Conflicts of Interest in the Regulation of Food Safety
A Threat to Scientific Integrity

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Conflicts of interest in medical research, education, and practice are well known to increase the risk of undue influence by corporate sponsors. Because conflicts of interest are so prevalent and troublesome, the Institute of Medicine (IOM) was asked to develop guidelines for dealing with them. An IOM committee reviewed the substantial body of evidence demonstrating that financial ties with pharmaceutical and medical device companies influence prescribing practices; the opinions of experts; and the design, conduct, and interpretation of research studies. The guidelines produced by the IOM focus on financial connections with industry, largely because such connections are easier to monitor than other conflicting interests, such as career advancement or personal favors.[1]

Although conflicts created by financial relationships with drug and device companies have been a source of concern for decades, concerns about the effects of food company sponsorship on nutrition research, practice, and policy are more recent. Nevertheless, financial ties with food and beverage companies are now recognized as influences on federal dietary guidelines, opinions of nutrition professionals, and the interpretation of nutrition studies.[2] Investigators have demonstrated impressive similarities between the actions of cigarette companies and food companies in promoting and protecting product sales.[3] Consistent with the observations by the IOM, most studies sponsored by food or beverage companies support the benefits of the sponsor's products, whereas most independently funded studies do not.[4]

Related article

The study by Neltner and colleagues[5] provides an important addition to the growing body of evidence for undue food industry influence on food safety policy. The study examined conflicts of interest among scientific experts serving on panels deciding whether food additives—substances that preserve, flavor, blend, and thicken food—should be deemed generally recognized as safe (GRAS) and exempt from Food and Drug Administration (FDA) premarket approval requirements. Their findings are alarming. An astonishing 100% of the members of 290 expert panels included in their review worked directly or indirectly for the companies that manufactured the additive in question. Even more alarming, the experts on these panels form a tight professional cadre. Although 850 people served on the panels, 10 experts served on 27 panels or more, and one of these 10 participated in three-quarters of the panels. The scientific substantiation used by manufacturers to support GRAS status is highly conflicted.

This state of affairs might not matter if all food additives were safe at current levels of intake. But some are not. A few additives once assumed to be safe, such as cyclamate salts and sulfites, are now banned or no longer considered GRAS. More recently, the FDA has issued warnings about caffeine in alcoholic beverages. Its decisions about the safety of GRAS substances such as *trans* fats and salt have been pending for years.

How is it possible that the FDA permits manufacturers to decide for themselves whether their food additives are safe? In 1958, Congress passed a law requiring companies introducing a new additive to provide evidence of safety before putting it on the market. The FDA's subsequent regulations did not require manufacturers to establish additive safety with absolute certainty. But they did demand reasonable assurance that an additive was unlikely to cause harm under conditions of intended use.

Because many additives had been in the food supply for a long time and were assumed to be safe, the law exempted GRAS substances from premarket approval requirements. Thus, no FDA review was required for additives that manufacturers believed qualified for a GRAS exemption. Because some manufacturers wanted written reassurance that the FDA agreed with their GRAS decisions, the agency allowed manufacturers to petition for GRAS status. Many did, and the FDA wrote "opinion letters" in response.

In 1997, the FDA responded to the Clinton administration's "Reinventing Food Regulation" initiative by announcing that it planned to streamline the GRAS process as an incentive for manufacturers to inform the FDA about new additives. The agency proposed to replace the petition system with a simple notification process.[9] Food companies could—at their own discretion—notify the FDA that experts generally agreed that a new additive was safe. Color additives were an exception; manufacturers would still have to submit them to the FDA for premarket approval and provide evidence for safety. It is astonishing that these rules, proposed 16 years ago, have never been issued in final form and are still pending.

At present, manufacturers of all food additives are permitted to decide on their own whether a substance is GRAS for human consumption, unless the additive affects food color. Companies also can choose whether to even notify the agency about a new additive. In practice, many manufacturers do inform the FDA. But, as Neltner et al[5] explain, about a thousand additives are believed to be in the food supply without the FDA's knowledge. For example, manufacturers added caffeine to alcoholic drinks without informing the FDA.

The study by Neltner et al[5] is based on review of the voluntary notification letters sent to the FDA. It is possible that expert panels reject some proposed GRAS exemptions, but such decisions would never come to the FDA's attention. When the FDA receives notification letters, it reviews and responds to them. The FDA has "no questions" about most notifications, thereby tacitly approving the additive as GRAS. However, approximately 15% of the letters are withdrawn from FDA evalu-

ation at the request of the manufacturer.[6] The FDA reviewers can raise scientific questions about the decisions of expert panels, but only when manufacturers choose to notify the agency.

The findings of conflicts of interest in GRAS exemption decisions by Neltner et al[5] have ample precedent. In 2010, in response to requests from Senator Tom Harkin (Democrat, Iowa) and Representative Rosa de Lauro (Democrat, Connecticut), the Government Accountability Office (GAO) issued an incredulous report on the FDA's limited oversight of GRAS decisions.[7] The reason for the report was the rapid, unregulated introduction of nanomaterials—molecular-sized particles—into foods and food packages. Although manufacturers consider nanoparticles to be GRAS, their safety risk is unknown. Because manufacturers do not need to tell the FDA about substances they consider GRAS, there is no way for the agency to monitor use of nanoparticles or their safety. The GAO recommended that the FDA take immediate steps to finalize its GRAS regulations and minimize conflicts of interest among GRAS reviewers.

Later in 2010, the FDA responded by reopening the comment period for the 1997 proposed rules.[10] The agency asked for comments on how to ensure the independence of members of expert panels, minimize and mitigate conflicts of interest, and whether GRAS notifications should include information about the independence of expert panels. Three years later, the FDA has still not issued final regulations.

The problems created by conflicts of interest for the FDA go well beyond those related to food additives and GRAS exemptions. A recent analysis of requests for waivers by people serving on FDA advisory committees views conflicts of interest as a severe threat to scientific integrity.[8] As Neltner et al[5] argue, the lack of independent review in GRAS determinations raises serious questions about the public health implications of unregulated additives in the food supply, particularly the additives that the FDA does not even know about. It also raises questions about conflicts of interest in other regulatory matters. By focusing attention on one blatant example, this study performs a great public service.

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