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July 30, 2004

Division of Documents Management
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

Re: Notice on the Critical Path Initiative, 69 FR 21839-40

The Association of American Medical Colleges represents all of the 125 U.S. medical schools, and over 400 teaching hospitals and 96 academic societies. The AAMC is pleased to offer brief comments on aspects of the FDA Critical Path document and *Federal Register* notice that are especially pertinent to our constituents in academic medicine.

We agree that the process of drug development (the Critical Path) is costly and time-consuming, and that improvements in any stage of this pathway could increase the rate and efficiency at which safe and effective new drugs are introduced into the market. We also believe that recent advances in the biological and natural sciences will provide new approaches that will accelerate the drug evaluation process. AAMC certainly supports the idea that improvements in regulatory science will benefit society as a whole.

While we applaud FDA's efforts to improve the drug development process, we are not convinced that the *major* cause of the seeming slowdown in new drug submissions derives from excessive regulatory burdens or the many uncertainties that characterize both clinical and pre-clinical testing. If this were the case, then one would expect to see evidence of a substantial accumulation of new biologically active molecules awaiting entry into phase I clinical trials. Rather, we believe that the problem derives mainly from the slow rate of drug discovery, a process that is intimately related to our current understanding of normal and abnormal biology. Although FDA is not directly involved in the discovery process, we would encourage the scientific community to consider this issue in greater detail.

Whatever the causes of the "dry pipeline," a few aspects of the Critical Path initiative are of potential concern to us. First, we object to the politically freighted presentation in Figures 1 and 2 of the Critical Path report of the stark contrast between the growth in NIH funding and the submission rate for new molecular entities. On its face, and without placing these data in their proper context, the attempt to correlate the rate of appearance of new drugs to levels of NIH funding can too easily give rise to the misleading impression that the biomedical research enterprise has somehow "failed" the public. For the past five decades, the central tenet of federal support of scientific research has been to invest in the creation of basic scientific knowledge, not in the production of products, which, with the singular exception of national defense, falls almost exclusively within the provenance of the private sector. Consistent with this tenet has been the strong political aversion to any federal policies that smack of "industrial planning."

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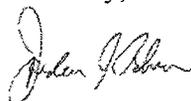
The vast majority of the NIH budget is for support of novel, hypothesis-driven research, which is distinct from the process of drug development. Certainly, the knowledge that derives from basic and clinical research provides the crucial insights required for the development of new and effective therapies. However, the translation of the former into the latter almost always involves some period of delay. For example, development of HIV protease inhibitors depended on elucidation of the pathogenesis of AIDS and a general understanding of the biology of retroviruses. These advances would have been impossible without prior development of the broad field of molecular biology. This and countless other examples serve to emphasize that basic research is a long-term investment that has repeatedly propelled the nation's productivity and economic leadership by yielding extremely valuable dividends that could not be predicted and were not evident originally.

Thus, AAMC believes that enhancing the rate of appearance of new prescription drugs in the marketplace is not the *primary* or immediate objective of federally funded biomedical research, although no one questions the importance of this goal.

Second, the Critical Path initiative calls for collaborative efforts among academia, industry, and government. These efforts involve a range of activities, from establishment of molecular databases to development of surrogate markers. We note that certain of these activities are embodied in the NIH Roadmap, an important objective of which is to strengthen the nation's clinical research enterprise. At the same time, in fostering greater collaboration across the scientific community, we urge that decisions that would commit greater NIH resources explicitly to solving problems in drug development (e.g., validation of biomarkers and surrogates) be approached with due consideration to the impact of corresponding reductions in support for basic and clinical investigation. This matter is of particular urgency to AAMC and the research community, given the impending restraint of growth of NIH appropriations at a time of unprecedented scientific promise. While we believe that partnerships among government, academia, and industry are laudable and can be very productive, we urge that all parties safeguard the resources that the public has allocated to laying the scientific foundations for tomorrow's progress.

Finally, with regard to the establishment of public-private partnerships, we would urge that you consider ways to reduce the formidable barriers created by the intense emphasis on the capture and protection of intellectual property that pervades nearly all sectors of the biomedical research community, and which has moved steadily "upstream" in the creative scientific process over the past two decades. There is compelling economic theory that warns of the perverse effects of premature privatization of fundamental knowledge on the translation of discovery into practice and social benefit. AAMC urges that any new public-private partnerships that are created to facilitate the drug discovery and development enterprise be established on a *pre-competitive* basis.

Sincerely,



Jordan J. Cohen, M.D.