FDA Recommends Third Pfizer Vaccine Booster Shot: Only for age 65 and high risk of severe COVID-19

September 17, 2021 — In an all-day meeting that became somewhat disorganized at the end, the Vaccines and Related Biologic Products Advisory Committee (VRBPAC) of the US Food and Drug Administration (FDA) recommended, by unanimous 18-0 vote, authorization for third booster doses of the Pfizer COVID-19 vaccine, officially now called Comirnaty, but restricted to those either age 65 and older or at "high risk of severe COVID-19." By informal poll, the committee also recommended including in the latter category health care workers and others at increased likelihood of exposure by virtue of occupation. Exactly who is at "high risk" will be left to the Advisory Committee on Immunization Practices (ACIP) of the US Centers for Disease Control and Prevention (CDC) who are expected to meet next week. Basic eligibility for booster doses kicks in six months after primary vaccination has been completed.

This unplanned vote was taken after the planned vote on authorizing third booster doses for the general public without age or other restrictions was resoundingly defeated, 16-2. The consensus expressed by the members seemed to be that the data provided by Pfizer with their application was of low quality and based on a study with small sample size of 330 test subjects. The cost-benefit balance was clearer, the committee clearly thought, with older people whose immune systems are naturally and normally less robust. Because vaccines work by teaching the immune system to recognize a virus, the effectiveness of a vaccine is ordinarily reduced with age.

The first vote was a blunt rejection of expressed desire for widespread booster dose authorization sought by Pfizer and the Biden administration. While the FDA is not obligated to follow the recommendations of its advisory committees of outside experts, it is extremely rare for them to be overruled.

Most of the questions from the committee were directed to guest experts from the Israeli Ministry of Health and the Weizmann Institute. Israel leads the world in vaccinating its population, approximately three months ahead of the US and the UK, and made the decision to authorize third booster doses beginning in July in phases, first to age 60 and older and eventually within a few weeks down to age 16 and older. The Israeli experts said that the virus reproduction rate, known as R0 ("R-nought"), was about 1.3 when booster doses began to be administered, a bad situation corresponding to a doubling of infections every 10 days, and fell to 0.96 by the end of August, a slight day-to-day decrease in total infections. They said that their model predicted that without booster doses the entire hospital capacity of the nation would have been exhausted by the beginning of September.

The Israeli experts emphasized that the vaccines even without a third booster dose remained very protective, but they observed a reduction in effectiveness from 97% after initially completing full vaccination to 85% six months later. While any vaccine more than 50% is medically valuable, they explained that these numbers implied a breakthrough rate of 3% (=100%-97%) rising to 15% (=100%-85%), a five-fold increase. Officially, the committee was supposed to consider only the data submitted by Pfizer with the application, using the Israeli data only for general guidance.

Because almost all useful data on the virus now must be derived from real-world observational studies rather than randomized controlled trials, it is difficult if not impossible to determine whether increasing occurrences of breakthrough infections are attributable to waning vaccine effectiveness per se or to other factors such as the nearly universal prevalence of the newer delta variant of the virus. Such statistical confounding factors left the committee unsure of how to compare risks and benefits. Ultimately, the committee was concerned that booster doses in young people might cause rare but significant adverse effects, such as myocarditis (inflammation of the heart muscle), and seemed to conclude that the data were insufficient to compare such risks to those resulting from COVID-19 infection.

There was a clear expectation that Pfizer would reapply for authorization of booster doses for the general public without age restriction once they had better data.