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## Global Research & Development

October 29, 2005

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

Dear Dockets Management:

Re: **Critical Path Initiative; Developing Prevention Therapies;  
Planning of Workshop**

[Docket No. 2005N-0311, 70 *Federal Register*, 44660, August 3, 2005]

Pfizer recognizes the importance of pharmaceutical development of preventive medicines and supports the FDA proposal to conduct a workshop to explore the challenges and opportunities in development of chemo-preventive therapies.

The scope of potential scientific and regulatory topics relevant to the development of drugs for disease prevention is wide-ranging and any set of the topics would enable interactive discussions. As such, Pfizer suggests planning for a series of workshops rather than attempting to cover multiple topics in a single 2-day meeting. For a first workshop, Pfizer recommends that the focus be on issues fundamental to chemo-prevention development, specifically:

- identification of key hurdles for the development of prevention therapies,
- discussion of the challenge of adequately identifying and modeling the benefits-risks for chemo-prevention therapies,
- identification of therapeutic areas and/or diseases with critical needs for prevention therapy strategies, and
- recommendations for defining a regulatory path for approval.

Subsequent discussion of disease-specific chemo-prevention development approaches and issues, would inform for future workshop topics. These subsequent workshops could focus on developing action plans to achieve therapeutic area-specific prevention therapy goals.

Suggested topics for the first broad issues workshop include the following:

**Novel Clinical Measuring Tools:**

- Development of chemo-prevention therapies requires the use and regulatory acceptance of novel clinical measuring tools including biomarkers, to demonstrate efficacy. These tools are needed for physicians and patients to enable monitoring of effective disease prevention. These tools are also needed by drug developers to enable clinical study in potentially cost-prohibitive prevention trials. Discussion of how the regulatory pathway for qualification and acceptance of novel clinical measuring tools for use in clinical trials can be expeditiously designed and employed, should be a key topic of this workshop. As this topic is developed, one can envision the use of disease or indication-specific case studies as illustrations of learnings or challenges to defining the regulatory path.

**Alternate Clinical Development Methods:**

- Discerning the benefit-risk profile of chemo-prevention therapies can be time consuming and expensive. Alternate development paradigms to allow initial approval and use of novel chemo-preventive therapies in defined patient subsets should be explored. How patient subsets should be defined, and how the application of post-launch monitoring and Phase 4 clinical study can be used to expand approved patient populations, should also be explored. Discussion of the regulatory, prescribing, information technology and monitoring tools needed to facilitate this approach, is a suggested workshop topic. This could also include discussion of possible study designs using specific examples such as the use of the Gail Model to assess breast cancer risk in support of tamoxifen use.

**Quantitative Frameworks for Benefit-Risk Analysis:**

- All drugs have associated risks as well as benefits. Developing therapies to prevent future disease in healthy individuals or subjects with very early disease requires that potential risks and benefits be both understood and compared in a quantifiable manner. Absent agreed quantitative measures of benefit and risk, the difficulty associated with both the development and the approval of novel preventive therapies increases. Discussion of potentially applicable analytical frameworks, including those used in other regulatory settings, to improve quantitative benefit-risk assessment in chemo-preventive intervention, is a recommended workshop topic.

**The Cost of Disease and the Value of Disease Prevention:**

- There are economic as well as health imperatives for developing a path for prevention therapy. A discussion of the economic impact of disease prevention would be an important aspect to consider for this workshop. For example, what is an appropriate cost-benefit model to assess the value of a therapy that would delay diabetic complications by five years in diabetes patients? How does this type of modeling contribute to the overall goal of developing prevention therapies?

To facilitate the breadth of discussion it may be advantageous to invite a range of participants beyond industry, industry trade associations, FDA, NIH, and medical academia. Suggested additional participants include:

- other professional societies such as the International Society for Pharmacoepidemiology (ISPE), the Society for Epidemiological Research (SER), the College of Preventive Medicine, the American Medical Association (AMA), and disease-specific associations,
- other government agencies that assess benefit-risk such as the EPA, the FAA, and NASA,
- payers/insurers including CMS and Academics in health economics, and
- experts in medical ethics.

We appreciate the opportunity to provide comments and commend the Agency for pursuing guidance on this topic. Additionally, we would invite direct dialog with the Agency if you would consider the opportunity valuable.

Sincerely,

A handwritten signature in cursive script that reads "Melissa S. Tassinari". The signature is written in black ink and is positioned above the typed name and title.

Melissa S. Tassinari, Ph.D., DABT  
Senior Director  
Pfizer Global Research and Development