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**BEFORE THE
SELECT SUBCOMMITTEE ON THE CORONAVIRUS PANDEMIC
COMMITTEE ON OVERSIGHT AND ACCOUNTABILITY
U.S. HOUSE OF REPRESENTATIVES**

“ASSESSING AMERICA’S VACCINE SAFETY SYSTEMS, PART 1”

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Introduction

Chair Wenstrup, Ranking Member Ruiz, and members of the Subcommittee, thank you for the opportunity to testify before you to discuss the Food and Drug Administration's (FDA or the Agency) coronavirus disease 2019 (COVID-19) response and vaccine safety and surveillance efforts to date and moving forward.

The American public can be assured of the simple fact that FDA-approved and authorized vaccines are high quality, effective, and safe. Vaccines work and save the lives of millions of children and adults every year by producing immune responses to bacteria or viruses that cause disease.¹ While they may not always prevent an infection or mild disease, vaccines often can prevent hospitalization and death. The vaccine development process, and FDA's stringent regulatory and scientific evaluation process, ensure that the health benefits of available approved and authorized vaccines far outweigh any risks.

Vaccines approved or authorized by FDA, including the COVID-19 vaccines, have undergone a rigorous research and development process and have been thoroughly evaluated by FDA prior to authorization for emergency use and prior to approval, in accordance with the Agency's rigorous policies, procedures, and standards. Furthermore, vaccine safety is closely and continuously monitored through multiple surveillance systems, which alert both FDA and the Centers for Disease Control and Prevention (CDC) should a potential concern arise.

Facilitating the Availability of COVID-19 Vaccines in the United States

FDA has consistently followed a science-driven process with transparency in mind when evaluating the safety and effectiveness of COVID-19 vaccine candidates.

FDA's Center for Biologics Evaluation and Research (CBER) has facilitated, and continues to facilitate, the development and availability of vaccines and other biological products to combat COVID-19. Through our transparent and rigorous process of scientific evaluation, FDA has issued Emergency Use Authorizations (EUAs) for four monovalent COVID-19 vaccines:

- the Pfizer-BioNTech COVID-19 Vaccine for use in individuals six months of age and older;
- the Moderna COVID-19 Vaccine for use in individuals six months of age and older;
- the Janssen COVID-19 Vaccine for use in certain individuals 18 years of age and older (the Janssen COVID-19 Vaccine is no longer authorized for use in the United States);² and
- the Novavax COVID-19 Vaccine, Adjuvanted for use in individuals 12 years of age and older.

FDA has also approved Comirnaty (known as Pfizer-BioNTech COVID-19 Vaccine under the EUA) for use in individuals 12 years of age and older and Spikevax (known as the Moderna COVID-19 Vaccine under the EUA) for use in individuals 12 years of age and older.

¹ https://www.who.int/health-topics/vaccines-and-immunization#tab=tab_1

² In April 2021, after a period of use under EUA, the use of the Janssen vaccine was limited to certain populations. This change was made after a serious adverse event (thrombosis-thrombocytopenia syndrome) became apparent through the United States' rigorous vaccine surveillance activities. The EUA was eventually revoked on June 1, 2023, and no Janssen COVID-19 Vaccine is currently authorized or available for use in the United States.

Additionally, as the science dictated and the SARS-CoV-2 virus evolved, FDA authorized two COVID-19 vaccines that had a bivalent composition (original and Omicron BA.4/BA.5) as a booster dose: Pfizer-BioNTech COVID-19 Vaccine, Bivalent; and Moderna COVID-19 Vaccine, Bivalent. While these were initially authorized for use as a booster dose, the Pfizer-BioNTech COVID-19 Vaccine, Bivalent was also authorized as a third dose in the three-dose primary series in individuals six months through four years of age. We note that these are no longer authorized for use in the United States given the evolution of SARS-CoV-2, because the bivalent versions were developed to target strains of SARS-CoV-2 that are no longer circulating.

