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VICE PRESIDENT
SCIENCE POLICY AND TECHNICAL AFFAIRS

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October 18, 2005

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

Re: Critical Path Initiative; Developing Prevention Therapies; Planning of Workshop
[Docket 2005N-0311, 70 *Federal Register*, Nos. 148 and 161, pages 44660-44662 and
48962 (August 3, 2004 and August 22, 2005)]

Dear Sir/Madam:

The Pharmaceutical Research and Manufacturers of America (PhRMA) represents the country's leading pharmaceutical research and biotechnology companies, which are devoted to inventing medicines that allow patients to live longer, healthier, and more productive lives. PhRMA members invested an estimated \$38.8 billion in 2004 in discovering and developing new medicines. PhRMA companies are leading the way in the search for new cures.

PhRMA believes that encouraging the development of medicines for use in *primary prevention* of disease is also an important public health objective and appreciates very much the opportunity to help develop a workshop to address this opportunity through the attached comments. We look forward to a continuing partnership with FDA, along with other stakeholders, in this endeavor.

Sincerely,

Alice E. Till, Ph.D.

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2005N-0311

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Pharmaceutical Research and Manufacturers of America

Prevention Workshop Proposal

Background

Per the 3 August 2005 Federal Register Notice, the FDA seeks to explore both the approaches and obstacles to developing drugs, biologics, disease biomarkers, medical devices and vaccines to prevent or reduce illness. In the Federal Register notice, FDA noted that the potential topics to be addressed in a workshop on prevention therapies are very broad, and for this reason they are soliciting input on the key topics that should be discussed.

PhRMA Perspective

PhRMA, too, believes the scope is very broad and that a single workshop would likely be insufficient to address the breath of issues for this topic. In addition, PhRMA believes many of the topics proposed in the Federal Register Notice presume agreement and alignment among stakeholders on the importance of prevention as a health goal. While PhRMA believes that prevention therapy development is critical for the public health, other stakeholders may not share this view.

As such, PhRMA proposes a two-part workshop with the first workshop focused on gaining alignment among stakeholders about the importance of the development of prevention therapies and to delineate key issues hampering the current development of these therapies. A follow-up workshop would then focus on the tactical aspects including discussion of specific applications in the therapeutics areas identified as having a critical need for prevention therapy development.

Scope Proposal for Workshop 1

The scope of the initial workshop should focus on:

- Evaluating the needs and interests in prevention therapy (drugs, biologics, vaccines, etc.) development among stakeholders;
- Alignment of these stakeholders on the key strategic issues in prevention drug development and identification of opportunities to move the field forward;
- Establishing the collaborative relationships necessary to develop tactical approaches to addressing these issues and removing barriers in a subsequent workshop.

Goal of Workshop 1

If the interest and importance of developing prevention therapies are manifest in the workshop proceedings, a successful outcome of the workshop would bring about a prioritized ranking of this initiative (i.e., development of prevention therapies) under the Critical Path Initiative with a commitment to subsequent workshops for action planning and implementation. This commitment should reflect the need for collaborative efforts of stakeholders who will work jointly with the FDA to effectively address the issues and barriers in prevention development.

Goal of Workshop 2

The goal of the second workshop is to develop prioritized action plans to address issues and barriers in prevention development. Consistent with the Critical Path initiative the action plans need to focus on the transition from bench to bedside. Thus, engagement of decision makers at the policy level and those in the specific therapeutic areas identified as critical needs areas are essential to determining high level policy changes and creating disease specific plans.

Proposed Outline of Workshop 1

DAY 1.

