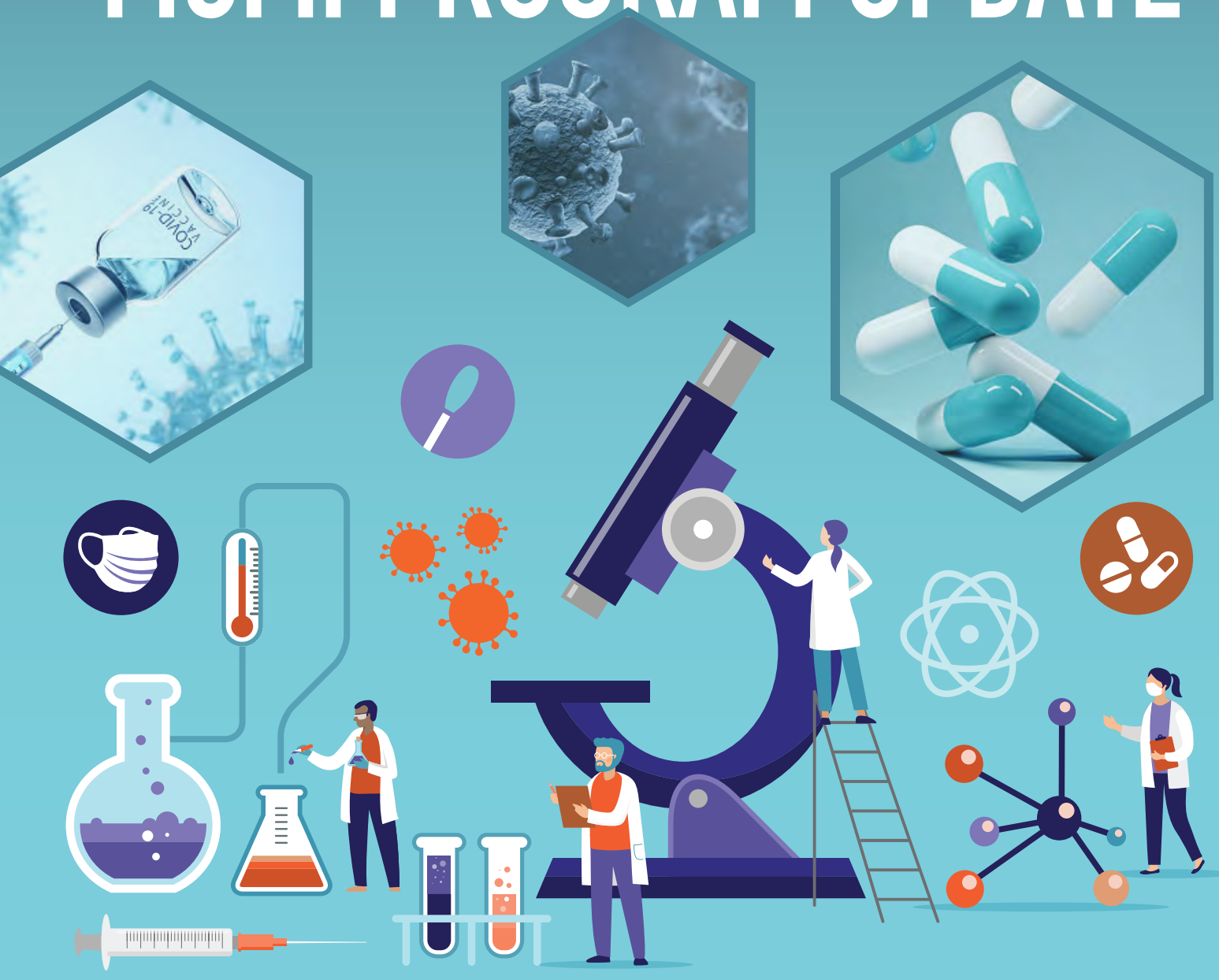
FDA

FY 2021

MCMi PROGRAM UPDATE



FDA MEDICAL COUNTERMEASURES INITIATIVE

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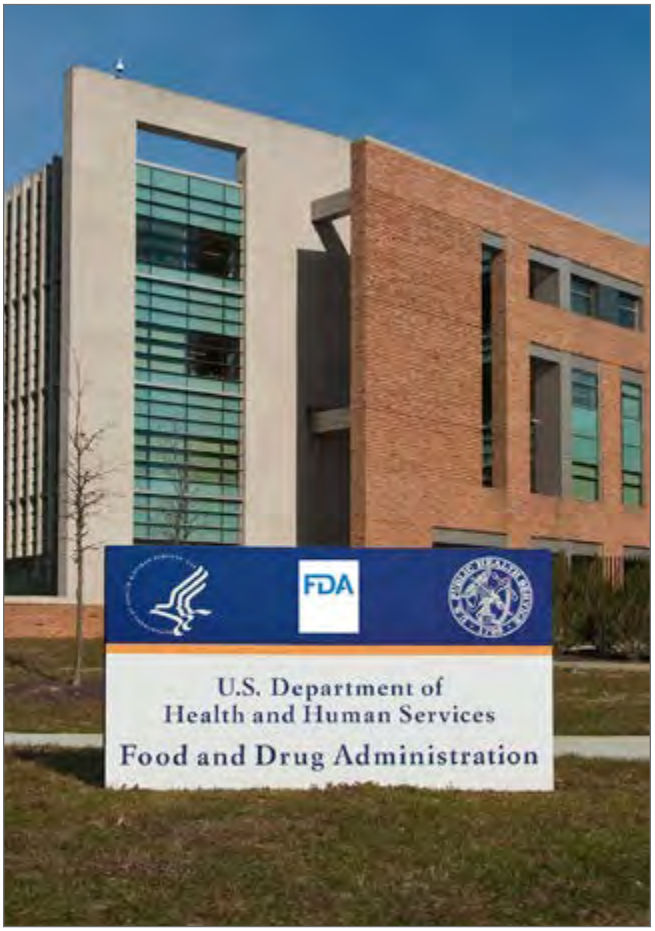
BACKGROUND



The United States (U.S.) Food and Drug Administration (FDA or agency) plays a critical role in protecting the U.S. from chemical, biological, radiological, nuclear (CBRN), and emerging infectious disease threats, such as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19). FDA is responsible for reviewing the safety and effectiveness of **medical countermeasures** (MCMs)—including drugs, therapeutic biologics, vaccines, and devices, such as diagnostic tests—to counter these threats.[a]

In addition to its regulatory responsibilities, FDA works closely with U.S. government (USG) partners, to build and sustain the MCM programs necessary to effectively respond to public health emergencies.[b] This includes the agency's unprecedented COVID-19 pandemic response efforts that began in December 2019, and continue today (see ***COVID-19 Response*** below). Interagency collaborations include numerous engagements through the U.S. Department of Health and Human Services (HHS) **Public Health Emergency Medical Countermeasures Enterprise** (PHEMCE, or the Enterprise). FDA also works closely with the U.S. Department of Defense (DoD) to facilitate the development and availability of MCMs to support the unique needs of American military personnel, including under a framework established in FY 2018 under Public Law 115-92 for enhanced FDA/DoD collaborations. FDA supports the PHEMCE and DoD by providing subject-matter expertise in MCM development and by providing scientific and regulatory input to inform MCM development, procurement, and stockpiling decisions. In addition, FDA facilitates access to available MCMs to respond to public health and military emergencies, even when products are still investigational or not yet approved for that particular use, provided certain criteria are met.[c,d]

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[a] MCMs include qualified countermeasures as defined in section 319F–1(a)(2)(A) of the Public Health Service Act (PHS Act) (42 USC. § 247d–6a(a))(2)(A); qualified pandemic or epidemic products as defined in section 319F–3(i)(7) of the PHS Act (42 USC. § 247d–6d(i)(7)); and security countermeasures as defined in section 319F-2(c)(1)(B) of the PHS Act (42 USC § 247d–6b(c)(1)(B)). Some medical products (e.g., traumatic brain injury (TBI) diagnostics), and some activities (e.g., combatting antimicrobial resistance) discussed in this report may not meet the statutory definition of MCMs or relate directly to products defined as MCMs, but were included in this report as examples of additional work supported by MCMi Program staff because of its connection to public health preparedness. Inclusion of such examples is not intended as comprehensive reporting on agency activities related to these topics.

[b] Section 2811-1 of the PHS Act (42 U.S.C. 300hh-10a).

[c] See e.g., sections 561 and 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

[d] For purposes of this document, "approved" refers to "FDA-approved, licensed, or cleared" under sections 505, 510(k), 512, 515, or 571 of the FD&C Act or section 351 of the PHS Act.

In 2010, FDA launched its Medical Countermeasures Initiative (**MCMi**) Program, building on the substantive MCM work ongoing at FDA and focusing increased resources on promoting the development of MCMs by establishing clear regulatory pathways for MCMs, instituting effective regulatory policies and mechanisms to facilitate timely access to available MCMs, and advancing MCM regulatory science to create the tools that support timely regulatory decision-making.

Many of FDA's activities under the MCMi Program foster the development and availability of MCMs, and FDA has also been given legal authorities to enable FDA to more effectively support preparedness and response efforts.[1] The Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (**PAHPRA**)[e] requires FDA to issue an annual report detailing its MCM activities. This report responds to that requirement for fiscal year (FY) 2021 (October 1, 2020 – September 30, 2021).[2]

FY 2021 RESOURCES FOR MCM ACTIVITIES

FDA obligated an estimated $356.2 million in FY 2021 to support CBRN, COVID-19, and pandemic influenza-related MCM activities (***Table 1***). These resources comprised a combination of base funding and no-year funding. This funding supported 626 full-time equivalents (FTEs).

Table 1: FY 2021 resources obligated to MCM activities (dollars in millions)

	FY 21 Estimate	FY 21 FTE Estimate
CBRN Base Funding	$76.2	297.5
Pandemic Influenza Base Funding	$34.5	118
MCMi Base Funding	$36.5	110.5
Subtotal	**$147.2**	**526**
COVID-19 Supplemental Funding	$209.0	100
Total	**$356.2**	**626**

[e] Public Law 113-5, 127 Stat. 161

OBJECTIVES, ACTIVITIES & ACHIEVEMENTS

FDA's overarching objective with respect to MCMs—which cuts across all FDA centers and offices engaged in MCM activities—is to facilitate the timely development of and access to safe and effective MCMs to counter CBRN and emerging infectious disease threats for civilian populations, as well as MCMs to support American military personnel.[f]

The following sections provide detail on achievements in FY 2021 with respect to these activities.

