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before the
Subcommittee on Health
Committee on Energy and Commerce
U.S. House of Representatives
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On PDUFA, Risk Evaluation & Mitigation Strategies, Clinical Trials, and Advisory Committee Conflicts

Mr. Chairman, Members of the Committee:

Thank you for the invitation to testify on this key legislative initiative to reform the FDA and improve the safety of the nation's prescription drugs.

Consumers Union is the independent, non-profit publisher of *Consumer Reports*.[1] For over two years we have been conducting a Prescription for Change campaign on behalf of state and national laws to strengthen the prescription drug safety system.

This is not a dry and abstract issue: it is a matter of life and death. In the hearing room today are families and individuals who have suffered from what we believe are adverse drug events that could have been avoided if we had stronger laws and a more aggressive safety effort in the FDA. Instead, these individuals – Patricia Slingo, Cathy Harter, Kim Witczak, Eric Swan, Mathy Downing, Marion Goff, Francine Esposito—all face a lifetime of heartbreak and grief because we have not done enough to ensure drug safety.

Ms. Slingo's story is described in an advertisement we ran this morning in USA Today – she took Vioxx for her arthritis pain but did not know about the drug's increased heart risk. She has since had angioplasty, stent placement and ultimately heart bypass surgery. As she puts it: "I can't say for certain Vioxx caused my heart problems, but I wish I would have known what the drugmaker knew."

That statement goes to the heart of the matter before us – the public is not being given the full story about all the potential risks of medications and devices, and therefore they can not make informed decisions about their health care. That is why we need to significantly strengthen our drug safety laws and adequately fund drug safety efforts at the FDA.

We have endorsed the Senate-passed Kennedy-Enzi bill, but hope it can be strengthened in the House. We thank all the Members who have worked on these issues, and have endorsed the Waxman-Markey, Hinchey-Stupak, and Tierney-Ramstad bills and hope their many good features can be included in the final law.

Chairman Pallone, we thank you and strongly congratulate you on the drug discussion drafts before us today: it combines several of the best features of all these other efforts, increasing the level of drug safety without slowing the approval of life-saving drugs.

How Discussion Draft Will Help Prevent Future Drug Safety Tragedies

REMS provisions: This proposal builds on the best provisions in the Senate-passed bill and the Waxman-Markey bill (HR 1561) to give the FDA the power to ensure that when safety issues warrant action, action can indeed be taken. Today, the FDA has limited authority to ensure post-market safety studies are actually conducted, or that labels can be changed quickly. Its enforcement tools are either too drastic or too weak. There is no system to regularly monitor a drug's history over its life cycle, and the adverse events reporting system is ineffective.

The bill would give the FDA an effective tool chest of authorities (Risk Evaluation and Mitigation Strategies or REMS) to give more attention to safety without slowing the approval of new drugs. The tools could be enforced by meaningful civil monetary penalties. As signs of trouble develop—such as the FDA reviewer's initial warning on Avandia—the FDA can use increasingly strong tools to determine if there is fire behind the smoke of warnings and, if so, act to protect the public.

Of particular note, all new drugs will carry for at least two years a symbol indicating their newness. Why? Because most drugs are approved after testing on a couple thousand usually healthy people for a year or less. Statistically, serious adverse effects or long-term injury will not show up before approval. The real test is when millions of people start using a drug over an extended period of time. Several years ago, a patient data monitoring company ran an advertisement in a drug trade press publication read by pharmaceutical industry employees that says it all:

> "How many prescriptions…
>
> "How many weeks in market…
>
> "UNTIL YOU'RE CONFIDENT THAT YOUR DRUG IS SAFE?"

Consumers should be aware of the newness of a drug, so that they are more conscious of the need to report adverse events to the FDA or, if the drug offers relatively little new advantage, they may choose to stay with an older, more tested drug.

The Pallone discussion bill allows the FDA to require disclosure of dangers in advertisements, and in a few rare cases, even allows a temporary moratorium on ads until we know more about the safety of the drug.

