TESTIMONY

OF

ROBERT M. CALIFF, MD
COMMISSIONER OF FOOD AND DRUGS
FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES

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AN UPDATE ON THE ONGOING FEDERAL RESPONSE TO COVID-19: CURRENT STATUS AND FUTURE PLANNING

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Introduction

Chair Murray, Ranking Member Burr, distinguished members of the Committee, thank you for the opportunity to testify before you today to describe the Food and Drug Administration's (FDA's or the Agency's) coronavirus disease 2019 (COVID-19) response efforts. All of our efforts are in close coordination and collaboration with our partners, both within the Department of Health and Human Services (HHS) and across the federal government, to help ensure the development, authorization, licensure, approval, and availability of critical, safe, and effective medical products to address the COVID-19 public health emergency.

I want to note that this testimony is just a snapshot of some of our extensive work and is in the context of efforts across the Agency to address this pandemic. There are thousands of FDA employees who have been working on COVID-19 response efforts non-stop since the start of the pandemic. I want to commend and recognize their efforts and thank them for their dedication and service. I also want to thank all FDA employees who have continued to work on the myriad issues the Agency is responsible for that do not directly involve COVID-19.

From the beginning of this public health emergency, FDA has taken an active leadership role in the all-of-government response to the COVID-19 pandemic, inspired by the resiliency of the American people and our great innovators. FDA stood up an intra-agency group that continues to ensure we are doing everything possible to protect the American public, help ensure the safety, efficacy, and quality of FDA-regulated medical products, and provide the industries we regulate with the guidance and tools to do the same. We continue to focus on facilitating the development and availability of medical countermeasures to diagnose, treat, and prevent COVID-19, surveilling the medical product and food supply chains for potential shortages or disruptions, and helping to mitigate such impacts, as necessary to protect the public health.

This includes working to quickly address any potential impacts of new variants. FDA continues to evaluate the potential impact of new variants on the currently available diagnostics, therapeutics and vaccines. We are closely monitoring changes to the virus and are committed to communicating with the public as we learn more. In response to the omicron variant, we

updated the *SARS-CoV-2 Viral Mutations: Impact on COVID-19 Tests* web page[1] to share new information on the variants and their impact on antigen diagnostic tests. FDA is committed to continuing to use every tool in our toolbox to fight this pandemic, including pivoting as the virus adapts, to arm ourselves with the best available diagnostics, life-saving therapeutics and vaccines to fight this virus.

At this time, the current vaccines remain highly effective at preventing serious clinical outcomes associated with a COVID-19 infection, including hospitalization and death. Additionally, currently available data from our international partners and vaccine manufacturers that has been evaluated by the Agency, suggests that an additional booster shot following the completion of a primary vaccination provides further protection. Data also suggest a second booster dose of either the Pfizer-BioNTech Vaccine or Moderna COVID-19 Vaccine could help increase protection levels for certain higher-risk individuals.

Getting vaccinated or receiving a booster with one of the currently available vaccines is the best thing Americans can do right now, in addition to standard precautions like wearing a mask, to help protect themselves and their families.

Biologics, Including Vaccines

FDA's Center for Biologics Evaluation and Research (CBER) continues to use every tool available to help facilitate the development and availability of vaccines and other biological products to combat the COVID-19 pandemic expeditiously and safely.

CBER is working on multiple fronts to address the COVID-19 pandemic, including:

- Helping to facilitate expedited clinical trials for vaccines and certain therapeutic biological products that hold promise to prevent or treat COVID-19 by providing timely interactions, scientific advice, and recommendations for individual sponsors and through issuance of guidance documents;

[1] *https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-viral-mutations-impact-covid-19-tests*

- Supporting product development and facilitating the scaling up of manufacturing capacity for high priority products to treat COVID-19 and conducting timely reviews;
- Expediting the review of Emergency Use Authorization (EUA) requests and Biologics License Applications (BLAs) for vaccines and other critical medical products to address COVID-19, including the evaluation of booster doses of COVID-19 vaccines and the use of COVID-19 vaccines in certain pediatric populations;
- Helping to ensure an adequate and safe blood supply; and
- Providing information to healthcare providers and researchers to help them submit expanded access investigational new drug application (IND) requests to permit the use of CBER-regulated investigational products for patients with COVID-19.

CBER's work on COVID-19 vaccines, as discussed below, has made a tremendous difference in addressing the pandemic by facilitating the availability of COVID-19 vaccines that meet the Agency's rigorous standards as expeditiously as possible. Through our transparent scientific evaluation process, FDA has issued EUAs for three COVID-19 vaccines: the Pfizer-BioNTech COVID-19 Vaccine for use in individuals 5 years of age and older; the Moderna COVID-19 Vaccine for use in individuals 18 years of age and older; and the Janssen COVID-19 Vaccine for use in certain individuals 18 years of age and older. FDA has also approved Comirnaty (known as Pfizer-BioNTech COVID-19 Vaccine under the EUA) for use in individuals 16 years of age and older and Spikevax (known as the Moderna COVID-19 Vaccine under the EUA) for use in individuals 18 years of age and older. In doing so, we have relied upon the Agency's rigorous standards for safety, effectiveness, and manufacturing quality. These COVID-19 vaccines were developed without cutting corners or compromising our regulatory and scientific standards. Intensive interactions between FDA and manufacturers minimized the time between different studies in the clinical development process; allowed seamless movement throughout the different phases of clinical trials; and simultaneously facilitated manufacturers proceeding with manufacturing scale-up before it was clear whether the safety and effectiveness data for a vaccine would support an EUA, allowing for quicker access to products once FDA reviewed the data and found the products met the Agency's rigorous standards for authorization or approval.

For the approved vaccines, as well as those that have been authorized for emergency use, our process included a thorough evaluation of the data by the Agency's career staff. We also

solicited input from independent scientific and public health experts through our public advisory committee meetings for the COVID-19 vaccines that we have authorized. Throughout our scientific and regulatory process, FDA took additional steps to facilitate transparency, such as posting sponsor and FDA briefing documents and key decisional memoranda.

The COVID-19 vaccines that are available in the United States have shown clear and compelling efficacy in large, well-designed phase 3 trials. These vaccines are helping the country in the fight against this pandemic and have met FDA's rigorous standards for safety and effectiveness to support either EUA or approval. The vaccines are approved or authorized to prevent COVID-19, and have been shown to significantly reduce the associated serious outcomes, including hospitalization and death.

As part of our continued efforts to be transparent and educate the public, we have a wealth of information on our website about the COVID-19 vaccines available for use in the United States. The information includes fact sheets for healthcare providers (vaccination providers) and fact sheets for vaccine recipients and caregivers in multiple languages, with important information such as dosing instructions; information about the benefits and risks of each vaccine; and topical Questions and Answers developed by FDA for the approved vaccines and each authorized vaccine.[2]

It is also important to highlight that, as part of each EUA or approval, manufacturers and vaccination providers are required to report serious adverse events, cases of Multisystem Inflammatory Syndrome (MIS), and cases of COVID-19 that result in hospitalization or death to the Vaccine Adverse Event Reporting System (VAERS), a national vaccine safety surveillance program jointly run by FDA and the Centers for Disease Control and Prevention (CDC).

COVID-19 vaccine safety is a top priority for the federal government, and we take all reports of health problems following COVID-19 vaccination very seriously. FDA and CDC have implemented a coordinated and overlapping approach for continuous safety monitoring of all

[2] *https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-frequently-asked-questions*

COVID-19 vaccines using state-of the art technologies. Specifically, the Agency's monitoring following authorization of the COVID-19 vaccines uses a multi-pronged approach including:

1) passive surveillance using VAERS consisting of safety reports submitted by healthcare providers,[3] patients, parents and other members of the public; combined with
2) active surveillance, using large population-based healthcare datasets.

These latter healthcare data systems offer a higher likelihood of detecting rare adverse events because they capture medical data on millions of Americans, cover diverse subpopulations (i.e., pregnant women, elderly, and patients with comorbidities), and can provide a longer duration of follow-up when compared to the prelicensure clinical studies. In addition, COVID-19 vaccine recipients are encouraged to enroll in CDC's v-safe After Vaccination Health Checker smartphone-based tool that uses text messaging and web surveys to check-in with vaccine recipients over time after they receive a COVID-19 vaccine. Through v-safe, they can quickly tell CDC if they have any side effects after getting a COVID-19 vaccine. Together, the passive and active safety surveillance provide a coordinated and overlapping approach to vaccine safety monitoring for COVID-19 vaccines.

On August 23, 2021, FDA announced the first approval of a COVID-19 vaccine. The vaccine previously known as the Pfizer-BioNTech COVID-19 Vaccine was approved and marketed as Comirnaty for the prevention of COVID-19 in individuals 16 years of age and older. The Pfizer-BioNTech COVID-19 Vaccine has continued to be available under an EUA and is currently authorized as a:

- Two-dose primary series for individuals 5 years of age and older; third primary series dose for individuals 5 years of age and older with certain immunocompromising conditions;

- homologous first booster dose (matching the primary vaccination) administered at least 5 months after completion of primary vaccination to individuals 5 years of age and older;

[3] Providers in the CDC COVID-19 Vaccination Program are required to report certain adverse events following COVID-19 vaccination to VAERS

- heterologous first booster dose (not matching the primary vaccination) administered after completion of primary vaccination to individuals 18 years of age and older (the dosing interval is the same as that authorized for a booster dose of the vaccine used for primary vaccination);

- homologous second booster dose administered at least 4 months after a first booster dose to individuals 50 years of age and older and individuals 12 years of age and older with certain immunocompromising conditions; and

- heterologous second booster dose administered at least 4 months after a first booster dose to individuals 50 years of age and older and individuals 18 years of age and older with certain immunocompromising conditions.

