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Subcommittee on Health

The critical role of public/private partnerships in creating applied regulatory science to advance the development of new Alzheimer's disease therapies

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Mr. Chairman, Members, and Committee Staff:

Thank you for the opportunity to provide testimony before the Subcommittee on this critically important topic. My name is Marc Cantillon, MD, Executive Director of the Coalition Against Major Diseases (CAMD) for the Critical Path Institute (C-Path). I am a practicing physician and neuroscientist with over 15 years of experience in research at the NIH, academia, and the pharmaceutical industry. C-Path is an independent, non-profit organization founded in 2005 by the U.S. Food and Drug Administration (FDA) and the Arizona community to build public/private partnerships that identify more reliable and efficient methods to test new medicines.

Critical Path Institute

C-Path was created in response to what, we believe, is a crisis in drug development, i.e. the rapidly declining productivity of the biomedical research and development enterprise. Our goal has been to create a forum for scientists from the FDA, academia, biomedical organizations, and the pharmaceutical industry to evaluate innovative testing methods for use in drug development- innovations that will give patients the earliest access to the safest possible medications. We believe that this type of collaboration, a public/private partnership, facilitated by a neutral organization such as C-Path, is essential to bring about needed changes in the way drugs are developed. C-Path focuses on "applied regulatory science", i.e. the science that improves the quality, accuracy and efficiency of decision-making by scientists in the FDA and in the regulated industry.

In order to serve as a neutral and trusted third party for collaborators, C-Path does not accept funding from the pharmaceutical industry or other companies that develop products regulated by the FDA. Since 2005, over $30 million in federal and foundation grant awards and $11 million in contributions from foundations and governments in Arizona have been received to support C-Path's work.

This funding is leveraged by in-kind support from a broad group of stakeholders and enables C-Path to manage five separate consortia with a total of over 750 participating scientists from FDA, NIH, academia and 30 of the largest global pharmaceutical companies. These stakeholders *share pre-competitive knowledge* and *develop consensus* on new drug development tools. These tools will improve the drug development process, make it more efficient and result in new drugs that are safer and more effective. C-Path supports projects that are identified as high priority by the FDA and are in the interest of public health.

CAMD: A Public Private Partnership

Thanks to the work of this Subcommittee, the FDA Amendments Act of 2007 included a provision for the FDA to create Critical Path Public/Private partnerships. Critical Path Institute's Coalition Against Major Diseases was one of the first of these partnerships launched by the FDA, and was formed to tackle brain disease beginning with one of today's most devastating illnesses, Alzheimer's disease (AD).

One of the greatest challenges facing biomedical sciences in the 21st century is the development of better treatments for neurodegenerative diseases. The two most prevalent of these, Alzheimer's disease and Parkinson's disease (PD), exert a heavy and growing human and economic burden on our society. Our lack of knowledge about the specific cause(s) of either disease is a major obstacle to the development of new treatments that have the potential to cure or prevent these devastating and tragic diseases.

In recent years, billions of dollars have been invested to develop new drugs for Alzheimer's disease but so far, all have failed to significantly impact the course of the disease. We firmly believe that new, applied regulatory science created through the public/private partnership of CAMD will result in new tools and methods that will accelerate the development of treatments for Alzheimer's patients that are effective much earlier in the disease.

Why Alzheimer's Disease for CAMD?

As the results of a 2009 study by the Alzheimer's Association make clear, the need for CAMD is compelling, The study revealed that the health care costs for American's over age 65 is three time greater if they have Alzheimer's disease. In the United States, 5.3 million people have Alzheimer's, costing the nation's healthcare system $148 billion annually. Alzheimer's has become the sixth leading cause of death in the United States. Someone in America develops Alzheimer's every 70 seconds, which means more than 450,000 new patients will be diagnosed next year.

As a practicing neuropsychiatrist, I am proud to serve as the leader of CAMD. I have been frustrated daily by the limited benefits patients receive from our current treatments for Alzheimer's disease. I have spent 15 years conducting clinical trials for Alzheimer's and Parkinson's disease patients at the NIH, in universities and in the pharmaceutical industry where several trials costing $200-500 million have failed. I am heartened that C-Path's CAMD is developing the needed tools that will help make it possible to find effective drugs quickly for patients.

CAMD seeks to *re*create the sense of urgency and open collaboration that made unprecedented, rapid progress against HIV/AIDS possible. Sharing of knowledge was a hallmark, and is generally accepted as the reason for early, and continued, successes against that epidemic.

Created jointly by C-Path and the Engelberg Center at the Brookings Institution in February 2008, CAMD is a public/private partnership that currently includes twelve major pharmaceutical companies (listed below), NIH and five organizations that represent patients (including the Alzheimer's Association and the Alzheimer's Foundation here testifying today), with advisors representing the FDA and its European counterpart, the European Medicines Agency (EMA), National Institute of Neurological Disorders and Stroke (NINDS), and National Institute on Aging. CAMD also collaborates with several other organizations, including the Michael J. Fox Foundation, the Metrum Institute, Ephibian, and the Clinical Data Interchange Standards Consortium (CDISC), as well as over 200 academic scientists around the world.