Box 1: Key FDA activities to facilitate development of and access to MCMs

- Supporting developers, manufacturers, researchers, and others in development of new and innovative MCMs to meet FDA's standards
- Providing regulatory advice, guidance, and technical assistance to sponsors developing investigational MCMs for CBRN or emerging infectious disease threat indications
- Discussing questions with potential product sponsors to help clarify requirements for approval[g] or Emergency Use Authorization (EUA)
- Reviewing MCM marketing applications and approving those that meet standards for approval
- Supporting the establishment and sustainment of an adequate supply of MCMs, including interagency collaboration on efforts to advance MCM supply chains
- Enabling access to available MCMs that are not yet approved for use—when necessary—through an appropriate regulatory mechanism, such as clinical trials or EUA
- Responding to emerging and re-emerging public health threats
- Establishing and sustaining Public Health and Security Action Teams to identify and catalyze the resolution of regulatory and scientific challenges associated with MCMs to address high-priority threats
- Developing capabilities to monitor and assess MCMs used during public health emergencies
- **Collaborating** with USG partners developing MCMs
- Sustaining the **MCMi Regulatory Science Program** to create tools, standards, and approaches to develop and assess MCM safety, efficacy, quality, and performance
- Encouraging manufacturers to develop innovative and emerging approaches to produce medicines through **advanced manufacturing** technologies
- Ensuring that the FDA **regulatory and policy framework** adequately supports MCM development and enables preparedness and response activities
- Sustaining the **MCMi professional development program** to ensure that FDA personnel maintain the requisite skills and abilities to support the MCM mission

[f] The publicly available list of high-priority threats identified by the Enterprise for which MCMs are needed can be found in the *2017-2018 PHEMCE Strategy and Implementation Plan* at: **https://www.phe.gov/Preparedness/mcm/phemce/Documents/2017-phemce-sip.pdf** (see Box 1, page 8). FDA is working with HHS to provide an updated publicly available list.

[g] For medical devices, the term "approval" will be used generally to mean marketing under a premarket approval application (PMA), 510(k) notification, or De Novo classification.

FDA COVID-19 RESPONSE

From the beginning of the COVID-19 public health emergency through the end of FY 2021 (September 30, 2021), FDA activities include:

REGULATORY ADVICE & GUIDANCE

- Issued 75+ COVID-19-related guidance documents
- Published 10 diagnostic test and 3 other medical device EUA templates
- Reviewed 470+ trials for COVID-19 therapeutics
- Worked with sponsors on 640+ drug development programs in planning stages

COVID-19 MCM APPROVALS*

*FDA-approved, licensed, or cleared

- 1 vaccine
- 1 treatment
- 1,000+ generic drug approvals for COVID-19 related treatments and supportive therapies
- 1 diagnostic test
- 492 personal protective equipment (PPE)
- 77 other devices

ADDRESSING FRAUD

- 1,500+ fraudulent and unproven products related to COVID-19 identified
- 260 warning letters sent to sellers
- 393 fraudulent test kits reported
- 320 online marketplace abuse complaints addressed
- 312 domain registrar abuse complaints addressed

EUAs

470+ EUAs issued enabling access to 750+ products

- 3 vaccines
- 13 drug and biological therapeutic products
- 390+ diagnostic tests and sample collection devices
- 18 PPE
- 44 other devices

COMMUNICATIONS

- 370+ COVID-19 update press releases
- 450+ new FDA web pages
- 11 Consumer Updates
- 15+ videos for consumers
- 16+ podcast episodes
- Thousands of tweets

STAKEHOLDER ENGAGEMENT

- 80+ MCMi email updates + hundreds more stakeholder emails
- 80 town halls on testing and PPE
- Answering public questions
  - 23,515 on COVID-19 drugs
  - 410,000+ on COVID-19 devices, including testing
  - 11,168 on COVID-19 vaccines
- Engaged with 2,200+ manufacturers on manufacturing capacity and supply chain issues

COVID-19 RESPONSE

The COVID-19 pandemic is unprecedented in modern history and has required an extraordinary response around the world. On January 31, 2020, the HHS Secretary issued a determination[3] that a public health emergency exists, and the World Health Organization (WHO) declared COVID-19 a worldwide pandemic on March 11, 2020—the first pandemic caused by a coronavirus.[4] Since December 2019, and throughout the remainder of FY 2020 and FY 2021—and beyond—FDA has been "all hands on deck," with thousands of FDA scientists, clinicians, lawyers, and other experts working around the clock to respond to COVID-19.

While FDA's work continues, this report offers a snapshot of response activities during the FY 2021 reporting period, October 1, 2020 through September 30, 2021.[5] FDA's COVID-19 response actions in FY 2021 include:

> In FY 2021, FDA approved the first COVID-19 treatment, vaccine, and diagnostic test.

Facilitating development of MCMs to diagnose, prevent, or treat COVID-19, including by working with medical product sponsors to clarify regulatory and data requirements necessary to rapidly advance development of products essential to supporting response efforts. In FY 2021:

- FDA approved the first **treatment**, first **diagnostic test**, and the first **vaccine** for COVID-19.
  - On October 22, 2020, FDA approved the antiviral drug Veklury (remdesivir) for use in adult and pediatric patients 12 years of age and older and weighing at least 40 kilograms (kg) (about 88 pounds) for the treatment of COVID-19 requiring hospitalization. To ensure continued access to the pediatric population, FDA also revised the EUA for Veklury to authorize the drug's use for treatment of suspected or laboratory confirmed COVID-19 in hospitalized pediatric patients weighing 3.5 kg to less than 40 kg or hospitalized pediatric patients less than 12 years of age weighing at least 3.5 kg. Clinical trials assessing the safety and efficacy of Veklury in this pediatric patient population were ongoing at the time of the October 2020 approval.[6]

  - On March 17, 2021, FDA granted marketing authorization of the **BioFire Respiratory Panel 2.1 (RP2.1)**, a diagnostic test for the simultaneous qualitative detection and identification of multiple respiratory viral and bacterial nucleic acids in nasopharyngeal swabs (NPS) obtained from individuals suspected of COVID-19 and other respiratory tract infections. The diagnostic test, which was previously authorized under an EUA, was granted marketing authorization using the De Novo premarket review pathway, a regulatory pathway for low- to moderate-risk devices of a new type. The granting of this De Novo request marked an important step in FDA's response to the COVID-19 pandemic because it is the first SARS-CoV-2 diagnostic test that will be permitted to be marketed beyond the public health emergency.[7]
  - On August 23, 2021, FDA approved the first COVID-19 vaccine, **Comirnaty**, for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and

older. FDA granted this application Priority Review; the application was submitted on May 18, 2021 and approved on August 23, 2021, months ahead of the January 2022 Prescription Drug User Fee Act (PDUFA) deadline. This vaccine, also known as the Pfizer-BioNTech COVID-19 Vaccine, continues to be available under EUA, including for individuals 5 through 15 years of age; for the administration of a third dose in certain immunocompromised individuals; and for a single booster dose in certain people.[8]

- Under the Coronavirus Treatment Acceleration Program (CTAP), a special emergency program launched in April 2020 for possible coronavirus therapies, FDA actively engaged with medical product developers on more than 110 drug development programs, and reviewed more than 120 clinical trials.[9] FDA enabled more than 470 studies of potentially effective medical products to proceed, including sending 263 "safe to proceed" letters in response to Investigational New Drug (IND) application requests for drugs, and 76 in response to biologics products. ***Table 2*** lists COVID-19 IND and Pre-IND requests received as of September 30, 2021.
- FDA issued or updated more than 20 **guidance documents** related to medical product development and availability for COVID-19.[10] New MCM-related guidances issued in FY 2021 include:
  - **Emergency Use Authorization for Vaccines to Prevent COVID-19** (issued in October 2020, and updated in May 2021)[11]
  - **COVID-19: Master Protocols Evaluating Drugs and Biological Products for Treatment or Prevention Guidance for Industry** (issued in May 2021)[12]

Enabling access to emergency use and investigational MCMs including accurate and reliable tests through an appropriate mechanism, such as **EUA** or IND.[13] FDA issued 179 new EUAs enabling the use of more than 575 medical products to support the COVID-19 response in FY 2021, including vaccines, drug and biological therapeutic products, and devices. ***Table 3*** and ***Table 4*** provide more information about EUA activities during the COVID-19 response, through September 30, 2021.

- In FY 2021, FDA issued new EUAs for three vaccines and seven drug and biological therapeutic products, including four EUAs for monoclonal antibodies (three of which are still in effect). FDA also authorized two of these monoclonal antibodies for post-exposure prophylaxis (prevention).[14]
- FDA also reissued more than 400 EUAs in FY 2021 to reflect, based on evolving information, data and circumstances, changes to conditions of authorization, authorized uses, authorized information, and product descriptions.
  - Since the first vaccine EUA was issued in December 2020, FDA reissued the three vaccine EUAs a combined total of 12 times in FY 2021 and granted numerous EUA amendments to authorize use for additional populations and booster doses, and also acted on dozens of EUA amendments to, among other things, update fact sheets with safety information, allow for more flexible storage and transportation conditions, and permit manufacturing changes to help increase the availability of COVID-19 vaccines,

Table 2: COVID-19 IND and Pre-IND requests received as of September 30, 2021[10]

Product type	Pre-IND submissions FY 2020	Pre-IND submissions FY 2021	IND submissions FY 2020	IND submissions FY 2021
Drugs	522	98	348	146
Vaccines	65	29	27	45
Hyperimmune products (Immune globulin and polyclonal antibody)	4	0	1	2
Product type	**591**	**127**	**376**	**193**

including nine additional batches of Janssen COVID-19 Vaccine,[15] and **extending the shelf life** of two COVID-19 vaccines.[16]

- To provide regulatory flexibility for medical devices, FDA's Center for Devices and Radiological Health (**CDRH**) published 13 EUA templates, and 28 guidance documents (including revisions).[17]
  - FDA has authorized more than 400 tests and sample collection devices, including direct-to-consumer tests with at-home specimen collection, tests for serial screening, over-the-counter (OTC) tests performed entirely at home that do not require a prescription, and multiplex tests that detect COVID-19, flu, and other respiratory viruses.
  - FDA provided additional flexibility for test developers in March 2021, issuing an EUA template for test developers seeking EUA of certain tests for screening with serial testing. As part of this new template for test developers, the agency provided recommendations aimed to streamline the authorization of screening tests with serial testing. For example, in certain circumstances, a point of care (POC) test or an at-home test could be authorized for OTC use without the need for validating its use in asymptomatic individuals prior to authorization. The FDA believes that evidence of a test's strong performance in symptomatic patients combined with serial testing can mitigate the risk of false results when testing asymptomatic individuals.[18]
  - FDA has authorized a wide variety of other medical devices for use in combating the pandemic, including personal protective equipment (PPE), ventilators, and other therapeutic devices. As of September 30, 2021, FDA authorized 260 PPE devices including 42 surgical masks, 205 filtering facepiece respirators (FFRs), and 13 systems for PPE decontamination or bioburden reduction, to meet a need at the time for these types of devices due to PPE shortages. In addition to granting EUAs, FDA has also cleared, through its premarket notification pathway, almost 500 PPE 510(k)s.
- FDA approved more than 580 emergency IND requests to enable access to investigational drugs in FY 2021.
- FDA understands the need to adapt and pivot to support modification or development of lifesaving MCMs as new variants of coronavirus are identified. In FY 2021, FDA took steps to address new virus variants, such as the delta variant, including:
  - Communicating with individual medical product sponsors to provide information as they evaluate the impact of COVID-19 variants on their products.[19]
  - Issuing a suite of guidances to guide medical product developers of vaccines, therapeutics, and diagnostics, to address the emergence and potential future emergence of variants of SARS-CoV-2.[20]
  - Authorizing revisions to fact sheets to address SARS-CoV-2 variants for monoclonal antibody products under EUA,[21] and working with ASPR on appropriate use and distribution of monoclonal antibody treatments that may be less effective to treat patients infected with certain variants.[22]
  - Providing information regarding the impact of viral mutations on COVID-19 tests, recommendations for clinical laboratory staff and health care providers, and information about certain tests for which the FDA has identified potential impacts on performance due to SARS-CoV-2 genetic mutations.
  - Revising the authorizations of certain molecular, antigen, and serological tests for COVID-19 by

> In FY 2021, authorized 3 COVID-19 vaccines, 4 monoclonal antibody treatments, and 160+ diagnostic tests for emergency use.