On January 31, 2022, FDA approved a second COVID-19 vaccine. The vaccine has been known as the Moderna COVID-19 Vaccine; the approved vaccine is marketed as Spikevax for the prevention of COVID-19 in individuals 18 years of age and older. The Moderna COVID-19 Vaccine has continued to be available under an EUA and is currently authorized as a:

- Two-dose primary series for individuals 18 years of age and older;

- third primary series dose for individuals 18 years of age and older with certain immunocompromising conditions;

- homologous or heterologous first booster dose administered after completion of primary vaccination to individuals 18 years of age and older (the authorized dosing interval for a homologous booster is at least 5 months after completion of a primary series, and the authorized interval for a heterologous booster is the same as that authorized for a booster dose of the vaccine used for primary vaccination); and

- a homologous or heterologous second booster dose administered at least 4 months after the first booster dose to individuals 50 years of age and older and individuals 18 years of age and older with certain immunocompromising conditions.

The Janssen COVID-19 Vaccine was originally authorized on February 27, 2021. On May 5, 2022, FDA limited the authorized use of the Janssen COVID-19 Vaccine to individuals 18 years of age and older for whom other authorized or approved COVID-19 vaccines are not accessible or clinically appropriate, and to individuals 18 years of age and older who elect to receive the Janssen COVID-19 Vaccine because they would otherwise not receive a COVID-19 vaccine.

At this time FDA is closely monitoring the emergence of new variants in order to determine what, if anything, needs to be changed in the composition of COVID-19 vaccines moving forward to best protect the population. The Agency has already issued COVID-19 vaccine-specific guidance to address the emergence and potential future emergence of variants of SARS-CoV-2, the virus that causes COVID-19.[4]

FDA recently held the following virtual meetings of its Vaccines and Related Biological Products Advisory Committee (VRBPAC) related to emergency use requests that have been publicly announced by COVID-19 vaccine manufacturers.

- On June 7, FDA convened VRBPAC to discuss an EUA request for a COVID-19 vaccine manufactured by Novavax to prevent COVID-19 in individuals 18 years of age and older.

- On June 14, FDA and its advisory committee of external experts met to discuss Moderna's EUA request for 6 years through 17 years of age.

- On June 15, FDA and its advisory committee of external experts met to discuss the Moderna EUA request for 6 months through 5 years of age and the Pfizer-BioNTech EUA request for 6 months through 4 years of age.

On June 28, FDA plans to convene the VRBPAC to discuss whether the SARS-CoV-2 strain composition of COVID-19 vaccines should be modified, and if so, which strain(s) should be selected for Fall 2022. This meeting is a follow-up to the April 6 VRBPAC meeting that

[4] *Emergency Use Authorization for Vaccines to Prevent COVID-19*, updated March 31, 2022: *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-vaccines-prevent-covid-19*

discussed general considerations for future COVID-19 vaccine booster doses and the strain composition of COVID-19 vaccines to further meet public health needs.

Figure 1


Vaccine Timeline
June 30, 2020
FDA issues guidance with recommendations for those developing COVID-19 vaccines for the ultimate purpose of licensure.
October 6, 2020
FDA issues guidance providing further information on the EUA process for investigational vaccines.
December 10, 2020
VRBPAC meeting on Pfizer's COVID-19 vaccine.
December 11, 2020
FDA issues first EUA for a COVID-19 vaccine, for the Pfizer vaccine.
December 17, 2020
VRBPAC meeting on Moderna's COVID-19 vaccine.
December 18, 2020
FDA issues EUA for Moderna vaccine.
February 26, 2021
VRBPAC meeting on Janssen's (J&J) COVID-19 vaccine.
February 27, 2021
FDA issues EUA for Janssen vaccine.
May 10, 2021
FDA amends Pfizer vaccine EUA to include adolescents 12 through 15 years of age.
June 10, 2021
VRBPAC meeting on data needed to support authorization and/or licensure of COVID-19 vaccines for use in pediatric populations.
August 12, 2021
FDA amends EUA for Pfizer and Moderna vaccines to allow for a third dose in certain immunocompromised individuals.
August 23, 2021
FDA approves Pfizer vaccine (now Comirnaty) for those 16 years of age and older. EUA remains for those 12 and older and for third dose in certain immunocompromised individuals.
September 17, 2021
VRBPAC meeting on Pfizer application for a booster dose in those 16 years of age and older.
September 22, 2021
FDA amends Pfizer vaccine EUA to include a booster dose in specified individuals.
October 14, 2021
VRBPAC meeting on amending Moderna EUA to include a booster dose in individuals 18 and older.
October 15, 2021
VRBPAC meeting on amending Janssen EUA to include a booster dose in individuals 18 and older. VRBPAC to discuss heterologous boosters.
October 20, 2021
FDA amends Moderna and J&J vaccine EUAs to include booster in specified individuals. Amends all EUAs to allow for each available COVID-19 vaccine as a "mix and match" booster dose in specified individuals.
October 26, 2021
VRBPAC meeting on amending Pfizer EUA to allow the use of its COVID-19 vaccine in children ages 5 through 11.
October 29, 2021
FDA amends Pfizer vaccine EUA to include children ages 5 through 11.
November 19, 2021
FDA amends Pfizer and Moderna EUA to include booster dose in those 18 years of age and older.
December 9, 2021
FDA amends Pfizer EUA to include booster dose in those 16-17 years of age.
January 3, 2022
FDA amends Pfizer EUA to include booster dose in those 12-15 years of age, shorten the time between the completion of primary vaccination and a booster dose to five months, and allow for a third primary series dose for certain children 5-11 years of age.
January 7, 2022
FDA amends Moderna EUA to shorten the time between the completion of primary vaccination and a booster dose to five months for those 18 and older.
January 31, 2022
FDA approves Moderna vaccine (now Spikevax) for individuals 18 years and older. EUA remains in place for those 18 and older, a third dose in certain immunocompromised individuals, and for a booster dose.
March 29, 2022
FDA authorizes second booster dose of Pfizer-BioNTech and Moderna COVID-19 vaccines for older people and certain immunocompromised individuals.
April 6, 2022
VRBPAC to discuss considerations for COVID-19 vaccine booster doses and the process for COVID-19 strain selection to address current and emerging variants.
May 5, 2022
FDA limits Janssen vaccine to individuals 18 years and older for whom other FDA-authorized or approved COVID-19 vaccines are not accessible or clinically appropriate, or who would otherwise not receive a COVID-19 vaccine.
May 17, 2022
FDA expands eligibility for Pfizer-BioNTech COVID-19 vaccine booster dose to children 5 through 11 years.
June 7, 2022
VRBPAC meeting on Novavax COVID-19 vaccine.

This pandemic is dynamic and evolving, with new data continuously emerging about vaccine safety and effectiveness. As we obtain more data about the safety and effectiveness of COVID-19 vaccines, including the use of booster doses, we will continue to evaluate the rapidly changing science and keep the public informed.

At this time, it is clear that the approved or authorized vaccines reduce the risk of severe illness; however, data are not yet available to make a determination about how long they will provide protection. Additionally, although we do not yet know the full range of SARS-CoV-2 variants that each of the vaccines will protect against, there is evidence that the available vaccines protect against severe disease caused by variants circulating in the United States.

To date, having three authorized vaccines and two approved vaccines that meet FDA's expectations for safety and effectiveness at this point of the COVID-19 pandemic is a tremendous achievement and a testament to the dedication of vaccine developers and FDA's career scientists and physicians. We are highly engaged in ensuring that all COVID-19 vaccines meet the high quality that the American public expects and deserves. The Agency is very proud of these efforts, and we believe that the vaccines will help bring this pandemic to an end.

In addition to its work on COVID-19 vaccines, CBER also has been actively involved in reviewing data related to COVID-19 convalescent plasma and on December 28, 2021, FDA updated the EUA for COVID-19 convalescent plasma. The update limits the authorization to the use of COVID-19 convalescent plasma with high titers of anti-SARS-CoV-2 antibodies for the treatment of COVID-19 in patients with immunosuppressive disease or who are receiving immunosuppressive treatment. These patients may be treated in outpatient or inpatient settings. Additionally, to help assure the manufacture of high titer COVID-19 convalescent plasma, the update to the EUA revises acceptable tests and increases qualifying result cutoffs to be used for manufacturing COVID-19 convalescent plasma with high titers of anti-SARS-CoV-2 antibodies.

