medical products, making the process faster, safer, smarter.
Critical Path Institute’s Programs

Everything the Critical Path Institute does is geared towards improving the medical product development process so that life-saving therapies can reach patients as quickly and safely as possible. Using the FDA’s Critical Path Initiative as a guide, Critical Path Institute works closely with scientists from government, industry and academia to collaborate so that the most reliable methods for testing are identified and qualified for use. The Critical Path Institute’s programs facilitate the development of guidance documents by the FDA which will provide industry with a more predictable, standardized and streamlined approach for developing new medical products.
Predictive Safety Testing Consortium (PSTC)

The tests that are used to determine drug safety today have not changed in decades. Companies have developed newer safety testing methods, but these are not generally accepted by the FDA as proof of safety because the tests have not been independently validated by a third party. Also, the methods used by companies are often different, leaving the FDA scientists unclear about which methods should be preferred.

In order to change this, the Critical Path Institute formed the Predictive Safety Testing Consortium in 2006 and invited pharmaceutical companies to join and share their internally developed methods and then test each other’s methods. The PSTC was announced by Health and Human Services Secretary Michael Leavitt, FDA Commissioner Dr. Andrew von Eschenbach and FDA Deputy Commissioner Dr. Janet Woodcock who identified this Consortium as “unprecedented” and a “shining example” of the type of work the FDA would like to see conducted.

This innovative program has gained international attention and now, the European counterpart of the FDA, the European Medicines Agency (EMEA) has appointed observers to work with the Consortium. In addition, the United Kingdom (UK) Academy of Medical Sciences, equivalent to the U.S. National Academy of Sciences, has also asked to be kept informed of the progress and offered to share the results of a similar UK initiative that is being created. Because of its success, the Critical Path Institute has been asked to report its experience at national meetings and to share the structure of the legal framework with other organizations forming consortia.

Since its inception, the PSTC has grown to 17 corporate members with more than 190 participating scientists. Seventeen FDA and eleven EMEA scientists participate as advisors with Critical Path Institute serving as the trusted third party collecting and summarizing the data. Out of this work, data are being generated that can provide the basis for an FDA Guidance to be formulated, which provides direction for the entire pharmaceutical industry on how to better test drugs for safety.

This year, an annual update meeting on the Consortium’s progress was held with Dr. Janet Woodcock as well as other FDA officials and the information presented was extremely well received. This meeting paved the way for the first ever formal submission of a biomarker qualification package to the FDA and EMEA. Subsequent discussions and follow-up data submissions culminated in a final PSTC-FDA-EMEA meeting held in October 2007 jointly in Washington, D.C. and London, with all regulatory questions addressed and “closed”. A final decision by both regulatory bodies is expected in 2008.

PSTC: Improving how new drugs are tested.
Molecular Assays and Targeted Therapeutics (MATT)

Advances in biomedical science have spawned a new generation of promising targeted therapies and molecular diagnostic tests. Molecular diagnostics have the potential to guide the choice of targeted therapy so that the patient receives the most effective therapy. However, this potential is often not realized because therapies and diagnostics are not developed in a coordinated fashion by industry. The leading health agencies of the U.S. government have encouraged creation of a new model for development of diagnostics and targeted therapy in cancer and asked the Critical Path Institute, due to its track record with the PSTC, to bring together the necessary parties to establish standards for assay validation and to design and coordinate the model study.

The Critical Path Institute is now leading a consortium that includes the FDA, National Cancer Institute (NCI) and Centers for Medicaid and Medicare Services (CMS) along with 20 diagnostic companies in a cross-industry collaboration to determine the best of class indicators that are predictive of response in patients with lung cancer.

A grant supporting this project was awarded by Science Foundation Arizona (SFAz) for $2.1 million over a two year period (July, 2007 – June, 2009). The Critical Path Institute is working with Ventana Medical Systems, Inc. and others to standardize the performance criteria for diagnostic tests. The FDA is very supportive and is watching closely as this is the first prototype model for assuring reliable performance of companion diagnostic tests.

Another major objective of this effort is to use the Ventana product development project as a proof of principle for the establishment of a new national laboratory in Arizona. This facility, tentatively named United States Diagnostics Standards (USDS), would be a national, standardized testing laboratory for evaluating new diagnostic tests. Diagnostics would be validated for performance characteristics and the data used in applications for FDA approval.

MATT: Making personalized cancer therapy possible.
Cardiovascular Biomarkers

In partnership with scientists at the University of Utah and Intermountain Healthcare, the Critical Path Institute is evaluating how genetic testing can be used to predict safer and more effective treatments for patients with heart disease. Specifically, this program is evaluating genetic tests for their ability to predict safer and more effective doses of the anti-coagulant warfarin (Coumadin®) by using each individual's DNA. Warfarin is a generic drug widely prescribed as a blood thinner to prevent dangerous blood clots. The optimal dose varies from patient to patient. If the dose is too high, the patient may have serious bleeding and conversely, if the dose is too low, the patient may suffer a stroke or embolism. In both of these situations, death can result.

