Public Citizen

Buyers Up • Congress Watch • Critical Mass • Global Trade Watch • Health Research Group • Litigation Group
Joan Claybrook, President

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PUBLIC CITIZEN'S HEALTH RESEARCH GROUP'S STATEMENT TO THE UNITED STATES HOUSE OF REPRESENTATIVES COMMERCE COMMITTEE ON THE IMPLEMENTATION OF THE FOOD AND DRUG ADMINISTRATION MODERNIZATION ACT (FDAMA) OF 1997

Public Citizen was opposed to the 1997 Food and Drug Administration Modernization Act (FDAMA), both for what was included in the legislation and what was not. While numerous provisions of FDAMA directly and indirectly weaken FDA authority to protect consumers from unsafe drugs and medical devices, badly needed new enforcement powers - civil monetary penalties for any drug-related violation of the Food Drug and Cosmetic Act, giving the FDA authority to require mandatory recalls and to be promptly notified of voluntary ones, and subpoena power for drug and other regulated industry records - were not included in the Act.

Nor did the agency receive additional funding to carry out FDAMA's significantly increased workload. (Renewal of the Prescription Drug User Fee Act [PDUFA] at a higher level exacerbates rather than alleviates FDA's resources problem, since the fees can be used only to approve new drugs but not for postmarketing safety monitoring or postmarketing advertising surveillance once the drugs are on the market.)

Under FDAMA, consumers and patients will be exposed to significant new health and safety risks, while a weakened, resources-strapped FDA will have less authority and fewer staff to protect them. Vigorous and critical Congressional oversight - aimed at identifying and minimizing dangers to public health and safety, not placing increased political pressure on the agency to approve drugs and medical devices when significant safety concerns are unresolved - is essential.

Our comments today will focus primarily on one highly controversial section of FDAMA - Section 401, which, for the first time since 1962, allows manufacturers to promote drugs for unapproved purposes. But before turning to problems with how FDA plans to implement this section, we would like to briefly address the urgent problem of prescription drug safety. Specifically, Public Citizen is deeply concerned

that the drug approval policies that FDA has been pressured into following since 1992 - now codified in FDAMA - have lowered U.S. drug safety standards, arguably once considered the world's best, to pre-1938 levels when the Food Drug and Cosmetic Act was passed.

We find it ironic that the Committee is holding its first and only FDA oversight hearing this year on the implementation of FDAMA, rather than investigating the recent rash of injuries and deaths suffered by Americans from new but redundant drugs - that is, "me too" drugs that duplicate products already available to patients and their physicians - that have been approved with known safety problems as a result of drug approval polices now embodied in FDAMA.

In a period of only nine months three new drugs approved since 1996 have been removed from the market for safety reasons.[1,2,3] Serious safety questions had been raised about each, questions that should have, and could have, been answered before they were approved. None of the three were shown to have any therapeutic advantage over numbers of other drugs in their classes. Lives were needlessly lost because these unsafe drugs were approved despite the fact that patients and their physicians had multiple treatment options available to them in other, older (and safer) drugs approved for the same medical uses as these three new redundant drugs.

Just as troubling as the unneeded drugs with unacceptable risk benefit ratios now coming on the market in this country is the fact that dangerous drugs have been removed from the market in the United Kingdom (U.K.) that remain available in the United States. Two such drugs were banned in the U.K. in 1997.[4,5]

Unquestionably, patients with serious or life-threatening diseases should have access to safe and effective new drugs as expeditiously as possible. But now under the pressure that created FDAMA new drugs in classes where there are multiple effective alternatives available are receiving expedited approvals only because they have new mechanisms of action, with the possibility of new mechanisms of toxicity, and

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[1] U.S. Department of Health and Human Services, HHS News: FDA Announces Withdrawal of Fenfluramine and Dexfenfluramine. September 15, 1997.

[2] U.S. Department of Health and Human Services, Food and Drug Administration. FDA Talk Paper: Roche Laboratories Announces Withdrawal of Posicor From the Market. June 8, 1998.

[3] U.S. Department of Health and Human Services, Food and Drug Administration. FDA Talk Paper: Wyeth-Ayerst Laboratories Announces the Withdrawal of Duract From the Market. June 22, 1998.

[4] Committee on Safety of Medicines. Volital (Pemoline) has been withdrawn. *Current Problems in Pharmacovigilance* 1997; 23:9-12.

[5] Committee on Safety of Medicines. Troglitazone (Romozin) withdrawn. *Current Problems in Pharmacovigilance* 1997; 23:13-16.

no evidence that they are as effective or as safe as older drugs. The new diabetes drug troglitazone (Rezulin) is one example.