Table 3: COVID-19 EUA and Pre-EUA requests received as of September 30, 2021

Product type	Pre-EUA submissions FY 2020	Pre-EUA submissions FY 2021	EUA submissions FY 2020	EUA submission FY 2021
Diagnostics	824	390	1,405	776
Other Devices	1,147	420	2,214	133
Drugs	3	1	50	18
Biologics	7	5	1	3
Total	**1,981**	**816**	**3,670**	**930**

Table 4: COVID-19 EUAs issued as of September 30, 2021

Product type	Number of EUAs issued in FY 2020	Number of new EUAs issued in FY 2021	Total EUAs issued through end of FY 2021*	Enabled access to medical products under EUA (cumulative)**
Diagnostic devices	233	161	394	420+
PPE, such as respirators, gowns, surgical masks	13	5	18	200+
Other devices, including ventilators	37	7	44	160+
Drugs and biological therapeutic products	6	7	13	13
Vaccines	0	3	3	3
Total	**289**	**183**	**472**	**796+**

**This total may include EUAs that are no longer active (i.e., EUAs that have been revoked or terminated). Multiple devices were authorized for use under a single "umbrella" EUA in some cases, including certain tests, PPE, and ventilators/accessories. Each umbrella EUA is counted here as a single EUA, while the total number of products authorized under the umbrella is captured in the last column.*

***Estimates of the number of medical products that EUAs enabled access to are based on lists of these devices that were reported publicly (i.e., listed individually in tables) on the FDA website as authorized under umbrella EUAs; certain types of products may not have been listed this way, and therefore are not counted here.*

requiring additional conditions of authorization concerning viral mutations.[23]

- Expanding the practice established in FY 2020 to monitor global sequencing databases for emerging variants and evaluate their impact on diagnostic tests.
- Funding regulatory science research on the immunological response to infection and vaccination, including potential impacts of emerging variants.[24]

Actively monitoring the medical product and food supply chains to address imbalances. FDA continues to screen and monitor millions of domestic and international products in the medical supply chain to help ensure COVID-19-related supplies coming into the U.S. are safe and distributed appropriately. In FY 2021, FDA continued working with U.S. and global manufacturers to address unprecedented disruptions in global supply chains, impacting medical products needed to respond to the COVID-19 pandemic. Actions by FDA in FY 2021 included:

- Assessed supply chain vulnerabilities, to identify potential supply chain issues early, and minimize disruptions.[25] CDRH alone contacted more than 1,000 medical device manufacturing sites in 12 countries.
- Conducted supply chain illumination to identify weaknesses in obtaining and distributing needed PPE and other medical products.
- Gathered data from distributors and other third parties to monitor the supply chain to look for early signs of medical product availability issues and to determine when to implement mitigations.
- Conducted an assessment of FDA-wide supply chain capabilities to identify successes, gaps, challenges, and opportunities to promote supply chain resilience.
- Worked with other agencies to monitor and address product shortages.
- Provided conservation strategies to health care providers to minimize the use of certain PPE to make the most of the supply and avoid running out of critical products.
- Cleared almost 500 PPE 510(k)s to increase the amount of PPE available in the market during the COVID-19 response.
- Issued more than 15 guidance documents to help protect the medical product supply and sustainment of the food supply for humans and animals.
- Participated in interagency efforts to address medical supply chain challenges, such as through the Federal Emergency Management Agency (FEMA)- and DoD-led Supply Chain Task Force and FEMA- and HHS-led international medical product donation efforts, and through White House-led COVID-19 response structures.
- In response to an August 2020 Executive Order,[26] FDA **identified a list** of essential medicines, MCMs, and critical inputs that are medically necessary to have available at all times in an amount adequate to serve patient needs and in the appropriate dosage forms. The goal of this work is to ensure the American public is protected against outbreaks of emerging infectious diseases, such as COVID-19, as well as CBRN threats.[27]
- Continually updated a **web page** listing specific authorities under the Coronavirus Aid, Relief, and Economic Security Act (CARES Act) to enhance FDA's ability to identify, prevent, and mitigate drug shortages.[28]
- The CARES Act, for the first time, provided statutory authority intended to help prevent or mitigate device shortages during, or in advance of, a public health emergency. These new authorities have enabled the agency to collect information submitted by manufacturers about supply chain disruptions to help prevent and mitigate the impact of critical shortages caused or exacerbated by the COVID-19 pandemic. As part of this work, FDA published a list of medical device shortages during the COVID-19 public health emergency, fulfilling a statutory obligation under section 506J of the FD&C Act, and is working toward establishing a new, permanent, **Resilient Supply Chain and Shortages Prevention Program** (RSCSPP). The RSCSPP will enhance FDA's capacity to enable rapid intervention to prevent and mitigate supply chain interruptions.[29]

Protecting the safety of the nation's blood supply and human cells, tissues, and cellular/tissue-based products for transplantation (HCT/Ps).

- Issued a final guidance to provide manufacturers of licensed and investigational cellular therapy and gene therapy (CGT) products with risk-based rec-

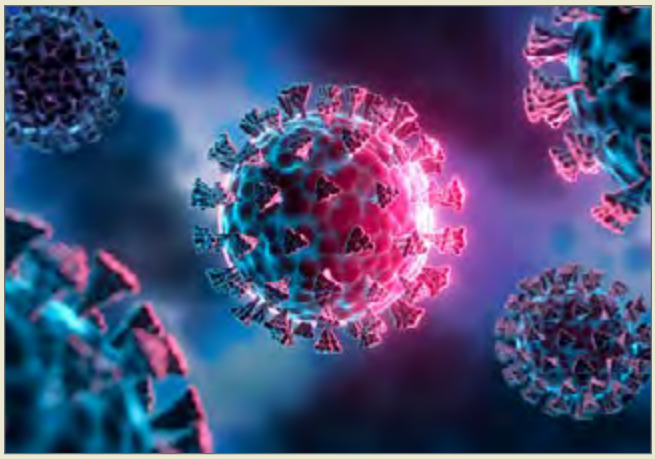
ommendations to minimize potential transmission of SARS-CoV-2.[30]

Protecting consumers against fraudulent products. Unfortunately, during emergency situations, fraudulent products claiming to prevent, treat or cure conditions associated with the emergency almost always appear for sale. The FDA monitors for fraudulent products and false product claims related to COVID-19 and other conditions and takes appropriate action to **protect patients and consumers**.[31]

- To proactively identify and neutralize threats to consumers, the FDA launched Operation Quack Hack in March 2020.
- In FY 2021, FDA identified more than 1,000 fraudulent and unproven medical products related to COVID-19, reviewed thousands of websites, social media posts, and online marketplace listings, resulting in 146 **warning letters** to sellers, 49 reports sent to online marketplaces, and 41 abuse complaints sent to domain registrars.[32]
- FDA also continued to identify hand sanitizer products that consumers should not use due to a range of issues including contamination with methanol, 1-propanol, benzene, acetaldehyde, or acetal; subpotency; or because it was packaged in containers that may appear as food or drinks and may put consumers at risk of serious injury or death if ingested. As of the end of FY 2021, more than 250 such hand sanitizer products had been identified, with 66 of them added to the **list of hand sanitizers consumers should not use** in FY 2021.[33]

Conducting and collaborating on regulatory science research to help ensure FDA's ability to quickly assess safety and efficacy of new SARS-CoV-2 MCMs, and to help diagnostic test developers validate and ensure the quality and performance of their tests. In FY 2021, FDA:

- Expanded several MCMi Regulatory Science Program **extramural research contracts** to support COVID-19 MCM development and evaluation including:
  - **University of Liverpool**, to better understand how COVID-19 develops and its severity, including for variants of concern. This work was co-funded by the Office of Biodefense, Research Resources and Translational Research, National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH).[34]
  - **Stanford University**, to identify biomarkers and immune correlates of protection to further understanding of diverse responses across populations, including race, ethnicity, sex, and age to aid the development and evaluation of medical countermeasures for all.[35] This work was co-funded with the Office of Minority Health and Health Equity (OMHHE).
  - **Wyss Institute for Biologically Inspired Engineering at Harvard University**, to develop new organs-on-chips (including non-human primate models) to aid development and testing of countermeasures for COVID-19.[36] This work was co-funded by the Office of Biodefense Research Resources, and Translational Research, Division of Microbiology and Infectious Diseases, NIAID, NIH.
  - **Broad Institute**, to better understand viral infection, pathogenesis, and immune responses to SARS-CoV-2 to inform development and review of MCMs for COVID-19.[37]
- Awarded an extramural research contract to help inform development and evaluation of COVID-19 MCMs, including a contract to the Commonwealth Scientific and Industrial Research Organization (**CSIRO**), Australia's scientific research agency, to strengthen coronavirus models through systems biology, artificial intelligence (AI), and machine learning.
- Awarded an extramural research contract to **Embleema and George Washington University** to develop quality metric tools for next-generation sequencing databases to support SARS-CoV-2 and influenza diagnostics. This project will also complement the MCM-supported **FDA ARGOS Database** (FDA Database for Regulatory Grade Microbial Sequences).[38]



Engaging with partners on innovative approaches to respond to COVID-19 as quickly and safely as possible.