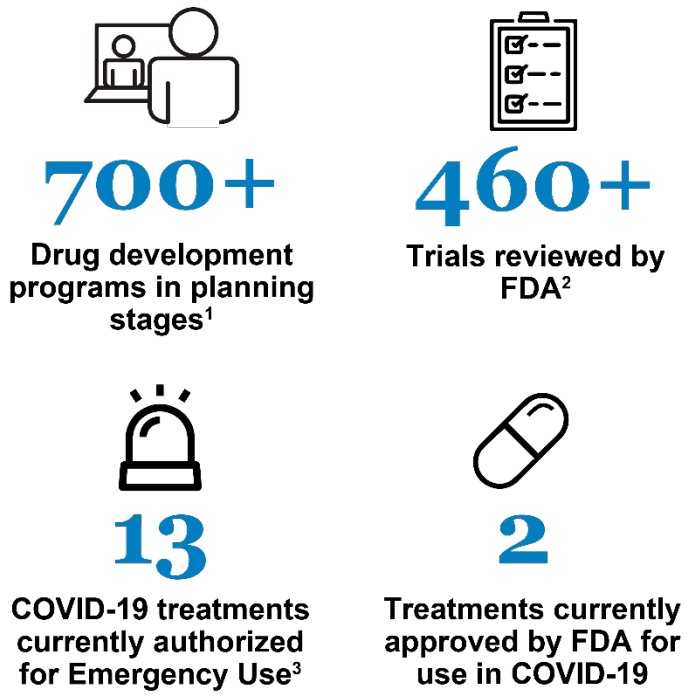
Drug Products

Since the beginning of the COVID-19 pandemic, FDA's Center for Drug Evaluation and Research (CDER) has been working tirelessly to facilitate the development and availability of

therapeutics for use by patients, physicians, and health systems as expeditiously and safely as possible. FDA accelerated the development and publication of guidance and other information for industry and researchers on developing COVID-19-related treatments. Further, FDA created an emergency review and development program for possible therapies for COVID-19, the Coronavirus Treatment Acceleration Program, or "CTAP." Under CTAP, FDA is using every available authority and regulatory flexibility to facilitate the development of safe and effective products to treat patients with COVID-19. As of May 31, 2022, there are more than 700 drug development programs in the planning stages and the Agency has reviewed more than 460 trials of potential therapies for COVID-19. These therapies include antivirals, immunomodulators, neutralizing antibodies, and combinations of these products, as well as cell and gene therapies regulated by CBER. The diversity of therapeutic approaches being investigated is important because it rapidly expands our understanding of the effect of different categories of potential treatments.

Figure 2

CTAP Snapshot as of May 31, 2022



1 Active Pre-INDs. Excludes vaccines.

2 Safe to proceed INDs. These only include ongoing trials (e.g., withdrawn or terminated trials are not included). Ongoing trials reviewed by FDA include antiviral drugs, immunomodulators, neutralizing antibody therapies, cell therapies and gene therapies; vaccines are excluded. These trials fall into two categories: early stage and late stage. Early stage trials (phase 0, 1 and 1/2) test safety and sometimes dosing. They rarely provide sufficient evidence to support Emergency Use Authorization or approval. Late stage trials (phase 2, 2/3, 3, and 4) assess safety and establish whether the treatment is effective. They may generate sufficient evidence to support the statutory standards for Emergency Use Authorization or approval. For additional information regarding the different phases of clinical trials, please visit: What Are the Different Types of Clinical Research?

3 Please see the Emergency Use Authorization webpage for more details. This number includes 1 EUA authorizing both medical devices and a drug for emergency use.

As of May 31, 2022, FDA has approved two drugs to treat COVID-19 and currently there are thirteen authorized therapeutics for emergency use. On December 8, 2021, FDA issued an EUA for AstraZeneca's Evusheld (tixagevimab co-packaged with cilgavimab and administered together) for the pre-exposure prophylaxis (prevention) of COVID-19 in certain adults and

pediatric individuals (12 years of age and older weighing at least 40 kilograms [about 88 pounds]).

On December 22, 2021, FDA issued an EUA for the first oral antiviral, Paxlovid, manufactured by Pfizer. Paxlovid (nirmatrelvir tablets and ritonavir tablets, co-packaged for oral use) is authorized for the treatment of mild-to-moderate coronavirus disease (COVID-19) in adults and pediatric patients (12 years of age and older weighing at least 40 kilograms or about 88 pounds) with positive results of direct SARS-CoV-2 testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death. In the large clinical trial that was conducted among high-risk patients, Paxlovid reduced the risk of hospitalization or death by nearly 90 percent compared to placebo.

On December 23, 2021, FDA issued an EUA for another oral antiviral, molnupiravir, manufactured by Merck. Molnupiravir is authorized for the treatment of mild-to-moderate coronavirus disease (COVID-19) in adults with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death, and for whom alternative COVID-19 treatment options authorized by FDA are not accessible or clinically appropriate.

On February 11, 2022, FDA issued an EUA for bebtelovimab, manufactured by Eli Lilly and Company. Bebtelovimab is authorized for the treatment of mild-to-moderate coronavirus disease (COVID-19) in adults and pediatric patients (12 years of age and older weighing at least 40 kg or about 88 pounds) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death, and for whom alternative COVID-19 treatment options authorized by the FDA are not accessible or clinically appropriate.

In considering EUA requests for therapeutics, we promptly and carefully evaluate the totality of the scientific evidence to determine whether the statutory criteria for issuance under section 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 360bbb-3) are met. Among other criteria, this evaluation considers whether the product may be effective for its

proposed authorized uses, and whether the product's known and potential benefits when used as proposed outweigh the known and potential risks of such product.

Our goal is to be as transparent as possible about the scientific basis for recommending that a drug or biological product be authorized for emergency use under section 564 of the FD&C Act or for recommending that an EUA be revised or revoked.[6]

FDA continues to work closely with manufacturers to mitigate and prevent shortages as the COVID-19 pandemic evolves. For example, the Agency has issued four EUAs to authorize the emergency use of certain therapeutic products intended to treat serious or life-threatening diseases or conditions (e.g., Acute Kidney Injury, Acute Respiratory Distress Syndrome) caused by COVID-19 after determining that sufficient FDA-approved alternatives to these products were not available to fully meet the emergency need. This has helped to alleviate shortages of some therapies that are essential for the care of critically ill COVID-19 patients. FDA is working with manufacturers to increase supplies to meet current demand by expediting review of applications. In addition, the Agency has prioritized the review of generic drug applications for potential treatments and supportive therapies for patients with COVID-19, such as sedatives used in ventilated patients, anticoagulants, and pulmonary medications. In June 2021, FDA reached a milestone of approving 1,000 original and supplemental generic drug applications since the start of the pandemic to help in the treatment of patients with COVID-19. This supports FDA's everyday mission of improving access to safe, effective, high-quality treatment options, especially during the COVID-19 pandemic.

Medical Devices

FDA's work to support access to devices for the COVID-19 response began in January 2020 – before the public health emergency was declared in the U.S. and two months before the pandemic was declared worldwide – due to the immediate need for COVID-19 tests and testing supplies, collection kits, personal protective equipment (PPE), ventilators, and other devices. The need for medical devices to respond to the COVID-19 pandemic has far exceeded what we experienced in any prior public health emergency. The first EUAs issued for the COVID-19

[6] *https://www.fda.gov/news-events/press-announcements/covid-19-update-fdas-ongoing-commitment-transparency-covid-19-euas*

public health emergency were for medical devices, and the volume of EUA requests quickly surpassed (by two orders of magnitude) that of any prior public health emergency or other situation. To help combat the COVID-19 pandemic, FDA and the staff of the Center for Devices and Radiological Health (CDRH) have continued to go well beyond normal operating procedures to help ensure the availability of appropriately safe and effective COVID-19-related devices as quickly as possible. From early in the pandemic, CDRH has actively reached out to and engaged other government agencies, medical device developers and international regulatory agencies, among other stakeholders. CDRH continues to hold weekly virtual town halls with industry to address COVID-19 test development and validation, as well as additional webinars and town halls addressing other policies and questions including PPE, 3D-printed swabs and manufacturing disruptions during the public health emergency. CDRH staff have also interacted frequently with test developers and manufacturers through the Pre-Emergency Use Authorization (pre-EUA) process, including rolling reviews of information that helped to further expedite EUA of critical medical devices for patients and health care professionals on the front lines. Since January 2020, FDA has received more than 8,000 EUA requests and Pre-EUA submissions for devices (including more than 1,000 so far in fiscal year 2022). The emergency use requests included submissions for devices that CDRH had never received EUA requests for during prior public health emergencies. This included ventilators and novel devices such as extracorporeal blood purification devices, as well as novel indications for devices such as continuous renal replacement therapy devices. CDRH continues to receive nearly 120 EUA requests and pre-EUA submissions each month, the majority for in vitro diagnostic (IVD) tests, and has begun receiving conventional submissions from firms intending to transition their products beyond emergency use.

Since the start of the pandemic, FDA has issued EUAs or granted marketing authorization to nearly 2,300 medical devices for COVID-19-related uses. In addition, FDA rigorously monitors safety signals and medical device reports, using the information to publish 23 letters to healthcare providers and 14 safety communications. FDA completed other pivotal work activities such as addressing supply chain shortages and counterfeit products related to COVID-19.

Diagnostic tests are the first line of defense in an outbreak, and FDA plays an important role to ensure these tests work through the EUA review. The EUA process expedites access to

appropriately accurate diagnostic tests during emergencies, when, without such access, information gaps and false results could adversely affect individual patient care and public health decision making. Through this process, molecular diagnostic tests are able to be developed, validated, authorized, and deployed within weeks rather than several months to over a year, as is typical for test development and traditional premarket submissions. The Agency employed its EUA authorities to facilitate availability of tests in six previous emergencies. Careful review of tests is critical because false test results can adversely impact the nation's response. In public health emergencies, FDA is generally open to receiving and reviewing EUA requests for tests from any developer, including commercial kit manufacturers and laboratories, for tests that address the public health need.

