

VIEWPOINT

COVID-19 Vaccination—Becoming Part of the New Normal

Peter Marks, MD, PhD
US Food and Drug
Administration,
Silver Spring, Maryland.

Janet Woodcock, MD
US Food and Drug
Administration,
Silver Spring, Maryland.

Robert Califf, MD
US Food and Drug
Administration,
Silver Spring, Maryland.

As the US emerges from the recent Omicron surge of the COVID-19 pandemic following close to a million deaths in the country attributable to COVID-19, many people are hoping that the worst is over.¹ Widespread vaccine- and infection-induced immunity, combined with the availability of effective therapeutics, could blunt the effects of future outbreaks. Nonetheless, it is time to accept that the presence of SARS-CoV-2, the virus that causes COVID-19, is the new normal. It will likely circulate globally for the foreseeable future, taking its place alongside other common respiratory viruses such as influenza. And it likely will require similar annual consideration for vaccine composition updates in consultation with the US Food and Drug Administration (FDA) Vaccines and Related Biological Products Advisory Committee (VRBPAC). A recent meeting of the VRBPAC on April 6, 2022, resulted in a lively discussion and agreement on many considerations for planning for upcoming approaches to COVID-19 vaccine strain composition decision-making, development, and recommendations.

COVID-19 vaccines, developed and deployed in record time based on foundational scientific and clinical research conducted over the preceding decade, have

Nonetheless, it is time to accept that the presence of SARS-CoV-2, the virus that causes COVID-19, is the new normal. It will likely circulate globally for the foreseeable future, taking its place alongside other common respiratory viruses such as influenza.

conservatively saved tens of thousands of lives in the US and many more across the globe.² Although data show that third doses of the mRNA COVID-19 vaccines provide more durable protection against the severe outcomes of hospitalization and death, only 45% of the US population has received a third vaccine dose, including only about 68% of those older than 65 years—the individuals at greatest risk of adverse outcomes from COVID-19.³ Because fourth doses of the mRNA COVID-19 vaccines were only recently authorized for those older than 50 years, it is too early to assess their effects on protection against serious outcomes of COVID-19 in the US. However, robust observational data from Israel with a large sample size showed additional protection against hospitalization and death in that population.⁴

During this coming fall-to-winter period, 3 factors may come together to place the country's population at

risk of COVID-19, particularly those who are unvaccinated or who are not up-to-date with vaccination. These factors include (1) waning immunity from prior vaccine or prior infection, (2) further evolution of SARS-CoV-2, and (3) seasonality of respiratory virus infection, waves of which are generally more severe in the fall to winter months when individuals move their activities indoors.

By summer, decisions will need to be made for the 2022-2023 season about who should be eligible for vaccination with additional boosters and regarding vaccine composition. Administering additional COVID-19 vaccine doses to appropriate individuals this fall around the time of the usual influenza vaccine campaign has the potential to protect susceptible individuals against hospitalization and death, and therefore will be a topic for FDA consideration.

Those at greatest risk who might benefit most from vaccination include immunocompromised individuals and people older than 50 years, given the prevalence of comorbidities that increase the risk of severe disease and death in this latter group. Additional groups that might benefit include those who are unvaccinated (including children) or not up-to-date with vaccination (eg, those who have received only 1 dose of a COVID-19 vaccine or have not received a booster dose).⁵ The benefit of giving additional COVID-19 booster vaccines to otherwise healthy individuals 18 to 50 years of age who have already received primary vaccination and a first booster dose is not likely to have as marked an effect on hospitalization or death as in the other populations at higher risk (noted above). However, booster vaccinations could be associated with a reduction in health care utilization (eg, emergency department or urgent care center visits).

Around the same time that a decision is made regarding who should be eligible for vaccination, a decision will also need to be made on the COVID-19 vaccine composition. To provide maximal benefit across the entire age spectrum, careful consideration will need to be given to the choice of the SARS-CoV-2 variant(s) to cover in the COVID-19 vaccines for the fall and winter of the 2022-2023 season. This is because the variant(s) covered by the vaccine may have an important influence on both the extent and duration of protection against a future SARS-CoV-2 variant(s) that may circulate. Better alignment between the variant(s) covered by the vaccine and circulating variant(s) of SARS-CoV-2 might be expected to prevent a broader spectrum of disease, potentially for a longer time. In the event of a major fall or winter wave, a vaccine with optimal variant coverage might facilitate significant reductions in lost productivity and health care utilization from both

Corresponding Author: Peter Marks, MD, PhD, Center for Biologics Evaluation and Research, US Food and Drug Administration, 10903 New Hampshire Ave, WO71-7232, Silver Spring, MD 20993 (peter.marks@fda.hhs.gov).

acute and chronic complications of COVID-19, including postacute COVID-19 syndrome.⁶ Of note, in the past, such an overall public health benefit in an otherwise healthy younger population has been considered during the annual influenza vaccine campaign.⁷

In terms of practical considerations, at the recent meeting of the VRBPAC, there was relatively uniform agreement that a single vaccine composition used by all manufacturers was desirable and that data would be needed to inform and drive the selection of a monovalent, bivalent, or multivalent COVID-19 vaccine.⁸ There was also general agreement that, should a new vaccine composition be recommended based on the totality of the available clinical and epidemiologic evidence, optimally it could be used for both primary vaccination as well as booster administration.