I. Analysis of Current Environment Related to Development of Prevention Therapies

- Didactic presentations, including at least two perspectives (payor /industry; regulatory/ academic research) for the topics outlined below, followed by a facilitated panel discussion of various stakeholders are suggested. The panel discussion should focus on key questions that will address alignment on importance of prevention therapy development.
- Facilitated Panel Discussion: The panel should consist of decision-makers and leaders among the key stakeholders prepared to discuss level of interest in prevention therapies development and commitment to tackling issues and barriers. Topics are listed below.
- Illustrative Examples of Stakeholders* to Include: Payors (Government - CMS, VA Medical Center Research Area; Private - Kaiser, United Health, BCBS), companies involved in preventive care product development, FDA, academic health economist, NIH or other academic clinical developer

*(*Note: As requested in the Federal Register Notice, examples of stakeholders to include are being presented in this response. The list is not intended to be all inclusive.)*

Topics

A. Current State and Potential Opportunities

1. Background on approved treatments for prevention
 - b. What is the utilization of current treatments?

Suggestions for Case Studies:

A. Current Public Investment:

Investment relative to total R&D investment, review areas funded publicly (NIH/NCI, VA, etc)

B. Existing Treatments:

1. *Vaccines* - regulatory/policy issues public health need driving development, regulatory role in development and approval, drug utilization, impact on disease burden and economy
2. *Cholesterol/ LDL* – lowering - public health need driving development, regulatory role in development and approval, drug utilization, impact on disease burden and economy
3. *Prevention of Diabetes* - (e.g., Metformin in high body mass index population) - public health need driving development, regulatory role in development and approval, drug utilization, impact on disease burden and economics
4. *Others* - antihypertensives, prevention of breast cancer (e.g., Tamoxifen), osteoporosis prevention

B. What are the stakeholder interests in developing new prevention therapies?

1. Public Health Needs and Goals

- a. What disease areas are in most dire need of development of prevention therapies (i.e., biggest public health impact)?
- b. What are the motivators to support development in these disease states (e.g. disease burden measures, evolving science, etc.)
- c. What are the patients' and prescribers' interests in prevention therapies?

Suggestion for Case Study:

Prevention of Cancer- stated public health goals (NCI/C-Change/ASCO); stakeholder engagement (patients, prescribers, industry, payors)

2. Lessons Learned that Positively or Negatively Impact Future Research and Investment in Prevention Therapies

- a. What examples exist to demonstrate the positive impact of prevention therapies? (per FR notice this includes cholesterol lowering agents, antihypertensives, aggressive control of blood glucose to reduce long-term consequences of diabetes. Additional suggestions include Metformin for prevention of Type 2 diabetes)
- b. What attracted development in these areas? (e.g., accepted use of surrogates, defining new disease states, health economics models, etc.)
- c. What were the obstacles in developing therapies in these areas? (i.e., bench to bedside transition, epidemiologic data, role of MOA)
- d. What policy and regulatory issues slowed or accelerated development in these areas? (e.g., guidance documents, promotional claims)

3. What examples exist that create uncertainty in development of prevention therapies? (Case Studies: e.g., per FR notice, estrogens for prevention of heart disease; colon polyp / cancer prevention; osteoporosis prevention)

- a. What attracted development in these areas? (acceptance of surrogates, defining new disease states, health economics models, etc.)
- b. What was learned in these examples?
- c. What policy and regulatory issues slowed or accelerated development in these areas?

II. Gaining Alignment on the Key Issues for Stakeholders

- Didactic presentations representing various perspectives highlighting the key issues for given stakeholders should provide a framework for a paired panel discussion. The goal of the panel discussion is to gain alignment of the key issues most critical to address in order to improve development of prevention therapies.
- Panel Discussion: The panelists should be prepared to assess the relative importance of each as a barrier to prevention research, development, and utilization. The panelists should come to agreement on a prioritization list. The prioritization list will be the focus of the breakout session for the following day action planning. The didactic and panel discussions should cover such topics as:
- Stakeholders to include those who could address:
 - Benefit/Risk Issues: Industry safety and risk management representative, FDA safety and risk management representative, National Consumer League, FAA or EPA safety and risk management representative, academicians involved in risk-benefit assessment (e.g., CERTS)
 - Regulatory and Policy Issues: FDA Office of Regulatory Policy, Office of New Drugs, ODE Representation, Academic/Research Institutes, Industry
 - Prescriber: Medical Associations (American Medical Association, ASCO, American Diabetes Association, American Heart Association), Industry
 - Health Economics: FDA, CMS, Industry, Health Economics, Private Payors, other

A. Benefit / Risk Issues -

- Baseline risk assessment and use of surrogates
- Improving efficiency in safety assessment and risk communication
- Discuss progress towards an agreed upon framework for benefit/risk assessment
- Address shift from short term to long term use
- Broadening use of drug in treatment setting to lower risk tolerant groups
 - Impact on treatment use
 - Managing risk/benefit communication
 - Others

B. Regulatory and Policy Issues

Assess the relative importance of each as a barrier to prevention research, development, and utilization from the aspect of the various stakeholders.