For the 2023-2024 fall to winter season, a process was implemented early in 2023 by FDA for making vaccine strain selection recommendations. This process was similar in many ways to that used for seasonal influenza vaccines and is based on prevailing and predicted variants. Strain selection by June was desirable to allow for vaccine production by September. Subsequently, on September 11, 2023, FDA took action approving and authorizing for emergency use COVID-19 vaccines updated to include the 2023-2024 Formula (XBB.1.5 monovalent composition) to more closely target circulating variants and to provide better protection against serious consequences of COVID-19, including hospitalization and death. The updated mRNA COVID-19 vaccines are each approved for individuals 12 years of age and older and are authorized for emergency use in individuals six months through 11 years of age. On October 3, 2023, FDA amended the EUA of the Novavax COVID-19 Vaccine, Adjuvanted for use in individuals 12 years of age and older to include the 2023-2024 Formula.

Vaccines Are Among the Safest and Most Effective Public Health Measures

Vaccines are among the safest and most effective public health measures ever introduced and are directly responsible for reducing suffering and saving innumerable lives around the world.

Thanks to safe and effective vaccines, we no longer routinely see the serious diseases that they prevent. For example, measles kills at least one in every 1,000 children infected with the virus.³ The measles vaccine is at least 96 percent effective in preventing illness,⁴ and tens of millions of children's lives have been saved across the globe since the vaccine became widely available.⁵

Similarly, because of vaccines, smallpox, a disease that killed about one in three individuals infected, has been eradicated worldwide.⁶ Except for rare cases, polio has been eliminated from circulation in the United States, and with continued vaccination, polio may also be eradicated worldwide in the not-too-distant future.⁷ The relationship between vaccination and the eradication of smallpox and the near elimination of polio is indisputable.

³ <https://www.cdc.gov/measles/symptoms/complications.html>

⁴ [https://www.usatoday.com/story/opinion/2023/12/14/covid-flu-rsv-vaccines-protect-holidays/71882946007/;](https://www.usatoday.com/story/opinion/2023/12/14/covid-flu-rsv-vaccines-protect-holidays/71882946007/)
<https://www.cdc.gov/vaccines/vpd/mmr/public/index.html>

⁵ <https://www.who.int/news-room/fact-sheets/detail/measles>

⁶ <https://www.who.int/news-room/spotlight/history-of-vaccination/history-of-smallpox-vaccination#:~:text=Over%20thousands%20of%20years%2C%20smallpox,most%20severe%20forms%20of%20dis,ease.>

⁷ <https://www.cdc.gov/polio/global-polio-eradication.html>

Appropriately targeted vaccines also provide protection against several other infectious diseases.⁸ In fact, vaccines have been so effective that we now often take for granted the protection that they provide us from countless serious and life-threatening diseases.

Similarly, vaccines that help prevent respiratory diseases save lives. Data from multiple studies indicate that since the beginning of the COVID-19 pandemic, tens of millions of lives have been saved by vaccination against COVID-19 globally.⁹ Although the benefits were most clear in older individuals, the vaccine continues to benefit all ages for which they are authorized or approved.¹⁰

During the course of the pandemic, those who remained unvaccinated had almost a 2.5 times higher risk of death from COVID-19 than those who had received even at least a single vaccine dose.¹¹ Additionally, data from the past two years also make it clear that people who stay up to date on vaccination have an even lower risk of hospitalization or death from COVID-19.¹²

COVID-19 Vaccine Safety Surveillance

FDA and its federal and state partners cooperate to conduct intensive monitoring of U.S. COVID-19 vaccine safety using a variety of overlapping approaches. FDA also collaborates with international partners to understand the safety of these vaccines globally.

During the COVID-19 public health emergency, over 270 million people received more than 676 million doses of COVID-19 vaccines in the United States. Vaccine safety is a top priority for the federal government, and we take reports of health problems following COVID-19 vaccination very seriously. We investigate all events that potentially indicate a safety concern. As detailed below, FDA and CDC have implemented a coordinated and overlapping approach for continuous safety monitoring of all COVID-19 vaccines using state-of-the-art methods.

