FEATURE

COMPETING INTERESTS

Centers for Disease Control and Prevention: protecting the private good?

After revelations that the CDC is receiving some funding from industry, **Jeanne Lenzer** investigates how it might have affected the organisation's decisions

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The Centers for Disease Control and Prevention (CDC) includes the following disclaimer with its recommendations: "CDC, our planners, and our content experts wish to disclose they have no financial interests or other relationships with the manufacturers of commercial products . . . CDC does not accept commercial support."[1]

The CDC's image as an independent watchdog over the public health has given it enormous prestige, and its recommendations are occasionally enforced by law.

Despite the agency's disclaimer, the CDC does receive millions of dollars in industry gifts and funding, both directly and indirectly, and several recent CDC actions and recommendations have raised questions about the science it cites, the clinical guidelines it promotes, and the money it is taking.

Marcia Angell, former editor in chief of the *New England Journal of Medicine,* told *The BMJ,* "The CDC has enormous credibility among physicians, in no small part because the agency is generally thought to be free of industry bias. Financial dealings with biopharmaceutical companies threaten that reputation."[2]

Industry funding of the CDC has taken many doctors, even some who worked for CDC, by surprise. Philip Lederer, an infectious diseases fellow at Massachusetts General Hospital and Brigham and Women's Hospital in Boston, Massachusetts, and a former CDC epidemic intelligence service officer, told *The BMJ* he was "saddened" to learn of industry funding.

The CDC's director, Tom Frieden, did not respond to a question about the disclaimer. He told *The BMJ* by email, "Public-private partnerships allow CDC to do more, faster. The agency's core values of accountability, respect, and integrity guide the way CDC spends the funds entrusted to it. When possible conflicts of interests arise, we take a hard, close look to ensure that proper policies and guidelines are followed before accepting outside donations."

Since its inception in 1946, the CDC has had a pivotal role not only in the prevention of infectious diseases but in reducing workplace hazards, motor vehicle injuries, and tobacco related deaths and in ensuring food safety.

One of the CDC's most important contributions, with an estimated eight million lives saved to date,[3] has been its work to educate the public about the dangers of tobacco. CDC spokesperson Thomas Skinner says the surgeon general's first report on smoking in 1964 was a "tipping point," when tobacco was first clearly identified as a health hazard by the US government. Skinner said the CDC's anti-tobacco campaign "serves as an important counter to the more than $950 000 [£630 000; €860 00] that the tobacco industry spends each hour—more than $23m a day—on cigarette advertising and promotion."

Opening up to private money

Funding of CDC took a turn in 1983, when the CDC was authorised to accept external "gifts" from industry and other private parties. In 1992, Congress passed legislation to encourage relationships between industry and the CDC by creating the non-profit CDC Foundation, which began operations in 1995.

The CDC Foundation raised $52m in fiscal year 2014, of which $12m was from corporations. The CDC itself in fiscal year 2014 received $16m in conditional funding from sources such as corporations, individuals, and philanthropy, including the CDC Foundation. Conditional donations are earmarked for specific projects. For example, in 2012, Genentech earmarked $600 000 in donations to the CDC Foundation for CDC's efforts to promote expanded testing and treatment of viral hepatitis. Genentech and its parent company, Roche, manufacture test kits and treatments for hepatitis C.

Numerous manufacturers give donations to the CDC Foundation. Janssen also contributed $1.5m in 2012-13,[1] and in 2011-12 contributors included Merck ($915 149), Genzyme ($762 000), Sanofi-Aventis ($600 000), and Abbott Laboratories ($550 000).

The CDC has recently issued controversial recommendations for screening tests and drugs,[2 4] and is currently overseeing several equally controversial studies.[5] Some of these are

associated with "conditional" industry funding, as the three examples below show.

Cohort screening for hepatitis C

The CDC issued guidelines in August 2012 recommending expanded (cohort) screening of everyone born from 1945 to 1965 for hepatitis C virus.[1] The agency cited new direct acting antiviral drugs and protease inhibitors to treat hepatitis C as part of its rationale for cohort screening, saying the drugs "can halt disease progression and provide a virologic cure (ie, sustained viral clearance following completion of treatment) in most persons."

The science behind cohort screening has been challenged[4] and is said to be "the subject of major debate."[6] The scientific debate along with the price tags of the newer drugs (over $84 000 per treatment course for the new drug sofosbuvir), raise questions about CDC's industry funding.

In 2010, the CDC, in conjunction with the CDC Foundation, formed the Viral Hepatitis Action Coalition, which supports research and promotes expanded testing and treatment of hepatitis C in the United States and globally. Industry has donated over $26m to the coalition through the CDC Foundation since 2010. Corporate members of the coalition include Abbott Laboratories, AbbVie, Gilead, Janssen, Merck, OraSure Technologies, Quest Diagnostics, and Siemens—each of which produces products to test for or treat hepatitis C infection.

