

## **May You Whistle While You Work at FDA?**

Guest editorial by Mark Cohen and Tom Devine\*

FDA commissioner Andrew von Eschenbach so believes his agency's view that cloning is safe that he apparently has copied his own body. How else to explain the two versions of him circulating in Washington these days? One is the champion of vigorous, robust scientific debate and a diversity of views at FDA. He swore to Congress his zero tolerance for FDA managers who pressure reviewers to change their conclusions, and that violators may be fired. But then there's his evil twin, the despot von Eschenbach, who before dozens of FDA staff threatened to "trade" reviewers who speak out against FDA's tacit approval of fraudulent clinical trials or who raise their voices against management pressure on reviewers to change scientific conclusions to the liking of drug sponsors. The latter von Eschenbach told a pro-PhRMA conference in February that it is "destructive" for FDAers to blow the whistle on safety and scientific integrity concerns to the public. He was probably thinking of Dr. David Ross.

Ross is, by his own estimation, an unlikely whistleblower. Soft-spoken, cerebral and possessed of a dry wit, the 40-something, Yale-trained Ross railed to his wife against his colleague, David Graham, when Graham rocked the Senate in 2004 with his revelations about the lethality of Vioxx and FDA's complicity in putting that drug on the market. But Ross's beef is no longer with Graham; on the contrary, it's with culture of drug approval at FDA that treats industry as its primary client rather than the public.

Ross served as both primary safety reviewer and safety team leader on Ketek (telithromycin), a Sanofi-Aventis antibiotic for respiratory tract infections. As early as 2000, he was troubled by evidence that the drug caused a variety of dangerous side effects, notably severe liver damage. Ross was further alarmed when the evidence mounted that a 24,000-person clinical trial on Ketek was mired in fraud. When he asked his supervisors about informing an advisory committee about this data integrity debacle, he was stunned to be told that doing so wouldn't be productive. Then a supervisor leaned on him to "soften" his negative review of Ketek; he reluctantly complied but submitted his original review as well and noted that he had changed the conclusion at her behest.

Ross tried to alert his FDA superiors that Ketek was a bust. But it was his superiors who were championing its approval. So Ross took what was, for him, the extraordinary step of sharing his story with members of the Senate and House, Republicans and Democrats. When the media took an interest – the Wall Street Journal, New York Times, ABC and more – FDA management circled the wagons and lashed out.

Last June, nine months into his tenure as acting FDA commissioner, von Eschenbach was the featured guest at an invitation-only meeting on Ketek at the White Oak campus. Curiously, Ross, who by then had transferred two years earlier to a different office at FDA, was nonetheless invited to this meeting. CDER director Steven Galson told the assembled group that the meeting was to respond to the negative publicity about Ketek, a drug he continued to praise. Von Eschenbach seconded Galson that FDA's decision-making on Ketek was proper, and he likened FDA to a football team in which differing views may be vented in the "locker room." But on the field, the team speaks with one voice and any FDAer who blows the whistle will be warned the first time, benched the second time, and traded the third time. With a straight face, von Eschenbach testified before Congress in March that he is sorry if anyone misunderstood his football analogy to mean other than he fully supports the legal rights of whistleblowers. Hmmm.

FDA management's heavy-handed approach to dissent helped drive Ross out of the agency, as it did to his colleague, John Powers. Until recently Powers was FDA's lead medical officer for Antimicrobial Development and Resistance Initiatives and is a recognized international expert on the proper design of clinical trials. But he too was censured by his superiors and denied the right to speak at meetings with drug companies. Powers's offense? He persistently drew attention to FDA's acquiescence in drug sponsors' use of inappropriate "non-inferiority trials" to demonstrate efficacy for relatively minor, self-resolving indications. Ketek, he noted, like 67 other antibiotics approved by FDA, had never been shown more effective than a placebo.

Ross and Powers – like Graham before them – were proven correct. Last December an FDA advisory committee, weighing the risks and benefits of Ketek, voted overwhelmingly to recommend that FDA withdraw approval for two of three indications for Ketek. For the lone remaining indication, it recommended that a black box warning be

required. (FDA has followed the withdrawal recommendation but balked at the black box warning for anything but the rare disease, myasthenia gravis.)

The Ketek case illustrates the upside-down world that is FDA. Dedicated professionals who risk their reputations and careers to blow the whistle on unsafe or unproven drugs are threatened, punished and pushed out. Those deceiving the public about life-threatening risks remain ensconced in the leadership of this critical public health agency.

This surreal environment persists because government scientists who "commit the truth" are treated like criminals with no realistic chance to defend themselves. They need the protections of the Whistleblower Protection Act but that law has degenerated into the Whistleblower Removal Act. While the paper rights in the WPA are outstanding, due to hostile court and agency decisions, they are as reliable as FDA safety kudos for Ketek or Vioxx. Since 1994 when Congress unanimously made this the strongest free speech law in history, whistleblowers have a 2-179 adverse track record for decisions whether their rights have been violated. The administrative board for their limited day in court has not found a single case of whistleblower retaliation during the Bush Administration.

Fortunately, we are on the verge of a reality breakthrough. By a 331-94 vote on 2/14, the House approved legislation to put enforcement teeth in the Whistleblower Protection Act for federal employees and contractors. The reform's foundation is normal access to court when their rights are violated. The House also went an extra step. Based on Graham's experience, it specifically authorizes challenges to - "(1) any action that compromises the validity or accuracy of federally funded research or analysis; (2) the dissemination of false or misleading scientific, medical, or technical information; [or] (3) any action that restricts or prevents an employee or any person performing federally funded research or analysis from publishing in peer-reviewed journals or other scientific publications or making oral presentations at professional society meetings or other meetings of their peers."

Hopefully the Senate will quickly follow suit. This reform could be a real life saver. For the professional lives of honest government scientists who fear that whistleblowing currently is the sound of professional suicide. For the lives of American families, endangered

when they trust government deception about drug safety. And for the lives of politicians, since a recent Democracy Corps poll found 79% of likely voters want the new Congress to pass strong whistleblower protection – second in priority only to eliminating illegal spending. There is no time to delay. Until the whistleblower reform becomes law, those who defend the public cannot defend themselves.

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