It takes about seven years for the average adverse event to be detected, and therefore it is important to periodically review a drug's safety profile. The discussion bill provides for

yearly reviews of the REMS for at least the first three years after approval, and a review on the 7th year. This is an excellent idea because it will force the FDA to review the history of a drug at a point in time when a sufficient amount of data should be available to improve on its labeling and usage.

Another important provision is the use of large databases (section 5), such as Medicare's, to detect short- and long-term safety problems in drugs and courses of treatment. This concept was first offered by former FDA Commissioner Dr. Mark McClellan and by Senators Gregg, Burr, and Coburn in S. 1024. As Dr. McClellan testified before the Senate HELP Committee on March 14, 2007, the use of such database surveillance might have helped detect the increase heart risk from Vioxx within months, rather than years:

> "…according to calculations by Richard Platt (Principal Investigator of the HMO Research Network CERT), electronic and other data actually used to determine a significant association between Vioxx use and serious cardiovascular events took almost three years to detect a statistically significant association, based on limited population data available for analysis at the time. If data from large health plans could have been pooled…as envisioned by this [section 201] strategy, the significant association could potentially have been detected within just several months…."

If this database monitoring system had been in place, it likely would have resolved the heart-risk questions that recently came to light about the diabetes drug Avandia – which has been on the market eight years – much sooner. We hope that as your refine the bill, you make it very clear that the research and patient *de-identified and privacy protected* data that comes out of section 5's public and privately-contracted research is made public and freely available to researchers everywhere.

However, our support of active database surveillance should not be misconstrued that this the sole fix needed for our nation's drug safety problems. The FDA needs the legislative authority of REMS to act on the warning signals it gets from Routine Active Surveillance and Assessment epidemiological studies. Section 5 without the rest of the REMS title would leave us where we are now: lots of signals of problems, and endless delays in dealing with them because of a lack of clear authority to take action.

We also urge that the Members ensure that this important public health project stresses the use of de-identified patient data, and that privacy protections and guarantees in Section 5 be strengthened to ensure that we fully guarantee privacy and individual rights.

No Federal Preemption: We support the discussion bill's recognition that nothing in these FDA drug bills pre-empts state tort laws. Controversy has arisen because the FDA recently added, without proper notice, ability to comment or clear congressional authority, a note in a preamble to a regulation that it believed its approval of a drug pre-empted a range of state tort actions. This note, if given credence by the courts, would effectively prevent consumers from holding drug companies accountable. We find it incredible that an agency which has such a track record in protecting the public against

dangerous products and company misrepresentation of data and safety results would dare to interfere with consumers' only effective recourse -- action in the courts. We hope you take even stronger action, and repudiate the FDA's gratuitous preamble language (as provided in Rep. Hinchey and Stupak's bill, HR 2273, section 6).

PDUFA provisions: Ideally, we would like to see the FDA fully and adequately funded out of the general Treasury. If user fees are needed, then there should be no strings attached, as Rep. Hinchey and Stupak have proposed in HR 2273.

We deeply appreciate the addition of $225 million over five years in new safety money to provide desperately needed resources to conduct post-market approval safety work and modernize the FDA's antiquated computer systems. Because PDUFA triggers some increased general treasury money and now involves safety funding, we strongly support the new idea of including patient and consumer representatives in the negotiations over any PDUFA renewal in 2012. This provision will help ensure more sunshine and public interest in what has been a very closed door private industry process.

Below, I would like to discuss areas of particular controversy or where we hope you can make further improvements on behalf of public safety and a modern FDA.

