What's Behind the FDA's Controversial Strategy for Evaluating New COVID Boosters

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The U.S. Food and Drug Administration is using a controversial strategy to evaluate the next generation of COVID-19 boosters. The approach is stirring debate as the agency works to make new, hopefully improved, boosters available in September to help prevent severe disease and save lives in the fall and winter. For the first time, the FDA is planning to base its decision about whether to authorize new boosters on studies involving mice instead of humans. "For the FDA to rely on mouse data is just bizarre, in my opinion," says John Moore, an immunologist at Weill Cornell Medicine in New York. "Mouse data are not going to be predictive in any way of what you would see in humans." But others defend the approach, arguing that the country has had enough experience with the vaccines at this point to be confident the shots are safe and that there's not enough time to wait for data from human studies. "We have 500 people a day dying of coronavirus right now. Those numbers sadly might very well rise in the fall and the winter. The question is: 'Can we do something better?'" says Dr. Ofer Levy, a pediatrics and infectious disease researcher at Harvard Medical School who also advises the FDA. "And I think the answer is: 'We can, by implementing this approach.'"

The U.K. just approved a new booster

The United Kingdom just approved a new booster that targets both the original strain of the virus and the original omicron variant, called BA.1 — a so-called bivalent vaccine. But the FDA rejected BA.1 bivalent boosters last spring. Instead, the FDA told the vaccine companies that make the mRNA vaccines, Moderna and Pfizer and BioNTech, to develop bivalent vaccines that target the dominant omicron subvariants — BA.4 and BA.5 — in the hopes they will offer stronger, longer-lasting protection. That's why the FDA decided to use a new, streamlined strategy for testing the new boosters. The agency is asking the companies to initially submit only the results of tests on mice. Regulators will rely on those results, along with the human neutralizing antibody data from the BA.1 bivalent booster studies, to decide whether to authorize the boosters. The companies will continue to gather more data from human studies; those results probably won't be available until late October or early November. But the big concern is the boosters may not work as well as the mouse data might suggest. Mouse experiments are notoriously unreliable. And with the government telling people not to get the old boosters now and rejecting the first bivalent vaccines, the FDA really needs good evidence that the BA.4/5 boosters are in fact better, critics say. "We need to make sure that we have solid immunogenicity data in people to show that you have a dramatically greater neutralizing antibody response against BA.4, BA.5," says Dr. Paul Offit of the University of Pennsylvania, who also advises the FDA. "I think anything short of that is not acceptable." Some also worry that the approach may further erode the long-faltering efforts to persuade people to get boosted. "I think it would be good to have neutralizing antibody data in a small group of humans," says Dr. Monica Gandhi, an infectious disease researcher at the University of California, San Francisco. "Otherwise, extrapolation may be considered too great."

But others agree the time constraints mean the country can't wait for more evidence. The billions of people who have gotten Moderna and Pfizer-BioNTech mRNA vaccines show how safe they are, those experts say. The new booster will be identical to the original vaccines except it will contain genetic coding for two versions of the protein the virus uses to infect cells — the protein from the original vaccine and proteins from the BA.4 and BA.5 omicron subvariants. And some scientists say health officials know enough about how vaccines work to start handling the COVID-19 vaccines like the flu vaccines, which are changed every year to try to match whatever strains are likely to be circulating but aren't routinely tested again every year. "We're going to use all of these data that we've learned through not only from this vaccine but decades of viral immunology to say: 'The way to be nimble is that we're going to do those animal studies," says Deepta Bhattacharya, an

immunobiologist at the University of Arizona College of Medicine in Tucson. "We're really not going out too far on a limb here." The companies are expected to submit their data to the FDA by the end of the month and the administration hopes to make millions of doses of the new boosters available starting in September.