

Testimony of Bruce M. Psaty, M.D., Ph.D.
Before the House Committee on Energy and Commerce
Subcommittee on Oversight and Investigations
March 22, 2007

Mr Chairman and members of the Committee,

My name is Bruce Psaty. A professor of medicine and epidemiology at the University of Washington, I served on the Institute of Medicine (IOM) drug-safety committee (1,2). The IOM review was undertaken at the request of the FDA after the withdrawal of Vioxx had raised questions about the integrity of the US drug-safety system. This testimony reflects my views as a public-health scientist.

According to one former FDA commissioner, the only novel IOM recommendation was the proposed 6-year term for future commissioners [IOM recommendation 3.1 (1)]. All the other recommendations had been made in one form or another in a dozen previous reports. Yet, in the FDA response to the IOM report (3), all actions are listed as “recently initiated,” “new,” or “planned” in PUDFA IV. What happened to the scores of previous recommendations? Whether, this time, FDA responses will eventually improve drug safety remains to be seen.

The FDA, which has many outstanding scientists, has a difficult job. The interests of the pharmaceutical industry in risks and benefits are not symmetrical; there is little short-term economic interest in safety; and some sponsors lack imagination when it comes to safety: hence, the need for strong science-based regulation to protect the health of the public.

The current drug-safety system, in which approval largely signals the end of evaluation, could hardly be weaker. The FDA centerpiece, the Adverse Event Reporting System (AERS), creates a “case series,” the weakest form of epidemiologic evidence. Other major drug-safety efforts are the post-market commitments made by sponsors. Their completion rate dropped from 62% in the 1970s down to 24% in recent years (4). As of September 2006, 899 (71%) of the 1259 post-market studies were still “pending” (5).

To improve the system, the IOM committee recommended a life-cycle approach to drug evaluation (1)--an on-going systematic effort to identify safety signals, translate them into high-quality studies, evaluate both health benefits and risks, integrate the information into risk-benefit analyses, and communicate the findings to patients and physicians.

FDA needs additional resources (IOM, 7.1). While some FDA responses to the IOM report were excellent or were limited by inadequate resources, others seem to embrace the culture, vision and values of the status quo at the Agency (3).

For all new molecular entities (NMEs), the IOM recommended a re-evaluation of post-approval data by FDA (IOM, 5.4), an idea will be pilot tested. Leaving the review of new safety data in the hands of industry may, on occasion, be a hazard to the health of the public.

The IOM recommended public release of the FDA’s risk-benefit analysis after the

completion of post-marketing studies (IOM, 4.13). FDA plans to do so only on a case-by-case basis. Transparency is, however, essential. Although the Agency usually needs to make one decision, physicians and patients deserve to hear, not one constrained voice, but the range and quality of evidence underlying regulatory decisions. Otherwise, FDA fails in its mission to serve as the trusted intermediary of complex information.

The IOM recommended joint authority for the Office of New Drugs (OND) and the Office of Surveillance and Epidemiology (OSE) in the post-approval setting (IOM, 3.4). The FDA planned a few pilot projects. This response, which fails to acknowledge even a future commitment to the spirit of joint authority for OSE, does not signal major cultural change at the FDA.

The IOM Committee recommended that a substantial majority of Advisory Committee members be free of significant financial conflicts (IOM, 4.10), yet FDA described no commitment to limit conflict of interest. The failure to recognize the importance of independent review provided by Advisory Committees is not in the spirit of broad cultural change.

These responses, taken together, do not represent “fundamental changes ... [that will] entail a cultural shift within the FDA” (page 5). A fundamental change would involve actively embracing an on-going lifecycle evaluation that includes both transparency and independent review. Cultural changes need to come first, from the top, and include leadership that relies on science in its decision-making process, leadership that values and harnesses scientific disagreement to improve drug approval decisions, and leadership that is at once courageous under outside pressures and passionate about the health of the public.

References

1. Committee on the Assessment of the US Drug Safety System, eds Baciou A, Stratton K, Burke SP. *The Future of Drug Safety: Promoting and Protecting the Health of the Public*. The National Academies Press, Washington, DC.
2. Psaty BM, Burke SP. Protecting the health of the public--Institute of Medicine Recommendations on drug safety. *N Engl J Med* 2006;355:1753-55.
3. Food and Drug Administration. *The future of drug safety--promoting and protecting the health of the public: FDA's response to the Institute of Medicine's 2006 Report*. US Department of Health and Human Services, January 2007; <http://www.fda.gov>.
4. Tufts Center for the Study of Drug Development. FDA requested postmarketing studies in 73% of recent new drug approvals. *Impact Report* July/August 2004;6(4):1-4.
5. Food and Drug Administration. Report on the performance of drug and biologics firms in conducting postmarketing commitment studies; availability. *Federal Register* 2007 Feb 2;72(22):5069-70.