ONE HUNDRED EIGHTH CONGRESS

Congress of the United States

House of Representatives

COMMITTEE ON GOVERNMENT REFORM

2157 RAYBURN HOUSE OFFICE BUILDING

WASHINGTON, DC 20515–6143

MAJORITY (202) 225–5074
FACSIMILE (202) 225–3974
MINORITY (202) 225–5051
TTY (202) 225–6852

www.house.gov/reform

June 7, 2004

Mr. Alan F. Holmer
President
Pharmaceutical Research and Manufacturers of America
1100 Fifteenth Street, NW
Washington, DC 20005

Dear Mr. Holmer:

I am writing about the failure of many pharmaceutical companies to submit information on their cancer clinical trials, as required by law, to a government website used by critically ill patients. This appears to be a disturbing example of the pharmaceutical industry refusing to make important information available to physicians and patients. I request that you address the industry's lack of participation in this initiative.

At issue is the website www.clinicaltrials.gov. This web site is supposed to list basic eligibility criteria and contact information for all clinical trials of the effectiveness of treatments for serious or life-threatening illnesses. It is intended to be a comprehensive resource for patients. However, according to data from the Food and Drug Administration (FDA), many industry sponsors of cancer research have not been posting information to this web site — despite a federal law requiring them to do so.

This failure has drawn the attention of senior FDA officials. At a recent Government Reform Committee hearing on cancer clinical trials, Dr. Richard Pazdur, the senior cancer drug reviewer at the agency, testified that he and his colleagues "are greatly concerned about the low participation of the industry."

Despite a request from the Committee, PhRMA did not send a witness to the hearing or submit written testimony. I ask that you address the industry's failure to comply with www.clinicaltrials.gov now.

The www.clinicaltrials.gov Registry

The website www.clinicaltrials.gov is a searchable online registry of clinical trials that patients with serious or life-threatening illnesses and their providers can use to see if they are eligible for participation. The registry was created under section 113 of the Food and Drug

Administration Modernization Act in 1997, and it applies to studies of effectiveness conducted under FDA's Investigational New Drug (IND) regulations for drugs and biologics.[1]

The statute states that any sponsor of a clinical trial for effectiveness of a treatment for a serious or life-threatening disease must submit information on the trial to the registry, unless the sponsor can demonstrate that submitting information would "interfere with timely enrollment of subjects."[2] The information must be submitted within 21 days of initiation of patient enrollment in a new trial.[3]

Despite these requirements, evidence shows that many private-sector sponsors of cancer-related clinical trials have not been submitting information to the registry. An April 2003 presentation by FDA staff showed that between January and September 2002, while 91% of cancer-related government-sponsored trials that fall under section 113 had been registered on www.clinicaltrials.gov, only 49% of such industry-sponsored covered trials had been registered.[4]

The failure of companies to comply with the law does not appear to be due to a lack of information about how to satisfy its requirements. FDA issued detailed guidances for industry about the registry in 2000,[5] 2001,[6] and again in 2002.[7] In October 2003, FDA reported sending more than 2,000 letters to private-sector drug companies "notif[ying]" them of their legal obligation to report clinical trials for effectiveness of drugs for serious and life-threatening

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[1] Section 113 of the FDAMA amended § 402 of the Public Health Service Act (42 USC § 282); 21 CFR § 312. Trials for effectiveness include all phase 2, 3, and 4 trials with "efficacy endpoints."

[2] 42 USC § 282(j)(4).

[3] 42 USC § 282(j)(3).

[4] J. Derbis et al., *FDAMA Section 113: Information Program on Clinical Trials for Serious and Life-Threatening Diseases*, Poster Presentation, FDA Science Forum (Apr. 24, 2003).

[5] FDA, *Guidance for Industry: Information Program on Clinical Trials for Serious or Life-Threatening Disease: Establishment of a Data Bank (Draft Guidance)* (Mar. 2000).

[6] FDA, *Guidance for Industry: Information Program on Clinical Trials for Serious or Life-Threatening Diseases: Implementation Plan* (Draft Guidance) (June 2001).

[7] FDA, *Guidance for Industry: Information Program on Clinical Trials for Serious or Life-Threatening Diseases and Conditions* (Mar. 2002) (online at http://www.fda.gov/cder/guidance/4856FNL.PDF).

illnesses.[8] FDA then sent another guidance for industry in January 2004 containing detailed instructions for submitting information.[9]

At a meeting with PhRMA representatives on May 6, Committee staff asked about the poor participation by companies in www.clinicaltrials.gov. PhRMA representatives responded that many PhRMA member companies make their clinical trial information available on the PhRMA website, and that a section of this website, called "New Medications in Development," provided contact information for sponsoring companies.[10]

The statute requiring registry of clinical trials does not contain any exemptions for trials that sponsors claim can be found elsewhere. Even if the law did have such an exemption, however, a review of the PhRMA website reveals that contact information is generally not provided with the clinical trials list. Nor does the site give any relevant information about eligibility or the parameters of the trial.

