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April 13, 2004

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Email: [jjohannessen@oc.fda.gov](mailto:jjohannessen@oc.fda.gov)

Re: Innovation or Stagnation? -- Challenge and Opportunity on the Critical Path to New Medical Products (“Critical Path White Paper”) – 69 Fed. Reg. 18094, April 6, 2004

Dear Dr. Johannessen:

Thank you for the opportunity to comment to the FDA and the Science Board as the Agency launches the program described in the Critical Path White Paper (or “Proposal” -- <http://www.fda.gov/oc/initiatives/criticalpath/whitepaper.html>). We are nonprofit and volunteer patient advocates working in the field of HIV/AIDS vaccine and treatment development dedicated to accelerating ethical research and global delivery of safe, effective and affordable drugs, biologics and microbicides to combat the AIDS pandemic. Development, assessment, manufacturing, approval and delivery of such products (those that exist and those that need to be marketed) have lagged behind the urgent needs created by this worst of modern infections. We therefore have a great interest in - and are encouraged by - the FDA’s Proposal to identify priorities and create new basic toolkits to mitigate some of those problems.

We understand the recent publication of the Critical Path White Paper is a first step to announce opportunities for public comment, that the Proposal will grow and be further defined, and that later comment will also be welcomed. For that reason, these comments are preliminary and lay out some initial principles that will be refined as the FDA’s Proposal is elaborated.

**1. Clear, Practical Means to Secure the Interests of Patient Populations Should be a Feature of the Proposal’s Development.**

The focus of the Proposal - removing barriers to “innovative medical therapies reaching patients” – is well stated. We hope the end result will reflect the concerns and anxieties that patients dealing with serious illness have as to the safety, reliability, and availability of products. Effective participation of patient populations in the design and implementation of the Proposal, including identification of the Critical Path Opportunities List, is necessary to overcome natural fears about safety of participants in research, acceptance of research results and benefits responsive to patients needs. Patients of course also have primary concerns that the promise of

cost saving innovations in product assessment and manufacturing will be reflected in genuine improvements in affordability and access.

At the same time, compared to commercial or funded research organizations, patient representatives and advocates often lack the resources to learn about and provide timely input into the FDA's broader programmatic changes, such as this one, or to travel to meetings where decisions are made. Minority or low income groups are especially challenged in participating effectively, and – as the Institute of Medicine and others have shown - they are groups experiencing disparities in joining research efforts or benefiting from the results.

We appreciate the invitation the Agency provides to include patient groups in these discussions, but wider efforts are also warranted. During the development of the Critical Path Proposal, we request that FDA engage in dedicated outreach to affected patients – especially in minority and low income groups – to explain the Agency Proposal and account for patient concerns. Working with community leaders, outreach could include targeted and solicited invitations to nonprofit and volunteer organizations, local meetings and community based communication.

## **2. The Toolkits Should be Developed So as to Gain Wide International Acceptance, Maintain Credibility and to Support Similar Problem Solving Efforts in Other Jurisdictions.**

We agree with the FDA's premise in creating new tools that “lowering safety standards.... is not a preferable solution” to address delays and development. Deservedly, the FDA's existing safety and effectiveness requirements are recognized as among the most rigorous and they should not be diminished.

Real obstacles to “medical therapies reaching patients” remain, however, when the FDA's standards are either not accepted quickly by other countries or when the FDA itself acts to use its approval requirements without extended evaluation of the comparability of standards used by others or the difficulties other countries face in review of products.

The FDA participates in harmonization activities through the International Conference on Harmonization and other avenues. However those mechanisms may be slow and not apply in all jurisdictions where products developed in the U.S. or elsewhere should “reach patients.” We request that the development of the Proposal include practical discussions of how the toolkits will be used and regarded by others to affect the delivery of products wherever they may be needed.

Countries where U.S. approved products are urgently needed often lack resources, systems or basic procedures to review and accommodate entry of new products. We request that the FDA and other U.S. agencies take steps not only to publicize the results of the Proposal, if they accomplish the stated objectives, but to support the ability and interest of other countries to accept and use the new tools in a reasonable fashion. Comparability of standards others employ should also be encouraged. Such efforts would have positive impact mitigating some of the

FDA's own concerns with the safety and reliability of products marketed or made outside the United States.