- FDA is working with several partners to capture relevant real-world data (RWD), for example, clinical outcome data to identify existing drugs that demonstrate possible COVID-19 treatment approaches.[39] One example is the Reagan-Udall Foundation **COVID-19 Evidence Accelerator**, which was launched at FDA's request, in collaboration with Friends of Cancer Research, in March 2020. Initial efforts focused on understanding the natural history of COVID-19 and therapeutics, as little was known at the time about the disease or potential medications that might be used to treat the virus effectively. The Evidence Accelerator lab meetings created a safe collaborative space to assimilate and evaluate data generated from across the country for organizations across the health data ecosystem: FDA, major health data/technology organizations, academia, professional societies, health systems, insurers, and drug and device industries. In May 2020, Reagan-Udall's **Diagnostics Evidence Accelerator** began reviewing RWD including test performance, surveillance trends, contemporaneous symptoms, and presentation.[40]
- FDA continues to leverage research collaborations with USG partners (e.g., NIH, DoD) to characterize host pathogen interactions to support development of MCMs against emerging viral diseases, including COVID-19.
- FDA is also teaming with NIH 3D Print Exchange (3DPX) and Department of Veterans Affairs (VA) Innovation Ecosystem to enhance access to critical medical products through **non-traditional manufacturing approaches**. The NIH **3DPX** COVID 3D TRUST collection included 625 designs, with more than 2 million views from nearly every country around the globe. The most popular downloads were face masks, face shields, and ear savers—favorites of small groups with desktop 3D printers responding to the urgent needs of frontline workers. (See more in ***Collaboration and Communication*** and ***Advanced Manufacturing***.)
- FDA is working with manufacturers outside of the medical product industry to produce or increase production of needed PPE, ventilators, and other medical products, including hand sanitizers. FDA met with these third-party manufacturers to determine hurdles to producing medical products and, when appropriate, allowed enforcement discretion of certain regulatory requirements through an EUA or immediately in effect guidance documents.
- FDA is partnering with the DoD and the Department of Homeland Security (DHS) to address questions about the safety of food that may have been exposed to coronavirus, specifically evaluating environmental stability of SARS-CoV-2 on food and food packaging, as well as whether the virus is infectious via oral exposure to contaminated food.
- FDA meets regularly with the U.S. Centers for Disease Control and Prevention (CDC) and Centers for Medicare and Medicaid Services (CMS) to address implementation issues associated with *in vitro* diagnostic (IVD) tests made available under EUAs. The Tri-Agency Task Force for Emergency Diagnostics (**TTFED**), established in FY 2019, has met routinely since January 2020 to discuss implementation of SARS-CoV-2 IVDs.[41]
- In November 2020, PrecisionFDA launched the **COVID-19 Precision Immunology App-a-thon**. The agency encourages the scientific and analytics community to develop innovative applications to explore the relationship between personalized immune repertoires and COVID-19 disease variables and associated factors.[42]

- In May 2021, FDA received an HHS grant to expand the CURE ID platform to explore COVID-19 treatments. The grant will fund expansion of the CURE ID platform to allow automated data collection from electronic health records (EHR) worldwide and clinical disease registries for COVID-19 and other difficult-to-treat infectious diseases.[43]
- FDA is working with the National Cancer Institute (NCI) at NIH to independently assess the performance of certain antibody tests, and leveraged this data for EUA authorizations.
- FDA meets weekly with NIH's RADx program and participants to provide advice to participants to assist with the program's goal to speed the development, validation, and commercialization of innovative diagnostics.

COVID-19 MCM-related actions are discussed in more detail later in this report, along with FDA's other MCM-related work during FY 2021.

Proactive COVID-19 communication

FDA has been as transparent as possible about our COVID-19 response activities, communicating early and often with stakeholders and the American public. In early February 2020, the agency instituted a COVID-19 Joint Information Center, or JIC, a task force of more than 100 communication professionals from across the agency responsible for coordinating FDA's response-related communications. FDA launched a frequently updated **COVID-19 response page** on January 27, 2020, and the FDA COVID-19 JIC published more than 70 new response-related web pages in FY 2021.[44] Other FDA communications in FY 2021 include:

- Issuing more than 150 COVID-19 **press announcements**, including 100+ COVID-19 Roundup press releases.[45]
- FDA leadership and scientific and policy experts **speaking** at hundreds of—mostly virtual—stakeholder, consumer, media, Congressional, and other events on various aspects of FDA's COVID-19 response efforts.[46]
- Publishing consumer-friendly information in plain language, including nine new or updated **Consumer Updates**,[47] five new **videos** for consumers,[48] 15 **FDA Voices** perspectives from FDA leadership,[49] thousands of **social media** posts,[50] weekly consumer email updates[51] featuring COVID-19 frequently asked questions, and six COVID-19-related episodes of the **FDA Insight** podcast.[52] Consumer-focused information, including regularly updated **COVID-19 frequently asked questions**,[53] is available in **multiple languages** including Spanish, Simplified Chinese, Korean, Vietnamese, Tagalog, Hmoob (Hmong), and Af Soomaali (Somali), and COVID-19 vaccine fact sheets were made available in more than 25 languages.[54]
- Continually communicating with stakeholders via email, including COVID-19 response recap **emails** twice weekly, and hundreds of topic- and center-specific emails.[55] FDA also published a variety of COVID-19 educational resources, including a **vaccine myths social media toolkit** available in six languages.
- Responding to 9,016 inquiries from health care providers, consumers, and manufacturers to the Center for Drug Evaluation and Research (CDER) Division of Drug Information, with questions on a variety of drug-related topics, including hand sanitizer safety and use.[56]
- Responding to more than 337,000 email and phone inquiries from diagnostic test developers, health care providers, and patients.
- Hosting a series of webinars including a twice monthly **virtual town hall for SARS-CoV-2 test developers**,[57] and periodic **webinars on respirators and other PPE for health care personnel use** during the COVID-19 pandemic.[58]
- CDRH issued several frequently asked questions (FAQs) and Letters to Health Care Providers to clarify information regarding EUA medical products and other topics.[59]
- CDRH sent millions of emails to stakeholders on COVID-19 topics.

Responding to misinformation

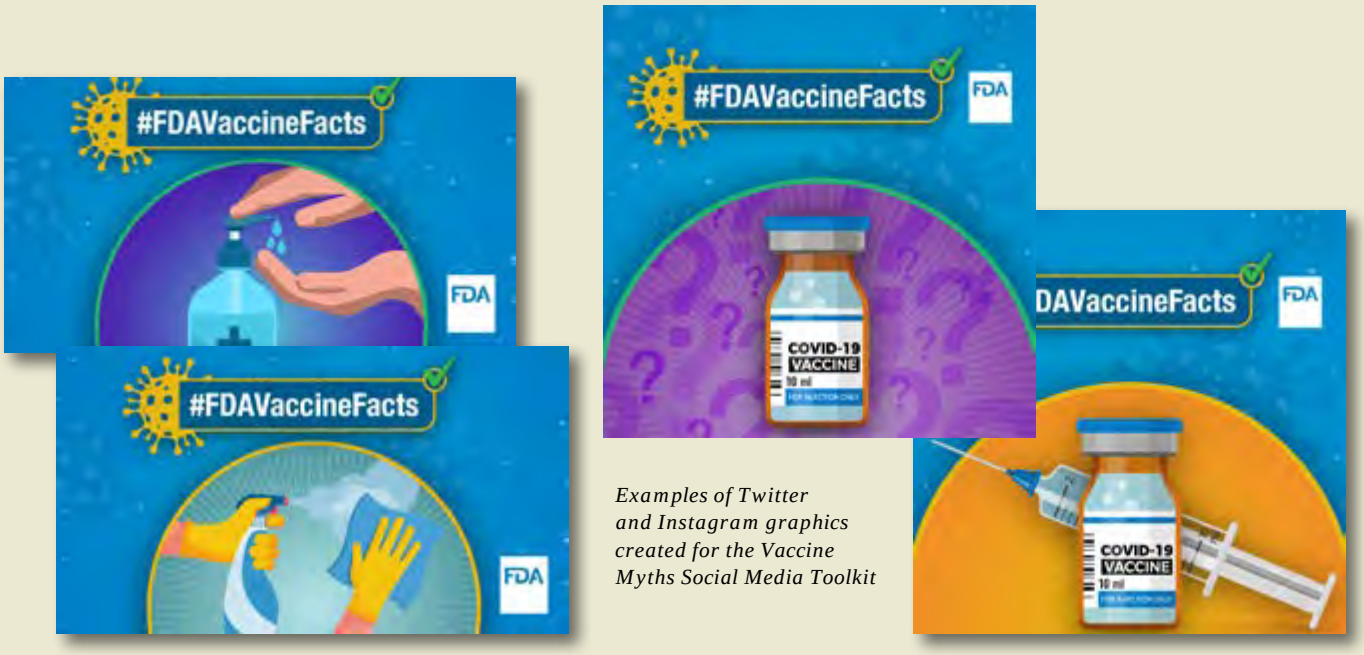
FDA responded to misinformation about COVID vaccines, diagnostics, and treatments by offering clear consumer information, including:

- A new **Consumer Update and video** to help people understand available COVID-19 treatments.[60]
- Information about why consumers **should not use ivermectin to treat or prevent COVID-19**.[61]
- Publishing a multilingual **COVID-19 Vaccines Myths** social media toolkit, with clear information to dispel rumors widely circulating on social media.[62]
- Advising against the use of antibody test results to evaluate immunity or protection from COVID-19[63]

Addressing COVID-19 health disparities

FDA also continued to support work addressing COVID-19 health disparities among racial and ethnic minority communities, including:[64]

- Holding listening sessions with diverse health professional organizations and other stakeholders to learn more about the gaps and needs of racial and ethnic minority communities and to share information on COVID-19 activities.
- Building awareness about **clinical trial diversity** (clinical trials are how medical products like vaccines get to the market).
- Launching bilingual (English/Spanish) and multilingual COVID-19 social media toolkits: **#VaccineReady**, and Multilingual COVID-19 Vaccines Myths (also noted at left, under ***Responding to misinformation***). These shareable toolkits allow stakeholders to have ready to use messages that can be shared with their communities to ensure accurate and consistent messaging.[65]
- Releasing **videos** in English and Spanish that talk about the importance of getting vaccinated.
- Hosting a **webinar** in March 2021 to shed light on the vaccine approval process and key information for minority communities to be aware of.[66]
- Funding regulatory science research to further understanding of diverse responses across populations, including race, ethnicity, sex and age to aid the development and evaluation of medical countermeasures for all.[67]



Examples of Twitter and Instagram graphics created for the Vaccine Myths Social Media Toolkit

MEDICAL COUNTERMEASURE APPROVALS

During FY 2021, FDA continued to review marketing applications for MCMs against CBRN and emerging infectious disease threats and approve safe and effective MCMs. FDA approved the majority of MCM marketing applications under review[h] in FY 2021 (see ***Appendix 1: FY 2021 Medical Countermeasure Approvals– Biologics and Drugs*** and ***Appendix 2: FY 2021 Medical Countermeasure Approvals–Devices***).[68]

> FDA approved treatments for COVID-19, smallpox, Ebola, radiation injuries, and thermal burns in FY 2021.

