Removing barriers
to a larger national investment in chemoprevention drug development
2008
Executive Summary & Recommendations

C-Change
Collaborating to Conquer Cancer

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Chemoprevention Strategic Initiative Goals

The C-Change Cancer Chemoprevention Research initiative aims to resolve major barriers -- limitations in patent and intellectual property law; uncertainty of reimbursement; lengthy clinical trial processes involving the emerging science of biomarkers; and the uncharted regulatory approval process -- to stimulate an increased intellectual and financial investment in chemoprevention and cancer vaccine research.

By accelerating the development of promising chemoprevention agents, cancer can be prevented.

About C-Change

C-Change is a not-for-profit organization whose mission is to eliminate cancer as a public health problem, at the earliest possible time, by leveraging the expertise and resources of our members. C-Change is the *only* organization that assembles cancer leaders from the three sectors – private, public, and not-for-profit – from across the cancer continuum – prevention, early detection, treatment, and quality of life.

Former President George Bush and former First Lady Barbara Bush are Co-chairs of C-Change and Senator Dianne Feinstein serves as Vice Chair of C-Change, a 501(c)(3). C-Change is comprised of approximately 130 of the Nation's key cancer leaders who share the vision of a future where cancer is prevented, detected early, and cured or is managed successfully as a chronic illness.

One of the underlying principles of C-Change is to serve as both a forum and a catalyst for identifying issues and major challenges facing the cancer community, and for initiating collaborative actions to complement the efforts of individual C-Change Members. C-Change invests in the resolution of problems that cannot be solved by one organization or one sector alone.

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Introduction

At C-Change, we envision a future where cancer is prevented, detected early, and cured or managed successfully as a chronic illness. We recognize that enabling the promise of emerging research in chemoprevention is one key element in achieving this end. Several major systemic barriers currently deter further investment in the research and development of chemopreventive agents: 1) the limited life of patents in agents requiring a prolonged development time due to their preventive nature; 2) the uncertainty of reimbursement; and 3) and an uncharted clinical trial design and regulatory approval process.

Background

In 2006, C-Change hosted a summit of multidisciplinary experts and leaders to further define the barriers and potential solutions facing the field of chemoprevention Several major systemic barriers were identified as major deterrents to further intellectual and financial investment in the research and development of chemopreventive and immunoprevention agents: 1) the limited life of patents in agents requiring a prolonged development time due to their preventive nature; 2) the uncertainty of reimbursement; and 3) and an uncharted clinical trial design and regulatory approval process.

A summary of the summit proceedings is contained in the following journal publication:

> "Cancer Chemoprevention and Cancer Preventive Vaccines - A Call for Action: Leaders of the Diverse Stakeholder Groups Present Strategies for Overcoming Multiple Barriers to Meet Urgent Need," Herberman, et al, Cancer Research 66(24) December 15, 2006

Since the summit, an advisory committee and several sub-committees have developed and/or commissioned white papers proposing solutions to these patent law, reimbursement, and regulatory/scientific barriers. Below is a summary of the proposed solutions which are informed by these collaborative works by C-Change as well as an industry survey that was performed by Friends of Cancer Research.

Patent Law

Recommendations for removing the barrier posed by patent law are based upon the following documents:

> Commissioned scholarly manuscript: “Impact of Economic, Regulatory and Patent Policies on Innovation in Cancer Chemoprevention,” Henry Grabowski and Jeffrey Moe, 2007.
>
> Journal publication: “Impact of Economic, Regulatory, and Patent Policies on Innovation in Cancer Chemoprevention,” Henry Grabowski and Jeffrey Moe, AACR’s Cancer Prevention Research, Published Online First on April 14, 2008 as 10.1158/1940-6207.CAPR-08-0048. www.aacrjournals.org.

Patent Law (continued)

Recommendations for legislative action, encouragement, and/or agency encouragement:

- Congress should give positive consideration to lengthening the data exclusivity period for new chemo-prevention, biologic prevention, or immunoprevention agents to 14 years.
- Proposals for an abbreviated regulatory approval process for follow-on biologics must not simply mirror the 1984 Hatch-Waxman Statute. Policymakers must give careful consideration to the significant scientific differences between chemical and biological agents that, among other things, make establishing equivalence very difficult. The failure to understand this, could lead to unintended adverse clinical outcomes and compromise drug safety.
- If legislation providing an abbreviated approval process for biopharmaceuticals is considered, it should include a substantial period of data exclusivity.
- In considering patent law reform, Congress should carefully weigh the impact of such proposed reforms on the incentive system for new drug research and development. While we strongly support steps to enhance the quality of patents and reduce the cost of patent litigation, we do not support provisions that add to the risk and cost of drug research or reduce the deterrents to infringement.
- Targeted incentives such as those included in the Orphan Drug Act should be extended to the development of chemoprevention or other types of prevention agents for cancer. This would include the 50 percent tax credit for clinical trials and FDA input regarding clinical trial protocols. Consideration should also be given to some period of market exclusivity protection balanced against the interests of competition and new research.