An example that comes to mind is the recent international meeting in Botswana where the U.S. government opposed the use of available fixed dose combination generic drugs produced outside the United States to combat HIV/AIDS in limited resource countries where the U.S. itself wants to expend scarce funds for the greatest benefit in drug delivery. A number of experts as well as some members of Congress support use of the generics – which meet WHO approval standards – as appropriate in those countries and consistent with treaties such as TRIPS and the related paragraph 6 of the Doha Declaration to permit importation of drugs. The U.S. objections were based, not on the use of generics per se in these limited resource situations, but on concerns with the safety, reliability and manufacturing quality of the generics. Whether or not those concerns are justified, they point to the need for FDA to export its own expertise for use by others who are trying to produce safe and effective products to “reach patients.” FDA's mission would be served if it works with other countries in the dissemination of the toolkits and actively supports the variety of international regulatory programs overseeing the manufacture of desperately needed lower priced products. The Proposal should address ways to accommodate the standards employed in other jurisdictions and to provide material assistance to agencies in other countries. Demonstrable benefits would result if the toolkits and other standards FDA develops are used and supported to increase the credibility of products developed elsewhere.

### **3. The Critical Path White Paper Should Include Evaluation Measures To Document Beneficial Results in Final Drug Pricing.**

The theory of the Critical Path White Paper – that high costs of medical product development can be lowered to mitigate pressure on spiraling prices – is appealing. Often the reality experienced by patients is quite different. It is difficult to show a clear correlation between lowered development costs for any individual medical product and reduced prices for patients who need that product.

We strongly support reduction in development costs when the solution consists of improved methods that do not compromise the safety, efficacy and quality of products. However, to make the FDA's Proposal credible, it should contain clear ongoing and end result evaluation measures to demonstrate that one of the reasons products “reached patients” was because patients could now afford them. We also request that FDA promote discussion among the Agency, patient groups, manufacturers and researchers to obtain comfort that implementing this Proposal will indeed yield lowered costs for medical products.

### **4. The Safety and Effectiveness Assessment Toolkit Should Be Developed With Consideration for Other Ongoing FDA Initiatives.**

We appreciate the discussion in the Critical Path White Paper that there is an urgent need for improved reliable measures of safety and effectiveness. Many of the problems and potential solutions FDA reviews are frontline urgent matters faced by investigators working with NIH and in pharmaceutical companies in the development of HIV/AIDS vaccines, drugs and

microbiocides. We look forward to opportunities to provide more technical comment on specific tools at a later time.

We also believe it makes sense that the proposed changes in safety and efficacy requirements be performed with consideration for other ongoing FDA proposals. Specifically, FDA published extensive proposed rulemaking last year to revise pre- and post marketing safety and adverse reporting requirements.(68 Fed. Reg. 12406, March 14, 2003). The public comment period for that proposal has ended. To the extent that the Proposal will adopt safety and efficacy measures that rely increasingly on newer models, surrogate markers and indirect evidence of safety or efficacy, the FDA should require a level of adverse event reporting sufficient to yield information that can answer questions of causation responsibly and consistent with FDA's mission to protect public health.

FDA has also recently published a draft guidance to address the ICH E2E: Pharmacovigilance Planning (PvP) document (<http://www.fda.gov/cber/gdlns/ichpvp.pdf>). In keeping with the FDA's premise that lowering safety standards is not a preferable solution, use of the new safety toolkits should be developed taking the principles of pharmacovigilance into account.

Thank you for considering these comments. We regret not being able to attend the April 22, 2004 meeting of the Science Board in person and we request that copies of this letter be offered to the Board members. Please contact Robert Reinhard (tel: 415/268-7469; email: [reinhar@mofo.com](mailto:reinhar@mofo.com) or by letter to the header address) if you have any questions.

Sincerely,



**on behalf of:**

**AIDS Vaccine Advocacy Coalition** (<http://www.avac.org>)  
**San Francisco AIDS Foundation** (<http://www.sfaf.org>)

cc:  
Richard Klein, FDA  
David Banks, FDA