FDA sought to facilitate COVID-19 test evaluation and authorization through the development and availability of templates for EUA requests. The templates provide recommendations for test validation and a fill-in-the-blank form to streamline the paperwork and make it easier for developers to provide information in support of a request for an EUA. Since providing the first template in January 2020, FDA has been in daily contact with test developers to answer questions and help them through the EUA process. This has proved to be a helpful tool for many. FDA had as many as ten posted templates and continues to update, add, combine, and remove templates as the science evolves and as necessary to support developers of COVID-19 tests. As of April 13, 2022, these templates have received over 618,543 hits from those visiting FDA's website. FDA also supported test developers through establishment of a dedicated mailbox, 24-7 toll-free hotline that ran until July 2020, the posting of over 100 frequently asked questions on our website, and by hosting 86 virtual town halls for test developers.

FDA has prioritized review of EUA requests for at-home tests since Spring 2020 – almost a year before other countries pursued expansive use of home tests – and has consistently actively engaged with test developers to support their development. To date, FDA has authorized 19 distinct over-the-counter (OTC) COVID-19 tests, 11 of which were authorized in four weeks or less, with five authorized within a week. The Agency first discussed this prioritization in the Spring of 2020, during one of its weekly virtual Town Halls on COVID-19 tests, due to their potential impact on test accessibility and public health. To further encourage such test development, on July 29, 2020, FDA posted a template for at-home diagnostic tests. This

template includes recommendations for validating OTC tests for screening asymptomatic individuals with general performance expectations that are lower than for lab-based tests. The Agency recognizes the benefits of increased availability of OTC tests, and these recommendations have helped to increase OTC screening test availability, particularly rapid antigen tests.

Throughout the pandemic, FDA has also monitored evolving circumstances and growing scientific knowledge and made adjustments when appropriate to help streamline and expedite the path to market for these and other tests as much as possible while assuring they are supported by sound science. In March 2021, FDA obtained results from a National Institutes of Health (NIH)-sponsored study that supported further streamlining of FDA's at-home test recommendations. Based on these data, on March 16, 2021, FDA issued an EUA that provides a streamlined path to authorize tests with at least 80 percent sensitivity in symptomatic individuals, with sensitivity falling in a range as low as 70 percent in certain circumstances, for developers to offer their test for OTC serial screening without additional data collection. Multiple tests were authorized under this approach within weeks.

FDA authorized the first at-home test on November 17, 2020. At-home tests, also referred to as self-tests, are those that can be performed by a lay user at home, or in other settings, with a self-collected sample. As of June 1, 2022, the 19 authorized OTC at-home tests have a combined manufacturing capacity of hundreds of millions of tests per month based on data provided to FDA by the manufacturers, and we understand many have scaled beyond their initial estimated capacity with additional government support.

FDA further streamlined the process for manufacturers developing over-the-counter at-home tests on October 25, 2021, by facilitating at-home single-use testing for symptomatic individuals for tests currently authorized only for serial testing. Developers of certain tests may request authorization to add single-use testing for symptomatic individuals without submitting additional data. This change would allow tests authorized for single use to be sold in singles, meaning more individual tests for sale potentially at a lower price.

On November 15, 2021, FDA published an update to its *Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency* that describes our review priorities based on the

current needs of the pandemic. In that update, FDA stated that going forward, the Agency generally intends to focus its review on EUA requests for the following types of tests:

- At-home and point-of-care (POC) diagnostic tests that can be manufactured in high volumes;
- Certain high-volume, lab-based molecular diagnostic tests (and home collection kits for use with such tests) that expand testing capacity or accessibility such as through pooling of specimens to increase throughput, testing specimens collected at home and shipped to the lab, screening asymptomatic individuals or detecting multiple different respiratory viruses at once;
- Certain lab-based and POC high volume antibody tests that can measure the amount of antibodies (fully quantitative antibody tests) or the amount of neutralizing antibodies; and
- Tests for which the request is from, or supported by, a U.S. government stakeholder, such as the Biomedical Advanced Research and Development Authority or NIH's Rapid Acceleration of Diagnostics (RADx) initiative.

These priorities help developers focus their prospective efforts where they are most needed and reduce inefficient use of developer and FDA time on tests with less public health impact. Ultimately, we anticipate we will receive EUA requests only for those tests identified in the guidance for which the public health need is greatest, and we will be able to focus our attention on the review of such tests.

FDA also partnered with the NIH to establish the Independent Test Assessment Program (ITAP),[7] which streamlines validation and authorization of at-home antigen tests with potential for large-scale manufacturing. This program is an extension of the NIH RADx program which has already supported development of several authorized tests, including the first OTC COVID-19 test. ITAP also supports studies on OTC tests and works with companies to provide complete, high-quality submissions for FDA review. The first two successful candidates to come through

[7] *https://www.hhs.gov/about/news/2021/10/25/new-hhs-actions-add-biden-administration-efforts-increase-access-easy-use-over-counter-covid-19-tests.html*

this process were authorized by FDA in the last week of 2021, which was weeks, if not months, ahead of schedule. FDA has authorized five OTC, at-home COVID-19 tests that participated in this program through this accelerated pathway – one manufactured by SD Biosensor and distributed by Roche, one manufactured by Siemens, a third manufactured by Maxim Biomedical, a fourth manufactured by Osang, LLC, and a fifth manufactured by Xiamen Boson Biotech Co., Ltd.[8] We are already seeing shorter review times for such EUA requests due to our partnership with ITAP in establishing the evaluation program that provides high quality data. The average FDA review time for a test evaluated under ITAP is just over a week, and can be as short as one day, after receipt of a complete data package.

Going forward, FDA continues to take steps to increase access to reliable, accurate rapid antigen tests. This includes continuing to prioritize review of EUA requests for at-home antigen tests and increasing staffing on the antigen test review team as resources permit. FDA is actively working to increase the pipeline of at-home tests by engaging with companies to obtain data that can be used to support their EUA, working with developers with authorized POC tests to expand their authorization for at-home use, continuing support of ITAP and engagement with RADx and international regulators, and conducting targeted outreach to manufacturers of home tests in non-U.S. markets.

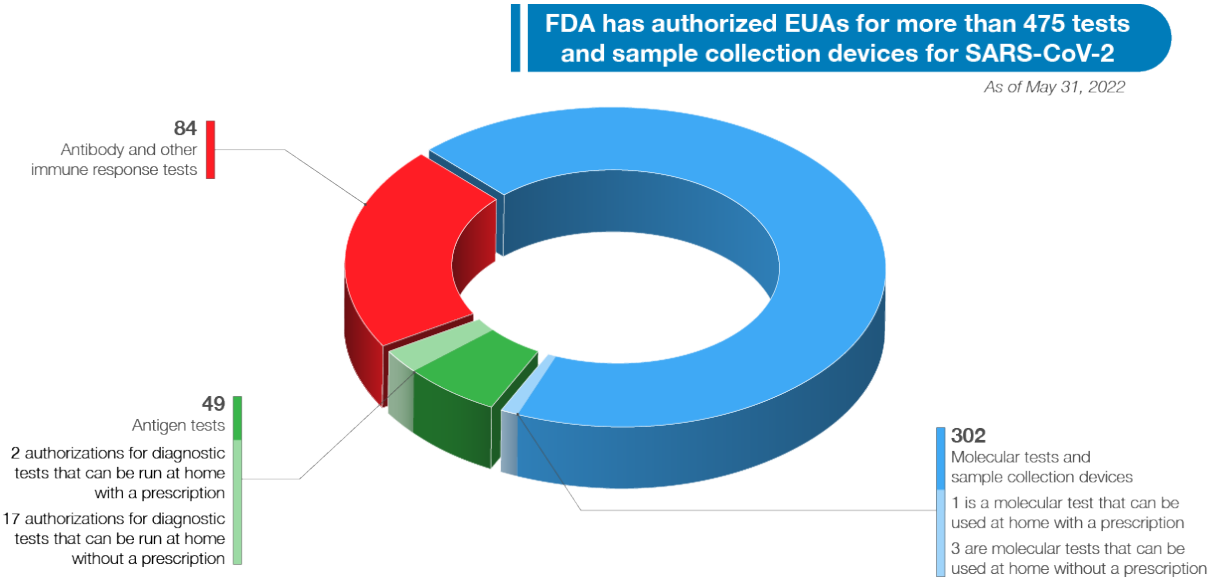
To date, FDA has engaged with over 1,000 developers and authorized more than 475 tests and sample collection devices that provide a wide array of test options. In addition to at-home diagnostic tests, these include other types of molecular and antigen tests, as well as serology tests; POC tests, home collection tests, multi-analyte tests that can detect both COVID-19 and flu; tests using various sample types, including saliva tests; and tests for pooling, screening, and serial testing.[9] Most recently, FDA issued an EUA for the first COVID-19 diagnostic test that detects chemical compounds in breath samples associated with a SARS-CoV-2 infection.[10]

[8] *https://www.nibib.nih.gov/covid-19/radx-tech-program/ITAP*
[9] *https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas*
[10] *https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-first-covid-19-diagnostic-test-using-breath-samples*

As noted in *Figure 3* below, as part of this effort, FDA has authorized 302 molecular tests and sample collection devices, 84 antibody and other immune response tests, and 49 antigen tests. We have also authorized 34 tests for serial screening programs (27 antigen and seven molecular).

The volume and variety of authorized tests is a testament to FDA's support of innovative test design and our commitment to public health. FDA will continue to adapt to address public health needs and increase access to tests for consumers, including at-home diagnostic tests, adopting an approach that is grounded in sound science.