Troglitazone (Rezulin) has a different mechanism of action than the multiple other drugs in its class. Because of this difference, that is of no known clinical significance, troglitazone was reviewed by the FDA in less than six months. Neither troglitazone nor the other drugs in its class have ever been shown to reduce the serious illnesses associated with diabetes. However, tragically, at least 26 people have died from troglitazone-induced liver toxicity. (260 deaths may be a more realistic figure, since the FDA estimates that only one in ten adverse reactions are reported.) Troglitazone was banned in Britain on December 1, 1997, but remains on the market in the U.S.

The FDA's primary mission of consumer protection appears to have been recast under industry pressure, exerted through Congress, as industry's "partner" in marketing new drugs. Under this pressure for fast approvals, the performance of the FDA is now gauged, according to one FDA medical review officer, by "linking of the productivity of FDA reviewers with approval of new products . . . even if the new drugs are not as good as what is available already."[6]

OFF LABEL PROMOTION

Before the final votes in the House and Senate that led to the passage of FDAMA, fenfluramine (Pondimin), one-half of the notorious "fen/phen" diet drug combination, and Redux were withdrawn from the market because of heart valve damage and primary pulmonary hypertension, an adverse drug reaction that is fatal about 50 percent of the time. At the crux of this catastrophe was the prescribing of "fen/phen" for off-label uses and its promotion to an unaware public by unethical diet doctors and an unscrupulous diet clinic industry. Because both the Congress and the President disregarded the "fen/phen" disaster and one of the tragic lessons of medical history - that people can needlessly die when they are prescribed drugs for uses that have not been shown to be safe and effective - the American public will be forced to relive this history.

Representatives of pharmaceutical companies, who stand to reap economic benefit from off-label promotion, have complained that the "FDA's proposed rule goes beyond the carefully-defined statutory scheme to impose significant new requirements and constraints to narrow Section 401."[7] This charge ignores the context in which Section 401 should be placed: the long, well-documented history of danger to

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[6] Letter to the Editor, Robert I. Misbin, M.D. A possible drug fix? *The Washington Post*, August 24, 1998.

[7] Letter to Michael A. Friedman, M.D., Acting Commissioner, Food and Drug Administration from Alan F. Holmer, Pharmaceutical Research Manufacturers of America dated June 26, 1998.

consumers and patients from drugs that have been prescribed for uses that have not been shown to be safe and effective. This history led to the enactment of the Food Drug and Cosmetic Act (FDCA) in 1938, and in 1962, the adoption of the Kefauver-Harris Amendments to FDCA (requiring proof of safety and effectiveness before a drug could be marketed).

The 1962 Amendments to the FDCA were based on extensive evidence documenting the fact that physicians relying on their uncontrolled observations in their offices, and their colleagues' anecdotes and testimonials cannot weed out, or prevent the public from receiving, worthless or even dangerous drugs. Consumer protection required that Congress enact standards for a drug's safety and effectiveness based on rigorous scientific evidence. Unfortunately, the circumstances that required the 1962 amendment to the FDCA still exist today.

A growing body of research, accumulating since the early 1980s, indicates that some physicians base their prescribing decisions on drug company promotional materials rather than on clinically relevant scientific research. Physicians who are influenced by advertising may, in fact, prescribe inappropriate or dangerous drugs when there are more effective, safer alternatives available.[8, 9, 10, 11, 12]

Proof that practicing physicians can make fatal mistakes by prescribing drugs for unapproved purposes is, unfortunately, readily available. If all physicians were able to evaluate the scientific literature, or read and understood the FDA approved labeling, or were immune from the influences of advertising not a single patient would have been killed or injured from the diet drugs "fen/phen" and Redux or the painkiller bromfenac (Duract) banned on June 22, 1998. Instead, all too frequently these drugs were prescribed by doctors for off-label uses, with tragic results.

Thus longstanding and recent drug safety history provides extensive documentation for the fact that off-label prescribing is *inherently* risky to consumers and patients. Yet members of Congress and proponents of off-label drug promotion

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[8] Avorn J, Chen M, Hartley R. Scientific verses commercial sources of influence on the prescribing behavior of physicians. *American Journal of Medicine* 1982;73: 4-8.

[9] Bowman MA, Pearle DL. Changes in drug prescribing patterns related to commercial company funding of continuing medical education. *Journal of Continuing Education of Health Professionals* 1988;8: 813-820.

[10] Lexchin J. The medical profession and the pharmaceutical industry: an unhealthy alliance. *International Journal of Health Services* 1988;18: 603-616.

[11] Orlowski JP, Wateska, L. The effects of pharmaceutical firm enticements on physician prescribing patterns. *Chest* 1992;102: 270-273.

[12] Siegel D, Lopez J. Trends in antihypertensive drug use in the United States: Do the JNC V recommendations affect prescribing? *Journal of the American Medical Association* 1997;278: 1745-1748.

repeatedly stated when Section 401 of FDAMA was under consideration that the section could, and would, be implemented in a manner that would adequately safeguard consumers and public health. Unfortunately, FDA's proposed rule falls far short of these assurances.

