Can the Institute of Medicine review the FDA?

To the editor:

A *Nature Medicine* News item[1] reported on the plan of the US Food and Drug Administration (FDA) to seek a review by the Institute of Medicine (IOM) of the National Academy of Sciences. The IOM would review the agency's "drug safety system and its relationship with drug companies." Is the IOM the appropriate body to conduct such a review?

The IOM maintains a carefully cultivated image of independent, Olympian wisdom on matters affecting the health of the American public. Congress and the public, in turn, receive pronouncements of the IOM with deference and respect. Congress and the public are mostly unaware that the IOM is riddled with conflicts of interest that bear directly on the institute's proposed new role.

Some of the most esteemed members of the IOM are employees and executives of major pharmaceutical corporations, the very industry that has come under fire recently for lack of candor concerning toxicity of their products, for failure to make generally known the negative studies of their drugs' efficacy, and for direct-to-consumer advertising that overstates efficacy while understating potential risks of medications. The 'big pharma' group includes IOM members employed by Abbott Laboratories, GlaxoSmithKline, Eli Lilly and Company, Merck and Co., Inc., Pfizer, Inc. and Schering-Plough Research Institute[2]. These members are not shy about representing their corporate interests in public forums. Indeed, IOM member Peter S. Kim of Merck recently participated in a sharply partisan public exchange about his company's behavior and interactions with the FDA in the Vioxx matter[3].

In addition, many smaller corporations involved in biotechnology research and development are represented in the membership of the IOM. These include the ALZA Corporation, BioCryst Pharmaceuticals, Inc., Celera Genomics, Corcept Therapeutics, Inc., Immusol, Inc., Innovative Drug Delivery Systems, Inc., Neurocrine Biosciences, Inc., Neurome, Inc., Perlegen Sciences Inc. and Quest Diagnostics, Inc. Some of these corporations, such as Neurocrine, already have matters pending with the FDA. Others, like Corcept, have received fast-track status from the FDA for products they hope to bring to market. All will sooner or later be negotiating with the FDA over clinical trials protocols, product approvals, labeling cautions and postmarketing surveillance. There is even a presence within IOM from the Chemical Industry Institute of Toxicology, which can be sure to take a lively interest in the FDA's positions on preclinical safety testing.

Moreover, most members of IOM are employees of medical schools that have extensive relationships with pharmaceutical corporations for research support, educational programs and endowments. Corporations routinely cultivate IOM members as 'academic thought leaders': it is not unusual for IOM members to have financial arrangements with big pharma and smaller companies as consultants, advisors, board members, stockholders, paid speakers and research contractors. One IOM member recently listed 46 such financial relationships with 21 corporations[3]. The potential for bias that attends these institutional and personal competing financial interests should disqualify most IOM members from reviewing FDA safety procedures and relationships with drug companies. The IOM must not imagine that mere disclosure of such conflicts of interest in any way mitigates the compromises they create.

Even more problematic are the informal, often reciprocating relationships among academic and corporate IOM members that create nontransparent conflicts of interest. These relationships, which are not readily discoverable by the IOM leadership, might take many forms: favorable editorial decisions that publicize clinical trials reports; fast-tracking of publications that aid start-up corporations to raise capital; the writing of favorable editorials and commentaries; 'product placement' in review articles; deflection of scientific criticism; sponsorship to advisory boards; and preferential treatment for research funding. Regardless of whether these relationships pass ethical muster, their existence creates the potential for bias in any review of the FDA by the IOM.

If its proposed review of the FDA is to be credible, the IOM will need to come to terms with these issues in a public way. Otherwise, the Institute of Medicine of the National Academy of Sciences will be viewed as just another compromised part of the academic-industrial complex in medicine. That would rather defeat the purpose of a review that is meant to restore trust in drug safety and in the FDA.

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3. Kim, P.S., Reicin & A.S. *N. Engl. J. Med.* **351**, 2875–2878 (2004).
4. Nemeroff, C.B. *J. Clin. Psychiatry* **65**, 1562 (2004).