Figure 3



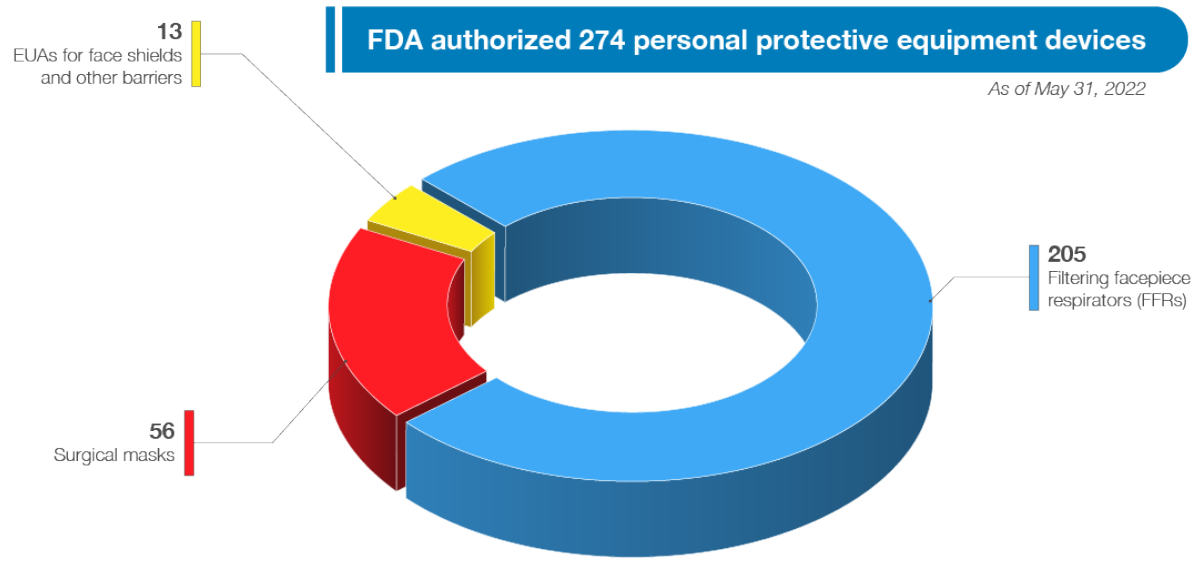
In addition to these efforts, FDA has been actively monitoring for the possible emergence of SARS-CoV-2 variants since early in the pandemic and has worked with test developers when a new variant (or mutation) emerges that could impact test performance. FDA also works with test developers, who are required to monitor their authorized test for the impact of viral mutations. As FDA's or the developer's analysis identifies tests whose performance could be impacted by SARS-CoV-2 viral mutations, these tests are added to FDA's SARS-CoV-2 Viral Mutations: Impact on COVID-19 Tests webpage.[11] This includes posting the latest information

[11] *https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-viral-mutations-impact-covid-19-tests*

on the omicron variant and testing implications as they become available. FDA also works with other agencies and divisions in HHS, such as NIH, as we monitor tests for potential effects of genetic variation on test performance on an ongoing basis.

FDA has authorized a wide variety of other medical devices for use in combating the pandemic, including a wide range of PPE, ventilators, and other therapeutic devices. As of May 31, 2022, FDA authorized 274 PPE devices, including 56 surgical masks, 205 filtering facepiece respirators (FFRs), and issued 13 EUAs for face shields and other barriers intended to protect the user from bodily fluids, liquid splashes, or potentially infectious materials. See *Figure 4*. In addition to issuing EUAs, CDRH has reviewed 510(k)s for and cleared over 1,400 devices that can be used for COVID-19 and certain similar diseases, including in future pandemics, with over 500 devices in fiscal year 2022 to date.

Figure 4



Since early 2020, FDA has adopted agile, interactive, and innovative approaches to review EUA requests for all types of devices. For example, FDA developed the umbrella EUA approach to efficiently authorize multiple devices of the same type falling within the scope of authorization and meeting the statutory criteria for issuance. The Agency has also issued 28 guidance documents outlining policies to help expand the availability of medical devices needed in response to COVID-19. For example, to help quickly increase availability of tests in the early

stages of the pandemic, FDA outlined a policy for developers of certain tests who offered their tests, upon validation and notification to FDA, while Agency review of the EUA request was pending. Additionally, FDA outlined flexible approaches for manufacturers of certain cleared and approved devices (e.g., remote monitoring systems, ventilators, infusion pumps) regarding certain limited modifications made to devices without submitting a premarket submission. Further, FDA made several improvements to our EUA review processes to make the most efficient use of our resources, including a front-end triage process to identify devices that would have the greatest impact on the public health. These improvements incorporate the latest information on device availability and shortages, prioritizing novel or critical devices not yet available on the market or those that would address significant device shortages.

For medical devices, review times have increased over time as the number of EUA requests and Pre-EUA submissions for medical devices have increased to unprecedented levels. This is demonstrated in the tables we have provided with review times for IVD EUA requests over time, and submission volume for IVD EUA requests over time (see Figures 5 & 6 below). At the beginning of the pandemic, FDA was authorizing tests and other devices in as little as 1 or 2 days upon receipt of complete data packages. Congress has provided critical, one-time funding that FDA has used to leverage contractors from outside organizations, to provide technical expertise to supplement our review staff in the review of EUA requests and other marketing submissions. These personnel are authorized to work alongside full-time employees, integrated into our internal review teams to help with the massive workload for tests, ventilators, PPE, and other devices, but the workload has continued to greatly exceed capacity even with the additional support.

Figure 5

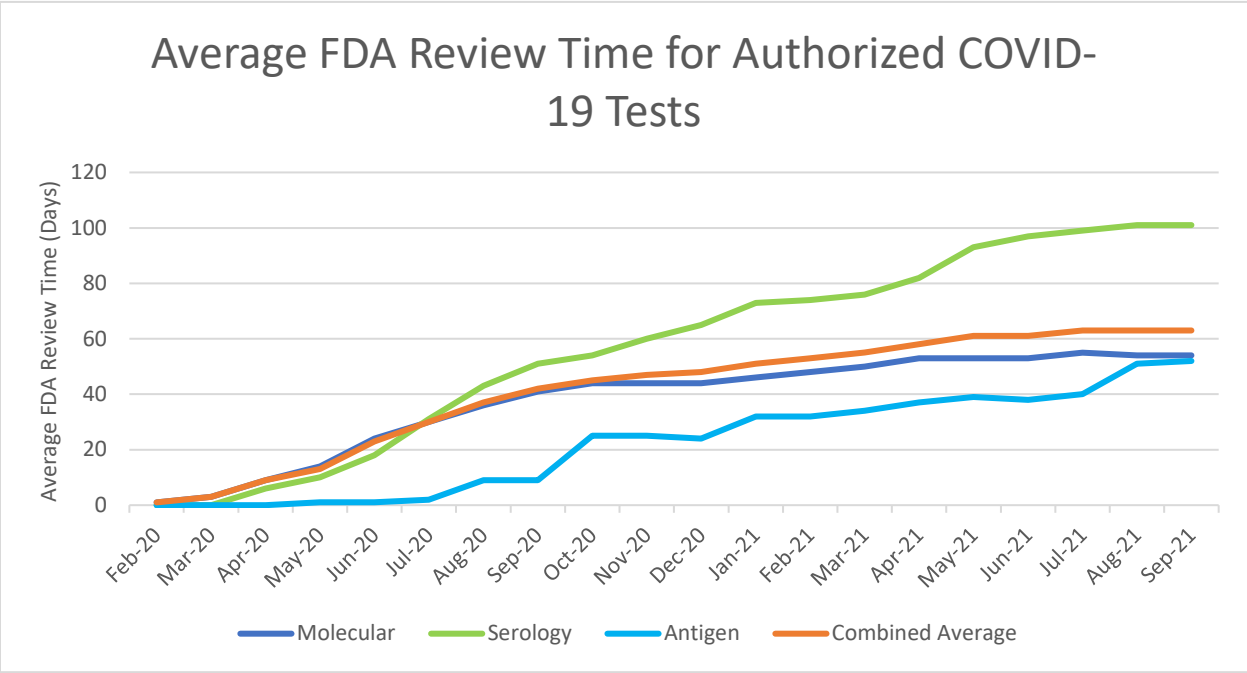
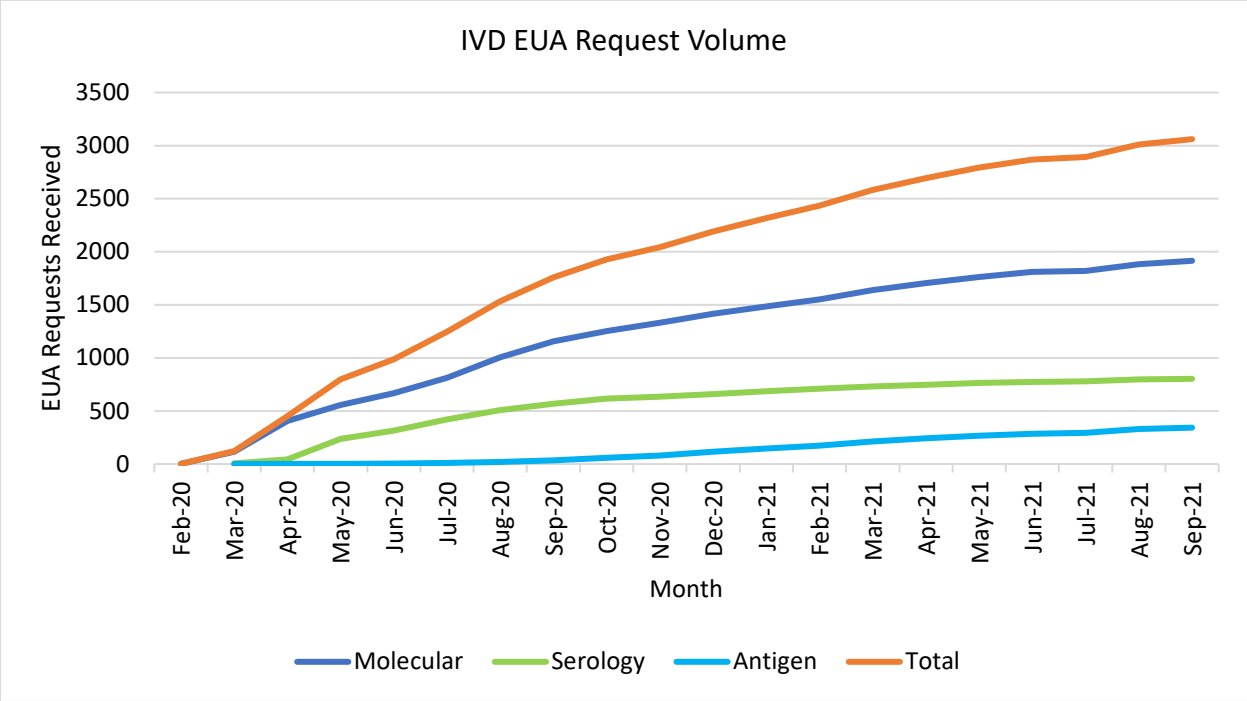