Culture, Openness, and Scientific Integrity within the FDA; Giving the Office of Drug Safety a Role

Scientific Integrity within the FDA: The Union of Concerned Scientists, the HHS Inspector General, and the Institute of Medicine have all reported serious morale and culture problems within the FDA. Too many staff feel pressured to approve drugs before all safety concerns are reviewed. There also is a belief that they are not free to raise questions or slow the PDUFA-and MDUFMA-driven approval timeframes. Turnover in the FDA is above average for Federal scientific agencies and there have been a number of resignations in protest.[2]

To help address this morale and culture problem, we urge you to include the Kennedy-Enzi S. 1082 section 210 which makes public the FDA Action letter, including a public statement of any dissents and disagreements. The discussion bill seems to make the action letters public, but there is no clear indication as there is in the Senate bill that scientific dissent and disagreement is a normal part of the scientific process and is not to be squashed or hidden, but instead be made part of the public record. Public knowledge of the areas of internal concern—for example, the FDA reviewer's concerns with Avandia—would allow researchers and outside experts to concentrate on answering scientific controversies more rapidly.

We urge you to include language like the Senate's section 501 on the right of staff to be able to publish in scientific journals or speak at scientific forums, but state it more clearly and more simply as contained in HR 1165:

> Officers and employees of the Food and Drug Administration, and individuals

> sponsored by such Administration, may publish in peer-reviewed journals and other scientific publications, and make oral presentations at professional society meetings and other meetings of their peers, unless publication or presentation of the data is subject to Federal export control or national security laws or regulations, or is proprietary information. The right to publish or present such data cannot be waived by any agreement, policy, form, or condition of employment.'

And to make both the Action letter dissent and the right to publish meaningful, we hope that you could include whistleblower protection language within the bill and an explicit prohibition against scientific misconduct or censorship. Rep. Markey's bill, HR 1165, has language that could be considered. The need for increased protection for those who raise safety questions is seen in the June 6, 2007, *New York Times* discussion of the Avandia situation. The FDA has just announced that it is asking for a Black Box Warning on the drug. Yet an FDA staffer who suggested that action a year ago, feels she was discriminated against:

> A supervisor in the drug safety office at the agency said in an interview yesterday that she was rebuked last year after calling for a stronger warning label on Avandia and a competing drug, Actos.
>
> The supervisor, Dr. Rosemary Johann-Liang, said that in March 2006 she approved a recommendation from a safety reviewer at the agency that the drugs be required to carry the strongest warning, a so-called black box warning, because they posed a risk of unusual swelling that could lead to heart failure.
>
> But after officials at the agency who dealt more closely with Glaxo complained, Dr. Johann-Liang said she was ordered to retract her approval of the warning, lost her power to approve such assessments and no longer supervised reviews of the safety of Avandia and Actos.
>
> "This was a very careful review that came to an inescapable conclusion," Dr. Johann-Liang said in the interview. "They decided to act like the review never happened and punish me for approving it."[3]

To further promote the status and integrity of science within the agency, we also urge you to consider including the Senate's provision, as recommended by the Institute of Medicine, for an Office of the Chief Scientist (section 222 of S. 1082).

Of course, all of these provisions should apply to vaccines and medical products, not just drugs.

Giving Status to the Office of Drug Safety: We have long supported legislation by Representatives Tierney, Hinchey, Stupak, and Ramstad (and Sens. Grassley and Dodd) that would create a separate office of drug safety, with actual power to order various safety actions. Today, the office of safety, called the Office of Surveillance and

Evaluation, is a small unit that is overwhelmed and, according to the GAO and IOM, often ignored by the much larger Office of New Drugs (OND). While the OND spends a great of deal time considering safety issues, its prime job is processing new drug applications.

In the Senate bill, there are references to the office of safety and the OND working together to adjust a REMS, but it is a very vague power.

We need a locus, a point of responsibility within the FDA where safety issues can be raised, vetted, and acted on.

If there is concern that a completely separate office would just 'slow things down,' and create a duplicate bureaucracy, there is an easy answer. It is the Grassley Senate floor amendment #1039 that failed by only one vote in the last minutes of debate. Basically, the proposal gives the Office of Drug Safety the power to ask for a REMS change—for example, a study to follow up on the warnings raised in the approval of Avandia. If the Director of the Office of New Drugs disagreed, the Commissioner would settle the dispute within a short time period (say a week). This would not slow actions down, but it would clearly make someone responsible for safety within the agency. Today, the voice of safety is too often lost in the drive to meet PDUFA approval deadlines, and as such, public safety suffers.