Conflict of interest forms filed by the 34 members of the external working group that wrote and reviewed the new CDC recommendation in 2012 show that nine had financial ties to the manufacturers.[1]

A report by the Office of the Inspector General in December 2009 found that external advisors to the CDC "play an influential role in decision making for the federal government." The inspector general evaluated conflicts of interest of advisors and concluded, "CDC has a systemic lack of oversight of the ethics program": 97% of disclosure forms filed by advisors were incomplete, and 13% of advisors participated in meetings without filing any disclosure at all.[7]

Although the CDC states it has addressed all of the deficiencies cited in the report, the agency did not restrict participation of the nine conflicted external advisors in the recommendation to broaden hepatitis C screening.[1] However, the CDC told *The BMJ* that external advisors acted in an "individual capacity" and are not designated as "special government employees." It said that their financial ties to industry didn't comprise a conflict of interest as the participants "had no relationships directly related to the task-reviewing evidence as a basis for an HCV testing guideline. The reported financial activities represent activities not directly related to this work but involving commercial and non-commercial entities that could be perceived to influence involvement in the task."

Oseltamivir for flu

Following criticism of the CDC and its foundation for accepting a directed donation from Roche for the agency's Take 3 flu campaign (Step 3 tells the public to "take antiviral medicine if your doctor prescribes it"),[2] the CDC posted an article on its website entitled, "Why CDC Recommends Influenza Antiviral Drugs."[8] The agency cited multiple observational and industry funded studies, including the recent meta-analysis by Dobson and colleagues,[9] which it described as an "independent" study. authors had financial ties to Roche, Genentech, or Gilead (the first two sell oseltamivir and Gilead holds the patent).[10]

Despite its extensive list of studies, the CDC did not cite the systematic review and meta-analysis by the Cochrane Collaboration.[11]

The CDC told *The BMJ* that it didn't include the Cochrane review because Cochrane "did not consider any data from uncontrolled observational studies of oseltamivir treatment. While such studies have inherent design limitations, they can inform clinical practice and public health, especially when data from RCTs [randomized controlled trials] are unavailable or have not been conducted among high-risk groups or hospitalized influenza patients, or because having a placebo group would be unethical since antiviral treatment is recommended for these groups."

The US Food and Drug Administration issued a warning to Roche that it could not claim that oseltamivir reduces pneumonia or deaths since it has never provided evidence to the FDA to support that claim.[2] Manufacturers are prohibited by law from making off-label claims about their drugs. However, doctors can legally recommend drugs for off-label uses. By funding the CDC's Take 3 campaign, Roche and other companies are not claiming their antivirals will reduce pneumonia or death. CDC director, Frieden, however, did make the off-label claim, telling the public that it could "save your life."[2]

Shannon Brownlee, senior vice president of the Lown Institute and former journalist covering the CDC, told *The BMJ*, "This looks like classic stealth marketing, in which industry puts their message in the mouths of a trusted third party, such as an academic or a professional organization."

CDC and the sugar industry

The CDC has also been criticised for its role in a series of studies into an epidemic of chronic kidney disease among men working in the sugar fields of central America.[5] The sugar industry is paying $1.7m to fund the studies, and critics say the fact the research is being funded by the men's employers raises concerns about how far it will probe industry's role in the disease outbreak. The CDC states it will provide "technical assistance and subject matter expertise," for the studies, with the foundation serving as the "grant administrator overseeing the donor funding and facilitating the research activities."

Researchers think that the epidemic, which has killed over 20 000 mostly young men,[12] is most likely to be caused by "two interdependent factors: the misuse of agrochemicals and the working conditions of the labor force."[13] The men are exposed to banned and dangerous pesticides, some of which are known to be nephrotoxic, and the working conditions cited include "regular exposure to very hot temperatures and extreme physical effort, lead[ing] to heat stress and dehydration."[13]

Daniel Brooks, associate professor of epidemiology at the Boston University School of Public Health, will lead the CDC research, which includes several observational studies examining genetics and biomarkers in children and a longitudinal study of the sugarcane workers and their families for an as yet undetermined time period. He defends the CDC's involvement, saying it provides two main benefits, creating a "firewall between donors and researchers" and enlisting the expertise of the CDC.

The sugar industry has trumpeted Brooks' earlier research into the epidemic as proof that conditions in the fields are not the

the idea that the disease has an occupational origin, telling a reporter with the International Consortium of Investigative Journalists, "We are fully convinced that there is no direct relationship between [chronic kidney disease] and the activities conducted in the sugarcane industry."[5]

The Pan American Health Organization has called the outbreak, "a serious public health problem that requires urgent, effective, and concerted multisectoral action."

Jerome R Hoffman, a methodologist and emeritus professor of medicine at UCLA, told *The BMJ*, the study was asking the wrong questions. "Epidemiologic studies can of course be tremendously useful in cases like this, but given the human suffering involved, we need to devise and test interventions that have a chance to prevent or ameliorate this substantial harm, as quickly as possible. It's inappropriate to focus on things that cannot protect these workers, such as identifying an unusual genetic predisposition to kidney failure, or evaluating a biomarker to follow the disease, while ignoring modifiable factors."