MCMs to treat or prevent diseases or conditions caused by CBRN threats

For radiological/nuclear agent preparedness, FDA approved **NPLATE** (romiplostim), a treatment to increase survival in adults and pediatric patients (including term neonates) acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome [H-ARS]). FDA approved this indication for NPLATE under the Animal Rule.[i]

For smallpox preparedness, FDA approved **Tembexa** (brincidofovir) to treat smallpox in adult and pediatric patients, including neonates, under the Animal Rule.[69]

MCMs to diagnose, treat, or prevent COVID-19

In addition to activities noted above to enable access to investigational MCMs to diagnose, prevent, or treat COVID-19, FDA approved the antiviral drug **Veklury** (remdesivir) for use in adult and pediatric patients (12 years of age and older and weighing at least 40 kg [about 88 pounds]) for the treatment of COVID-19 requiring hospitalization.[70] Under that October 2020 approval, Veklury should only be administered in a hospital or in a health care setting capable of providing acute care comparable to inpatient hospital care. At the time of that approval, FDA also continued to make this therapeutic **available** under EUA for emergency use by licensed health care providers for the treatment of suspected or laboratory-confirmed COVID-19 in hospitalized pediatric patients weighing 3.5 kg to less than 40 kg or hospitalized pediatric patients less than 12 years of age weighing at least 3.5 kg.[71]

FDA also approved **Comirnaty** (COVID-19 Vaccine, mRNA) for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 16

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[h] For purposes of this document, "under review" indicates that a marketing application has been submitted to FDA for approval by the product's sponsor.

[i] Before a medical product can be approved by FDA, the sponsor must prove the product's safety and its efficacy for its intended use. The FD&C Act generally requires that sponsors demonstrate efficacy through studies conducted in human subjects. However, FDA has regulations, commonly known collectively as the Animal Rule, that describe the very limited circumstances under which the FDA may consider the statute's effectiveness standard for approval to have been met based on adequate and well-controlled animal studies when the results of those studies establish that the product is reasonably likely to produce clinical benefit in humans. The product sponsor must still demonstrate the product's safety in humans. The Animal Rule can be used only for drug and biological products that have been studied for their safety and efficacy in preventing or ameliorating serious or life-threatening conditions caused by exposure to lethal or permanently disabling toxic chemical, biological, radiological, or nuclear substances when definitive human efficacy studies cannot be conducted because: 1) it has not been feasible to study the product's effectiveness after accidental or hostile exposure, and 2) it would not be ethical to deliberately expose healthy human volunteers to the substance. The Animal Rule also only applies to products that cannot be approved through other existing regulatory pathways. Also see Animal Rule Information at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-regulatory-science/animal-rule-information**

years of age and older. This vaccine also continues to be **available** under EUA, including for individuals 5 years of age and older; for the administration of a third dose in certain immunocompromised people; and for a single booster dose in people 12 and older.[72]

FDA also granted the first marketing authorization using the De Novo review pathway for the **BioFire Respiratory Panel 2.1 (RP2.1)** for the simultaneous qualitative detection and identification of multiple respiratory viral and bacterial nucleic acids in NPS obtained from individuals suspected of respiratory tract infections, including COVID-19.

MCMs to treat or prevent diseases or conditions caused by other emerging infectious diseases

To support Ebola preparedness, FDA approved two Ebola treatments in FY 2021. In October 2020, FDA approved **Inmazeb** (atoltivimab, maftivimab, and odesivimab-ebgn), a mixture of three monoclonal antibodies, as the first FDA-approved treatment for *Zaire ebolavirus* (Ebola virus) infection in adult and pediatric patients. Inmazeb was evaluated in 382 adult and pediatric patients with confirmed *Zaire ebolavirus* infection in one clinical trial (the **PALM trial**[j]). The PALM trial was led by the NIH and the Democratic Republic of the Congo (DRC) Institut National de Recherche Biomédicale with contributions from several other international organizations and agencies. Inmazeb received an Orphan Drug designation and Breakthrough Therapy designation from FDA.[73] In December 2020, FDA approved **Ebanga** (ansuvimab-zykl), a human monoclonal antibody, for the treatment for *Zaire ebolavirus* infection in adults and children.[74]

Pandemic influenza preparedness

FDA licensed a BLA supplement for a four-strain (quadrivalent) version of **Flucelvax Quadrivalent** (influenza vaccine) to extend the use of this vaccine to persons 2 years of age and older. FDA also **expanded the approved indication** for Xofluza (baloxavir

marboxil) to include post-exposure prevention of influenza (flu) for patients 12 years of age and older after contact with an individual who has the flu. Xofluza, previously available only in tablet form, is also now available as granules for mixing in water. Xofluza was originally **approved** in 2018 for treating uncomplicated flu in patients 12 years of age and older who have been symptomatic for no more than 48 hours.[75]

FDA also cleared one new influenza test. FDA has also issued EUAs for 25 multi-analyte (SARS-CoV-2 + Influenza) diagnostic tests and home collection kits (22 molecular and 3 antigen) as of October 1, 2021, and has issued two immediately in effect guidance documents that provide regulatory flexibilities intended to ensure availability of influenza tests and test supplies during the COVID-19 public health emergency. FDA authorized three EUA requests for home collection of specimens intended for use with multi-analyte tests.

These steps forward in influenza prevention and diagnostics facilitate preparedness for both seasonal and pandemic influenza, as new tests and technologies may be applied more rapidly to emerging

> To support pandemic influenza preparedness, FDA licensed a BLA supplement for a four-strain flu vaccine to extend its use to persons 2 years of age and older.

[j] Pamoja Tulinde Maisha [(PALM) "Together Save Lives" in the Kiswahili language]

pandemic influenza strains once approved for seasonal influenza use.

All-hazards preparedness

To help with preparedness of U.S. military personnel that are stationed in locations where tick-borne encephalitis (TBE) is endemic, FDA approved Pfizer's TBE vaccine (**Ticovac**) for active immunization to prevent TBE in individuals 1 year of age and older. Ticovac is the only FDA-approved vaccine against the TBE virus for individuals visiting or living in areas where TBE is endemic.

For preparedness in the event of a large-scale event involving thermal burns, FDA approved Stratatech's burn product **StrataGraft** for the treatment of adult patients with thermal burns containing intact dermal elements (remaining deep skin layers) for which surgical intervention is clinically indicated (also referred to as deep partial thickness burns). FDA granted StrataGraft regenerative medicine advanced therapy (RMAT), Priority Review, and Orphan Drug designations for this indication.

FDA also approved **I-STAT TBI Plasma Cartridge With The I-STAT Alinity System**, a rapid handheld traumatic brain injury (TBI) blood test, and the **MeMed BV** diagnostic tool, to rapidly determine whether an infection is bacterial or viral. Development of the MeMed tool was supported by the Defense Threat Reduction Agency's (DTRA) Chemical and Biological Technologies Department in its role as the Joint Science and Technology Office (JSTO) for the DoD Chemical and Biological Defense Program.[76]

Additional marketing applications in progress

Twenty-two additional marketing applications for new MCMs or new MCM indications were under review in FY 2021; these reviews were still ongoing at the end of the reporting period for this report. While FDA anticipates meeting the goal date for a decision for each of these submissions, FDA is generally prohibited from disclosing any determinations regarding the filing or approvability of any marketing application for a medical product under applicable statutory and regulatory provisions unless the application is approved or other grounds for disclosure apply.[77]

SUPPORTING AN ADEQUATE SUPPLY OF MEDICAL COUNTERMEASURES

In addition to actively monitoring the medical product supply chains, FDA continued efforts to support supplies of MCMs in other ways during FY 2021.

Working to resolve MCM shortages as quickly as possible when they occur is another way FDA helps ensure an adequate supply of MCMs. In addition to extensive COVID-19-related supply chain monitoring and mitigation activities, as noted on page 9, in FY 2021, FDA continued to collaborate with U.S. government partners and manufacturers of auto-injector products used for the treatment of nerve agent and insecticide poisoning to help prevent shortages of these products. FDA reviewed applicable scientific data, including through the Shelf-Life Extension Program (**SLEP**), to assess whether, if properly stored, certain lots of auto-injector products held for emergency use can continue to be used beyond the original labeled expiration date for a period specified by FDA, to help ensure ready access to these products. FDA also reviewed scientific data to assess whether certain lots are no longer useable and, therefore, should be properly disposed of.[78]

FDA also responded to numerous stakeholder inquiries on nerve agent auto-injector **expiry dating extensions** to assist in determinations about whether stockpiled auto-injector products made by the same manufacturer should be retained. Meanwhile, FDA continued to work with the applicant on manufacturing issues.

To help ensure an adequate supply of MCMs for potential emergencies, FDA may extend the expiration dating of MCMs based on FDA's review of scientific data.[79] For example, FDA issued final guidance to support government public health and emergency response stakeholder testing to support FDA extensions of the expiration date of specific lots of doxycycline hyclate 100 mg capsules held in strategic stockpiles for anthrax emergency preparedness and response purposes.[80]

Previously issued FDA-authorized extensions under the recommendations of the draft guidance were extended through July 2022. Based on government stakeholder needs, FDA continues to review scientific data to determine whether additional extensions of other MCMs may be supported outside of the SLEP.

Vaccines and biological therapeutics authorized for emergency use–as products that are not approved under a Biologics License Application (BLA) and are still being studied under IND applications–do not have fixed expiry dates. For those doses that are close to expiry, if they are being held under appropriate conditions for ensuring their integrity for use, they can potentially be quarantined to see if data on new stability studies warrant extension of the initial expiry date according to appropriate policies and procedures. In FY 2021, FDA **extended the expiration date** of several lots of Pfizer-BioNTech COVID-19 Vaccine, Janssen COVID-19 Vaccine, and the monoclonal antibodies bamlanivimab and etesevimab.[k]

FDA also continued to support SLEP, a federal fee-for-service program for extending the useful shelf life of military-significant and contingency use medical products, including MCMs that are owned by components of DoD or other federal program participants such as the **Strategic National Stockpile** (SNS). SLEP is designed to defer drug replacement costs for date-sensitive stockpiles of drugs by extending their useful shelf life beyond the manufacturer's original labeled expiration date. FDA laboratory personnel test and evaluate drugs submitted for shelf-life extension to assure stability and quality before an expiry dating extension is granted. In FY 2021, as a result of SLEP testing that ensured drug stability and quality, FDA granted shelf-life extensions for approximately 1,331 lots (batches) of MCM drugs.

