

**Testimony to the U.S. Senate Committee on Health, Education, Labor and Pensions**  
**Building a 21st Century FDA: Proposals to Improve Drug Safety and Innovation**

**Thursday, November 16, 2006**

My name is Steven E. Nissen, M.D. I am Chairman of the Department of Cardiovascular Medicine at Cleveland Clinic and the President of the American College of Cardiology (ACC). My testimony does not reflect the views of either Cleveland Clinic or the ACC. As an individual who has frequently served as the “point on the end of the spear” during the public debate on drug safety, I appreciate the opportunity to provide an independent perspective on the “Enhancing Drug Safety and Innovation Act of 2006” introduced by Chairman Enzi and Ranking Member Kennedy.

We face a crisis in public confidence in the FDA following an unprecedented series of revelations about drug and device safety. The American people no longer trust the FDA to protect their health. Unfortunately, patients are increasingly suspicious of new therapies and sometimes are reluctant to accept potentially life-saving medications or devices. Strong and decisive legislative action is now essential to improve the safety of drugs and medical devices and restore public confidence in this critically important regulatory agency.

The initiative now before you represents the best opportunity in many years to fix these chronic problems. We need new laws to strengthen the authority of the FDA. Currently, the Agency must “negotiate” with industry to make even simple changes in drug labels. I served on a 2001 Advisory Panel that recommended a warning label for Vioxx, but it took 14 months before the FDA could secure agreement from the company to accept a weakly written warning. Companies routinely make commitments to perform Phase IV studies, but never actually launch the promised clinical trials and the agency is powerless to act. When drug studies reveal toxicity or lack of efficacy, the Agency is not permitted to release the results and the findings are often not published, thereby denying patients and physicians access to vitally important safety information.

This problem of “negative publication bias” – the practice of suppressing and never publishing unfavorable studies has a catastrophic effect on the drug development

system. 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.

The post-marketing surveillance system for drugs and devices functions poorly. Adverse event reporting is voluntary and studies show that only 1 to 10% of serious adverse events are ever reported to the Agency. Accordingly, the actual incidence of serious or life-threatening complications cannot be calculated accurately.

The current legislation proposed by Senators Enzi and Kennedy addresses many of these problems in a thoughtful fashion. The bill's authors sought to simultaneously facilitate development of innovative therapies, while aggressively protecting public safety. The proposed Risk Evaluation and Mitigation Strategy is a step toward a more robust post-marketing surveillance system. The system for dispute resolution is fair to the industry, but makes certain that safety concerns are promptly addressed. The requirement to register clinical trials is essential and the establishment of a mandatory Clinical Trials Results Registry will guarantee that society reaps the benefits of knowledge, whenever a study is conducted in human subjects. Finally, the improvements in the Advisory Committee process will help to ensure that FDA consultants are less likely to be influenced by financial conflicts of interest.

Although this bill is a major step forward, I would like to see further legislative actions. The Agency should be better funded. Virtually, every American takes one or more medications, so drug safety affects every one of us. However, the annual expenditure for drug regulation approximates only about \$500 million and is largely supported by user fees, creating a conflict in loyalty for FDA employees. We cannot expect outstanding performance for an Agency operating on a poverty budget.

For high-risk drugs, another approach to drug approval should be considered – “provisional approval” – a limited term approval that would automatically expire unless certain criteria for efficacy and safety are met.

I believe that Direct to Consumer (DTC) Advertising requires legislative action. The standard for acceptable DTC advertising should require demonstration of a compelling public health benefit for this type of communication. Drugs with an addiction potential, such as sleeping medication, should be specifically prohibited from consumer advertising.

Finally, there is an important drug safety problem not addressed in this bill – the nutraceutical industry. I recognize that the H.E.L.P. committee has made progress by unanimously approving legislation requiring serious adverse event reporting for dietary supplements. However, more needs to be done. These products are often worthless and occasionally harmful. It must also be recognized that some patients take such dietary supplements instead of effective medications with negative implications for their health.

The current bill is an important step toward improving the safety of drugs and devices and restoring public confidence in the FDA. I strongly support its passage and commend the Senators for their bipartisan leadership.