The intent of this FDA-funded project is to improve patient outcome and reduce adverse events from warfarin.

The Critical Path Institute's role is to evaluate the methods used in clinical trials to assure the FDA that the results can be used to write dosage recommendations for warfarin that are based on genetic testing. The FDA also supports work to evaluate biomarkers that predict the safety of drugs used in the treatment of cardiovascular disease, especially heart failure.

The Critical Path Institute is also leading a consortium of diagnostic companies and the National Institutes of Health (NIH) in the planning of a large-scale diagnostic clinical trial to accurately identify the best genetic tests to determine the correct individual dose of warfarin. This project was analyzed by The Brookings Institute and is predicted to save many lives and as much as $1 billion annually in health care costs in this country.

Common Adverse Drug Reaction Project (CADRe)

One of the goals of personalized medicine is to provide the right drug at the right dose to the right patient at the right time. A requirement of this personalized approach is to understand the causes of adverse drug reactions (ADRs) and the patient population at risk. To do this, an improved understanding of the mechanism of these adverse events is required to better tailor a safe and effective course of therapy. In addition, genetic testing to identify patients at risk for adverse events is needed to reduce the morbidity that can occur. Invited by the FDA and supported by a planning grant, the Critical Path Institute recently launched CADRe to bring these necessary pieces together in order to identify the genetic basis of ADRs and then use the information clinically (e.g., in dosing) to reduce risk.

True to its mission, the Critical Path Institute is bringing together experts in government (FDA, NIH, Agency for Healthcare Research and Quality (AHRQ)) as well as academia and industry to compile a list of drugs that merit consideration and then develop a framework to assess candidate ADRs in relation to specific drugs. The Critical Path Institute will also develop a plan for clinically qualifying any identified genetic markers and for validating the tests for these markers in target populations to determine specificity and sensitivity, so that these genetic markers can inform clinical decision-making and improve patient outcomes.

Warfarin: Safer dosing protocols.

CADRe: Preventing common adverse drug reactions.
ArizonaCERT: Improving patient safety and outcomes.

ArizonaCERT

Through a $4 million grant from the Agency for Healthcare Research and Quality (AHRQ), the Critical Path Institute hosts one of 14 national Centers for Education and Research on Therapeutics (CERTs). The ArizonaCERT is a collaboration with The University of Arizona College of Pharmacy and its mission is to conduct research and provide education that will improve therapeutic outcomes and reduce adverse events caused by drug interactions, with a special focus on those affecting women.

The specific aims of the ArizonaCERT are to improve patient safety and health outcomes by using a systems approach to examine the underlying human and systems factors responsible for the co-prescription, co-dispensing and co-administration of drug combinations that have the potential to interact and cause adverse reactions.

The ArizonaCERT leverages the federal funding for this grant through partnerships that extend its reach and currently has very productive collaborations with a variety of organizations including the Veterans Administration Healthcare System, Sonora Quest clinical laboratories, El Rio Community Health Centers, and the Mariposa Community Health Center in the border community of Nogales, Arizona. These extensions allow ArizonaCERT to both educate patients and physicians as well as evaluate the effectiveness of alerts to physicians for preventing the prescription of potentially harmful drug combinations.

ArizonaCERT also has the internationally recognized website, www.QTdrugs.org, which is currently being made more interactive utilizing data from the FDA Adverse Event Reporting System. Together with the FDA and the American Medical Association (AMA), ArizonaCERT will inform providers and patients about drug-drug interactions and new gene-based dosing recommendations for the anticoagulant warfarin, through multiple approaches including a series of educational brochures.
“The Critical Path Institute is a major part of Arizona’s growing innovation economy. The pathways to innovation that the Institute opens surely represent an excellent return on our public investment and are just as important to the many people around the world who will benefit from collaborative efforts that lead to new medicines.” — Governor Janet Napolitano

Financial Status

The Critical Path Institute started out with more than $10 million in pledges from the local community. In return, our promise was to replace those commitments over time with long-term sources of funding. We also were expected to help grow the number of high-paying jobs in the biosciences sector. Fully 83% of all revenues go to support our programs. The Critical Path Institute has competed successfully for a number of multimillion dollar federal and state grants which will provide $7,490,337 in funding over the next several years. For every dollar of public funding we received in fiscal 2007, six dollars in private and federal funding were brought into the local economy. On the job creation front, the Critical Path Institute opened its doors with three employees and ended fiscal 2007 with 17. We expect to more than double in size in the next two years.

Audited Statement of Financial Position

Fiscal Year 2007 Ending June 30

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We gratefully acknowledge the following donors who have given support to the Critical Path Institute through December 31, 2007.

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