Not just the carrot—but the stick

Corporations have not only been offering gifts to the CDC; they have also used a heavy stick—with consequences that continue to hobble critical research. In 1996, the National Rifle Association, which is underwritten in large part by gun manufacturers, mounted an offensive against CDC's research into gun violence. The association lobbied Congress, and pro-gun representatives slashed $2.6m from the CDC budget—the exact amount the agency had spent in the previous year on firearm injury research. The funding was later restored, but the bill prohibited any of the restored funds from being used to "advocate or promote gun control."

Frederick Rivara, one of the team members who conducted gun research for the CDC before the cuts, told *The BMJ* that firearms research has "plummeted dramatically," and that gun violence remains a major public health concern in the US, where nearly half a million people have died from gunshot wounds since the funding cuts.

After multiple mass murders, including the shooting of 20 first grade children at the Sandy Hook Elementary School in Newton, Connecticut in 2012, President Obama asked Congress for $10m to fund research into preventing gun violence; however, Congress has not approved the funds to date. The president renewed this request for the 2016 budget.

Professional reaction

Neil Calman, president and chief executive of the Institute for Family Health in New York, a large community health center network in 31 locations with over half a million patient visits a year, says the institute has relied on CDC guidance largely because of its prestige as an independent agency, free of industry relationships. Calman told *The BMJ,* "Industry funding undermines trust and introduces a bias in the presentation of results and treatment recommendations that is deplorable for a government agency. If the allegations of industry funding and influence are true, we will have to look very carefully at recommendations we are following now and those made in the future by the CDC."

Calman said, "Industry claims their scientific methodology ensures their studies are unbiased—just as the CDC claims money doesn't affect their recommendations. Yet multiple studies clearly—and repeatedly—show that who sponsors a study, or issues a guideline, makes a difference."

Hoffman said, "Most of us were shocked to learn the CDC takes funding from industry. Of course it is outrageous that industry apparently is allowed to punish the CDC if the agency conducts research that has the potential to cut into profits. But it was our government that made this very bad arrangement, so the way to fix it is not to ask the CDC to 'pretty please be more ethical, and avoid conflicts of interest'; rather, as a society, we have to get the government to reject this devil's bargain, by changing the rules so this can no longer happen."

John Mandrola, a cardiologist in Louisville, Kentucky, reacted to the news of industry funding, saying that the CDC "must have the highest of moral ground. For if we are to believe them about public health matters, there can be no conflicts of interest. The public good, pure evidence, that is all."[14]

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1 Recommendations for the identification of chronic hepatitis C virus infection among persons born during 1945-1965. *Morbid Mortal Wkly Rep* 2012;61:1-36. www.cdc.gov/mmwr/pdf/rr/rr6104.pdf.
2 Lenzer J. Why aren't the US Centers for Disease Control and Food and Drug Administration speaking with one voice on flu? *BMJ* 2015;350:h658.
3 Holford TR, Meza R, Warner KE, et al. Tobacco control and the reduction in smoking-related premature deaths in the United States, 1964-2012. *JAMA* 2014;311:164-71.
4 Koretz R, Lin K, Ioannidis JPA, Lenzer J. Is widespread screening for hepatitis C justified? *BMJ* 2014;350:g7809.
5 Chavkin S. CDC launches industry-funded study of mystery kidney ailment. *Global Muckraker.* 2014 Dec 2. www.icij.org/blog/2014/02/cdc-launches-industry-funded-study-mystery-kidney-ailment.
6 European Association for Study of the Liver. EASL clinical practice guidelines: management of hepatitis C virus infection. *J Hepatol* 2014;60:392-420.
7 Levinson DR. CDC'S ethics program for special government employees on federal advisory committees. 2009. https://oig.hhs.gov/oei/reports/oei-04-07-00260.pdf.
8 CDC. Why CDC Recommends Influenza Antiviral Drugs. 2015. www.cdc.gov/media/haveyouheard/hyh-antiviraldrugs.html.
9 Dobson J, Whitley RJ, Pocock S, Monto AS. Oseltamivir treatment for influenza in adults: a meta-analysis of randomised controlled trials. *Lancet* 2015;385:1729-37.
10 Lenzer J. CDC, conflicting (conflicted?) info, Tamiflu & unquestioning news reporting. *HealthNewsReview* 2015 Feb 10. www.healthnewsreview.org/2015/02/conflicting-study-reports-tamiflu-and-unquestioning-news-reporting/.
11 Jefferson T, Jones M, Doshi P, et al. Oseltamivir for influenza in adults and children: systematic review of clinical study reports and summary of regulatory comments. *BMJ* 2014;348:g2545.
12 Ramirez-Rubio O, McClean MD, Amador JJ, Brooks DR. An epidemic of chronic kidney disease in Central America: an overview. *Postgrad Med J* 2013;89:123-5.
13 Ordunez P, Martinez R, Reveiz L, et al. Chronic kidney disease epidemic in central America: urgent public health action is needed amid causal uncertainty. *PLoS Negl Trop Dis* 2014;8:e3019.
14 Mandrola J. Public trust, the CDC and Tamiflu. *Dr John M* 2015. Feb 13. www.drjohnm.org/2015/02/public-trust-the-cdc-and-tamiflu/#comments.

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