

Increasing the Nation's Investment in Cancer Chemoprevention Research: C-Change's Effort to Remove Barriers in Patent and Intellectual Property Law

Executive Summary and Call for Action by the C-Change Patent Law Advisory Committee* December 2007

Based upon the commissioned scholarly work
by Henry G. Grabowski and Jeffrey L. Moe of Duke University,
"Impact of Economic, Regulatory and Patent Policies on Innovation in Cancer Chemoprevention"

Scope of C-Change Initiative - Background

In the summer of 2006, C-Change convened the Cancer Prevention Research Summit - a meeting of scientists, oncologists, pharmaceutical researchers, governmental representatives, public policy experts, and patient advocates to discuss the barriers to research and development of chemoprevention drugs and unleash the potential of this promising field. Four major barriers were identified as deterrents to progress: limitations in current patent law and intellectual property (IP) protection; the impact of emerging science on the uncharted clinical trial design and drug approval processes; uncertain reimbursement mechanisms; and limited public participation in clinical trials. Proceedings from the summit were published in *Cancer Research* 66(24) December 15, 2006, "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."

Following this groundbreaking meeting, three complementary efforts ensued to propose solutions to the legal, regulatory, and financial barriers impeding the field. This document reports on the work and recommendations of the Chemoprevention Patent Law Advisory Committee. The complementary work of the other two groups will be released in the near future. C-Change believes the findings and recommendations of the three task forces, when viewed as a whole, will reflect a considered strategy to enhance research and development on chemoprevention agents in the future.

Focus of the Chemoprevention Patent Law Advisory Committee

The Chemoprevention Patent Law Advisory Committee is comprised of leaders with perspectives from the private, public, and not-for-profit sectors who have significant experience in the scientific and commercial development of pharmaceuticals. The deliberations of the group focused on whether there was something in the nature of chemoprevention drugs that discouraged research in the field and whether there were aspects of the current IP system that contributed to the problem. It also discussed whether a targeted set of incentives were needed to attract R&D investment to chemoprevention. From the professional experience of the Committee Members, there was a

general understanding of the significant risk, time and cost associated with the new drug development process. It was also understood that the current drug approval system was more geared towards treatment drugs as opposed to prevention agents. Did these forces combine to make it more risky, more time consuming and more costly to develop chemoprevention drugs such that the reward system of current IP law was insufficient to drive investment to this field? If true, what changes in the IP regime should be considered and were additional more targeted incentives warranted?

To better address these questions, C-Change commissioned a scholarly study to assess the current climate and explore potential improvements to the patent law and IP environment. A grant was awarded in response to a competitively issued RFP to Henry Grabowski and Jeffrey Moe of Duke University. Their study, entitled “*The Impact of Economic, Regulatory and Patent Policies on Innovation in Cancer Chemoprevention*”, was completed in October 2007 and can be found on the Department of Economics website at:

<http://www.econ.duke.edu/Papers/PDF/BarrierWorkingPaper.pdf>. The paper has been submitted to a law journal for peer review and publication. A condensed version is being developed for publication in AACR’s new Cancer Prevention Research journal.

Key Findings of the Grabowski-Moe Study

- The new drug research and development process is complex, costly, risky and time consuming. More than 80 percent of new chemical entities that enter clinical trials fail to ever get FDA approval.
- Chemoprevention agents face greater scientific, regulatory and economic barriers than other pharmaceutical agents. They are particularly reliant on basic research discoveries, an arena in which there is a growing funding gap. Clinical trials for these drugs must generally be larger and longer, significantly adding to the cost of development. They face a regulatory system geared towards treatment agents and liability exposure more akin to that confronting the vaccine industry before the current vaccine compensation system was put in place.
- Patent protection is critical to new drug development. Approximately sixty percent of drugs would not have been developed without patent protection. In fact, IP rights are a core part of the US R&D eco-system. A limited period of market exclusivity is granted to reward the innovator and, in exchange, there is disclosure and dissemination of the discovery to further scientific progress.
- Patent protection and data exclusivity are two separate, but complementary, forms of intellectual property protection for pharmaceuticals and biologics. Data exclusivity recognizes the substantial investment in developing the safety and efficacy data required for new drug approval.