Clinical Trial registration:
International effort moving to include Phase 1 trials; US legislation should be supportive.

We strongly support the registration of Phase 2-4 clinical trials language. By public registration of trials as they start, we can help patients find appropriate trials to participate in. But also, by publicly establishing what a trial is to measure, for how long, on how many people, etc., the FDA and researchers will be able to determine whether certain research results may have been hidden or doctored when it is ultimately made public. This was the abuse that occurred in Paxil's trials on use in younger people, and the bill's language would prevent that kind of scientific dishonesty.

The clinical trial registration movement was driven substantially by the International Conference of Medical Journal Editors' call two years ago for registration as a condition of journal publication. On June 4th, the ICMJE announced that beginning with trials commencing after June, 2008, it would also require the registration of Phase 1 trials, "because these studies can guide future research or signal safety concerns." We support this international movement and hope that the legislation would be expanded to registration of Phase 1 trials. While Phase 1 trials involve tests on only a handful of people, they are important, contribute to the statistical base of knowledge, and—when unsuccessful—can save other human beings from undergoing dangerous tests. Dr. Steven Nissen testified before the Senate HELP Committee on November 16, 2006:

> When drugs show serious toxicity in patients, the results are rarely published. Accordingly, other companies subsequently expose patients to closely-related drugs without knowing that their competitors' study of a similar agent showed significant harm. I am aware of a class of drugs where more than a dozen compounds showed serious toxicity, resulting in termination of development, but without a single publication of results. In my view, when a patient volunteers to participate in a drug or device study, there is an implicit moral obligation that the patient's participation will benefit medical science. When studies are not published, we learn nothing from the experiment and make the same mistakes over and over again. [Underlining added.][4]

For the sake of science and for those who volunteer their health in these trials, all trials should be registered, and as quickly as possible, the results made public.

We hope that you can include language that will encourage more initial diversity in clinical trials. All too often, we are testing on middle-aged Caucasians and have little or no understanding of the impact of a drug on other races, older citizens, and in particular, older women. And again, all of these provisions should apply to vaccines and medical products, not just drugs.

Results of Clinical Trials: House Language Gives Us Certainty that Trial Results will be Public

We strongly support your proposal's requirement that all Phase 2-4 Clinical Trial Results will be honestly and accurately made public in a timely manner, in both a non-technical, unbiased form for the average consumer, and in more detail for the medical and scientific community. This should apply to all medical products tested in clinical trials.

The original Enzi-Kennedy bill looked a great deal like your proposal. But we understand that many in the industry were fearful that the detailed information would be too confusing to the consumer and cause too much uncertainty. We at Consumers Union find that argument insulting.

What is more serious, is that experts at the National Institutes of Health and the National Library of Medicine have expressed concern that some trials are scientifically worthless and in many cases, just promotions or a marketing pitch for the drug studied. As the former editor of *The Lancet* said in 2004, "Journals have devolved into information laundering operations for the pharmaceutical industry."[5] How does the government insure that trial results are honestly presented, when so much of the process has been corrupted?

To try to answer the question of how to honestly present trial results, the Senate bill includes a study and a negotiated rule-making leading to a final regulation 30 months after the bill's enactment that would describe the "what, when, and how" of trial reporting. In the interim 30 months, there will be a link to public data (including the

excellent idea of a link to Section 210's Action Package) "for those clinical trials that form the primary basis of an efficacy claim" or are a Phase IV post approval safety trial.

These Senate provisions could be a major problem. All trials should be made public, not just those that are the 'primary basis of an efficacy claim.' And after the 30 months of study in the Senate bill, we have no idea what will be made public, how quickly, and in what detail. We see no guidance to these questions.