The timeframe to determine the composition of the COVID-19 vaccine for the 2022-2023 season, to use alongside the seasonal influenza vaccine for administration in the Northern Hemisphere beginning in about October, is compressed because of the time required for manufacturing the necessary doses. A decision on composition will need to be made in the US by June 2022. Because of this timing, the FDA, in consultation with the VRBPAC, will need to arrive at a recommendation for the future composition of the US COVID-19 vaccines for 2022-2023 based on the available evidence and predictive modeling, with the understanding that there will be some inherent residual uncertainty about the further evolution of SARS-CoV-2. To date, the original, or prototype, vaccine composition deployed has been reasonably good at protecting against severe outcomes from COVID-19. However, a greater depth and du-

ration of protection might be achieved with a vaccine covering currently circulating variants.

As plans are being developed for the coming fall and winter, it is critical that patients and caregivers understand the profound benefit of a booster dose of the mRNA vaccines or a second vaccine dose of any kind after the Janssen/Johnson & Johnson vaccine and that this understanding leads to action now in the face of a current uptick in infection rates. Clinicians should not be susceptible to inertia and should continue to recommend that patients get their COVID-19 vaccination status up to date, meaning primary vaccination and relevant booster(s). There is no evidence that getting vaccinated now will have adverse effects or toxicity that would preempt the administration of an additional vaccine dose in the fall months if there is evidence of waning of immunity, a new variant, or an adverse seasonal pattern.

Vaccines, as public health interventions, have been responsible over the past century for reducing an unimaginable amount of morbidity and for saving millions of lives. The eradication of smallpox and near elimination of several other infectious diseases are an unambiguous triumph of modern medicine. During the 2022-2023 COVID-19 vaccine planning and selection process, it is important to recognize that the fall season will present a major opportunity to improve COVID-19 vaccination coverage with the goal of minimizing future societal disruption and saving lives. With the plan for implementation of this year's vaccine selection process, society is moving toward a new normal that may well include annual COVID-19 vaccination alongside seasonal influenza vaccination.

ARTICLE INFORMATION

Published Online: May 2, 2022.
doi:10.1001/jama.2022.7469

Conflict of Interest Disclosures: Related to roles held prior to his confirmation as FDA commissioner, Dr Califf reported receiving personal fees from Alphabet Inc (Google LLC and Verily Life Sciences LLC), Centessa Pharmaceuticals PLC, Clinetic Inc, Cytokinetics Inc, and Medicxi Ventures (UK) LLP outside the submitted work. No other disclosures were reported.

Additional Information: Dr Marks is director of the Center for Biologics Evaluation and Research, Dr Woodcock is principal deputy commissioner, and Dr Califf is commissioner, all at the US Food and Drug Administration.

REFERENCES

1. Centers for Disease Control and Prevention. COVID data tracker. Accessed April 13, 2022. <https://covid.cdc.gov/covid-data-tracker>

2. Gupta S, Cantor J, Simon KI, Bento AI, Wing C, Whaley CM. Vaccinations against COVID-19 may have averted up to 140,000 deaths in the United States. *Health Aff (Millwood)*. 2021;40(9):1465-1472. doi:10.1377/hlthaff.2021.00619

3. Thompson MG, Natarajan K, Irving SA, et al. Effectiveness of a third dose of mRNA vaccines against COVID-19-associated emergency department and urgent care encounters and hospitalizations among adults during periods of Delta and Omicron variant predominance: VISION Network, 10 states, August 2021-January 2022. *MMWR Morb Mortal Wkly Rep*. 2022;71(4):139-145. doi:10.15585/mmwr.mm7104e3

4. Bar-On YM, Goldberg Y, Mandel M, et al. Protection by a fourth dose of BNT162b2 against Omicron in Israel. *N Engl J Med*. Published online April 5, 2022. doi:10.1056/NEJMoa2201570

5. Ferdinands JM, Rao S, Dixon BE, et al. Waning 2-dose and 3-dose effectiveness of mRNA vaccines against COVID-19-associated emergency department and urgent care encounters and

hospitalizations among adults during periods of Delta and Omicron variant predominance—VISION Network, 10 states, August 2021-January 2022. *MMWR Morb Mortal Wkly Rep*. 2022;71(7):255-263. doi:10.15585/mmwr.mm7107e2

6. Nalbandian A, Sehgal K, Gupta A, et al. Post-acute COVID-19 syndrome. *Nat Med*. 2021;27(4):601-615. doi:10.1038/s41591-021-01283-z

7. Grohskopf LA, Alyanak E, Ferdinands JM, et al. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices, United States, 2021-22 influenza season. *MMWR Recomm Rep*. 2021;70(5):1-28. doi:10.15585/mmwr.r7005a1

8. US Food and Drug Administration. Vaccines and Related Biological Products Advisory Committee April 6, 2022 meeting announcement. Accessed April 13, 2022. <https://www.fda.gov/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-april-6-2022-meeting-announcement>