- Ideally, data exclusivity would delay abbreviated filings (ANDA's) and patent challenges until innovators have had an opportunity to earn a positive return on the new drugs that make it through the approval process.
- The “socially optimal exclusivity time” requires a balancing of incentives for new product development versus market competition. Where the R&D process is more costly and risky, data exclusivity periods need to be longer. This is especially true where there are important external benefits to society as is the case with new medicines.
- The 1984 Hatch-Waxman statute has had a significant impact on the pharmaceutical marketplace and the economics of new drug development. While designed to foster competition by facilitating generic drug approvals and to spur R&D investment through patent term restoration, there is evidence that the statute's long-term net effect has tilted the balance away from the research-based industry. According to the CBO, the present value of cash flows from new drug introduction declined an average 12 percent as a result of generic competition facilitated by the 1984 Act. The increasingly rapid loss of sales post-generic entry has outweighed the benefits of patent term extensions.
- Other more recent adverse trends impacting new drug development include rising R&D costs, fewer NCE's, declining exclusivity periods, even more rapid post-generic entry losses, and vastly increased Hatch-Waxman patent litigation. The latter is linked to the 5-year data exclusivity period and has interjected a new uncertainty into the new drug development process.
- Proposals for establishing an abbreviated approval pathway for so-called follow-on biologics should be particularly mindful of the scientific differences between chemical and biological agents and the changing economics of new drug development.
- Data exclusivity is of particular importance to biopharmaceuticals in view of the fact that early stage development is so concentrated in start-ups and so reliant on venture capital. The levels of intellectual property protection, perceived risk and levels of uncertainty guide such investors.
- New chemoprevention agents are most likely to be based upon new indications for existing oncological products and are most likely to be biopharmaceuticals. To the extent the cost and risk of pursuing these new indications grows due to the manner in which Congress addresses the bio-similar or follow-on biologics issue it will have a significant impact upon chemoprevention drug development.
- Without endorsing any specific pending proposals, the authors suggest that the current 5-year data exclusivity period for pharmaceuticals seems inadequate. An analysis of economic data for new drugs and new biologics introduced in the US suggests a 14-year period would more closely align the protection with the time necessary for a new agent to

earn a positive return on the large, upfront R&D investment for new drug development and approval and more closely align the US with global competitors in science and industry.

- Patent law reform legislation pending in the 110th Congress could also have an impact upon the economics of new drug development, including chemoprevention agents. To the extent the legislation improves the quality of patents and reduces the cost of litigation, this development will be positive. At the same time, there are a number of provisions in the proposed legislation that could increase uncertainty and reduce deterrents to infringement. In the authors view, the increased uncertainty associated with open-ended post-grant patent review provisions could be especially problematic for pharmaceutical innovation. Moreover, the proposed apportionment of damages provisions could lead to increased willingness of parties to infringe patents.
- Other policy alternatives to increase R&D investment in chemoprevention drug development include “push” strategies that target government grants or subsidies to such investments. By having the effect of lowering R&D costs and risks, they help bridge the funding gap that characterizes the early stages of the R&D process, especially in the chemoprevention arena.
- The goal of increasing chemoprevention research and development might also be served by looking to the lessons of the Orphan Drug Act. This statute includes three provisions that reduce R&D costs. First, it provides for a 50 percent tax credit for clinical trials. Second it includes a modest research grant program targeted at early stage development. Third, it requires the FDA to advise drug sponsors on acceptable research protocols. These measures are combined with the additional incentive of a guaranteed 7 year market exclusivity period.

Recommendations for Action from the Chemoprevention Patent Law Advisory Committee

- Congress should give positive consideration to lengthening the data exclusivity period for new chemo-prevention 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 agents. 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.

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