We urge you to support the House discussion language on clinical trial results. If there is concern about the integrity of the data being made public, study that issue over 30 months, and provide for future regulations to ensure the honest presentation of data. But in the interim, don't give up on your bill's requirement that all Phase 2-4 trials must be public in a reasonable period of one to two years. In the interim, whether perfect or not, make the data public so that the world's researchers can help detect the areas where there are problems.

We also urge you to make public observational studies conducted by drug companies. While these are not the 'gold standard' that randomized clinical trials are, they can provide incredibly useful information to physicians and researchers -- the recent case of Bayer's Trasylol observational study, which found an increased risk of death, serious kidney damage, etc., but which was not volunteered to a recent FDA Advisory Committee meeting, is a prime example of the public value of these studies.[6]

Moratorium on Direct-to-Consumer Advertising as Part of REMS Tool Chest

Although complete safety risks are often unknown for years after approval, pharmaceutical companies invest huge amounts in the immediate promotion of approved drugs, including billions of dollars in Direct-To-Consumer (DTC) advertising. We have seen, too many times, the devastating effects of such DTC advertising. At least one study has commented on how DTC advertising contributed to the overuse and misuse of Vioxx by both consumers and physicians, which led to an unnecessary increase in the number of people at risk of heart attack and stroke.[7]

> [Vioxx] was the most heavily advertised drug to consumers in 2000 and retail sales quadrupled from 1999 to 2000….In 2003, Pfizer spent $87.6 million promoting celecoxib directly to consumers. Recent data highlight that marked increases in COX-2 inhibitor use occurred primarily among patients at low risk of adverse events from less expensive non-steroidal anti-inflammatory drugs….This inappropriate increase in COX-2 inhibitor use among patients for whom NSAIDs could be used accounted for more than 63% of the growth between 1999 and 2002. That this growth was due solely to DTCA is, again, unlikely, but Dai et al describe succinctly the important role that DTCA probably played in this trend—a trend that may have resulted in as many as 140,000 serious adverse cardiovascular events.[8]

In addition to the safety concerns, DTC advertising of Vioxx increased costs to consumers and health plans alike, which were paying significantly more for a new drug that added little or no benefit.[9]

Some defend the use of DTC advertising, asserting that it promotes patient-physician dialogue and increases awareness of diseases and treatments. One study shows, however, that these ads are rarely educational; while many advertisements gave the name of the drug and the condition being treated, very few provide any additional health information on alternative treatment of the condition.[10] The study reports that out of a possible 11 educational codes (specific educational points), the average number of codes present in advertisements was 3.2. Despite the lack of truly educational information in DTC advertising, consumers tend to believe the pharmaceutical industry's message that only the safest and most effective drugs appear in advertisements.[11] This is particularly dangerous given the fact that the goal of this advertising is to sell a costly product that can potentially have serious safety risks.

Although the perception is that only the safest and most effective drugs are advertised, a revealing poll by PricewaterhouseCoopers reported in January 2007 "that 90 percent of consumers and those involved with the industry do not think that direct-to-consumer advertising provides complete and useful information, while 40 percent of pharma executives thought that it does." This implies that a majority of drug company executives do not believe their own ads provide complete and useful information. Although therer are frequent problems with the accuracy and fairness of ads, *Consumer Reports* has carried a number of stories about how the FDA seldom acts against misleading and false ads, how the level of warnings and penalties has declined, and how some companies have repeatedly violated the truthful advertising regulations.[12]

As a part of REMS, the proposed bill gives the FDA authority to require the pre-clearance of advertisement to ensure specific disclosures of a serious risk listed in the labeling of the drug (REMS discussion bill, pages 15-18). In light of the promotional nature of DTC advertising and the long history of abuses in DTC advertising, and given that such advertising strongly influences consumers, Consumers Union recommends a requirement that **all** advertisements,[13] including the growing use of ads in the Internet and other non-traditional sites, be pre-cleared by the FDA for accuracy and honesty.[14]

We believe that if you provided an automatic, substantial penalty for any advertisement found to be misleading or false, companies would seek pre-clearance, they would use the new voluntary DTC user fee program, and the FDA would be able to prevent false and misleading ads, something it has failed to do under the existing process.

