COVID vaccine for kids under five: What happens next?

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The FDA will consider authorizing two doses of a COVID-19 vaccine for kids under five on an emergency basis, with the possibility for a third.

It's anticipated that a third dose may be needed because the antibody response with two doses in some of these youngest kids was not as robust as that seen in children in age groups where the vaccine is already authorized—which is the usual standard for authorization of the vaccine in a new age group.

Jason Pogue, clinical professor at the College of Pharmacy at University of Michigan, discusses what happens next.

There have been conflicting and confusing reports about the efficacy and plan for the vaccine in kids under five years old. Can you help us understand how the clinical trial process works for pediatric vaccines?

Pediatric vaccine trials really start to move forward after the vaccine has been proven efficacious in older age groups. Then, a moderate size clinical trial (in the case of children under 5, roughly 4,500 children were enrolled) is performed comparing children who receive the vaccine to those who receive a placebo injection. These studies are designed to assess the safety, tolerability and immunogenicity of the vaccine. The safety and tolerability analysis ensures no unique or potentially serious adverse events specific to this age group are present.

Pfizer reported that the two-dose vaccine (a lower dose of 3 micrograms) was well tolerated in kids under 5. Since these studies are relatively small, they may not be able to show efficacy of the vaccine at preventing COVID-19, because the number of children getting infected over the study period may be too small to allow a robust comparison. Therefore, "efficacy" in these trials is primarily assessed by a process called "immunobridging"—assessing antibody responses in children receiving the vaccine and comparing them to antibody responses in another age group where the vaccine was demonstrated to be effective.

For the Pfizer COVID-19 vaccine, this comparison arm is 16- to 25-year-olds. If the antibody response in the children in this trial is similar to those 16 to 25 in the other trial, then the expectation is that it will be equally effective in kids.

What did those results show so far?

In December, Pfizer reported that while the results of the immunobridging analyses were positive in kids six months to two years of age, the antibody response appeared inferior in kids 2 to 4 years old. Therefore, Pfizer decided to assess a third dose in kids six months to less than five years old, given at least two months after the second dose.

Since then, omicron surged. Given the large number of children being infected, researchers have the ability to assess the efficacy of preventing COVID-19 in this clinical trial, after receipt of two doses. For this reason, the FDA encouraged Pfizer to submit what they had to date, so that the FDA could begin reviewing the application while awaiting more data about the immunogenicity and clinical efficacy with the third dose.

We have not seen the immunogenicity data, the safety data, nor the clinical efficacy data yet, so it is impossible to truly comment on where we are with this vaccine. This package has been submitted to the FDA, which will review all of this and determine the path forward.

However, this assessment and subsequent recommendations will follow the same process as other vaccines in the pandemic. The data will be presented to an external panel of experts, which will make recommendations to the FDA. If the FDA ultimately allows an emergency use authorization in children under 5, the Advisory Committee on Immunization Practices will then independently review the data and make recommendations to the CDC on whether or not vaccination should be recommended for kids of this age group. The

CDC director has final say on the recommendation, but usually follows the advice of ACIP.

What does it mean that the vaccine had a less robust antibody response in kids 2 to 4 years old?

I think we need to keep in mind that while antibody responses/levels are important, they are just one part of an impressive and complex immune response to vaccination. Though the antibody response may have been lower in an age group (we haven't seen that data to know how much lower), remember that we just use that as a surrogate for clinical efficacy, and ultimately the most important piece of information is how well it fared in preventing COVID-19. Because of how intense the omicron surge has been, we may be better suited to answer that question.

You mentioned that omicron causing so many infections helps assess the efficacy of the vaccine. Anything else we should consider as we see results emerge during the omicron wave?

We need to keep in mind that the efficacy of two doses of the vaccine against symptomatic COVID-19 in adults against omicron appears to be lower than that of previous variants. Therefore, if the vaccine has a lower but still substantial (greater than or equal to 50%) efficacy against preventing COVID-19 during the omicron wave, this would not necessarily mean that it is inferior to the clinical efficacy (greater than or equal to 90%) seen with two doses of the vaccine in the trials in adults against the ancestral strain of SARS CoV-2—careful analysis and consideration needs to be given to the interpretation of those data.

There are many complexities to these data and the subsequent analyses and we are extremely fortunate in this country to have a robust process of expert analyses prior to any recommendations being set forth.

If authorized, will the vaccine become compulsory, like other school vaccines? Who makes this decision?

Mandatory vaccines for school children are made at the state level by the government. Given how mandates have been handled in this country to date, I would not anticipate this occurring anytime soon and certainly not before full FDA approval was given.

Will vaccinating this age group hasten herd immunity? Or, is that not the right question to ask anymore?

I feel very comfortable saying that vaccinating these children will protect them directly by decreasing the chance of infection. Further, by decreasing the number of infections in children, vaccination will help limit the spread of SARS CoV-2 and subsequently help protect other vulnerable individuals.

However, given what we have seen with delta and omicron, I do not think herd immunity is a realistic expectation. We will need to live with this virus moving forward. One of the best ways we can live with this virus is by vaccinating as many eligible people as possible.

How should parents decide if they should get a child vaccinated?

I encourage parents to speak with their pediatricians and listen to health care experts. At this point, it's impossible to recommend the vaccine for kids under five both because it is not authorized for use, but also because we haven't seen any of the safety or efficacy data. Once those things occur, I would encourage parents to speak with their trusted sources of

health care information and, importantly, their child's pediatrician.

I will say this though—the Pfizer vaccine has shown remarkable effectiveness in children five and up. While it is completely true that severe outcomes are rare in children, they do happen, including long COVID, hospitalization, multisystem inflammatory syndrome, and even death. What the real-world data in children 5 to 18 years of age have shown us is you can almost eliminate these risks with vaccination. If the data in children under five follows this same trend, I would recommend that all parents (barring legitimate medical contraindication to the vaccine) vaccinate their children.

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