

**Growth of Public Health Expenditures, as Compared with Private Spending, since 1965 and Projected Contributions for 2015.**

Data are from the Centers for Medicare and Medicaid Services.

viding a medical home for patients where their personal physician is paid to coordinate care.

The struggle over the reauthorization of SCHIP reflects the recurring discussion over the role that government should play in providing health coverage to the population. Every time, combatants come to the question with fervor, believing their arguments reflect the values of the American people. In a recent survey conducted by the *Wall Street Journal* and NBC, respondents who expressed pessimism about the future were asked to identify the source of their viewpoint; next

to the Iraq war, failures of the health care system drew the most nods.<sup>5</sup> Whether politicians are able to capture this concern in the form of an expanded SCHIP or reaffirm Bush's belief in the private market as the preferable solution is a question that will be addressed over the course of the coming presidential election campaign and beyond. As long as no political party holds a commanding margin in Congress, this debate will continue without a clear resolution in sight.

However, the growth of public health expenditures has far outstripped private spending since

1965 because, in the absence of affordable private insurance, the federal government has expanded coverage of populations considered appropriate recipients of public support. This trend will only accelerate with the coming retirement of baby boomers (see bar graph). And as it does, there is no question that the role of government will expand along with the fiduciary responsibilities of policymakers, regardless of who is in the White House.

**An interview with Professor Sara Rosenbaum, Chair of the Department of Health Policy at the George Washington University School of Public Health and Health Services, can be heard at [www.nejm.org](http://www.nejm.org).**

Mr. Iglehart is a national correspondent for the *Journal*.

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## Sidelining Safety — The FDA's Inadequate Response to the IOM

Sheila Weiss Smith, Ph.D.

Having been commissioned by the Food and Drug Administration (FDA) to evaluate the U.S. drug-safety system, the Institute of Medicine (IOM) published a report, *The Future of Drug Safety*, in September 2006 identifying weaknesses in the laws, regulations, re-

sources, and practice of ensuring drug safety.<sup>1</sup> Some of the IOM's recommendations were directed toward Congress, which it believed should increase FDA funding and regulatory authority. Some outlined ways in which other federal agencies could work in partnership

with the FDA for the public good. But most of the report outlined deficiencies that the FDA itself — or the Department of Health and Human Services (DHHS), to which it belongs — should correct.

In general, the IOM implored the agency to “embrace a culture

of safety” by increasing the priority accorded to the safety of patients. Such an emphasis could have ramifications for medical care that would be as broad and positive as those that the 1999 IOM report on medical error, *To Err Is Human*,<sup>2</sup> has had for the health care system. Sadly, the FDA's official response falls far short of what the American public expects and deserves.<sup>3</sup> Indeed, it highlights the very reason that the agency — with which I have had some firsthand experience — is in need of monumental change: its philosophy is no longer aligned with its regulatory mandate.

The basic criterion for approval of a new drug is that its benefits outweigh its associated risks — so benefits must be considered in light of the drug's toxicity and known safety problems. In its response to the IOM report, however, the FDA described its “fundamental dilemma” as weighing the “tradeoff between safety and access.”<sup>3</sup> Under the 1992 Prescription Drug User Fee Act, resources were provided to accelerate access to new drugs, and the FDA shortened review times and began to approve certain drugs earlier in the clinical development process.<sup>4</sup> Safety was affected in several ways. First, some drugs were approved on the basis of surrogate end points and fewer safety data than had previously been required. Second, user-fee funds could not be used for postmarketing safety assessments; this restriction changed in 2002, but even now such use is permitted only in limited circumstances. Third, mechanisms intended to speed access to potentially lifesaving medicines were broadly interpreted. Drugs for the treatment of common chronic condi-

tions such as diabetes (troglitazone), obesity (dexfenfluramine), and pain (rofecoxib) were approved under expedited programs and later were withdrawn from the market for safety reasons.

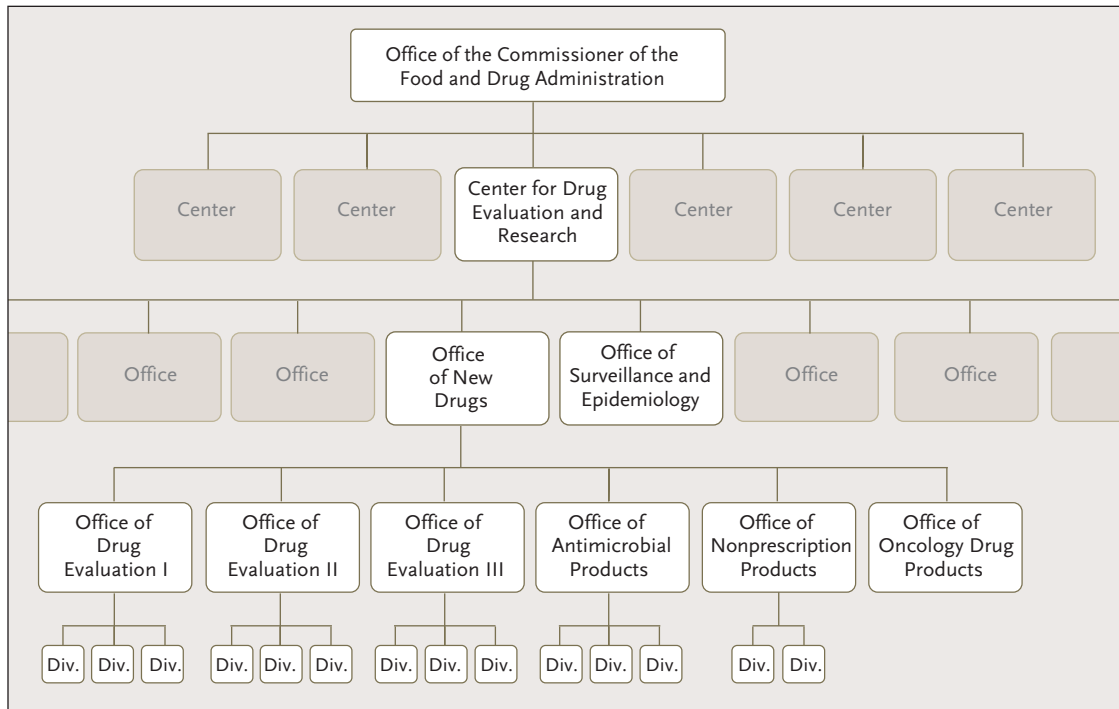
The public expects the FDA to be the final arbiter of drug safety. Accelerated development programs and expedited reviews hasten the introduction of lifesaving drugs, but they should not be an option for treatments intended for chronic conditions; these drugs should have safety standards that tolerate minimal uncertainty. By pitting safety directly against “access and innovation,” the agency betrays its mandate to ensure that U.S. drugs are both safe and effective.