CBER monitors the safety of approved and authorized COVID-19 vaccines through both passive and active safety surveillance systems in coordination and collaboration with other federal agencies such as the CDC, and other academic and large non-government healthcare data systems. In addition, CBER actively participates in ongoing international pharmacovigilance efforts, including those organized by the International Coalition of Medicines Regulatory Authorities (ICMRA). These efforts are in addition to the pharmacovigilance efforts being undertaken by the individual manufacturers for approved and authorized vaccines.

Overview of Vaccine Surveillance

Passive surveillance is defined as unsolicited reports of adverse events that are sent to a central database or health authority. In the United States, these are received and entered into the Vaccine Adverse Event Reporting System (VAERS), a national vaccine safety monitoring system co-managed by FDA and CDC.

⁸ <https://www.who.int/news-room/feature-stories/detail/counting-the-impact-of-vaccines>

⁹ <https://www.commonwealthfund.org/blog/2022/two-years-covid-vaccines-prevented-millions-deaths-hospitalizations>; <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9537923/>

¹⁰ <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-09-12/11-COVID-Wallace-508.pdf>

¹¹ https://www.cureus.com/articles/163598-unveiling-the-impact-of-covid-19-vaccines-a-meta-analysis-of-survival-rates-among-patients-in-the-united-states-based-on-vaccination-status?score_article=true#!/

¹² <https://www.usatoday.com/story/opinion/2023/12/14/covid-flu-rsv-vaccines-protect-holidays/71882946007/>

After an adverse event is reported, the information is processed and sent to CDC and FDA. Physicians and scientists then collaborate on evaluating the reports. These reports, which range from mild reactions, like soreness and fatigue, to more severe complications, are reviewed by VAERS staff within days to identify potential patterns of concern. In the case of reports related to the COVID-19 vaccines, for example, FDA and CDC experts assess relevant data from serious reports and share important findings with each other. Serious reports are defined by the following outcomes: death, a life-threatening adverse event, inpatient hospitalization or extension of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect.

Scientists also perform further analyses using other *active safety surveillance* systems such as CDC's Vaccine Safety Datalink (VSD)¹³ or FDA's Biologics Effectiveness and Safety system.¹⁴ The latter systems can compare individual health status prior to and after vaccination, or alternatively, these systems can compare unvaccinated to vaccinated individuals, which enables analyses that can help determine the relationship between an adverse event and a vaccine. These systems are more powerful than VAERS in helping to assess health risks and shed light on whether the vaccine caused the adverse event.

Passive Vaccine Surveillance Using VAERS

During the pandemic, reports in VAERS were used in conjunction with other vaccine safety systems to monitor the occurrence of certain adverse events including serious adverse events, as providers of COVID-19 vaccines were required to report these to VAERS. For example, we were able to evaluate severe allergic reactions following vaccination with the authorized mRNA-based COVID-19 vaccines. Through this work, we came to understand that these reactions are quite rare, occurring in fewer than five in one million vaccine doses administered.

While VAERS is arguably the most visible piece of the U.S. vaccine safety surveillance system, VAERS is not always well understood. Unfortunately, some use the publicly available, unverified information to inaccurately claim that VAERS reports show that vaccines definitively caused certain adverse or harmful health outcomes. VAERS relies on individuals, including healthcare providers, vaccine manufacturers, vaccine recipients, and the public to submit reports of adverse events following vaccination. Some of these reported events may be true adverse reactions to a vaccine, while other events may not be related. Often, the more robust active vaccine surveillance systems noted above are needed to understand the relationship between an adverse event and a vaccine.

Ultimately, the fundamental question in vaccine safety is whether an event is directly caused by a vaccine. A thorough examination of the facts underlying reports to VAERS is necessary to determine whether an adverse event is related to the administration of a vaccine. Further studies utilizing population-based surveillance systems are often conducted involving comparisons of the rate of an event to rates of the same event in populations that have not been vaccinated, or who have been vaccinated at a different point in time. Since most events that occur after

¹³ <https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/vsd/index.html>

¹⁴ <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/cber-biologics-effectiveness-and-safety-best-system>

vaccination also occur in people who are not vaccinated, these comparisons are critical to sorting out if the event was coincidental or could have been caused by vaccination.