In addition, in those extremely rare cases of drugs with serious potential of danger, the REMS process allows the FDA to impose a three-year moratorium on DTC advertising for drugs. Given the amount of influence this type of advertising has on consumers, and given the potential serious adverse drug reactions that may occur years after approval, Consumers Union supports including up to a three-year moratorium on DTC advertising as part of the REMS safety tool chest.[15]

We hope that you will encourage the FDA to require the inclusion of a 1-800-FDA number in all DTC and other drug ads where consumers can report adverse drug reactions.[16] Currently, most consumers probably have no idea that there is an adverse event reporting system or how to participate in that process. Adding a toll-free number to all drug ads could help improve the level of information on areas of safety trouble.

Ethics in FDA Advisory Committees:
Improvement over Senate language; zero conflict-of-interest policy urged

The Senate-passed bill does almost nothing to address an area of great controversy: FDA Advisory Committee members who are ethically conflicted. There are cases where the votes of ethically conflicted Advisory members made a difference in the outcome of a drug-safety issue.[17] But mostly, allowing conflicted members to vote casts a cloud over some of this expert advice. A recent poll from the Consumer Reports National Research Center found that six in 10 consumers disapproved of allowing doctors and scientists with a conflicting financial interest to participate on advisory boards, and 84 percent of consumers agree that drug companies have too much influence over the government officials who regulate them.

The discussion bill is much stronger than the Senate bill, in that it permits the FDA to grant only one waiver per meeting to permit a conflicted expert to participate in the Advisory Committee process.

The FDA itself has recently moved to exclude from Committees those with more than $50,000 in conflict, and to permit those with less than $50,000 to participate, but not vote. The problem is, the act of being on the Committee is where the socialization and influencing occurs, and transcripts have shown one or two Advisory Committee members can dominate deliberations even when they cannot vote because of a conflict.

We believe you should legislate a zero-conflict policy. If an individual is conflicted or had a financial relationship in the last 36 months, they could testify before the Committee like any other citizen, but not participate as a member of the Committee. Opponents of this change will say that there are not enough experts in a field who lack such conflicts. We don't believe the FDA has tried hard enough to find academic or NIH-funded researchers and other experts who are not conflicted.

We urge you to require the aggressive recruitment of non-conflicted experts in a wide diversity of fields (epidemiology, toxicology, statistics, etc.). To remove doubts of integrity problems, we hope you will codify a no-waiver policy: if an individual is conflicted, they cannot participate in that session of the Advisory Committee. If there is concern that this would create a shortage of experts, phase this zero tolerance requirement in over the next five years, while the FDA conducts a true search for conflict-free experts.

Also on the issue of improving Advisory Committees, there has been a history of FDA expert staffers who have been critical of a drug being considered by a Committee actually

being prohibited from addressing that Committee. We hope you will include language that gives any FDA staffer who requests time to make a presentation, the right to do so without retaliation.

MDUFA

The Draft Discussion version of the Medical Devices User Fee Act (MDUFA) is a clear improvement over the MDUFMA bill that was negotiated by device companies and the FDA and included without any revisions in the Senate bill. We know that the Senate received the negotiated bill too late to be able to focus on it before passage, and we congratulate you for the improvements you made. We support your efforts to maintain the already very speedy process for medical devices [80% of 510(k) reviews completed within 90 days, for example].

