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**COMMENTS**

**of the**

**WASHINGTON LEGAL FOUNDATION,  
ABIGAIL ALLIANCE FOR BETTER ACCESS  
TO DEVELOPMENTAL DRUGS, AND  
LORENZEN CANCER FOUNDATION**

**to the**

**U.S. DEPT. OF HEALTH AND HUMAN SERVICES**

**concerning**

**STIMULATING INNOVATION  
IN MEDICAL TECHNOLOGIES**  
*[Docket No. 2004S-0233]*

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August 20, 2004

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August 20, 2004

The Hon. Tommy G. Thompson  
Secretary  
U.S. Department of Health and Human Services  
200 Independence Ave., S.W.  
Washington, D.C. 20201

**Re: Stimulating Innovation In Medical Technologies [Docket No. 2004S-0233]**

Dear Mr. Secretary:

The Washington Legal Foundation (WLF), the Abigail Alliance for Better Access to Developmental Drugs, and the Lorenzen Cancer Foundation commend you for your decision to establish a cross-agency task force to examine barriers to innovation in medical technology and ways to encourage such innovation. We are submitting these comments in response to the request for input issued by the task force.

In HHS's announcement of the task force, you rightly stated, "Often, a new technology must clear several hurdles in different parts of HHS before it can reach consumers. By better coordinating this process across HHS, we can streamline the way we do business and make safe, effective medical technologies more quickly and readily accessible to Americans who could benefit from them." As detailed below, we believe certain HHS policies are unjustifiably deterring medical innovation or are chilling communications about medical innovations to doctors and patients; we recommend a number of strategies for reforming these policies.<sup>1</sup>

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<sup>1</sup> These comments are responsive to questions 1 and 6 in the Solicitation of Comments.

## **I. Interests of Commenters**

Commenter WLF is a nonprofit public interest law and policy center based in Washington, D.C., with supporters nationwide. Since its founding in 1977, WLF has engaged in litigation and advocacy to defend and promote individual rights and a limited and accountable government, including in the area of patients' rights. For example, WLF successfully challenged the constitutionality of Food and Drug Administration restrictions on the ability of doctors and patients to receive truthful information about off-label uses of FDA-approved medicines. *See Washington Legal Found. v. Friedman*, 13 F. Supp. 2d 51 (D. D.C. 1998), *appeal dismissed*, 202 F.3d 331 (D.C. Cir. 2000).

Commenter Abigail Alliance is a nonprofit organization based in Arlington, Virginia, dedicated to helping terminally ill patients obtain access to the medicines they need. Abigail Alliance was founded in 2001 by Frank Burroughs, who is now its president. The group is named for Burroughs's daughter, Abigail, an honors student at the University of Virginia. Abigail died of cancer on June 9, 2001, after she was stymied in her efforts to obtain new cancer drugs that her oncologist believed could save her life, but which were still in clinical trials. Abigail Alliance has numerous members and supporters who are suffering from terminal illness or who have lost family members to terminal illness.

Commenter Lorenzen Cancer Foundation is a nonprofit organization based in Monterey, California, providing assistance to patients fighting pancreatic cancer. The Foundation maintains a large database of clinical trials of pancreatic cancer therapies, as well as current medical news, to aid these patients and their physicians in keeping up to date on the range of available

treatment options for pancreatic cancer. The chairman of the Foundation is Lee Lorenzen, who founded it in response to the diagnosis and subsequent passing of his brother Gary Lorenzen due to metastatic adenocarcinoma of the pancreas.

WLF, the Abigail Alliance, and the Lorenzen Cancer Foundation previously submitted comments to the Centers for Medicare and Medicaid Services on February 10, 2004, regarding two national coverage reviews pending for certain off-label anti-cancer therapies based on FDA-approved medicines, and submitted comments to CMS on June 25, 2004, concerning the inclusion of off-label uses in CMS's Section 641 Demonstration Project for self-administered medicines.

## **II. HHS Should Strive For Greater Transparency in Regulating Industry Practices**

Major expansions in civil or criminal liability for industry practices should be undertaken openly, through standard legislative or regulatory processes. Theories of liability that are introduced on an *ad hoc* and retroactive basis by prosecutors will undermine the legal predictability that is needed by companies contemplating massive investments in new medical products. For this reason, FDA and CMS should normally have the lead in defining the scope of permissible behavior for pharmaceutical and medical device companies – doing so through written regulations.