Moreover, the very structure of the FDA marginalizes safety. All regulatory authority lies within the drug-evaluation divisions of the Office of New Drugs (OND) in the Center for Drug Evaluation and Research (see organizational chart); staff members in these divisions evaluate and approve drugs, negotiate labeling, and request risk-management programs and postmarketing studies. Despite the agency's theoretical emphasis on epidemiology, such expertise is often absent from these divisions. The FDA's safety experts work in a separate Office of Surveillance and Epidemiology (OSE) — which is not even a part of OND — and serve only as consultants to the review divisions, having no direct regulatory authority. Although they may be asked to provide background information as context for interpreting an application, they do not regularly participate in drug reviews.

Several IOM recommendations speak to the importance of including safety experts as integral players in the drug-review process. Yet instead of undertaking a

fundamental restructuring to integrate the relevant offices, the FDA merely initiated two pilot projects that involve OSE personnel in drug reviews to determine the “logistics and value” of doing so. But something akin to a pilot had already been done. More than 10 years ago, Greg Burkhart moved from the Epidemiology Branch (now the OSE) to the Division of Neuropharmacological Drug Products (now the Divisions of Neurology Products and Psychiatry Products in one of the Offices of Drug Evaluation). His successor in the latter post, Judith Racoosin, who had trained as a postdoctoral fellow in the OSE, spoke to the IOM committee in January 2006 about her work as a safety team leader.<sup>1</sup> It is partially on the basis of her experience that the IOM report argues that a critical step in promoting a culture of safety is to change the role of the safety expert from occasional consultant to vital participant in the day-to-day work of regulatory decision making.

Of course, even with such participation in preapproval reviews, premarketing clinical trials would have limited ability to identify uncommon adverse events. A safety data set supporting a new drug application for treatment of a chronic disease typically includes fewer than 3000 patients, some of whom have had only a single exposure to the drug. Postmarketing surveillance for adverse events and ad hoc safety studies are therefore crucial, but although responsibility for these activities falls to the OSE, all regulatory authority remains with the division that approved the drug. In the postmarketing realm, the IOM committee recommended establishing joint regulatory authority, so that either the OND or the OSE could take



#### Current Structure of the Food and Drug Administration.

The Division of Neurology Products and the Division of Psychiatry Products are part of the Office of Drug Evaluation I.

regulatory actions. The agency responded by creating two process-review teams, hiring external consultants to improve communications, and developing standard operating procedures that will, it says, “articulate the division of responsibility between OND and OSE” in presenting safety data to advisory committees. Although the FDA claimed that it is committed to ensuring that the “safety staff has a strong voice” in safety-related decision making, it did not confer any regulatory authority on the OSE.

The sidelining of safety experts extends to the FDA’s external advisory committees, which are composed of physicians with expertise in a given therapeutic area, along with a biostatistician, a patient representative, and an industry representative. Safety experts

serve on a separate Drug Safety and Risk Management Advisory Committee, which sometimes meets with other advisory committees, and individual safety experts are sometimes asked to consult on particular safety issues. In response to an IOM recommendation that scientists with expertise in pharmacoepidemiology or public health be included as regular members of all scientific advisory committees, the agency has proposed that it include such expertise “when safety issues are an important component of the issues before the Committee.” But safety should always be on the agenda. Such expertise is critical for evaluating and interpreting often sparse safety data at the time of drug approval, for evaluating proposed postmarketing studies, and for assessing risk-manage-

ment action plans. The FDA’s response once again highlights the low priority it assigns to its responsibility for arbitrating drug safety.

Recognizing the pervasiveness of this marginalization at the agency, the IOM recommended that DHHS appoint an external management advisory board to help find ways of transforming the agency’s culture. The FDA responded, instead, with a series of internal initiatives, pilot studies, and further evaluations that leave safety experts working largely in isolation, with limited resources and outdated technology.<sup>5</sup>

In my view, the FDA’s response to the IOM report demonstrates a lack of understanding of the magnitude of the changes required to create a culture of safety. Apparently, the agency’s leadership has

yet to recognize that the adoption of such a culture would benefit all stakeholders — industry, the community of scientists, and most important, the American public.

Dr. Smith reports having served on a number of FDA advisory committees as an ad hoc member and having served as a consultant to the IOM panel. She reports receiving grant support from PhRMA and Sanofi-Aventis, serving as a consultant on lawsuits for Bayer and Spectrum and against Abbott Laboratories, and serving on Covance's scientific advisory board on isotretinoin risk management. No other potential conflict of interest relevant to this article was reported.

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