We strongly support your efforts to question the 510(k) process, which is used for 98% of medical device reviews. Although the 510(k) review is limited to products that are "substantially equivalent" to devices already on the market, the FDA defines "substantial equivalence" to include products made of completely different materials and using completely different technologies – not at all similar or equivalent as most of us would define those terms. There is reason to be very concerned that implanted medical devices are being cleared for market through the 510(k) process, often without the FDA requiring or reviewing clinical trials. This concerns us because clinical trials are almost always necessary to determine if a product is truly safe and effective. And, it is important to note that these products are usually not available through Medicare, Medicaid, or most insurers until clinical trials prove that they are safe and effective. In other words, CMS and the health insurance companies have higher standards than the FDA, and most consumer will not benefit from quicker approvals because the proper testing has not been completed that would make sure that these products are safe and effective, or to meet criteria that would make them reimbursable through insurance.

One other device issue, we commend the Members of the Committee, such as Rep. Doyle, Dr. Burgess, and others, who are working on efforts to establish a unique device identification number for medical devices—a key step to being able to form registries that can be used when there is the need for a recall or to report adverse events.

Help for Consumers

Finding a full set of objective data about the effectiveness and safety of a drug can be like finding a needle in a haystack. The FDA is trying to improve its website for consumers, but we hope you will include S. 1082's section 209 that pulls all the information about a drug into one website.

Conclusion

Again, we thank you for your hard work on this key health safety issue, and we look forward to working with all of you on the enactment of this important legislation.

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[1] Consumers Union is a nonprofit membership organization chartered in 1936 under the laws of the State of New York to provide consumers with information, education and counsel about goods, services, health, and personal finance. Consumers Union's income is solely derived from the sale of Consumer Reports and ConsumerReports.org, its other publications and from noncommercial contributions, grants and fees. In addition to reports on Consumers Union's own product testing, Consumer Reports and ConsumerReports.org, with approximately 6.5 million combined paid circulation, regularly carry articles on health, product safety, marketplace economics and legislative, judicial and regulatory actions that affect consumer welfare. Consumers Union's publications carry no advertising and receive no commercial support. EXPERT • INDEPENDENT • NONPROFIT®

[2] In testimony to the Senate Finance Committee on November 18, 2004, Dr. David Graham, associate science director of the Office of Drug Safety at the FDA, alleged that FDA officials attempted to suppress and delay results regarding a study which concluded that individuals taking Vioxx had an increased risk of heart attack and stroke. In the same testimony, Dr. Graham mentioned a similar experience held by Dr. Andrew Mosholder, senior epidemiologist at the FDA, whose concerns that Paxil increased suicidal behavior in children were dismissed by higher FDA authorities. In August 2006, the Union of Concerned Scientists (UCS) released their survey of the FDA; their findings echoed those reported by the Office of Inspector General (OIG) in 2003. In response to the question: "Have you ever been pressured to approve or recommend approval for an NDA despite reservations about the safety, efficacy, or quality of the drug?" 41 respondents out of 217 Center for Drug Evaluation and Research (CDER) staff (nearly 19%) answered "yes." Nearly one-fifth (18.4 percent) said they "have been asked, for non-scientific reasons, to inappropriately exclude or alter technical information or their conclusions in a FDA scientific document."

[3] Stephanie Saul & Gardiner Harris, "Diabetes Drug Still Has Heart Risks, Doctors Warn," NYT, 6/607.
[4] "Clinical Trial Registration, Looking Back and Moving Ahead," C Laine, et al. JAMA, June 4, 2007.
[5] PLoS Medicine, May 2005, Richard Smith, "Medical Journals Are an Extension of the Marketing Arm of Pharmaceutical Companies."
[6] FDA Public Health advisory, Feb 8 and Sept 29, 2006.
[7] Dai C, Stafford RS, Caleb GC. National Trends in Cyclooxygenase-2 Inhibitor Use Since Market Release: Nonselective Diffusion of a Selectively Cost-effective Innovation. Arch Intern Med. 2005; 165: 171 - 177.
[8] Matthew F. Hollon, MD, "Direct-to-Consumer Advertising, A Haphazard Approach to Health Promotion," JAMA, April 27, 2005, p. 2030.
[9] Ibid.
[10] Bell RA, Wilkes MS, Kravitz RL. The educational value of consumer-targeted prescription drug print advertising. J Fam Pract 2000;49:1092-1098.
[11] Bell RA, Kravitz RL, Wilkes MS. Direct-to-consumer prescription drug advertising and the public. J Gen Intern Med 1999;14:651-657.
[12] See, for example, Consumer Reports, February 2003, "Free Rein for Drug Ads?"