The purpose of the www.clinicaltrials.gov registry is to give patients a single website at which all relevant information can be found. In contrast, the purpose of PhRMA's site appears to be touting ongoing industry research without providing usable information for seriously ill patients.

The May 13 Hearing

On May 13, the Government Reform Committee held a hearing on clinical cancer research. I asked Dr. Richard Pazdur, the Director of the Division of Oncology Drug Products at FDA's Center for Drug Evaluation and Research, if increased industry compliance with www.clinicaltrials.gov would benefit patients. He responded:

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[8] *A Milestone for ClinicalTrials.gov Web Site*, FDA News (Oct. 27, 2003) (online at www.fda.gov/bbs/topics/NEWS/2003/NEW00965.html).

[9] FDA, *Guidance for Industry: Information Program on Clinical Trials for Serious or Life-Threatening Diseases and Conditions* 7 (Jan. 2004) (online at http://www.fda.gov/cber/gdlns/clintrial.pdf).

[10] The website is www.phrma.org.

> The answer to your question is emphatically yes. We also are greatly concerned about the low participation of the industry in listing their trials on [www.clinicaltrials.gov]. We've taken a concerted effort to try to find why, what is the reason, and I really don't have a good reason at that time, if I could say, "This is the reason why industry is not placing studies on the web site." One would think they would have every reason to place their trials on.
>
> If we're talking about poor accrual to clinical trials, industry can't cry about poor accruals to clinical trials if they're not putting it on the web site. In our own division and at the FDA in general after every phase two meeting and industry meeting, we have a written bullet that is part of the minutes to that meeting that specifically informs the sponsor of the existence and their obligation to list the web site. That is a written part of the minutes of every end of phase two meeting. We've taken concerted efforts to talk to patient groups to encourage patient advocates to advocate for participation of commercial sponsors to look for trials. In addition to that, we've taken a concerted effort of talking to industry about this.[11]

Dr. Pazdur's comments illustrate both FDA's extensive efforts to facilitate industry compliance and the lack of any reasonable explanation for the failure of industry to participate.

As you know, the Government Reform Committee requested that PhRMA send a witness to this hearing. However, despite a reported budget of $72.7 million for federal lobbying this year,[12] your organization was apparently unable to find a single executive, official, administrator, spokesperson, lobbyist, board member, or representative of a member company to testify. Nor did PhRMA submit written testimony.

Request for Information

Section 113 was enacted because people with serious or life-threatening illnesses and their doctors should have access to information about clinical trials for new medications. It was not enacted as a resource for sponsors of clinical trials to use for recruiting when they choose and to ignore when they deem their enrollment sufficient. Gaps in compliance with section 113 deny seriously ill patients access to information and clearly violate requirements placed on IND sponsors.

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[11] Testimony of Richard Pazdur before the House Government Reform Committee, *Hearing on Cancer Clinical Trials* (May 13, 2004).

[12] *Drug Companies Increase Spending on Efforts to Lobby Congress and Governments*, New York Times (June 1, 2003).

The failure to list studies on www.clinicaltrials.gov fits a disturbing pattern of the pharmaceutical industry failing to disclose important information on clinical trials to patients and their doctors. Recently, companies have proposed a voluntary registry of clinical trials, with results.[13] It is hard to imagine how effective such a system would be, given that companies are not participating in a mandatory registry containing simple enrollment information for critically ill patients.

I would like to know what steps PhRMA or its member companies have taken to improve compliance with the submission requirements for www.clinicaltrials.gov. Please provide any documents that PhRMA has sent to members concerning compliance with the law, any information that you feel is relevant in explaining the extremely low compliance rates discussed above, and a description of the actions PhRMA or its member companies are planning to improve compliance.

There is no guarantee that randomized clinical trials will provide a therapeutic benefit. But in some circumstances, these trials may represent one of the only options for terminally ill patients. I look forward to your cooperation in improving patient access to potentially lifesaving information.

Sincerely,

Henry A. Waxman

Henry A. Waxman
Ranking Minority Member

[13] *Two Studies, Two Results, and a Debate over a Drug*, New York Times (June 3, 2004)