Figure 6



FDA has significantly improved IVD EUA review times. The average total time to decision (TTD) for Original IVD EUAs received in CY 2021 is 54 days, with 91 percent of the 2021 submissions closed.

Given the magnitude of the COVID-19 public health emergency, FDA recognizes that continued flexibility, while still providing necessary oversight, will be appropriate to facilitate an orderly and transparent transition back to the eventual resumption of normal operations. In December 2021, FDA issued draft guidance for public comment to help manufacturers begin to plan a return to normal operations, including a proposed phased-in transition period and recommendations relating to submitting marketing submissions. As proposed, FDA would announce the Advance Notice of Termination (ANT) in the Federal Register, which would give manufacturers 180 days to come into compliance with regulatory requirements and submit a conventional marketing submission (e.g., 510(k) or PMA). Provided that the submission is accepted by FDA by this time (180 days after the ANT), FDA does not intend to object to these devices to continue to be distributed and used while the submission is pending review. FDA is working to address stakeholder feedback and timely finalize this guidance and a companion guidance for devices that fall within COVID-19-related enforcement policies. The transition plan for device EUAs and other actions FDA is undertaking are intended to provide transparency to our stakeholders and to avoid market disruptions and shortages as the Agency and broader device ecosystem transition back to normal operations.

FDA recognizes that medical devices, particularly tests, will continue to play an important role in the next phase of the pandemic response. The Agency is continuing to monitor its policies, the marketplace, and national needs, and will continue to adapt as the circumstances of the evolving pandemic warrant.

Human and Animal Food (Center for Food Safety and Applied Nutrition, Center for Veterinary Medicine, and the Office of Food Policy and Response)

Throughout the pandemic, FDA has worked with federal, state, and local partners, as well as industry, to help ensure a safe and adequate food supply for both humans and animals.

While there is no evidence to show that SARS-CoV-2 is likely to be transmitted by food, some components of the food system are experiencing challenges and supply chain imbalances. We saw this at the outset of the pandemic with the dramatic shift in where people were eating, and most recently, we are seeing that the broad supply chain issues impacting so many commodities are also impacting food. Overall, food production and manufacturing in the U.S. has been remarkably resilient, but we continue to monitor the food supply and apply mitigation strategies for products for which availability has been impacted in part by pandemic-related issues.

In response to the pandemic, FDA's Foods Program developed *21 Forward*, a food supply chain data management tool, to help identify where risks for interruptions in the continuity of the food supply may be greatest. As part of *21 Forward*, FDA conducted targeted outreach to the food industry to offer additional resources and technical assistance in addressing challenges. As highlighted in the U.S. Department of Agriculture's (USDA's) Agri-Food Supply Chain Assessment report, developed in response to Executive Order 14017 on America's Supply Chains with input from FDA, a dynamic, interconnected, supply chain monitoring platform and robust data sets are necessary to be most effective in monitoring food supply chains, managing risks, and identifying and quickly addressing supply chain disruptions to reduce impacts on consumers.

FDA also recognizes that food supply chain stability and workers' safety are two sides of the same coin. Thus, a stable and robust food supply depends on the safety and health of the nation's food and agricultural workforce. Along with our federal, state, and local partners, we have provided best practices for food and agricultural workers, industry, and consumers on how to stay safe, and help ensure the continuity of operations in the food and agriculture critical infrastructure sector during the pandemic.

In collaboration with HHS, CDC, Health Resources and Services Administration (HRSA) and U.S. Department of Agriculture (USDA), data from *21 Forward* on the estimated numbers and distribution of food and agricultural workers have been made available to assist states with their vaccine distribution efforts to workers in the food and agriculture sectors, including migratory and seasonal agricultural workers. In addition, FDA has worked with its Federal partners to provide both COVID-19 and flu vaccination encouragement messages for the food industry.

FDA's Coordinated Outbreak Response and Evaluation team has been working throughout the pandemic looking for signs of foodborne illness outbreaks and initiating responses as needed. FDA's Center for Veterinary Medicine (CVM) is monitoring the animal food supply and initiating needed foodborne illness and natural disaster responses. In terms of inspectional work, FDA's Office of Regulatory Affairs (ORA) investigators continued to conduct mission-critical inspections domestically and abroad, including inspections and investigations in response to foodborne outbreaks, throughout the pandemic. FDA resumed standard operations for domestic surveillance inspections in July 2021, and since March 2022 has been conducting prioritized foreign inspectional work, including surveillance and other inspections. FDA continues to screen every line of every imported food shipment entering the U.S. utilizing our Predictive Risk-Based Evaluation for Dynamic Import Compliance Targeting (PREDICT) tool. We continually adjust the algorithm in PREDICT to place increased scrutiny on shipments from facilities where foreign surveillance inspections have been postponed. FDA has made greater use of our Foreign Supplier Verification Program (FSVP) regulation to review importer records for information showing that foreign suppliers are using processes and procedures consistent with FDA Food Safety Modernization Act (FSMA) requirements. The shift to remote FSVP inspections, along with other tools utilized by the foods program, was critical to ensuring the safety of human and animal food from foreign suppliers during the COVID-19 pandemic. Since March 2020, FDA has conducted approximately 3,423 FSVP inspections. Additionally, FDA continues to identify human and animal foods that are unsafe, misbranded, or may cause a serious health concern for the public at the border with over 15,324 lines being refused admission since March 2020.

In July 2020, FDA announced the New Era of Smarter Food Safety Blueprint outlining the Agency's plans over the next decade to create a more digital, traceable, and safer food system. The Agency has learned from its response to the pandemic that there is an accelerated need for certain goals in this blueprint, especially those involving supply chain continuity and resilience, modernized inspectional approaches, strengthening food safety infrastructures with regulatory partners, and the safety of foods ordered by consumers online. The number of consumers ordering food online has been steadily increasing over the years, but it has skyrocketed during the COVID-19 pandemic. Last year, FDA hosted a virtual Summit on E-Commerce, to help the Agency improve its understanding of how human and animal foods are sold through e-commerce

models and to identify courses of action for addressing potential food safety vulnerabilities, including those that may arise in the "last mile" of delivery.

Imports, Inspections, Compliance and Protecting the Medical Supply Chain

Similar to their work protecting the food supply, import investigators have been on site protecting the medical supply chain at our ports of entry, courier facilities, and the international mail facilities (IMFs) throughout the pandemic, with uninterrupted support from ORA laboratories. Through continued vigilance, FDA has prevented unsafe and unproven pharmaceuticals and other medical products from entering the country. Since March 2020, with the cooperation of and in coordination with the U.S. Customs and Border Protection (CBP), FDA has refused and destroyed more than 119,000 products, totaling over 21,232,063 capsules, tablets, and other dosage forms of violative drugs shipped via international mail.

Since March 2020, FDA has maintained the same level of screening for products offered for import as pre-pandemic and refused approximately 160,464 lines violative medical products offered for import. FDA has focused examinations on COVID-19 relief supplies to ensure that reviews of compliant products are expedited while maintaining our commitment to refusing medical products that appear to be unsafe, misbranded, unapproved, counterfeit, or may cause serious illness or injury to the public. Import investigators have evaluated donations of shipments destined for the Federal Emergency Management Agency (FEMA) and have been instrumental in expediting the importation of vaccines and related shipments and other COVID-19 necessities starting with the first vaccines (Pfizer Belgium) shipped into the United States in December 2020.

Despite generally pausing domestic and foreign surveillance inspections in March 2020 to safeguard the health and well-being of our staff, as well as employees at facilities we inspect, our investigators continued to conduct mission critical inspections both domestically and abroad and to do other prioritized domestic inspectional work when possible, to ensure FDA-regulated industries were meeting applicable FDA requirements. FDA developed a rating system to assist in determining when and where it was safest to conduct prioritized domestic inspections until we resumed standard inspectional operations for domestic surveillance inspections in July 2021.