[13] We note that the voluntary review/user fee provision in the Senate-passed bill and the discussion PDUFA bill define DTC television ads as those less than 2 minutes in length. Recently, there has been controversy about a 2.5 minute ad on a drug which has had safety issues. We see no reason to limit the definition to 2 minutes.
[14] DTC on the InterNet is growing rapidly, and is estimated to be $1.3 billion in 2008. As research firm eMarketer said August 18, 2006, "The spending increase is spurred by federal regulatory crackdowns on pharmaceutical advertising, and the fact that 31.6 million Americans turn to the Internet first for health care information."

[15] "The Court has developed a four-pronged test to measure the validity of restraints upon commercial expression. Under the first prong of the test as originally formulated, certain commercial speech is not entitled to protection; the informational function of advertising is the First Amendment concern and if it does not accurately inform the public about lawful activity, it can be suppressed. Second, if the speech is protected, the interest of the government in regulating and limiting it must be assessed. The State must assert a substantial interest to be achieved by restrictions on commercial speech. Third, the restriction cannot be sustained if it provides only ineffective or remote support for the asserted purpose. Instead, the regulation must "directly advance" the governmental interest. The Court resolves this issue with reference to aggregate effects, and does not limit its consideration to effects on the challenging litigant. Fourth, if the governmental interest could be served as well by a more limited restriction on commercial speech, the excessive restriction cannot survive. The Court has rejected the idea that a "least restrictive means" test is required. Instead, what is now required is a "reasonable fit" between means and ends, with the means "narrowly tailored to achieve the desired objective." Central Hudson Gas & Electric Co. v. Public Service Comm'n, 447 U.S. 557 (1980). Quote from http://caselaw.lp.findlaw.com/data/constitution/amendment01/17.html

[16] Section 9 of the Best Pharmaceuticals for Children Amendments of 2007 calls for the issuance of a rule on the 1-800 adverse event reporting number, and this section could be expanded to cover all drugs advertisements in all media.

[17] Although certain FDA experts have been refused permission to testify at advisory committee meetings, many outside scientific experts are free to participate in such meetings despite outstanding conflicts of interest. For example, at the February 2005 joint meeting of the Arthritis Advisory Committee and the Drug Safety and Risk Management Advisory Committee to discuss the safety of cyclooxygenase-2 (COX-2) inhibitors, it was disclosed that 10 of the 32 voting panel members had financial associations with the manufacturers of these drugs (such as the receipt of consulting fees or research support). All 10 members were issued general waivers that allowed them to participate in the meeting. 28 out of the 30 votes cast by these 10 members favored marketing of Bextra, Celebrex and Vioxx, whereas only 37 out of the 66 votes cast by the remaining 22 members favored marketing of these drugs. If the 10 panel members with conflicts of interest had not participated in the meeting, the committee would have voted to remove Bextra from the market, and to keep Vioxx from returning to the market (Merck voluntarily withdrew Vioxx from the market in 2004). Instead, due to the inclusion of the votes from the 10 conflicted panel members, the committee voted to keep these drugs on the market. The FDA consequently announced that it had asked Pfizer to voluntarily withdraw Bextra from the market, which it did in April 2005, two months after the advisory committee meeting. Vioxx remains off the market today. Sources: Center for Science in the Public Interest. Conflicts of interest on COX-2 panel. February 25, 2005. (Accessed October 30, 2006, at http://cspinet.org/new/200502251_print.html.); Harris G, Berenson A. 10 Voters on panel backing pain pills had industry ties. New York Times. February 25, 2005.