



School of Pharmacy
Biopharmaceutical Sciences

2004 N-0181

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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Critical Path Initiative [Docket No. 2004-N-0181, 69 Federal Register, 21839 (April 22, 2004)]

Dear Commissioner Crawford:

Scientists and leadership in the University of California San Francisco (UCSF) Schools of Pharmacy and Medicine and the Institute of Quantitative Biology share the concerns expressed in the Critical Path report, i.e., that bold new advances based on creative translational research are greatly needed to accelerate the development of new medical products to diagnose and treat human disease. Below, we comment on the Critical Path Initiative and how UCSF is positioned to contribute to accomplishment of its goals.

From an academic point-of-view to understand the current issues of stagnation in medical product development, as highlighted in the Critical Path report, it is important to note that there has been little funding for product development sciences through NIH, the traditional funding source for research in academic institutions. Thus, there is a shortage of scientists in universities interested in problems along the product development pathway. This, in turn, has led to a lack of training of Ph.D., Pharm.D., M.D. or other scientists focused on problems relevant to medical product development sciences.

We recommend and strongly support the funding of creative translational research activities in medical product development sciences, which have as their primary goals accelerating and improving all aspects of the development pathway from identification of therapeutic targets through the development of statistical/mathematical/pharmacometric models of clinical trials.

In particular, we recommend that the FDA fund comprehensive Centers in Translational Product Development Sciences analogous to the National Cancer Institutes "Cancer Centers." Like a Cancer Center, which includes basic research, translational research and clinical practice, these Centers would be

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focused on research along the entire medical product development pipeline including the following areas (as outlined in the Critical Paths report):

- Therapeutic agent discovery including computational and bioinformatics methods to identify new therapeutic targets; Systems biology methods to understand the entire disease and therapeutic response pathways and identify multiple therapeutic targets;
- Pre-clinical medical product development including the rationalization and modernization of animal toxicology testing, development of shared resources for pre-clinical drug evaluation (e.g., knockout or humanized mouse models of transporters and enzymes, cell lines expressing enzymes and transporters, siRNA methods directed towards enzymes and transporters, genomics and proteomic methods to evaluate drug toxicities; in silico mathematical models to predict drug absorption, distribution, metabolism and excretion (predictive ADME) and drug toxicities and response;
- Clinical development of medical products (traditional small molecules and biotechnology products, diagnostic and therapeutic devices, alone or in combination with drugs) including pharmacokinetic/pharmacodynamic studies and models and statistical methods to optimize clinical trial efficiency, informativeness, and economy; the development of biomarkers, including imaging methods and other device technologies to assess drug efficacies and toxicities and improve diagnostic certainty, genomic, pharmacogenomic and other biomarkers for assessing variation in drug response and side effects;

In addition to the research focus, these Centers should sponsor training programs in medical product development and regulatory sciences (including FDA and industry scientists as faculty). These programs could range from degree granting programs (e.g., Ph.D. or M.S. in Drug Development Sciences) to short courses for industrial or regulatory scientists or training of visiting scientists.

We recommend that the Centers be housed primarily in academia, but that they include industry and regulatory agency partners. The partners would participate in all aspects of the research and educational missions of the Centers.

The University of California, San Francisco Schools of Pharmacy and Medicine have a longstanding interest in drug discovery and development sciences, and in conjunction with newly incorporated intellectual resources are prepared to make a major contribution to the Critical Path Initiative. Pharmacokinetics and pharmacometrics, key tools in drug development and regulatory sciences, grew out of research in the Schools of Pharmacy and Medicine at UCSF. More recently, UCSF, together with UC Berkeley and UC Santa Cruz has established an Institute of Quantitative Biology, focused on quantitative sciences. Key recruitments of quantitative scientists in chemistry, mathematics, bioinformatics, computational and systems biology to the Institute together with outstanding Schools of Pharmacy and Medicine have positioned UCSF to become a

leader in advancing drug development sciences. Recently, we have established a drug development pipeline in-house where we can study and hopefully optimize it. We are also founder members of and active participants in Pharmastart, a consortium mentioned in the Critical Path report. Further, we have the largest funded NIH center grant in pharmacogenomics, which has as its goal the development of rational drug therapies and genomic biomarkers, highlighted as one of the major areas of research in the Critical Paths report. Finally, this Fall UCSF will intensify these efforts by incorporation of the Georgetown Center for Drug Development Science into its academic team to advance its global strategy for radically improving medical product development science.

We would like to commend the FDA for its bold, visionary Critical Path report. Funding of research in medical product development by the FDA, the agency that has the greatest awareness of issues in product development, is important. We support the notion of partnering with the NIH, which has been increasing its support of translational research, and other regulatory agencies, as well as the pharmaceutical industry. Many of the issues related to product development are pre-competitive, and partnerships between industry, academia and regulatory agencies are needed at the level of program development, research and education.

Sincerely,

A handwritten signature in cursive script that reads "Kathleen M. Giacomini".

Kathleen M. Giacomini
Chair
Department of Biopharmaceutical Sciences

Cc Executive Director Regis Kelly, Institute of Quantitative Biological Research
Dean Mary Anne Koda Kimble, Dean David Kessler, Professor Leslie Benet