### Testimony before the Senate Committee on Health, Education, Labor and Pensions Hearing on S. 3807, Enhancing Drug Safety and Innovation Act of 2006

November 16, 2006

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In early 2005 a combined Food and Drug Administration ("FDA") advisory committee reviewed the safety of COX-2 inhibitors, and concluded that the three drugs in this class, including Vioxx, were safe enough to keep on the market. Ten of the 32 scientists on that panel had financial ties to manufacturers of the drugs. Had their votes been eliminated, two of the drugs in the class would have been voted down by the panel.

The advisory committee process is an important safeguard in the FDA's regulatory system. Not all drugs require advisory committee approval. Only when the agency is uncertain or needs corroboration for its judgment does it turn to an advisory committee for outside advice, which it almost always follows.

Some have argued that conflicts of interest on advisory committees are of no consequence. The committees almost always reach unanimous or near-unanimous decisions. Moreover, the Vioxx case was an anomaly. Discounting the votes of conflicted scientists that have been allowed to sit on advisory committees would almost never change the ultimate decisions.

But these arguments ignore the dynamics of the advisory committee process. Clinicians, statisticians and scientists with conflicts of interest usually have strong opinions that flow from their ties with industry. Even if few in number, they can dominate the discussions that take place. Moreover, their presence crowds out other, nonconflicted scientists who may be interested in asking questions that a conflicted scientist may not see as crucial to the drug or device approval process: issues like safety, drugdrug interactions or the impact of the new drug or device on other diseases that the patient may have. At the least, their presence on these committees undercuts the public's faith in the integrity of the process. The best way to solve all these problems – without undermining the quality of the advice offered to the FDA – is to completely eliminate conflicts of interest from these committees.

Yet instead of this simple test, which would restore the original intent of the Federal Advisory Committee Act to FDA advisory committee deliberations, Title IV of S. 3807 creates a complicated scheme for managing the selection of scientists with conflicts of interest. It identifies four types of conflict of interest – defined as "any financial interest in a product that is under consideration or a competing product" (page 96, lines 32 et seq.) – for members of FDA's advisory committees: low magnitude, medium magnitude, high magnitude, and non-waivable. Committee members with a low magnitude conflict would not require a waiver to vote; committee members with a medium or high magnitude conflict would be able to vote only if the FDA grants a waiver (page 99, lines 25 et seq.). The FDA would not be able to grant a waiver if the scientific work of the panel member is under consideration or if the member or the member's immediate family member "could gain financially from the advice given to the" FDA (page 102, lines 6-25). S. 3807 directs the FDA to publish guidance – including criteria for defining "low," "medium," and "high" – within 270 days on how it will administer this four-tier regulatory scheme (page 103, lines 9 et seq.).

On behalf of our 800,000 members in the United States, the Center for Science in the Public Interest urges that Title IV of the Enhancing Drug Safety and Innovation Act of 2006, S. 3807, be substantially simplified by prohibiting any conflicted member of an advisory committee from voting on the committee's recommendations to the FDA (conflicted members could still offer their expertise to the committee as a witness if the agency or committee desired it). This simplification is necessary in order to give Americans confidence in the future recommendations of FDA advisory committees while ensuring that the FDA continues to get the best advice available.

The FDA justifies using conflicted scientists on two grounds. First, the agency's leadership has stated that it is very difficult to find qualified advisory committee panel members who are totally free from any previous association with manufacturers. Second, if the agency were forced to eliminate scientists with conflicts of interest, it would have to use less experienced or less qualified scientists, which would hamper the agency's ability to protect and advance the public health. Neither of these arguments is valid.

#### It is possible to find experts who do not have conflicts of interest.

The best examples of an organization that is similar to FDA and successfully takes a "no conflicts allowed" approach is the Office of Medical Applications of Research (OMAR) within the National Institutes of Health. OMAR holds consensus panels three to five times a year to discuss controversial medical problems. Its goal is to develop clinical practice guidelines representing the best clinical trial evidence. A recent panel on menopause management, for instance, called for de-medicalizing the condition and limiting hormone replacement drug therapy to women with the severest symptoms.

OMAR follows a simple rule in appointing the 12 to 15 scientists who sit on each panel: No conflicts of interest allowed. A scientist who consults with industry is allowed to sit on the panel only if that company has absolutely nothing to do with the topic under discussion. Even if the scientist consults with a company on a completely different topic, if that company has a stake in the outcome of the panel's deliberations, then that scientist is not eligible to sit on the committee.

OMAR panels require the same specialized expertise found on FDA advisory panels: biostatisticians expert in interpreting clinical trial data; clinicians expert in treating the disease; and scientists who understand the underlying biology. They perform the same tasks: understanding the science, evaluating clinical trials, weighing industry and public presentations and synthesizing published materials. OMAR can find unconflicted scientists. So can FDA if it just looks hard enough. For example, at the March 14, 2006 meeting of the Pediatrics subcommittee of the Oncology Drugs Advisory Committee, five of 12 panel members had their conflicts of interest waived so they could vote. Yet at the annual meeting of the American Society of Clinical Oncology that was held three months later, nearly half of the 726 oncologists who made presentations had no conflicts of interest, according to conference disclosures. If these unconflicted scientists were sufficiently expert to make presentations to the 29,000 oncologists attending ASCO's annual meeting, weren't some of them sufficiently qualified to serve on an FDA advisory panel considering pediatric oncology drugs?

OMAR officials admit that it has become more difficult in recent years to find experts without ties to firms with a stake in the outcome of its panels' deliberations, especially when the topics involve rare diseases. That organization has sometimes resolved this dilemma by turning to scientists in related fields and giving them background material in advance of meetings. "We use the Supreme Court analogy," said Susan Rossi, deputy director of OMAR. "These are smart, critical thinkers, senior people in their fields though not the field under consideration." In those rare disease cases when the best experts are almost all conflicted because there are so few of them, the FDA could employ a similar strategy.

# <u>Unconflicted experts are also highly qualified. Not all "thought leaders" in a field have close ties to industry.</u>

The assertion that FDA should only use the best advisers assumes there is a rigid hierarchy of expertise within medicine and the agency has identified the most qualified persons in every case. Numerous state agencies around the country have taken a different approach, believing there is a pool of highly qualified, untapped experts without ties to industry who are alternative "thought leaders" within their fields. The states are leading the way in identifying these experts as they struggle to hold Medicaid spending in check.

There are now 13 states affiliated with the Center for Evidence-Based Policy (CEBP) at Oregon Health Sciences University, which is run by former Gov. and physician John Kitzhaber. CEBP's goal is to analyze all clinical trial evidence in a field to determine which drugs, biologics and devices provide the best medical outcomes. This evidence is then turned over to states for use in establishing Medicaid formularies. CEBP maintains a strict "no conflict-of-interest" policy for its contractors, which include the University of North Carolina, Oregon Health Sciences University and Southern California Rand. These organizations provide evidence specialists, who write the systematic reviews. They cannot have any ties to companies whose products might be considered in the evaluation. Those reviews, once completed, are evaluated by a panel of leading clinicians, who also may not have ties to manufacturers.

## <u>With a little work, the FDA can identify experts in the field and build a</u> reservoir of "thought leaders" without conflicts of interest for its advisory panels.

Thank you for considering this testimony.