FDA strengthens its stance against unethical researchers

Until not too long ago, scientists who acted unethically in clinical trials did not necessarily face swift justice. Some debarment cases had been pending for over a decade. Now, the US Food and Drug Administration (FDA) says that it is trying to streamline the process of preventing unethical researchers from conducting clinical trials.

In May, the FDA issued a set of updated guidelines to the disqualification process. Kathleen Pfaender, a senior health policy analyst at the FDA, says the agency "has been working hard" to make sure that the disqualification and debarment of unethical researchers balances timeliness with fairness. Whereas the guidance document does not establish any new legally enforceable statutes, FDA officials said the agency hopes to publish a rule change to the disqualification process by the end of this year.

Disqualification and debarment of researchers and companies are separate processes, but they have slightly similar outcomes. Disqualification by the FDA means that an investigator is not eligible to conduct any new clinical trials on drugs, biologics or medical devices. Debarment is more serious and usually follows a misdemeanor or felony conviction related to drug products. Debarred researchers cannot work for anyone with an approved or pending drug product application at the FDA, and debarred companies may not submit new drug applications.

These efforts are, in part, a response to a September 2009 report from the US Government Accountability Office, which criticized the slow pace of disqualification and disbarment procedures, saying that the absence of established timeframes and competing priorities of FDA officials "may have contributed to the length of time taken to complete [disqualification] proceedings."

"The problem of the FDA having too many responsibilities and too few people is pretty well known," says Daniel Carpenter, a professor of government at Harvard University in Cambridge, Massachusetts. "Politicians often complain of so-called 'unfunded mandates'—well, the FDA gets a lot of them."

The FDA touts the fact that all disqualification cases initiated before 2009 have now been resolved, save one. The remaining case is that of Maria Palazzo, a clinical researcher at New Orleans Hospital, which opened in 2003. She is accused of falsifying diagnoses of obsessive-compulsive disorder in a number of patients to qualify them for a clinical trial of Paxil.

Although bioethicists welcome the FDA's updated guidelines, some say the agency can't see the proverbial forest for the trees.

"My wish is that the FDA would act against companies that have a history of submitting falsified data," says Samuel Richmond, co-director of the bioethics center at Cleveland State University. "It's often not just the individual investigator that's responsible; it's the company financing the study."

But proving bad faith on the part of entire companies is much harder than convicting individual researchers. "Going after firms would require testimony from investigators or really hard evidence that the firm encouraged them" to act unethically, says Carpenter.

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Gene test kit oversight could prove a mixed blessing for research

Last month, the US Food and Drug Administration (FDA) sent letters to five commercial providers of direct-to-consumer genetic tests, stating that the companies' devices must receive regulatory approval before they can be marketed. The move, which stops short of requiring the tests to be pulled from the market, may eventually increase consumer trust, but it could curtail current research.

"If [the companies'] ability to acquire genetic information slows down, their research may be slowed," says Geoff Ginsburg, director of the Center for Genomic Medicine at the Duke Institute for Genome Sciences & Policy in Durham, North Carolina. "The FDA process could put some sand in the gears."

For example, Mountain View, California-based 23andMe, known for its consumer-driven research programs, is currently gathering volunteer user survey data about migraine headaches for an association study to pinpoint genetic variations associated with the condition. If a drawn-out regulatory battle ensues, this research could be put on hold.

But Elissa Levin, director of genomic services at Navigenics, a Foster City, California-based company also cited by the FDA, says the ruling should not affect Navigenics's ongoing investigations. The company is currently partnering with academic centers including the Scripps and Mayo Institutes to explore whether personal genomic testing can be used as a primary research discovery tool. "We don't see any reason why there should be any impact our existing relationships," Levin says. "These are all [Institutional Review Board] approved studies and these are all research collaborations."

Research at deCODE genetics should similarly be minimally affected, according to Kári Stefánsson, the company's chairman and president of research. Since deCODE was first founded in 1996, the Icelandic company—also on the FDA's watch list—has maintained an active research program, including a genetic and medical database of more than half the adult population of Iceland. But the company does not use results from their consumer genetic test for research purposes, notes Stefánsson. "We've been doing research in this field for a long time, and we will continue to do so," he says.

The two other companies to receive letters are Knome and Illumina, based in Cambridge, Massachusetts and San Diego, California, respectively. Knome provides whole-genome sequencing to individuals, including researchers, and Illumina sells a human DNA array used by both 23andMe and deCODE genetics. Academics pursuing research with such platforms should not be affected by the FDA decision, predicts Ginsburg.

Although FDA regulation of direct-to-consumer genetic tests may seem like a barrier now, the added oversight could prove a boon to the industry in the long run, many scientists believe. "The recent activity by the FDA is a welcome step for all concerned," says Jim Evans, a medical geneticist at the University of North Carolina at Chapel Hill and editor-in-chief of the journal *Genetics in Medicine*. "[Research] will thrive only in an arena in which tests and the claims made for them can be trusted."

Stefánsson agrees. "It's going to increase the credibility of the field," he says. "In the end, I think this is good news for those who want to do this testing and believe in the quality of what they're doing."

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