Recent trends in federal prosecutions and investigations, however, have sought to render manufacturers liable for promotional practices, including communications about off-label uses, based on novel theories under the False Claims Act and Anti-Kickback Statute. In the recently-

settled Pfizer/Warner-Lambert case involving Neurontin, for example, the government made no allegation (so far as we can determine) that the company disseminated *any* untruthful or misleading information regarding the safety or efficacy of the drug. Rather, federal prosecutors claimed, apparently for the first time, that pharmaceutical companies such as Warner-Lambert are liable for “false claims” submitted to Medicaid by doctors – not because the pharmaceutical company was ever involved in the paperwork, but because the Medicaid programs of eight states do not reimburse for off-label uses, and the company encouraged off-label prescribing by doctors.

There are signs that this trend in policymaking by prosecution has yet to reach its high-water mark. In the May 21, 2004, issue of the trade journal *Rx Compliance Report*, Assistant U.S. Attorney Thomas Kanwit was quoted as saying, “There is regulatory language to suggest that it [an off-label use] may be an intended use if the company is aware of the use” – *i.e.*, that it is a criminal violation for a company to do nothing to stop off-label use of its products when it becomes aware of that use. Mr. Kanwit then ventured a “personal view” that the Government “probably” would not bring a case solely on that basis. Mr. Kanwit was also quoted as stating that a claim for Medicaid reimbursement can still be a “false claim” even when the off-label use is one listed in a recognized medical compendium. The newsletter presumably sought Mr. Kanwit’s views because he is the assistant who handled the May 13, 2004, plea agreement with Warner-Lambert.

We do not doubt that the vast majority of government attorneys involved in these cases have the public interest – *as they perceive it* – uppermost in their minds. But prosecutors have

neither the expertise nor the responsibility to make national health policy. HHS must exercise that responsibility by promulgating openly-accessible regulations (with appropriate safe harbors based on First Amendment limitations and sound policy) to define improper practices, particularly with respect to communications with doctors and patients.

### **III. HHS Should Recognize the Critical Importance of Off-Label Prescribing**

As is well known, once the FDA approves a new drug for marketing, physicians may prescribe the drug for indications other than the specific ones for which the FDA has given marketing approval. The recent prosecutorial actions noted above, along with statements by HHS's Office of Inspector General, have perpetuated the notion that when pharmaceutical companies communicate with doctors about off-label uses, or even when the companies fail to suppress off-label uses, the companies are preying on gullible doctors.

Off-label use is vitally important as a source of medical innovation and as a pathway for bringing the benefit of new medical knowledge to patients. Off-label prescribing allows physicians to take advantage of the most current research and experience concerning a drug's properties for the benefit of their patients. "Off-label prescribing is common in the areas of obstetrics, oncology, pediatrics, and infectious disease (particularly with AIDS patients)."

V. Henry, *Off-Label Prescribing: Legal Implications*, 20 J. Legal Med. 365, 365 (Sept. 1999). Physicians, the FDA, private insurers, and CMS have long understood that off-label prescribing represents the standard of care for many seriously ill patients.

Congress has also recognized the importance of off-label uses and of reimbursement for

those uses. In the late 1980's and early 1990's, Members of Congress learned of reports that the Medicare program, through the exercise of contractor discretion, was denying reimbursement in some instances for off-label uses of cancer medicines. A General Accounting Office survey and analysis released in 1991 confirmed that off-label prescribing is integral to oncology practice: One-third of all drug administrations to cancer patients were found to be off-label, and over half of all cancer patients were found to receive at least one off-label drug. The study also revealed that federal and private denials of reimbursement were directly affecting the quality of care. Some 62 percent of oncologists in the survey reported that they had admitted patients to hospitals within the past three months to avoid anticipated problems with reimbursement for cancer medicines. Eight to ten percent of oncologists reported altering therapies on account of expected reimbursement problems. Thus, on a broad scale, cancer patients were either being subjected to unnecessary hospital stays or being deprived of the therapy of choice for their cancer. Oncologists named the reimbursement policies of Medicare contractors as the number one cause of these unwanted practices.<sup>2</sup> Recognizing the benefits of off-label prescribing, Congress properly decided to put an end to this situation with respect to oncology patients in the Medicare program in 1993.<sup>3</sup>

Federal policies that demonize off-label prescribing, or that deny reimbursement for needed off-label prescriptions, will undermine a long-established and accepted means of

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<sup>2</sup> General Accounting Office, *Off-Label Drugs: Reimbursement Policies Constrain Physicians in Their Choice of Cancer Therapies* 3, 5 (Sept. 1991) (GAO/PEMD-91-14); *General Accounting Office, Off-Label Drugs: Initial Results of a National Survey* 21, 23-24 (Feb. 1991) (GAO/PEMD-91-12BR).

