**North Carolina Legislature, Senate Subcommittee Meeting**
**Thursday, March 29th, 2:00 p.m.**

**Curt Daniel Furberg, M.D., Ph.D – Remarks**

***Introduction/Qualifications:*** I am a physician and Professor of Public Health Sciences at Wake Forest Baptist Medical Center-Wake Forest School of Medicine in Winston-Salem, North Carolina, where I chaired the Department of Public Health Sciences until 1999. I have four decades of experience in epidemiology and prescription drug clinical trial design, conduct, and interpretation. I am an author of "Fundamentals of Clinical Trials," now in its Fourth edition, which is a seminal textbook on clinical trial design. I have performed safety data monitoring for over 50 prescription drug clinical trials, both with private pharmaceutical companies and with the National Institutes of Health. I was a charter member of United States Food and Drug Administration's ("FDA") Drug Safety Advisory Committee until 2006; since then, I have continued to serve as a drug safety expert at several FDA meetings. More recently, I have also served as a medical-legal consultant for the drug industry and victims of prescription drugs.

I am here today to speak against the proposed bill providing immunity to drug companies for drugs that are FDA-approved. I felt it was my obligation to speak out, because this bill is based upon misconceptions about how the FDA actually works and about how prescription drugs are regulated.

**1. The FDA Does Not Conduct Clinical Trials - Drug Companies Do:**

The FDA does not conduct clinical trials or otherwise safety test drugs. FDA relies on the Drug Companies to conduct the clinical trials, interpret the data, and in significant part, monitor and report problems with their drugs once they are on the market. Prescription drugs are only a fraction of the FDA's overall responsibilities. FDA is responsible for overseeing the safety of all food products sold in this country; blood supply, medical devices, vaccines, veterinary products and cosmetics. The part of FDA that's actually responsible for prescription drugs – CDER – has only ***72*** full-time medical officers who are responsible for overseeing about ***11,000*** drugs.

When the FDA approves a prescription drug as "safe and effective"...that does ***not*** mean the drug is safe. Instead, it means only two things: first, it means that based on a few thousand, who were exposed to the drug during clinical trials

that the drug appeared to work for its intended purpose, i.e., that it was effective. Second, FDA approval means that whatever side effects the drug companies reported in the small pool of people exposed to the drug during clinical trials – that the benefits of the drug ***outweighed*** the risks. It is impossible to detect all drug side effects during clinical trials. But once the drug is on the market, and millions of people start to take it, only then do the side effects become apparent. In the last ten years, we have seen more serious side effects, and more prescription drugs recalled, than in the entire history of the FDA. The drug names may sound familiar, Vioxx, Fen-Phen, Avandia, Rezulin, Baycol, Ketek, Darvocet, Trasylol, and the list goes on.

The Question here is will Drug Company immunity from state law claims make drugs safer? You may be familiar with the United States Supreme Court's recent decision in ***Wyeth v. Levine.***[1] The Supreme Court held in that case that FDA approval of a drug does ***not*** preempt state law failure-to-warn claims. During the case, the Supreme Court heard from two former FDA Commissioners, Dr. Donald Kennedy and Dr. David Kessler, who both argued that state law failure-to-warn claims ***should*** be allowed.[2]

Drs. Kessler and Kennedy told the Supreme Court:

> "The scientific demands on the Agency far exceed its capacity to respond. This imbalance is imposing a significant risk to the integrity of the...regulatory system, and hence to the safety of the public...The fundamental problem FDA faces is that, by necessity, drugs are approved on the basis of less-than-perfect knowledge. ... [The FDA] cannot single-handedly perform the Herculean job of monitoring the safety of every one of the 11,000 or so drugs on the market. The emergence of safety hazards that were unknown or not well understood at the time of a drug's approval...is commonplace. FDA's approval process is not a warrant of a drug's absolute safety, but an assessment of whether the drug's benefits outweigh potential risks based on the evidence available to FDA at the time. But once a drug enters the marketplace... unanticipated adverse effects...begin to emerge."

According to the Government Accountability Office (GAO), FDA's surveillance programs detect "at most a small fraction of adverse effects of drugs."

These former FDA Commissioners wanted the Supreme Court to understand that drug companies have much more information about their drugs' side effects than FDA does. Drug companies almost invariably find out about dangers of their drugs long before FDA. So it's a myth to assume that FDA has equal access to information about a drug's side effects. Drs. Kennedy and Kessler finally stated: "Manufacturers have superior resources committed to overseeing the safety of the drugs they market. As a result, manufacturers invariably get safety information before FDA does, and have access to information that is not available to FDA." And they pointed out that time and again "Failure-to-warn litigation has uncovered safety information that was known to the drug company but was not provided to, or otherwise available to, the FDA." Taking away an injured patient's right to bring a claim may actually make prescription drugs less safe.

**2. Drug Companies Have Superior Knowledge About Drug Risks And A Poor Track Record Of Sharing Information With FDA.**

Failure-to-warn claims almost invariably involve risks that were known to the Drug Company but not disclosed to FDA at the time it approved the drug or for years after the risks were known. I am aware of cases in which the Drug Company had reports of side effects that they did not send to FDA; or they conducted studies that documented a risk of their drug and then they did not publish the study or share it with FDA. When the FDA learns about a drug risk that has been concealed from them, often years later, FDA reverses its earlier decision that the drug was safe and effective and may ask the manufacturer to recall it from the market. But this takes time, drug companies do not disclose all data and we have seen delay tactics -- and by then it's too late.