Public Citizen believes that to provide a minimum level of protection for the American public from the substantial, known risks of off-label promotion, there must be a source of objective comparative drug information written for consumers placing the risks and benefits of prescription drugs in a context that can be used to make informed decisions about their drug treatments. The implementing regulations for Section 401 of FDAMA must be amended to require the following three critical safety elements:

1. **Labeling for Patients**

   a. Drug companies must be required to include labeling written specifically for patients as a part of the professional product labeling for each drug that a company chooses to promote for an off-label use.

   b. Patient labeling for drugs promoted for off-label uses must clearly notify consumers that the drug has been promoted for an off-label use and indicate the FDA-approved uses for the drug.

   c. Patient labeling must include sufficient, understandable information about the potential risks of the drug

2. **Full Public Access to Submissions, Requests, and Applications.** The regulations must require full public access to all drug company submissions, requests, and applications seeking permission to promote drugs for off-label uses whether or not the FDA approves the request. In addition, the regulations must require full public access to all submissions, requests, and applications made by drug companies seeking to promote their drugs for off-label use that have been denied by the FDA, including the reason for the denial.

3. **Full Public Access to Safety and Effectiveness Information.** The regulations must require full public access to all information held by the FDA pertaining to the safety or effectiveness of drugs that will be promoted for off-label uses.

Numerous sections of FDAMA, other than its off-label promotion provision, benefit multinational pharmaceutical companies and special interests at the expense of the American public by lowering our once high standards for consumer protection to a level that existed before the passage of the FDCA in 1938. These include:

- The pharmacy compounding provision creates a dangerous double drug standard in this country: (1) FDA approved drugs; and (2) drugs compounded and sold by pharmacists without proof of safety and effectiveness, and produced

outside the bounds of good manufacturing practices.

- Allowing private, for-profit firms to review and recommend approval of medical devices creates a system in which conflict of interest is inherent.

- Eliminating mandatory tracking and postmarket surveillance of implantable, high risk medical devices puts patients with those implanted devices at risk.

- Allowing the dissemination of health care economic, or pharmacoeconomic, information that is not based on valid scientific standards is nothing more than another platform for possibly misleading promotion of drugs by their manufacturers.

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Joan Claybrook, President

October 7, 1998

Honorable Thomas J. Bliley, Jr., Chairman
House Commerce Committee
U.S. House of Representatives
Washington, D.C. 20510

RE: Oversight Hearing on the Food and Drug Administration Modernization Act of 1997 (FDAMA)

Dear Chairman Bliley:

Since 1972, Public Citizen's Health Research Group has been actively monitoring the Food and Drug Administration (FDA) on behalf of consumers and patients. We promote research-based, system-wide changes in health care policy, as well as advocating for the appropriate prescribing and use of prescription drugs and medical devices. We testify before Congress and petition FDA on drug and medical device safety issues.

Together with the Patients' Coalition, Public Citizen's Health Research Group and Congress Watch were the major representatives of independent consumer and patient groups (i.e., those receiving no funds or subsidies from the pharmaceutical or medical device industries) in monitoring and critiquing FDAMA as it progressed through the legislative process. We expressed specific concerns with the potential adverse impact of numerous FDAMA provisions on consumer health and safety last year; we have submitted comments to FDA on our health and safety concerns with the implementing regulations this year.

We are writing to express two points about today's oversight hearing:

1. Drug Safety Issues Ignored. This will be the first, and only, FDA oversight hearing conducted by Congress this year - despite the fact that in the nine-month period between September 1997 and June 1998 - an unprecedented three new drugs were removed from the market for safety reasons. These drugs were approved with known safety problems, when numerous other drugs in the same classes were available, and caused the needless deaths and serious injuries of an undetermined number of American citizens. A drug approval process that emphasizes record numbers of new drugs rather than the public's safety appears to be the cause. Yet, FDAMA codifies the policies that led to the approval

of these drugs. Given this record, Congressional inquiry into how to protect the public from the approval of unsafe new drugs - and the impact of FDAMA on the drug approval process - is badly overdue.

2. Independent consumer and patient groups excluded. We find it very disturbing that the Committee has not invited any representatives of independent patients and consumer groups to testify today, given that representatives of the regulated industries will be appearing. This imbalance lends credence to the charge that FDAMA recasts FDA's primary mission from consumer protection to one of partnership with regulated industries in marketing their products.

Attached is testimony which we would have liked to present to the Committee today. We would request that it be included in the record of the hearing.

Sincerely,

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Public Citizen's Health Research Group

Maura Kealey
Public Citizen's Congress Watch

cc: Honorable John Dingell, Ranking Member and
Honorable Members, House Commerce Committee