

Statement of Senator Tom Coburn, M.D.
Regarding H.R. 3580, the Food and Drug Administration
Amendments Act of 2007
September 20, 2007

Today the full Senate will probably agree to legislation—H.R. 3580, the Food and Drug Administration Amendments Act of 2007—that constitutes a massive overhaul and expansion of the Food and Drug Administration's (FDA) authorities. Up until a couple days ago, determining the scope and details of the bill was an open and bi-partisan process. Unfortunately, all of that changed at the 11th hour and we were locked out of discussions to determine what a final product would look like. Now we are forced to either accept what we do not fully agree with or cause thousands of FDA employees to lose their jobs. This is not the way to ensure that we "get it right" with drug safety.

While this bill achieves the important and necessary objectives of reauthorizing the Pediatric Research Equity Act, the Best Pharmaceuticals for Children Act, the Pediatric Medical Device Safety and Improvement Act, the Prescription Drug User Fee Amendments, the Medical Device User Fee Amendments, and establishing a scientifically-based surveillance system for drug safety risks. There was still important work to be done to complete a bi-partisan product. Because of unfair Democratic Majority tactics I and my colleagues have no opportunity to further amend and perfect this legislation.

Furthermore, I am frustrated that certain important provisions were removed from the final language of the bill at the last minute. We lost a provision to provide incentives for developing new antibiotics—a disastrous decision at a time when we're seeing a huge rise of antibiotic resistance in this country. Last-minute negotiators also refused to recognize that patients desiring marijuana for medical purposes deserve to know critical information about its whether or not marijuana can be safely used. Finally, the final bill did not contain an important Senate-passed resolution to protect American pharmaceutical companies' intellectual property rights around the globe.

This legislation is a very delicate balancing act. No drug is completely safe--otherwise a doctor's prescription wouldn't be needed--but we do have to ensure that life-saving medicines are able to get to patients. New authorities in the area of Risk Evaluation and Mitigation Strategies (REMS), labeling, and post-market commitments should not be taken lightly. These new authorities we are giving the FDA need to be used based on a measured assessment of risk vs. benefit in the intended patient population. For instance, labeling changes should only be undertaken when reliable data clearly shows safety problems that aren't already reflected in the drug's label. If that data happens to come from a third party unknown to the application holder they should have the opportunity to review it along with the Agency so that appropriate labeling changes can be made based on sound science.

Another new authority granted to the FDA in a REMS is possible restrictions on distribution and use. If used, this restriction has the potential to impede patient access to important therapies and therefore should not be imposed where less burdensome approaches are available. This concept of a "less burdensome approach" is an important one and it is essential that product manufacturers have the opportunity to present alternative proposals to the Agency that would accomplish the goal of safety without imposing unduly restrictive actions to products and ultimately to patients. This legislation establishes that the FDA will not limit or restrict distribution or use unless a drug has been shown to actually cause an adverse event. We absolutely need FDA to have all the tools necessary to ensure the safety and efficacy of drugs, but doctors need tools as well, and one of those important tools is new drugs on the market. I appreciate the significant changes that were made in this language of the bill between Senate HELP Committee markup and full Senate consideration. These improvements remain in the final bill and are critical to ensure that physicians--not the FDA--can make risk/benefit decisions with their patients.

This bill ensures that the FDA has broad and exhaustive authorities to make sure that drug companies are doing the right and scientifically-justified thing when it comes to drug safety and the labeling of their drugs. This authority is placed rightly in the hands of highly-trained scientists at the FDA. It's clear that Congress relies on the scientists at the FDA to assess safety risks and drug

labeling and this should be squarely and solely the FDA's role—that is why we've spent months and months trying to get this issue of drug safety right. The newly expanded role of the FDA does and should pre-empt State law when it comes to drug safety and labeling. In order to ensure scientific drug safety the last thing that we need is the regulatory nightmare of every state court being a mini-FDA.

Let me be clear, the FDA is the expert Federal agency charged by Congress with ensuring that drugs are safe and effective and that product labeling is truthful and not misleading. Appropriate preemption of State jurisdiction includes not only claims against manufacturers, but also against health care practitioners for claims related to dissemination of risk information to patients beyond what is included in the labeling.

Product liability lawsuits have directly threatened the FDA's ability to regulate manufacturer dissemination of risk information for prescription drugs. I note a recent case in California (*Dowhal v. SmithKline Beecham*) where trial lawyers tried to assert that a drug company had failed to warn consumers that nicotine-replacement products allegedly cause birth defects—even though there wasn't scientific evidence to back that up. In this case, the FDA had previously told SmithKline Beecham that they should not include such unscientific warning in its label because it would clutter up the label's warnings that actually were scientifically justified. A California court asserted that more warnings were always better. Subsequently, that assertion was overruled unanimously by the California Supreme Court as the FDA again asserted that its scientific judgment should prevail. The case was not properly before the court by operation of the doctrine of primary jurisdiction. Unless State law is pre-empted in this area, State law actions can conflict with the FDA's interpretations and frustrate the FDA's implementation of its statutory and scientific mandate.