I'd like to give you just two recent examples of cases where that's happened. The FDA issues warning letters each year to drug companies that have withheld information, submitted false information, or there are problems with the integrity of the Drug Company data. The examples below illustrate how dangerous drugs remain on the market for years, increasing the drug company's profits while harming the unsuspecting public, and without resulting in any "final agency action" by the FDA.

> **Vioxx**: Merck's arthritis drug Vioxx was approved by the FDA as safe and effective in 1999, but pulled from the market five years later in 2004, due to an alarming number of heart attacks in patients taking the drug. Vioxx was one of the most widely-used drugs ever to be withdrawn from the market; and during the five years it was sold in the United States Merck earned

billions of dollars. But as early as 2001, Merck was aware from its own studies that Vioxx patients were three times more likely to die of a heart condition than patients taking a placebo or sugar pill. Now in the case of Vioxx, the FDA was also aware of other studies (although Merck didn't send them all of the data) and based on what they had, FDA asked Merck to add a "warning" about the risk of heart attack to the Vioxx label. But the company refused.

It is important to understand as you consider granting immunity to Drug Companies, based on the fact that FDA approved the warning label for a drug, is that Drug Companies submit the proposed label to FDA. It took the FDA more than a year to finally convince Merck to agree to add a statement about increased risk of cardiovascular events to the Vioxx label. Merck fought them on adding a "warning" because Merck's market research had shown that a warning (as opposed a "precaution") in the drug's label would cause a 50% reduction...in Vioxx sales – which were running about $2.5 billion a year at that point. So for over a year while Merck negotiated with FDA there was no mention in the Vioxx label of any risk of heart attack. And in the end, Merck won out: FDA accepted a compromise: they agreed that Merck could add the reference to heart attacks in the *Precautions* section of the label – but they didn't have to put it in *Warnings*. Testifying about this at a later Congressional hearing, FDA officials acknowledged that the Agency simply did not have the power to compel Merck to add a "warning" to the Vioxx label.[4]

**Ketek**: In 2000, drug manufacturer Aventis submitted fraudulent and fabricated data and misled the FDA into approving the drug Ketek for sinus infections. One of the clinical investigators in a multicenter study fabricated data on 350 patients, forged consent forms, and faked results. The clinical investigator pleaded guilty to fraud in 2003 and was sentenced to 57 months in prison.

An external auditor under contract with Aventis testified at a Congressional hearing that Aventis had concrete knowledge of the blatant fraud and forgery. The auditor repeatedly told officials at Aventis about the numerous problems until Aventis fired the auditor with a warning not to speak to the FDA. In addition to the evidence from the criminal case and congressional hearings, two FDA special agents concluded in separate investigations that Aventis knowingly submitted fraudulent data to the FDA. So the investigator who fabricated data went to jail, the auditor lost his job, people

who took Ketek for a common cold died of liver failure, but the drug company only had its fingers slapped.

Yet, by the time the FDA withdrew approval of Ketek in 2007, the dangerous drug had been on the market for almost three years, doctors had written over 5 million prescriptions for Ketek, and Aventis had made over $400 million dollars. There was never a final FDA determination of fraud.

### 3. The "fraud exception" has never been applied by FDA.

Now you may be asking -- doesn't concealing the potential drug safety data from the FDA constitute fraud on the FDA? And doesn't the proposed bill have an exception for "fraud on the FDA?"

Well, the answer to both questions is – **No**. First, merely withholding negative safety information from the FDA has been held not to constitute fraud. Second, as I understand that the proposed bill it defines fraud as "an intentional misrepresentation to the FDA, in violation of applicable regulations...as determined by the FDA."

That is an exception that will never be invoked because the FDA has ***never*** determined that a prescription drug company committed fraud by withholding safety information. Such a determination by the FDA would likely bar the Medicare and Medicaid programs from purchasing any of that company's drugs which would be an untenable situation. For that reason, when FDA has determined that a Drug Company has withheld significant safety information in the past, the consequence has always been a plea bargain, monetary fines, or "corporate integrity agreements" – none of which would seem to qualify as a determination of fraud under this bill.[7] So the "fraud exception" to the bill is not really an exception at all. And neither are the "exceptions" for promoting the drug for off-label use, or selling the drug after an order recalling it from the market, or bribing agents of the FDA. The pharmaceutical industry made over $31 million in campaign contributions last year,[8] but they've never been convicted of bribery of an FDA medical officer. In short, these fraud exceptions are so narrow that they are meaningless. Make no mistake, if this bill passes, failure-to-warn claims in North Carolina will simply be barred.

### Conclusion

By any common-sense metric, the North Carolina Attorney General is right: this bill would sell-out basic rights of North Carolina's citizens, in order to protect

Drug Companies from claims when they knowingly conceal safety information from the FDA, Doctors and Patients. And who pays for patient injuries when the drug companies are immune? The people do. They pay in the form of higher taxes to care for patients who have no health insurance. They pay in the form of higher medical insurance premiums for those with insurance. If a Drug Company withholds or fails to disclose important safety information, and a patient is injured or dies as a result, they should be responsible. I urge you to vote against this bill. Thank you.

## References


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2. Brief of Amici Curiae Former FDA Commissioners Dr. Donald Kennedy and Dr. David A. Kessler in Support of Respondent, 208 WL 3587489
3. GAO, *Drug Safety: Improvement Needed in FDA's Postmarket Decision-Making and Oversight Process 18* (2006)
4. Kessler & Vladeck, 96 Geo. L.J. at 480, n. 82.
5. Mangano, "The Risk Associated with Aprotinin in Cardiac Surgery," *New England Journal of Medicine* (2006)
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11. *Attorney General v. Merck*, 292 Mich. App. 1 (March 17, 2011)
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