[k] Bamlanivimab is currently authorized for emergency use only when administered together with etesevimab. FDA also extended the shelf life of certain lots of etesevimab from 12 months to 18 months on October 22, 2021, and again on December 21, 2021, in FY 2022. For more information, see Expiration Dating Extension, COVID-19 Therapeutics at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/expiration-dating-extension#COVIDtherapeutics**

ENABLING ACCESS TO MEDICAL COUNTER-MEASURES UNDER FDA'S EMERGENCY USE AUTHORIZATION AUTHORITY[l]

During FY 2021, FDA continued to work with USG partners, including DoD and other PHEMCE partners, and product sponsors to enable access to unapproved MCMs when necessary.[m] One way FDA does this is by issuing **Emergency Use Authorizations**. The EUA authority allows FDA to authorize the use of an unapproved medical product, or the unapproved use of an approved medical product, in anticipation of a potential emergency or during an actual emergency involving CBRN agents, or, for DoD purposes, other agents that may cause, or are otherwise associated with, an imminently life-threatening and specific risk to U.S. military forces, if certain statutory criteria are met.[n] A list of **current EUAs** is published on the FDA website.

> In FY 2021, FDA issued 183 EUAs, enabling access to 575+ medical products to support COVID-19 response efforts.

In addition to the extensive EUA work ongoing in response to COVID-19, in February 2021, FDA revised an EUA for a Zika diagnostic test initially authorized in 2016.[81]

In addition to issuing EUAs when necessary, FDA engages in the ongoing pre-EUA submission processes where FDA works with product sponsors or government agencies, such as the CDC and DoD, to facilitate the development of pre-EUA packages that may form the basis of an EUA request and issuance when the statutory criteria are met. During FY 2021, FDA continued to work with USG partners and industry on pre-EUA activities for MCMs against a diverse array of threats, in addition to intensive COVID-19 response efforts.[o, 82]

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[l] Section 564 of the FD&C Act (21 USCS § 360bbb-3)

[m] This support includes numerous activities including availability of pre-IND consultations for drug development proposals and pre-market consultations for device development proposals, advice, and feedback on clinical trial preparation, discussions related to expanded access protocols and pre-EUA discussions.

[n] The Project BioShield Act of 2004 [PL 108-276] established section 564 of the FD&C Act, granting the Secretary of HHS the authority to declare that circumstances exist that justify the authorization of "emergency use" of unapproved MCMs, or unapproved uses of approved MCMs, under certain terms and conditions. The authority to issue EUAs, after the declaration by the Secretary that issuance of such EUAs is justified, was delegated to the FDA Commissioner. Section 564 of the FD&C Act was amended by PAHPRA in 2013, the 21st Century Cures Act (Cures Act) in 2016 [PL 114-255], and PL 115-92 in 2017.

[o] A pre-EUA package contains data and information about the safety, quality, and efficacy of the product, its intended use under an EUA, and information about the potential emergency situation that might unfold. The pre-EUA process allows FDA scientific and technical subject matter experts to begin a review of information and assist with the development of conditions of authorization, fact sheets, and other documentation needed for an EUA in advance of an emergency. For more information about EUAs, see Emergency Use Authorization of Medical Products and Related Authorities at: **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities**

EUA transparency

While EUAs have received increased attention during the COVID-19 public health emergency, EUAs are not a new tool to the FDA. FDA recognizes that disclosing information from the scientific review documents supporting the issuance, revision, or revocation of EUAs for drugs and biological products, including vaccines, contributes to the public's confidence in the agency's rigorous review of scientific data and the appropriate use of authorized products.

FDA **announced** in November 2020 that our drug and biological product centers intended, to the extent appropriate and permitted by law, to publicly post their reviews of the scientific data and information supporting the issuance, revision or revocation of EUAs for all drug and biological products, including vaccines, as part of our COVID-19 response.[p, 83] The centers have since been posting this information to the FDA website as it becomes available.[84]

To help health care providers understand the benefits, risks, and proper use of FDA-authorized products, FDA has always posted letters of authorization (which spell out the conditions under which use of the product is authorized), fact sheets for patients, fact sheets for health care providers, and instructions for use, and Federal Register notices. When appropriate for the COVID-19 response, FDA has translated these materials into other languages to ensure the information is more broadly accessible. In addition, FDA has posted other supportive information such as letters granting amendments, product-specific frequently asked questions and information documents, and dear health care provider letters. Altogether, these documents provide helpful information and transparency to the public.

In March 2021, as part of its FDA Adverse Event Reporting System (FAERS), FDA published a new COVID-19 EUA FAERS Public Dashboard, which provides weekly updates of adverse event reports submitted to FAERS for drugs and therapeutic biological products used under EUA during the COVID-19 public health emergency.[q]

For device EUAs, FDA reorganized the SARS-CoV-2 ***In Vitro* Diagnostics EUAs** content on FDA's website to help make it easier to find specific categories of device EUAs and related information and updated its **FAQs on EUAs for Medical Devices During the COVID-19 Pandemic**. FDA also created new product codes for certain medical devices authorized for emergency use under EUA. An applicable product code has been assigned to each authorized device category. The product codes are listed in the tables for each category of devices that have EUAs. The categories of devices are available on the **Coronavirus Disease 2019 (COVID-19) Emergency Use Authorizations for Medical Devices** page, with codes listed in the EUA tables for each type of non-IVD device.

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[p] Consistent with FDA's longstanding practice of posting the relevant scientific reviews after new drug and biological product approvals, we will disclose information from EUA review documents as appropriate after our disclosure review and process is complete. As a part of this process, the FDA may redact certain information that is protected from disclosure under the law. The redacted information may vary depending on the type of data contained in the reviews and whether the requestor consents to the release of information that is protected from disclosure under the law.

[q] The COVID-19 EUA FAERS Public Dashboard is available at: **https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-public-dashboard**. After launching the FAERS Public Dashboard, click on the COVID-19 EUA link at the top of the home page to open the COVID-19 EUA FAERS Public Dashboard.

Additional EUA transparency resources from FDA include:

- **A conversation with the FDA Chief Scientist: Learn about the EUA Process** (Health Equity Forum podcast, June 2021)
- **The Path for a COVID-19 Vaccine from Research to EUA** (infographic)
- **Emergency Use Authorization for Vaccines Explained**
- **The FDA's Vaccines and Related Biological Products Advisory Committee and its Role in Advising the Agency on COVID-19 Vaccines** (FDA Voices, October 2020)
- **Vaccine EUA Questions and Answers for Stakeholders**, with answers to legal questions

3d rendered image of Ebola virus

RESPONDING TO EMERGING INFECTIOUS DISEASE PUBLIC HEALTH THREATS

During infectious disease outbreak and epidemic responses, FDA works proactively with U.S. government partners, medical product developers, and international partners (including the WHO and international regulatory counterparts) to provide scientific and regulatory advice to help facilitate the development and availability of MCMs.

In addition to responding to specific threats, including COVID-19 and Ebola, FDA also engages in numerous activities to support public health emergency preparedness for a variety of threats. In addition to COVID-19 response activities noted on page 6, emerging infectious disease-specific response activities in FY 2021 included:

Ebola

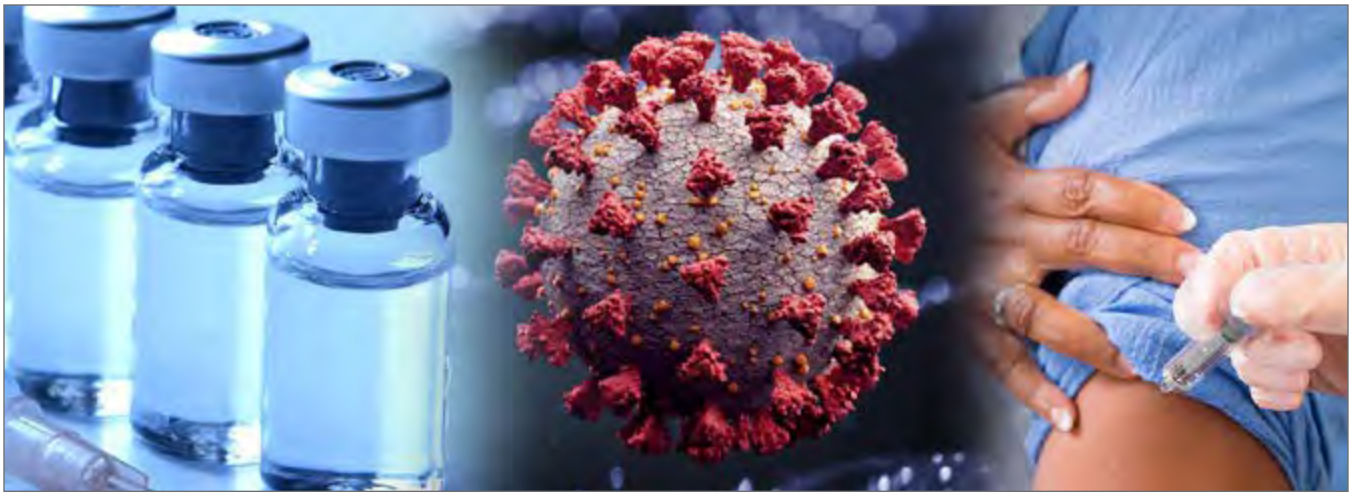
FDA continued to support the international response to outbreaks of Ebola virus disease, including follow-up activities related to the 2014-2016 West Africa outbreak and ongoing response to the most recent outbreaks in Guinea and DRC continuing into 2021. In FY 2021, FDA:

- Continued to work closely with interagency partners, medical product developers, the WHO, and international regulatory counterparts to help move candidate medical products for Ebola forward in development as quickly as possible. For example, FDA participated in discussions of potential clinical trial approaches including a trial comparing several investigational therapeutics against a control arm that began in 2018 and issued preliminary results in 2019.[85] Based on preliminary findings in this NIH trial, FDA continued to provide regulatory guidance to product developers in FY 2021.[86] FDA also provided to WHO study recommendations for the evaluation of rapid Ebola antigen-based diagnostic tests to facilitate data

Box 2: Key FDA emerging threat response activities
Collaborating closely with HHS, other federal agencies, and international partners in preparedness and response decisions regarding MCM development and use
Providing **review and feedback** on development proposals including clinical trial design and data assessment
Maintaining contact with drug, vaccine, and device (including diagnostic test) developers, and **expediting the regulatory review** of data for products that are currently in the pipeline and products that are still very early in development
Advising on design and set-up of **clinical trials** for establishing the safety and efficacy of investigational products for the treatment and/or prevention of emerging infectious diseases, including COVID-19, Ebola and Zika
Supporting FDA's ongoing efforts to **protect the safety of the nation's blood supply** and human cells, tissues, and cellular and tissue-based products (HCT/Ps) for transplantation
Enabling **access to investigational MCMs**—when necessary—through an appropriate mechanism such as under an expanded access protocol or for emergency use under an EUA, including review of expanded access protocols that may be used in Ebola outbreaks when a suitable clinical trial is not available, and updating EUA information for Zika and Ebola diagnostics that have not yet met requirements for full marketing clearance
Addressing issues related to the **import and export** of investigational MCMs
Preparing to implement **safety surveillance** programs for adverse events associated with MCM use and take appropriate action if safety issues are identified
Monitoring the **MCM supply chain** to identify product shortages and distribution of misbranded/counterfeit products
Monitoring **false product claims**, and taking appropriate action when necessary to protect consumers

collection for future marketing submissions.