When potential adverse events are verified, including after first being reported in VAERS, FDA acts swiftly to take appropriate measures to protect public health. While not without limitations, VAERS has proven to be vital in detecting both potential and actual safety issues and informing vaccine policy decisions that protect the health of the American public. It has helped identify notable COVID-19 vaccine safety concerns. For example, after VAERS detected an increase in rare, life-threatening allergic reactions just weeks after the first vaccines were authorized, CDC and FDA provided information and guidance to help prevent and manage these reactions. Just days after VAERS detected that six out of the more than six million patients who received the Janssen COVID-19 Vaccine had developed a rare and severe type of blood clot, CDC and FDA recommended pausing the use of that vaccine to better understand this adverse event. Another example of the utility of VAERS is the detection of myocarditis following the mRNA COVID-19 vaccines, which led CDC to provide advice to healthcare providers about the potential risk and to recommend that some people, primarily teen and young adult males, space out their vaccines. Additionally, FDA authorized revisions to the vaccine recipient and provider fact sheets to reflect the suggested increased risks of myocarditis and pericarditis following vaccination.

Active Surveillance

Active surveillance involves proactively obtaining and performing timely analysis of information occurring from millions of individuals recorded in large healthcare data systems to further evaluate safety signals identified through passive surveillance or to detect additional safety signals that may not have been reported as adverse events to passive surveillance systems. FDA conducts active surveillance using the Sentinel BEST (Biologics Effectiveness and Safety) System and collaborates with other federal and non-federal partners.

BEST

The BEST system makes use of multiple data sources and enables queries to detect or evaluate adverse events as well as studies to answer specific safety questions for vaccines. The major partners for the COVID-19 vaccine safety studies conducted in BEST currently are Acumen, IQVIA, Carelon Research, CVS Health, and Optum.¹⁵ Using BEST, CBER monitors about 15 pre-specified, potential adverse events of special interest that have been studied in other approved vaccines but have not been associated with a safety concern for an approved or authorized COVID-19 vaccine at this time. Adverse events of special interest are chosen based on real world observations of adverse events with related or unrelated vaccines or based upon prior experience observed with vaccines in clinical trials. These include death, Guillain-Barre Syndrome, myocardial infarction, stroke, anaphylaxis, and myopericarditis, among others. CBER further plans to use the BEST system to conduct more in-depth analyses should additional safety concerns be identified from sources such as VAERS.

In summary, in collaboration and coordination with CDC and several different partners, CBER has assembled passive and active surveillance systems that can detect and refine safety findings

¹⁵ <https://bestinitiative.org/best/about/collaborators>; <https://www.carelonresearch.com/perspectives/sentinel-data-partner-and-scientific-collaborator>

with the approved and authorized COVID-19 vaccines in a relatively rapid manner. These systems can also potentially be leveraged to assess safety in specific subpopulations and to assess vaccine effectiveness, including against emerging variants.

Conclusion

Vaccines are one of the most highly effective public health interventions, responsible for saving millions of lives each year. In the United States, authorized or approved vaccines must be manufactured with high quality, and their safety and effectiveness must be demonstrated. Their safety over time is also closely and continuously monitored through multiple overlapping passive and active safety surveillance systems, including VAERS, VSD, and the BEST Sentinel Initiative. As set forth above, these systems help to ensure that the health benefits of available authorized and approved vaccines continue to far outweigh any risks.

Unfortunately, due to vaccine hesitancy, some Americans have avoided getting the vaccines they need to best protect themselves from infectious diseases, including from the most severe consequences of influenza and COVID-19. This has led to unnecessary death, severe illness, and hospitalization. These tragic outcomes not only have a devastating effect on individuals and their families, but they also create a tremendous strain on our healthcare systems and clinicians. COVID-19 vaccines have been shown to be safe. COVID-19 vaccines have been shown to be effective. They are supported by the best available scientific data; they underwent FDA's rigorous regulatory authorization and approval processes; and their safety over time is closely monitored. Staying up to date on vaccination is the best way to reduce the risks of death and serious illness or hospitalization from diseases like COVID-19.