CAMD members are:

Abbott	Alliance for Aging Research	Alzheimer's Association
Alzheimer's Fdn. of America	AstraZeneca Pharmaceuticals LP	
Bristol-Myers Squibb Co.	CHDI Foundation, Inc.	Eli Lilly and Company
F. Hoffmann-La Roche Ltd	Forest Research Institute	Genentech, Inc.
GlaxoSmithKline	Johnson & Johnson	Michael J. Fox Foundation
National Health Council	Novartis Pharmaceuticals	Parkinson's Action Network
Parkinson's Disease Fdn.	Pfizer, Inc.	sanofi-aventis

CAMD's Progress to Date

CAMD's accomplishments have already changed the way we attack this devastating disease. Several examples are:

- CAMD researchers compared the way they had been scoring a person's dementia in clinical trials and found over a dozen inconsistencies in the way a score was determined for the standard tool, the Alzheimer's Disease Assessment Scale-Cognition or ADAS-cog. With these inconsistencies eliminated, it is possible for these investigators, and the FDA, to compare the results from study to study. This standardization process for ADAS-cog is a great example of "applied regulatory science".
- In CAMD and for the first time ever, pharmaceutical companies are sharing their clinical trial data with one another. CAMD has been able to pool data from 11 clinical trials conducted by seven different pharmaceutical companies. This is now the largest publicly available Alzheimer's disease database and it describes the natural course of the disease in over 4000 patients. Normally to generate new data for this number of patients, it would cost $300-600 million and take more than six years in new clinical trials. Today, only a few months later, the database has more than 200 users from academia and industry in over 34 countries. More information and how to apply for access to the database can be found at https://codr.c-path.org.
- A quantitative disease model that describes the natural progression of Alzheimer's disease has been developed using data from the Alzheimer's Disease Neuroimaging Initiative. This model is now being tested and improved with the larger and regulatory standard database of industry clinical trial data described above. The disease model will be used to help design new clinical trials, and has been submitted to the FDA and EMA for initial review. Scientists around the world are already using the database and models in innovative ways. For example, in the past, scientists designed trials based on their personal experience or what they read in the medical literature. Now, thanks to this database, they have the individual data for exactly how Alzheimer's progressed in each of over 4000 patients. This is far more precise than their personal understanding of the disease or what they have gleaned from text books. This database and mathematical models of the disease allow them to more accurately predict the outcome for a given clinical trial, how long the trial must be conducted, how many patients must

be enrolled, how genetic subsets of the population could respond, etc. CAMD is now working with the NIH and academic investigators to pool their data to further enrich this exciting leading edge tool.

- CAMD is helping define the FDA's new "Qualification" process, described in the new draft guidance released by FDA. (Guidance for Industry: Qualification Process for Drug Development Tools, U.S. Food and Drug Administration, October 2010) In this work, CAMD is submitting data and requesting that the FDA recognize certain imaging tools and cerebrospinal fluid tests as "qualified" for identifying patients much earlier in their disease, when there is still brain function to be saved. In this work, CAMD scientists are identifying imaging, biochemical, genetic, and molecular biomarkers that have the greatest potential to uncover patient populations that are pre-symptomatic and therefore have more potential benefit from new therapies. A research plan was submitted in fourth quarter to FDA and EMA.
- For the first time, we now have mutually agreed upon data standards for Alzheimer's clinical trials. CAMD investigators, working with the standard setting body, CDISC, posted these standards for public comment in an Implementation Guide on Dec 17, 2010. These common data elements will be used by all CAMD members, but are also now published for use by anyone. Having a common data format will enable rapid data sharing and accelerated research and drug development. In the near future, all data submitted to the FDA for this disease should be in a common format greatly accelerating the FDA's ability to quickly evaluate applications.

Having these new tools is allowing drug companies to more quickly evaluate potential therapies and find those that have a beneficial effect on disease progression – and also to more quickly stop working on therapies that show no benefit. This will allow them to optimize resources and bring therapies more quickly to the FDA and, therefore, more quickly to patients.

We need your help

Although CAMD is already improving applied regulatory science for Alzheimer's disease at the FDA, we need your help. Understaffing is a serious problem throughout the FDA and is especially critical for CAMD. The FDA needs your support to be able to dedicate the required number of scientists and staff to participate in CAMD and other critical path partnerships. CAMD's work is the kind of "applied regulatory science" that is changing the way drugs are tested and evaluated today, not ten years from now.

I thank you for the opportunity to provide this testimony and everyone at Critical Path Institute and CAMD thanks you for your leadership and foresight in authorizing the FDA's Critical Path Public/Private Partnerships that are giving new hope to patients and families at risk for this devastating disease.

I respectfully request that my full testimony be accepted to the record. Marc Cantillon, MD