- Continued work to facilitate access to available medical products through appropriate regulatory mechanisms when necessary and to protect consumers from fraudulent products and false product claims related to Ebola.
- Continued to work with manufacturers of authorized Ebola diagnostics to make rapid tests available, as well as advance these products toward market approval.
- Continued extramural research to expand a biobank of plasma and peripheral blood mononuclear cell (PBMC) samples to help support the development of MCMs against Ebola virus. (Also see ***Medical Countermeasure Regulatory Science***)



ACTION TEAMS

Under the MCMi Program, FDA established multidisciplinary Public Health and Security Action Teams (Action Teams) as necessary to advance MCMs for priority threats by working with internal and external entities—as appropriate—to identify and catalyze the resolution of regulatory and scientific challenges to MCM development. The following information summarizes activities of the Action Teams that were active in FY 2021.

Microbial Sequencing and Multiplex *In Vitro* Diagnostics Action Team

This Action Team continued its work to support sequence-based diagnostic device development. Such diagnostics may include multiplex diagnostic devices, which test for multiple pathogens simultaneously from a single clinical specimen, providing valuable information when responding to a public health emergency.

Key activities during FY 2021 included:

- Continuing collaboration with the National Center for Biotechnology Information (NCBI), the Lawrence Livermore National Laboratory (LLNL), and the Institute for Genome Sciences at the University of Maryland to establish quality criteria for microbial reference databases that will be critical to developers seeking to validate their candidate next-generation sequencing (NGS)-based IVD tests.
- Continuing to facilitate the population of a publicly available **database** for reference-grade microbial genomic sequences, **FDA-ARGOS**.[r] In FY 2021, FDA continued to seek **SARS-CoV-2 reference-grade sequence data** for the FDA-ARGOS database.[87]
- Continuing collaboration with the National Institute of Standards and Technology (NIST) to develop mixed microbial reference materials that will be critical to developers seeking to validate their candidate NGS-based IVD tests, and produce both microbial and human reference genome samples and materials to support the development and validation of NGS. instrumentation/software platforms for sequencing microorganism and human nucleic acids.
- Sustaining an interactive collaboration with DoD on the development of its Next-Generation Diagnostic System (NGDS Increment II).

FDA/DoD Enhanced Engagement Action Team

This Action Team[88] continued its efforts to facilitate the development and regulatory assessment of MCMs and related technologies primarily to support U.S. military personnel and trauma victims. Key FY 2021 activities included:

- Working with DoD partners to support COVID-19 response efforts, including:
  - The Joint Rapid Acquisition Cell-Screening and Diagnostics Capability (JRAC-SDC) to assist shortage analysis supporting diagnostics industrial base expansion efforts for HHS and the DoD Clinical Laboratory Supply Working Group to understand critical clinical lab supplies, reagents, and consumables currently in short supply as a result of SARS-CoV-2.
  - The use of EUA diagnostic tests.

[r] FDA-ARGOS was established in FY 2014, through NCBI, to sequence approximately 2,000 isolates. This database is being expanded to generate 150 high-quality, nearly complete draft genome sequences of mosquito-borne viral pathogens, including Zika virus sequences. As part of this project, FDA set up collaborations to acquire the following prospective samples: 1) clinical isolates from Children's Hospital and George Washington University in Washington, D.C., to enhance diversity of GenBank, 2) biothreat and near-neighbor isolates/gDNA from the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID)/Critical Reagents Program (CRP), 3) Ebola isolates/gDNA from Public Health Canada/NIAID) collaboration and USAMRIID/CRP, 4) antimicrobial resistance (AMR) isolates from Children's Hospital, and 5) difficult-to-acquire isolates from the American Type Culture Collection (ATCC). The FDA-ARGOS database is available at **https://www.ncbi.nlm.nih.gov/bioproject/231221**

  - The development of new ventilators, and the 3D printing of medical products, including PPE.
  - With the U.S. Army Medical Research and Development Command's (USAMRDC) Telemedicine and Advanced Technology Research Center (TATRC), supporting the rapid development, deployment and testing of the National Emergency Telecritical Care Network (NETCCN) to support the COVID-19 response.
- Continuing a **joint program** established under **Public Law 115-92** to prioritize the efficient development of safe and effective medical products intended for deployed American military personnel, including:
  - Working closely with DoD's **Office of Health Affairs** to better understand the military's medical needs for deployed personnel;
  - Expediting the review of priority DoD medical products in a manner similar to products under the **breakthrough therapy designation program**; and
  - Providing ongoing technical advice to DoD to aid in the rapid development and manufacturing of medical products for use by the military.[s]
- Continuing a formal fellowship program between FDA and DoD to support the training of DoD scientific and medical personnel in medical product development and FDA's regulatory processes. Two DoD laboratory experts are currently being cross-trained in regulatory review at FDA.
- Discussing the development of autonomous systems and closed-loop control technologies in medical care as part of a continued collaboration between FDA and DoD on the development of autonomous systems.

[s] In FY 2019, FDA and DoD **signed** a Memorandum of Understanding (MOU) setting forth the framework for the ongoing partnership and the creation of a robust program that can better serve the health care needs of American military personnel. This MOU, available at: available at: **https://www.fda.gov/about-fda/domestic-mous/mou-225-19-001**, builds upon the work of both agencies to foster and prioritize the efficient development of safe and effective medical products intended to save the lives of American service members.

- Sharing regulatory considerations and updates on additive manufacturing. FDA and the U.S. Army Medical Logistics Command conducted a meeting on additive manufacturing of medical devices and medical device components, and continuing regular discussions on this topic.

Acute Radiation Syndrome (ARS) Action Team

This Action Team continued its efforts to clarify the regulatory requirements for development of radiological/nuclear (rad/nuc) MCMs, which include products for improving survival and mitigating or treating injuries from rad/nuc events, and products for determining subject exposures in a nuclear detonation. Key activities during FY 2021 included:

- Facilitating cross-agency interaction and supporting FDA rad/nuc MCM activities. In FY 2021, FDA hosted two meetings with NIAID to discuss cutaneous radiation injury animal model development and testing and one to discuss regulatory and scientific issues related to developing MCMs for gastrointestinal ARS (GI-ARS).
- Continuing interaction with BARDA to address regulatory issues related to development of radiation biodosimetry medical devices.
- Interacting with NIAID on MCM development for radiation-induced thrombocytopenia.
- Providing regulatory input on draft FEMA guidance for planning response to a nuclear detonation.
- Providing regulatory input on draft HHS Assistant Secretary for Preparedness and Response (ASPR) and Global Health Security Initiative (GHSI) Nuclear Detonation Playbook to support emergency preparedness.
- Sharing with FDA reviewers the latest scientific research and review related to radiation-induced skin injuries and discussing issues and challenges in development of products for cutaneous radiation injuries.

REGULATORY ADVICE AND GUIDANCE

During FY 2021, FDA continued to provide regulatory advice and guidance to sponsors and applicants of MCMs and our federal partners funding MCM development, to help foster the development and availability of various MCMs. FDA provides regulatory advice and guidance through a variety of mechanisms including direct engagement with sponsors and applicants, issuing **guidance documents**, and holding **Advisory Committee** meetings and public workshops. As noted previously, FDA is committed to providing timely recommendations, regulatory information, guidance, and technical assistance necessary to support rapid COVID-19 response efforts. In addition to continually communicating with stakeholders in frequent web updates, emails, and responses to individual inquiries, in FY 2020 and FY 2021, FDA issued 76 **guidance documents** (62 in FY 2020, and 14 in FY 2021) to provide updated policies, transparency, and regulatory flexibility, as appropriate, to address the vital medical products and public health issues facing

> FDA issued more than 75 guidance documents in FY 2020 and FY 2021 to provide updated policies, transparency, and regulatory flexibility during COVID-19.

the U.S. during this pandemic; the agency continues to update these guidances, including expiring temporary COVID-19 guidances when circumstances warrant. These guidances include diagnostics, PPE, ventilators, other medical devices, conduct of clinical trials of medical products, blood supply, hand sanitizers, and other topics.[89] FDA also issued additional guidance documents that help foster MCM development and availability, and sought input from a variety of stakeholders through webinars, workshops, town hall meetings, and

other engagements.

FDA medical product review centers engage with MCM sponsors and applicants throughout the product life cycle. For example, FDA reviews IND applications and Investigational Device Exemptions (IDEs) and responds to questions from sponsors, applicants, and federal agencies supporting product development. FDA medical product review centers have extensive interactions to discuss testing, data requirements, and nonclinical development plans to move candidate MCMs into clinical development and assess progress as these specialized product candidates move through clinical development toward a marketing application. FDA also continues to engage with sponsors and applicants to address any issues that arise during regulatory review as well as during the post-marketing phase for these MCMs.

FDA has established policies and procedures for conducting formal meetings with product sponsors or applicants. For detailed information on meetings about product development with CDER and the Center for Biologics Evaluation and Research (CBER), see the revised draft guidance **Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products**.[90] Formal meetings are held—as needed—at the request of a product sponsor or applicant, and requests for meetings are granted unless there is a substantive reason for denying the request (e.g., the product for which the meeting is requested is not sufficiently developed to warrant the type of meeting sought).[t] When FDA denies a request for a meeting, the sponsor or applicant is provided feedback on steps required to warrant a meeting.

CBER and CDER categorize formal meetings with product sponsors and applicants as Type A, B, and C. Type A meetings are meetings to help an otherwise stalled product development program proceed (such as a dispute resolution meeting, a meeting to discuss a clinical hold,[u] and a Special Protocol Assessment (SPA) meeting[91]).