On May 5, 2021, FDA issued a report titled, "Resiliency Roadmap for FDA Inspectional Oversight," [12] outlining the Agency's inspectional activities during the COVID-19 pandemic and its detailed plan to move toward a more consistent state of operations, including FDA's priorities related to this work going forward. The report was updated on November 22, 2021.[13]

The report described our oversight work during the pandemic and outlined the inspectional activities that the Agency had postponed due to travel restrictions or inability to ensure the safety of our workforce or the workforces within the industries the Agency regulates. The report also outlined the number of mission-critical inspections FDA completed during that time, such as inspections of facilities for which there was a drug shortage, inspections needed for the approval of novel drugs or drugs related to the potential treatment of COVID-19, support of pre-market and pre-license applications, and response to foodborne disease outbreaks or other food safety risks such as food contaminated with pathogens.

Additionally, the Resiliency Roadmap outlines FDA's continued, successful use of alternative tools and approaches where inspections are not feasible, including remote assessments (e.g. requests to regulated establishments to remotely view records as well as remote interactive evaluations that include remote livestreaming video of operations), teleconferences, or screen sharing, and leveraging information from trusted regulatory partners. For example, ORA made over 2,100 requests to human and animal drug and biological product manufacturers to remotely view records, to support on-time regulatory decision actions. Our review of records requested under section 704(a)(4) of the Federal Food, Drug, and Cosmetic Act supported more than 350 approval recommendations for new or abbreviated drug applications, as well as support for authorization decisions for EUA requests, potentially allowing new products to come to market and provide access to lower cost generic drugs to patients more quickly than may have otherwise been possible.

Notably, FDA's bioresearch monitoring program staff have conducted more than 200 remote assessments that were directly used in application decisions.[14] The new tool was incentivized for

[12] *https://www.fda.gov/media/148197/download*
[13] *https://www.fda.gov/media/154293/download*
[14] *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/remote-interactive-evaluations-drug-manufacturing-and-bioresearch-monitoring-facilities-during-covid*

and supported by industry and continues to provide the Agency with valuable information to assist with risk-based targeting for inspections. FDA recognizes that remote approaches do not replace inspections, and that there are situations where only an inspection is appropriate, based on risk and history of compliance with FDA regulations.

The Resiliency Roadmap further outlined the ongoing steps the Agency is taking to resume standard operational levels of inspection activities, including how it intended to prioritize domestic and foreign inspections that could not be performed during the pandemic. FDA began to transition back to standard operations for domestic surveillance inspections and other prioritized operational work on July 1, 2021, and exceeded the goals that were detailed in the May Resiliency Roadmap. We also exceeded our performance goal related to following up on previous inspections classified as official action indicated (OAI).

Since October 1, 2021, FDA has been performing domestic inspections at normal operational levels and recently began to conduct foreign facility inspections, including surveillance and other inspectional work, as well. As FDA works through the inventory of postponed surveillance inspections, the Agency is prioritizing higher-risk establishments. For example, a sterile manufacturing site that has not been previously inspected and is making narrow therapeutic index drugs would likely be deemed a higher risk than a site that had a well-known inspectional and compliance history that is making solid oral dosage form drugs. This means that postponed inspections will be prioritized based on risk and conducted over a longer period of time, ultimately increasing the amount of time between inspections of certain lower-risk facilities in order to focus on products that present the greatest risk to public health.

The Agency launched a multi-year modernization effort in July 2021 to further transform our data enterprise platforms and cross-program interoperability infrastructure to better support innovation related to its regulatory oversight role. This includes adopting technology to support regulatory assessments to improve our remote receipt, review, and analysis of industry data and records, and improve remote interactions with industry entities to be easier, more efficient, more consistent, and more secure. This modernization effort includes a review of inspectional approaches using next-generation assessment technologies and improvements. FDA established an Agency-wide Inspectional Affairs Council (FIAC) that provides coordination of inspection

approaches and assessment processes. The Agency intends to share more information on these efforts as this work progresses. FDA will continue to leverage and maximize every available tool and resource to meet its regulatory oversight responsibilities, while achieving optimal public health outcomes.

Compliance and Enforcement

FDA exercises its regulatory authority by, among other things, issuing warning letters and pursuing civil and criminal enforcement actions against firms and individuals who do not comply with regulatory requirements, including those distributing unapproved products with false or misleading claims that the products prevent, treat, mitigate, diagnose, or cure COVID-19. In March 2020, FDA launched Operation Quack Hack, which leverages the Agency's expertise and advanced analytics to protect consumers from fraudulent medical products, including unproven treatments, illegitimate test kits, and substandard or counterfeit respirators. FDA has sent hundreds of abuse complaints to domain name registrars and internet marketplaces. The Agency also has sent 285 warning letters to sellers of unproven products claiming to treat, prevent, or cure COVID-19. Working with the Department of Justice (DOJ), FDA has sought and obtained preliminary and permanent injunctions that require defendants to halt the sale of unproven products claiming to treat or prevent COVID-19, including one product, "Miracle Mineral Solution," that, when used as directed, is equivalent to industrial bleach. In addition, since the start of the COVID-19 pandemic, FDA has issued 22 warning letters to owners and/or operators of illicit internet pharmacy websites that offer unapproved and misbranded drugs purporting to treat COVID-19 for sale to U.S. consumers.

In addition, ORA's Office of Criminal Investigations (OCI), working with other federal and local law enforcement agencies, has conducted criminal investigations involving unproven COVID-19-related products. In one such example, OCI investigated a physician who attempted to profit from the pandemic by marketing and selling an unproven COVID-19 treatment. The physician marketed and sold treatment kits—which included hydroxychloroquine—as a cure for COVID-19. In May 2022, the physician was sentenced to 30 days' imprisonment and one year of home confinement after pleading guilty to, among other things, trying to smuggle hydroxychloroquine into the United States to sell in his COVID-19 "treatment kits." In another case, OCI investigated an individual who attempted to import approximately 1,000 unlawful COVID-19

test kits from China, which were intercepted at a FedEx facility in Memphis, Tennessee. As a result of OCI's investigation, the individual was fined and sentenced to 36 months of probation in October 2021 after pleading to a felony smuggling charge. OCI also has conducted criminal investigations to bring to justice those who tamper with COVID-19 vaccines. For example, OCI investigated a hospital pharmacist who tampered with COVID-19 vaccine doses at a Wisconsin hospital where he worked. On two successive nights, the pharmacist purposefully removed a box of COVID-19 vaccine vials from the hospital's refrigeration unit intending to render the vaccines inert and no longer effective. Before the full extent of his conduct was discovered, 57 people received doses of the vaccine from these vials. In January 2021, the pharmacist pleaded guilty to two counts of attempting to tamper with consumer products with reckless disregard for the risk that another person will be placed in danger of death or bodily injury. He has been sentenced to three years imprisonment, followed by three years of supervised release, and he must pay approximately $83,800 in restitution to the hospital.

In addition, FDA investigators remain on the front lines at ports of entry, quickly examining, reviewing, and sampling import entries, and refusing admission of violative products where appropriate. We protect the supply chain in two equally critical ways: first, we help ensure safe products are coming in; and second, we help prevent illegal, dangerous, and fraudulent products from getting into the country. These efforts include partnering with U.S. Customs and Border Protection (CBP) in establishing satellite laboratories at selected International Mail Facilities (IMFs) with scientists using state-of-the-art screening tools to rapidly identify unapproved, counterfeit and illicit products.

In March 2020, OCI, with the help of domestic law enforcement partners and foreign counterparts in the United Kingdom, led the investigation of fraudulent COVID-19 "treatment kits" that were falsely declared as "water treatment." Import examination of these shipments found misbranded "kits" intended to treat COVID-19. As a result of this investigation, a British national was sentenced to 10 months of confinement after pleading guilty to shipping mislabeled and unapproved products. In May 2020, FDA worked with CBP to intercept several shipments of counterfeit facemasks, with the result that they were refused and destroyed before entering U.S. commerce.

FDA also has taken steps to address hand sanitizer products that pose safety concerns, such as products that do not meet the required ethanol or isopropanol levels or that contain or may contain toxic ingredients like methanol or 1-propanol. FDA has tested several hundred products using field-based and laboratory-based tools and found more than a hundred violative products. FDA also has taken steps to help ensure that these dangerous or subpotent products do not enter domestic commerce, including coordinating with CBP to identify such products, and we have listed products made by more than 70 manufacturers on import alert. FDA also placed all alcohol-based hand sanitizers from Mexico on a countrywide import alert to help stop products from entering the U.S. that appear to be in violation until the Agency is able to review the products. That action marked the first time the FDA has issued a countrywide import alert for any category of drug product.

In addition to the use of compliance and enforcement tools, FDA also used targeted communication to alert the public and address misinformation about the efficacy of products purported to treat COVID.

Medical Product Supply Chain

FDA monitors and responds to worldwide demand and supply chain disruptions for medical products caused by the COVID-19 pandemic.[15] We work closely with manufacturers, within our current resources and authorities, to help ensure they continue to notify the Agency of any permanent discontinuance or interruption of drug (human and animal), biological product, and device manufacturing in a timely manner, and we are working to better position the Agency and our health care system to assure a strong domestic supply chain in future emergencies.

This is especially important as the COVID-19 pandemic has exposed major vulnerabilities in the supply chain that FDA continues to face as it works to help ensure access to the treatments and devices that patients and healthcare providers need.

