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March 21, 2006

Michael Leavitt
Secretary of the Department of Health and Human Services
200 Independence Avenue, SW
Room 615F
Washington, DC 20201

Dear Secretary Leavitt:

Thank you for your thoughtful comments at the March 16th PhRMA session. This letter is intended as follow-up to my question at that meeting regarding disease prevention initiatives.

In early 2004, Health and Human Services hosted a multi-industry roundtable discussion to engage in a dialogue on the growing societal problem of an aging population, rising health care costs, and the importance of health promotion and disease prevention in addressing these problems. The benefits and costs of investing in prevention as well as opportunities for strategic partnerships between the public and private sectors were discussed. The purpose of this letter is to ask the administration to swiftly reengage on the critical issue of preventive medicines.

Prevention of disease represents a large unmet medical need. The aging U.S. population presents not only a challenge of increasing afflictions but also increasing patient expectations for treatment options. As healthcare cost structures shift, these baby boomers are becoming informed decision makers and demanding more proactive healthcare options. The success of the statin drugs is one clear example of the public's desire to be more proactive in managing their health risks. The role of chemoprevention in modifying the risk of cardiovascular events has unequivocally played a major role in reducing cardiovascular deaths in the last decade.

In spite of this hallmark example, the current drug development paradigm remains "treatment". However, far greater social and economic impact could be realized in settings such as cancer, diabetes, osteoporosis, Alzheimer's disease, and other devastating diseases as scientific advances allow us to identify those at risk and treat them with drugs that can halt, reverse or prevent the biochemical processes that lead to disease. The NCI and C-Change have identified development in prevention as vital to the mission to reduce suffering and death due to cancer by the year 2020. Also, the threats of bioterrorism and pandemic flu acutely highlight the need for preventive medicines.

Currently, there are significant clinical, regulatory and economic barriers that are impeding research in this critical area of public health. Because of these barriers, few companies have any apparent focus on

Answers That Matter.

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primary prevention (excluding vaccines). Only 25 drugs, or 1% of all drugs in active development, are directed to a prevention indication.¹

Among these impediments to bringing a new prevention drug to physicians and their patients are the clinical and regulatory challenges. Prevention claims require more complicated and protracted drug development processes than treatment indications. Conducting prevention research requires additional time to develop and validate biomarkers and to validate clinically meaningful endpoints. Phase III trials for primary prevention indications tend to be more expensive, longer and larger due to the need to disprove an endpoint. The safety hurdles are much higher when a drug is given to disease-free patients for long periods of time. The current registration process is complicated due to ambiguous or lack of guidance regarding drug development for prevention therapies. Therefore, all else being equal, there is a natural bias to invest finite research and development resources on treatment rather than prevention.

There also are economic barriers to developing drugs for prevention. Existing intellectual property incentives are not well suited for prevention drugs. The patent clock for these drugs begins to run at the time the patent application is filed and continues to run during clinical development. As noted above, prevention trials typically are lengthy and could consume a substantial portion of a drug's patent life. Regulations that restore a portion of a drug's patent life consumed during the clinical development and approval phase (patent term restoration) and grant exclusivity upon marketing approval (data package exclusivity) in most cases are too limited to provide meaningful incentives. These barriers to innovation were recognized by the National Academy of Sciences and the Institute of Medicine in their 2005 report "Rising above the Gathering Storm." Among several improvements in the US intellectual property system, this report called for an increase in the length of data package exclusivity protection for pharmaceutical products.

Other economic barriers present significant challenges to the development of a preventive medicine. The lag effect between treatment and outcome means payors for prevention therapies may not receive the benefit; Medicare likely will. In order for a payer to cover a preventive medicine, the public health imperatives must be obvious and a specific patient targeted. Payors, practitioners and patients do not believe in surrogates or prevention economics. The current state of health care practice and reimbursement simply does not provide incentives for practicing prevention.

Clearly more needs to be done to tear down these barriers, create appropriate incentives and facilitate development and review processes so that people have every benefit of modern technology to stay healthy. The following clinical, regulatory and health policy reforms are recommended to facilitate the development of preventive medicines:

- Creation of a national task force of experts that represent all participants in chemoprevention and specifically cancer research to provide leadership and direction on these essential reforms.
- Development of comprehensive guidance by FDA on how to accelerate the drug approval process for prevention drug candidates.

¹ Lilly Research, data on file.

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- Development of standards for granting interim approvals based on surrogate endpoints associated with reduction of the targeted disease, especially in high-risk populations.
- Increased protection of data exclusivity for innovative medicines in the U.S.

Lilly regulatory staff has studied many of the barriers facing primary prevention and have shared these views with senior leadership at FDA (Including Drs. Woodcock, Galson, and Temple, June 30, 2004) and NCI (Dr. Andrew von Eschenbach, May 25, 2004). Our collective challenges are many but not insurmountable. Expedited attention is needed by HHS, FDA and others in order to remove or alter the impediments in the development of prevention therapies. Lilly is willing to collaborate and contribute intellectual capital to address the barriers that are slowing the development of drugs that prevent disease. We would be delighted to discuss this topic further with you or your staff at your convenience.

Sincerely,



cc: Andrew von Eschenbach, M.D.
Tim Franson, M.D.
Steve Paul, M.D.
Jen Stotka, M.D.
Janet Woodcock, M.D.
Billy Tauzin