1. Research and Development Incentives / Barriers

- Discuss current paradigm for development of prevention therapies
 - Use of established drugs in treatment setting
 - Duration of trials and hurdles for regulatory approval
- Discuss unique or enhanced intellectual property issues in developing prevention therapies
 - Effective patent life
 - Innovation incentives (e.g., Intellectual property protection biomarkers, surrogates)

2. Regulatory Process

- Establishing / Validating surrogates and disease biomarkers
 - What is an acceptable model for establishing surrogacy?
 - What needs to be done to accelerate validation and acceptance in registration trial designs?

- Regulatory mechanisms to facilitate development and approval processes
 - Guidances for prevention drug development
 - Recognizing “new” diseases with surrogate endpoints
 - Approval Mechanisms
 - Risk Management Plans
 - Alternative development and approval mechanisms for novel preventive therapies

C. Prescribers

- Obstacles in practice related to prevention therapies
 - What are the patient concerns?
 - Patient motivation issues
- Litigation and liability issues

D. Health Economics

Assess the relative importance of each as a barrier to prevention research, development, and utilization from the aspect of the various stakeholders.

- Cost-benefit assessment of prevention therapies
- Role of payors in determining patient eligibility for treatment
- Effect of risk stratification on patient insurability
- Disease states suggestive of health economic benefits from preventive therapies

III. Opportunities for Collaboration Across Stakeholders

Stakeholders who should present: Open to all to discuss topics including:

A. Stakeholder Roles

- Discussion by key stakeholders in driving prevention therapy development, policy, or technical expertise.
 - FDA
 - Payors
 - CMS/HHS
 - Private
 - Therapeutic Area Approaches
 - ASCO/NIH/C-Change
 - ADA
 - AHA
 - Others
 - Industry

B. Effective Partnering

- Academia/Industry/Government/Regulators/Patients/Payors
 - Identify demonstration projects or proof of concept studies

DAY 2.

A. BREAKOUT SESSIONS – 4 facilitated breakout sessions run simultaneously

1. Breakout Session: Development of Benefit / Risk Issues Action Plans

- What needs to be done to overcome these issues/barriers?
- Who are the key stakeholders in addressing the issues?
- Is there enough information to make a recommendation for specific actions to address these issues (e.g., in follow-on workshop)
- What other information is needed?

2. Breakout Session: Development of Regulatory / Policy Issues Action Plans

- What needs to be done to overcome these issues/barriers?
- Who are the key stakeholders in addressing the issues?
- What is the international perspective?
- Is there enough information to make a recommendation for specific actions to address these issues (e.g., in the follow-on workshop)?
- What additional information is needed?

3. Breakout Session: Development of Patients / Prescribers Issues Action Plans

- What needs to be done to overcome these issues/barriers?
- Who are the key stakeholders in addressing the issues?
- Is there enough information to make a recommendation for specific actions to address these issues (e.g., in the follow-on workshop)?
- What other information is needed?

4. Breakout Session: Development of Health Economics Issues Action Plans

- What needs to be done to overcome these issues/barriers?
- Who are the key stakeholders in addressing the issues?
- Is there enough information to make a recommendation for specific actions to address these issues (e.g., in follow on workshop)?
- What additional information is needed?

B. COORDINATED DE-BRIEF AND ACTION PLANNING FOR WORKSHOP 2

1. Debrief from each breakout session
2. A follow-up workshop should be planned to address:
 - the overarching prevention development issues identified in Workshop 1,
 - and therapeutic breakouts focused on the key disease states identified in Workshop 1 for specific, tactical action planning.

Additionally, identifying thought leaders and decision-makers to own the critical issues and establish effective collaborations should be a focus of the initial workshop that would then further invigorate interest in moving forward on this Critical Path Initiative.

C. FDA Conclusion / Next Steps

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