[15] *https://www.whitehouse.gov/wp-content/uploads/2021/06/100-day-supply-chain-review-report.pdf*

In addition to our usual communications with drug manufacturers, we work closely with healthcare and pharmacy systems, hospitals, providers, and others on the frontlines of COVID-19 patient care to identify problems with access to critical care drugs used to treat COVID-19.

FDA understands the significant impact shortages can have on patient care, and we are using our authorities to help prevent and alleviate disruptions. When we identify a shortage, we react swiftly to help mitigate the impact to U.S. patients and health care professionals, and quickly share that information with the public. Restoring and increasing the supply of approved drugs has been the Agency's priority. In addition, where necessary, FDA has issued temporary policies during the COVID-19 emergency to respond to reports from hospitals of increased demand and interruptions in supply, some of which have not resulted in a drug shortage but caused concern about continuing access to drugs to support hospitalized patients with COVID-19. We issued temporary policies for outsourcing facilities registered with FDA and pharmacists in state-licensed pharmacies or federal facilities, regarding the compounding of certain drugs used for hospitalized patients with COVID-19. The Agency has published guidances to help applicants and manufacturers provide FDA with timely and informative notifications about changes in the production of certain human drugs, including biological products, and certain animal drugs. We urged the timely submission of these notifications, which may assist in our efforts to prevent or mitigate shortages of such products. In addition, section 503B(a)(2)(A) of the FD&C Act permits outsourcing facilities to use bulk drug substances to compound drug products that appear on the drug shortage list in effect under section 506E of the FD&C Act at the time of compounding, distribution, and dispensing, when all conditions of section 503B are met.

The Coronavirus Aid, Relief, and Economic Security Act (CARES Act), signed into law on March 27, 2020, included authorities intended to enhance FDA's ability to identify, prevent, and mitigate possible drug shortages by, among other things, enhancing FDA's visibility into drug supply chains. The CARES Act expanded the requirement for manufacturers of certain drugs to provide information on permanent discontinuances and interruptions in manufacturing that may lead to a meaningful disruption in supply to FDA, and required FDA to prioritize and expedite, as appropriate, the review of certain applications and inspections that could help mitigate or prevent a shortage of a drug covered by section 506C(a) of the FD&C Act.

Our experience with COVID-19 only reemphasized that a strong domestic supply chain depends on a resilient supply chain for medical devices. Even before the pandemic hit the U.S., there were disruptions in the medical device supply chain due to higher demand for devices in other nations where COVID-19 was already prevalent and shutdowns in locations from which supplies were sourced. As a result, FDA began shortage mitigation activities for medical devices in January 2020 before the public health emergency was declared in the U.S., and two months before a pandemic was declared worldwide. At that time, the Agency did not have any dedicated funding or explicit authority regarding prevention or mitigation of medical device or animal drug shortages. The Agency lacked dedicated staff necessary to mitigate supply chain disruptions and/or shortages. Nevertheless, the Agency took several actions to rapidly respond to medical device supply chain needs, including reassigning over 130 staff to perform shortages work across CDRH and contacting over 1,000 manufacturing facilities in 12 countries in just a few weeks' time to get as much information as possible about critical devices. However, because the Agency lacked any explicit shortages authority at this time, only about one-third of facilities that were contacted responded even in part to CDRH requests because response was voluntary. This lack of explicit authority, staff and supply chain information significantly hampered our efforts to mitigate and prevent shortages at the outset of the pandemic.

The CARES Act gave FDA, for the first time, authority related to device shortages (see section 506J of the FD&C Act). The enactment of the CARES Act at the height of the initial pandemic response gave some authority to help prevent or mitigate medical device shortages during the public health emergency.[16] Throughout COVID, FDA has dealt with hundreds of thousands of device units that have been in shortage. FDA used the information it received from its CARES Act authorities to prevent or mitigate shortages including diagnostic testing supplies such as swabs and viral transport media; blood collection tubes; PPE (respirators, surgical masks, gowns,

[16] Specifically, section 506J of the FD&C Act requires manufacturers to notify FDA of a permanent discontinuance in or interruptions in the manufacture of certain devices that are likely to lead to a meaningful disruption in supply of that device in the United States during, or in advance of, a public health emergency. Section 506J also requires FDA to maintain a publicly available list of devices the Agency has determined to be in shortage, as well as devices that have been discontinued. The Agency is also directed to, as it deems appropriate, prioritize and expedite inspections and review of premarket submissions to help alleviate the supply chain constraint.

gloves); ventilators; pediatric trach tubes; dialysis products; infusion pumps and accessories; saline flush syringes, sharps containers, needles and syringes.

Specifically, FDA uses the information it receives from the CARES Act to:

- Expedite review of devices and changes to devices;
- Allow/expedite importation;
- Grant enforcement discretion, including outlining flexible approaches for manufacturers of certain cleared and approved devices (e.g., remote monitoring systems, ventilators, infusion pumps) regarding certain limited modifications made to devices without submitting a premarket submission;
- Provide clinical impact assessments to the Assistant Secretary for Preparedness and Response (ASPR) and the White House supply chain coordinator to support informed decision making regarding shortages;
- Authorize EUAs;
- Communicate with healthcare providers about devices in shortage;
- Inform conservation strategies; and
- Provide assessments that allow for informed decision making on medical device shortages across the United States Government.

FDA is using this information to develop shortage assessments that inform potential mitigations. This work has helped to protect patients and health care providers around the nation from critical shortages of devices.

In addition to the implementation of the new device shortages authorities, FDA has conducted horizon scanning to assess demand for devices needed to respond to the pandemic, including PPE, ventilators, diagnostic supplies, infusion pumps, and non-contact infrared thermometers; and established a rapid response team, working with field personnel to address fraudulent imports. The Agency has likewise worked to prevent and mitigate shortages of testing supplies and other critical medical devices. For example, FDA collaborated with U.S. Cotton, one of the world's largest manufacturers of cotton swabs, to develop and produce a polyester-based swab for testing. FDA also collaborated with laboratories and clinical investigators validating potential alternative sources of control materials, transport media, and swabs. As individual developers validated these alternative components, FDA requested their permission to share their

findings publicly so that others could benefit, and we posted these alternatives on our website. In this way, FDA has been serving as a clearinghouse for scientific information that the entire community can leverage to mitigate shortages and increase testing capacity. FDA continues to post this information on a rolling basis on an FAQ website so that labs have access to the latest information regarding alternative controls, transport media, extraction, instruments, and swabs.

FDA has also worked across the medical device ecosystem to address systemic challenges to our supply chain due to sterilization issues and resin shortages. The impacts of supply chain disruptions caused by a natural disaster (Texas Winter Storms) have significantly impacted our most vulnerable populations. Most recently, devices used to compound total parental nutrition for critically ill neonates were impacted by the lack of availability of resins. FDA has worked with manufacturers and suppliers to help mitigate this disruption.

FDA continues to work to implement and operationalize the new device shortage authority, as well as utilize one time funding from COVID supplementals and $5 million in the first annual appropriations it received in FY 2022 to stand up a new state-of-the-art Resilient Supply chain Program (RSCP). Medical device shortages not only put patients in harm's way but also jeopardize our health care workers on the front lines, during public health emergencies like the COVID-19 pandemic and every day in our health care system. Moreover, device shortages disproportionately affect at-risk populations and exacerbate health disparities. For these reasons, FDA continues to do all it can within its current authorities and resources to mitigate shortages and supply chain interruptions for COVID-19 and within the U.S. health care system generally, and why the Agency has requested additional authorities and funding in FY 2023 to improve our device supply chain readiness going forward

Congress has acknowledged the importance of FDA's work on shortages in our health care system and we want to continue working with this Committee and others to make sure FDA has the resources and authorities needed to ensure U.S. patients and health care providers have the medical products they need each day. To ensure the U.S. is properly prepared now and in the future, we must take action to secure our medical device supply chain, including related materials, parts, and components. FDA recognizes that this will take resources and expanded authority. The pandemic has demonstrated that by the time a public health emergency is

declared, it is often too late to effectively prevent or mitigate device shortages. Moreover, there are situations that occur frequently that do not rise to the level of a public health emergency – such as cybersecurity attacks, natural disasters, recalls and spot shortages that may impact one region of the country or one particular hospital system, but for which device shortages could significantly impact patient care. After the COVID-19 emergency ends, these authorities remain tied to a public health emergency – that is, during or in advance of a public health emergency. This limits FDA's ability to identify supply chain vulnerabilities and work with the industry to respond to early signs of supply constraints or a potential shortage situation. One need only look at the ongoing resin supply chain issue, noted above, to see the wide-spread impacts that have lasted for over a year and resulted in shortages of multiple devices to include pediatric trach tubes, blood collection tubes, diagnostic tests, and catheters. Most recently, a critical device component was impacted by this shortage which resulted in an inability to delivery total parental nutrition for neonates [17] Unfortunately, FDA will be very limited in our ability to proactively identify and address device shortages after the COVID-19 emergency ends while its device shortages authorities remain tied to a public health emergency – that is, during or in advance of a public health emergency.

Conclusion

FDA continues to advance its mission to protect and promote public health by helping to ensure the safety of human and animal food, and the safety and effectiveness of medical products. We take our public health mandate very seriously and will continue to work each day to help end this pandemic. We continue to communicate with the American public and make regulatory decisions based on data and sound science. I look forward to continuing to work with the Committee on these efforts and thank you again for the opportunity to testify today.

[17] *https://www.childrenshospitals.org/content/public-policy/letter/critical-shortages-fda-letter*