Reimbursement

Recommendations for removing the barriers posed by the uncertainty of reimbursement are based upon the following document:

White paper: "Considering Reimbursement for Cancer Preventive Agents," C-Change/Pyenson, et al.

Recommendations for legislative action, encouragement, and/or agency encouragement:

- CMS should provide benefit coverage for approved cancer preventive agents and sponsor demonstration projects with newly approved cancer preventive agents to reduce the uncertainty of reimbursement for developers and to evaluate the long term economic value of cancer preventive agent regimens.

Clinical Trials / Regulatory Approval

Recommendations for removing the barrier posed by the uncertainty of reimbursement are based upon the following document:

> White paper working title: "Therapeutic Prevention for Cancer Risk Reduction: Proposed Pathway to Regulatory Approval for Chemoprevention," C-Change / Meyskens, Curt, et al. (Completion pending - Fall 2008).

Recommendations for legislative action, encouragement, and/or agency encouragement:

- FDA should define guidelines, criteria, and/or procedures for chemopreventive drugs and immunologic or other biologic preventive agents for:
  - Qualifying biomarkers as indications for agent use as well as agent efficacy, and safety
  - Utilizing biomarkers in cancer preventive clinical trial design
  - Advancing clinical trials from initial, proof of concept phase II trials in subjects with very high risk for developing invasive cancer to large scale phase III trials in populations with moderately or highly increased risk for developing invasive cancer
  - Defining parameters for acceptable drug side effect profiles for preventive cancer agents among populations at differing risk for developing cancer
- Congress should provide substantially increasing funding for preclinical and clinical research to develop promising and innovative agents for prevention of cancer, and for identifying and validating biomarkers to facilitate the development and appropriate application of preventive agents to the relevant populations.

Acknowledgement

C-Change wishes to thank the leaders from the private, public, and not-for-profit sectors who collaborated to advance this emerging field of cancer chemoprevention research. Without their expertise and cooperation, these thoughtful works and the actions based upon them would not have been possible. In addition to all of the contributors listed below, C-Change would like to specially acknowledge Dr. Ronald Herberman who has tirelessly led this complex initiative. C-Change would also like to recognize the leadership of the sub-group committee chairs, Catherine Bennett, Bruce Pyenson, Dr. Frank Meyskens, and Dr. Gregory Curt.

All C-Change committee members participated voluntarily. The participation of federal agency employees was limited to providing information regarding existing policies and practices and providing expertise on scientific matters.

Chemoprevention Advisory Committee

Ron Herberman, Chair	University of Pittsburgh Cancer Institute
Carolyn (Bo) Aldige	Cancer Research and Prevention Foundation
Anna Barker	National Cancer Institute
Gregory Curt	AstraZeneca
Marge Foti	American Association of Cancer Research
Gary Gordon	Abbott
Mark Mendenhall	American Association for Cancer Research
Homer Pearce	Eli Lilly, retired
Eddie Reed	Centers For Disease Control And Prevention
Ellen Sigal	Friends of Cancer Research
Robert Young	Fox Chase Cancer Center
Janet Woodcock	Food & Drug Administration

Chemoprevention Patent Law Advisory Sub-Committee

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Jeff Allen	Friends of Cancer Research
Daniel Kracov	Arnold and Porter LLP
Mark Mendenhall	American Association of Cancer Research
Homer Pearce	Eli Lilly and Company (retired)
Caroline Sigman	CCS Associates
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Chemoprevention Reimbursement Sub-Committee

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Kathryn Phillips-Campbell	National Business Group on Health
Scott Ramsey	Fred Hutchinson Cancer Research Center
Jayson Slotnik	Hogan & Hartson
Robin Zon	American Society for Clinical Oncology

Chemoprevention Clinical Trials & Biomarkers Sub-Committee

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Frank Meyskens, Co –Chair	University of California – Irvine
Dean Brenner	University of Michigan
Powell Brown	Baylor College of Medicine
James Crowell	National Cancer Institute
Jack Cusik	Cancer Research UK
Bob Dorr	University of Arizona
Craig Eagle	Pfizer
Scott Emerson	Fred Hutchinson Cancer Center
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Neil Gibson	OSI Pharmaceuticals
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