<sup>3</sup> Omnibus Budget Reconciliation Act of 1993, Title XIII, 103 Pub. L. 66, 107 Stat. 312 (1993), § 13553(b). In this legislation, Congress amended 42 U.S.C. § 1395x(t) to require the Medicare program to reimburse for off-

enabling doctors to give their patients the benefit of the latest medical advances, especially for patients with conditions having few or no FDA-approved treatment options.

#### **IV. HHS Should Greatly Broaden the Availability of Investigational Drugs to Seriously Ill Patients**

Current FDA rules governing the use of investigational drugs present a significant barrier to the availability of life-saving or life-extending medical innovations to patients who need them. Some evidence of an investigational drug's safety and effectiveness, and its risks, is often known to patients, physicians and others well before the FDA completes its process and makes a decision. From the perspective of terminally ill patients who may benefit from investigational drugs, and who have no approved treatment options, treatment with those drugs may well present a worthwhile tradeoff of risk and potential benefit. Yet current policies deny those patients the choice to opt for treatment with investigational drugs in consultation with their physicians.

In the context of life-threatening diseases, the traditional public health rationale for limiting access to investigational drugs has substantially diminished force. Participants in the clinical trials are able to obtain a drug that may prolong their lives, while the excluded patients face an increased risk of dying in the near term from their disease because it is being left untreated or inadequately treated. We believe many thousands of Americans die every year for lack of access to investigational medicines that could save or prolong their lives – even though these same medicines are available to patients who have secured one of the relatively few places

in clinical trials or in the sponsor's compassionate use or expanded access program.

Commenters WLF and the Abigail Alliance filed a Citizen Petition with the FDA on June 11, 2003, urging the agency to adopt a program for earlier availability of lifesaving drugs during the approval process. (FDA Docket No. 2003P-0274/CP1.) We are encouraged by HHS's announcement that a proposed rule to govern treatment use of investigational drugs is among the agency's priorities for the second half of 2004; however, we also note with dismay that the initiative was first published as a priority in HHS's regulatory agenda issued in December 2003, more than eight months ago, with no public action taken since that time. We would be glad to further assist HHS in identifying the objectives that should be met by the proposed rule, and in mapping out the details that will allow those objectives to be met.

**V. HHS Should Examine the Role of Knowledge-Based Development in Drug Testing and Approval Policies**

In the last decade, much progress in drug development has come from knowledge-based invention – drug discovery based on rapidly expanding biomedical knowledge that is transforming our understanding of disease and bringing us new, better treatments. The fundamentals of our regulatory approach to clinical trials and endpoints, in contrast, were designed decades ago to confirm the effectiveness of drugs discovered largely by trial and error. Regulators laboring under the same limitations as researchers were, naturally, constrained to rely heavily on purely statistical, knowledge-blind approaches to assessing safety and efficacy.

The increasing role of a new model of drug development, based on knowledge of a

drug's activity at the molecular level, presents policymakers with important questions: In this emerging era, to what extent should regulators consider non-statistical information in approving new medicines? Should clinical judgment and direct scientific knowledge of disease and treatment mechanisms become more central to approval decisions, at least for serious and life-threatening diseases? While continuing to exploit the value of statistical methods, can FDA regulators and their advisory committees adopt new approaches to approval that will more effectively serve the needs of patients? By examining these questions now, HHS can assure that the United States drug approval process keeps pace with advances in medical understanding.

## CONCLUSION

The Washington Legal Foundation, the Abigail Alliance for Better Access to Developmental Drugs, and the Lorenzen Cancer Foundation respectfully request that HHS's task force on medical innovation address the need for transparent regulatory policies, the importance of off-label prescribing, the urgency of broadening the availability of investigational drugs to seriously ill Americans, and the potential utility of giving drug approval authorities a wider array of decision-making tools.

Respectfully submitted,

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