Should the FDA's scientific judgment on drug safety and labeling be set aside, we would risk eroding and disrupting the truthful representation of benefits and risks that medical professionals need to make decisions about drug use. As a physician, I know that exaggeration of risk can discourage the important and right use of a clinically therapeutic drug. Superfluous liability concerns can create pressure on manufacturers to expand labeling

warnings to include merely speculative risks and limit physician appreciation of potentially far more significant contraindications and side effects.

I note that the FDA has previously stated that "labeling that includes theoretical hazards that are not well grounded in scientific evidence can cause meaningful risk information to 'lose its significance.' Over-warning, just like under-warning, can similarly have a negative effect on patient safety and public health." In this bill, we have created a clear labeling pathway between the FDA and a drug sponsor in this bill to ensure that consumers get scientifically accurate and appropriate warning of drug safety risks.

Furthermore, if not pre-empted in drug safety information and labeling, State law could conflict with achieving the full objectives of Federal law if it precludes a firm from including certain labeling information. If a manufacturer then complies with State law, the firm would be omitting a statement required under § 201.100(c)(1) as a condition on the exemption from the requirement of adequate directions for use, and the omission would misbrand the drug under 21 U.S.C. 352(f)(1). The drug might also be misbranded on the ground that the omission is material within the meaning of 21 U.S.C. 321(n) and makes the labeling or advertising misleading under 21 U.S.C. 352(a) or (n).

While it's true that a manufacturer may, under FDA regulations, strengthen a labeling warning on its own, it's important to understand that in practice manufacturers typically consult with FDA before doing so. Otherwise they could risk enforcement action if the FDA ends up disagreeing.

Some misunderstand the FDA's labeling requirements to be a minimum safety standard and have used State law to force manufacturers to supplement safety regulation beyond that required by FDA. I want to be clear that the FDA's labeling requirements establish both a "floor" and a "ceiling." Therefore, risk information beyond what is required by the FDA could be considered unsubstantiated or otherwise false or misleading. Given the comprehensiveness of FDA regulation of drug safety, effectiveness, and labeling—additional requirements for the disclosure of risk information are not necessarily more protective of patients.

Finally, I want to specifically comment on language in H.R. 3580 that includes a new mechanism to further encourage the timely and accurate communication of new safety information on prescription drug labels. That mechanism reiterates the FDA's primacy in determining the content of prescription drug labeling, including through the new power to command a safety labeling change. New section 505(o)(4)(I) also makes clear that this enhanced safety labeling mechanism does not affect the obligation of a company to maintain a drug product's labeling in accordance with FDA's regulations, including 21 C.F.R. § 314.70. This provision is meant to confirm the basic obligation of a drug's sponsor to propose (or, in some cases, make) changes to the approved labeling to reflect changes in the conditions established in the approved application and/or new information. Nothing in this rule of construction changes that obligation or FDA's ultimate authority over drug labeling; nor is it intended to change the legal landscape in this area. That is because there is an overriding Federal interest in ensuring that the FDA, as the public health body charged with making these complex and difficult scientific judgments, be the ultimate arbiter of how safety information is conveyed. In this manner, there can be confidence that uniform drug labeling conveys clear, consistent, and scientifically-justified safety and medical information.

In fact, the courts have repeatedly upheld FDA's supremacy over prescription drug labeling in cases brought under state law. Nearly twenty years ago, the U.S. Court of Appeals for the Fifth Circuit emphasized that ". . . manufacturers cannot change the language in the product insert without FDA approval," and accordingly "[i]t would be patently inconsistent for a state then to hold the manufacturer liable for including that precise warning when the manufacturer would otherwise be liable for not including it." *Hurley v. Lederle Labs. Div. of Am. Cyanamid Co.*, 863 F.2d 1173, 1179 (5th Cir. 1989). As a more recent Court expressed this bedrock principle, allowing a state to decide what warnings are appropriate, and thus potentially subject companies to liability for otherwise FDA-approved labeling, would upset the careful benefit-risk balance that FDA has struck in approving a product for market," and doing so would "undermine FDA's authority to protect the public health through enforcement of the prohibition against false and misleading labeling of

drug products in the Federal Food, Drug and Cosmetic Act.”
Sykes v. Glaxo-SmithKine, 484 F. Supp. 2d. 289, 312 (E.D.
Pa. 2007) (internal quotation omitted).