Type B meetings are meetings held at pivotal points during product development to help products move into and through clinical development to marketing application (i.e., pre-IND application meetings, certain end-of-phase 1 meetings, end-of-phase 2/pre-phase 3 meetings, and pre-New Drug Application (NDA)/BLA). Type B meetings also include pre-EUA meetings, Risk Evaluation and Mitigation Strategies (REMS) meetings, and certain meetings for breakthrough therapy-designated products, as explained in the revised draft guidance Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products.

Type C meetings are any meetings other than a Type A or Type B meeting, and can address a range of issues related to product development (e.g., discussions related to data requirements, scientific issues related to product development and manufacturing, post-marketing commitments or requirements, etc.). Meetings that are not categorized as Type A, B, or C are non-PDUFA meetings such as meetings on a sponsor's compliance status or follow-up on post-marketing commitments.

To provide general considerations to assist sponsors in preparing pre-IND meeting requests for COVID-19 related drugs for the duration of the COVID-19 public health emergency, in May 2020, FDA issued the guidance **COVID-19 Public Health Emergency: General Considerations for Pre-IND Meeting Requests for COVID-19 Related Drugs and Bio-**

[t] Formal meetings may also be rescheduled or canceled based on criteria described in FDA guidance.

[u] A clinical hold is an order issued by FDA to a product sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. See 21 Code of Federal Regulations (CFR) 312.42 for more information on clinical holds.

Table 5: FY 2021 formal meetings between CBER/CDER and MCM sponsors or applicants

Meeting Type	CBER	CDER
Type A	0	1
Type B	24	13
Type C	13	4
Total	**37**	**18**

Table 6: FY 2021 formal meetings between CDRH and MCM sponsors or applicants

Meeting Type	CDRH
Pre-Submission	63
Submission	9
Total	**72**

logical Products.[92] As described in further detail in this guidance, FDA recommends that sponsors initiate all drug development interactions for COVID-19 related drugs through Pre-IND meeting requests.

In FY 2021, CBER held 37 formal meetings with MCM sponsors or applicants and 215 other (non-PDUFA) meetings, and CDER held 18 formal meetings (***Table 5***) and 15 other (non-PDUFA) meetings.

CDRH categorizes its formal meetings with product sponsors as Pre-Submission (Pre-sub) and 510(k)/PMA Submission meetings. Pre-sub meetings are designed for FDA staff to provide feedback in response to specific questions related to product development, including planned nonclinical evaluations, proposed clinical study protocols, regulatory pathways, or data analysis recommendations prior to making a submission.

CDRH reviewed 90 Pre-subs and 6 Submissions (marketing submissions) for MCM medical devices in FY 2021. FDA provided extensive written feedback on the Pre-subs, and many of these sponsors elected to cancel additional formal follow-up meetings after receiving this information, as they did not see the need for the originally requested formal meeting. If the sponsor wanted to further discuss the written Pre-sub feedback, a formal Pre-sub meeting was held. Submission issue meetings are sometimes held to discuss deficiencies identified during premarket review of device marketing applications and to provide clarification of FDA's questions or to discuss an approach to address any complex issues identified. In FY 2021, CDRH provided written feedback for 90 MCM Pre-sub or Submission applications and held 63 formal Pre-sub and 9 formal Submission meetings with MCM sponsors or applicants (***Table 6***).

In addition to the marketing applications discussed in the previous paragraph, CDRH had significant interactions with MCM sponsors during the pre-EUA and EUA Interactive Review process. The **Interactive Review** process was developed to facilitate the efficient and timely review and evaluation of pre-EUA and EUA submissions through increased interaction between FDA and sponsors, including the exchange of scientific and regulatory information.[93] In FY 2021, CDRH reviewed and provided written feedback on numerous pre-EUAs and EUA submissions, with many submissions involving multiple rounds of written feedback provided during interactive review, and held pre-EUA and EUA meetings to facilitate validation and development (telecons).

FDA also issued in May 2020 a guidance document, **Effects of the COVID-19 Public Health Emergency on Formal Meetings and User Fee Applications — Questions and Answers**[94] for drugs and biologics, and in June 2020, **Effects of the COVID-19 Public Health Emergency on Formal Meetings and User Fee Applications for Medical Devices - Questions and Answers**.[95]

In addition, eligible MCM sponsors or applicants can request a Regulatory Management Plan (RMP), setting forth a process whereby the terms for interactions between FDA and the product sponsor or applicant can be delineated.[v] FDA did not receive any written MCM-related RMP requests in FY 2021.[96]

[v] Under PAHPRA, MCMs eligible for RMPs are security countermeasures with respect to which the Secretary of HHS has entered into a procurement contract under section 319F-2(c) of the PHS Act (42 USCS § 247d-6b(c)); or MCMs with respect to which the Biomedical Advanced Research and Development Authority (BARDA) has provided funding under section 319L of the PHS Act (42 USCS § 247d-7e) for advanced research and development. (FD&C Act Sec. 565(f); 21 U.S.C. § 360bbb-4(f)). While RMPs are

FDA also conducted enhanced inspection and compliance activities to support early identification of any problems that might impede MCM product development. FDA provided technical advice to minimize risk during MCM product manufacturing, including pre-approval inspections or site visits to ensure that manufacturing establishments are capable of adequately manufacturing MCM products, and that submitted application data are accurate.

In addition to its direct work with MCM sponsors and applicants, FDA also issues guidance documents that help foster MCM development and availability.[w] Guidance documents issued during FY 2021 directly related or applicable to MCMs policies or regulatory issues are listed in ***Appendix 3: MCM-Related Guidance Issued in FY 2021***.

FDA also holds Advisory Committee meetings and public workshops to obtain independent input and expert advice on scientific, technical, and policy matters to facilitate MCM development. Key meetings and public workshops held during FY 2021 are listed in ***Appendix 4: Key MCM-Related Meetings Held in FY 2021***. In addition to these FDA-hosted meetings, FDA experts continued to participate in and present at a wide variety of other meetings, workshops, and conferences.[97, 98]

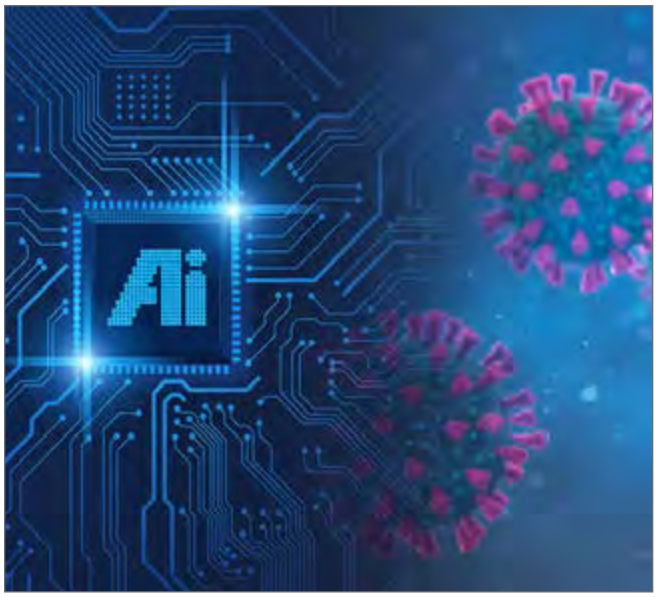
COLLABORATION AND COMMUNICATION

During FY 2021, FDA continued to **collaborate** extensively with other USG components, including with PHEMCE and DoD partners, to foster the development and availability of MCMs. FDA provided subject matter expertise and technical assistance to approximately 70 standing interagency and HHS/PHEMCE- and DoD-specific committees and working groups that develop MCM requirements, plans, priorities, and policies and conduct program oversight and integration. These standing committees and working groups met on a weekly, monthly, bimonthly, quarterly, semi-annually, or as-needed basis depending on the requirements of the issues at hand. These committees and working groups addressed a range of topics across the full spectrum of activities associated with MCMs including threat assessment, requirements setting, product development, procurement, stockpiling, utilization, and **monitoring and assessment** of MCMs after they have been dispensed or administered. In addition, FDA supported USG partners by providing subject matter expertise for various MCM-related proposal reviews. FDA also continues to support implementation of the 2018 National Biodefense Strategy.[99]

FDA continued to work with state, local, tribal, and territorial (**SLTT**) public health authorities and responders and public health non-governmental organizations (NGOs) to support MCM preparedness and response capabilities at the state and local levels, including responding to numerous legal and regulatory inquiries concerning EUA and other emergency use authorities, and MCM stockpiling, expiry dating,

to be established for all security countermeasures for which they are requested, the Director of BARDA, in consultation with the FDA Commissioner, prioritizes which otherwise eligible MCMs may receive RMPs if resources are not available to establish RMPs for all eligible MCMs for which requests are submitted. (FD&C Act Sec. 565(f)(7); 21 U.S.C. § 360bbb-4(f))(7)

[w] Guidance documents are documents prepared for FDA staff, applicants/sponsors, industry, and the public that describe FDA's interpretation of or policy on a regulatory issue. Guidance documents include, but are not limited to, documents that relate to: the design, production, labeling, promotion, manufacturing, and testing of regulated products; the processing, content, and evaluation or approval of submissions; and inspection and enforcement policies. (21 C.F.R. § 10.115(b))



distribution, and dispensing. FDA continues to participate in multiple national-level workshops and meetings on public health and legal preparedness. For example, FDA continues to sustain support for and participate in:

- The annual Public Health **Preparedness Summit** convened by the National Association of County and City Health Officials (NACCHO).
- The National Academies of Sciences, Engineering, and Medicine, Health and Medicine Division (NASEM-HMD) **Forum on Medical and Public Health Preparedness for Disasters and Emergencies**, to provide national leadership in coordinating ongoing efforts among members from federal, state, and local government; business; and professional associations to develop sustainable partnerships between the public and private sector so that communities are adequately prepared for natural or human-made catastrophic events.
- **TTFED**, launched in February 2019, to help leverage the expertise of each agency to better coordinate implementation of diagnostic tests in clinical and public health laboratories during public health emergencies.[100]

Other key collaborations in FY 2021 include:

NIST

In January 2021, FDA created a new collaboration with NIST through an **MOU**.[101] This MOU is intended to increase U.S. medical supply chain resilience and advanced domestic manufacturing of drugs, biological products and medical devices through adoption of 21st century manufacturing technologies. These include smart technologies, such as AI and machine learning, and emerging manufacturing processes. The MOU signals alignment between senior leadership at both institutions in recognition of the importance of **modernizing regulatory frameworks** as well as industry practices to meet public health needs in the U.S.[102]

NIH and VA

On March 27, 2020, FDA, NIH, and VA **signed an MOU** to share data, and coordinate on open-source medical products for the COVID-19 response with other stakeholders such as America Makes.[103] Within 3 days after the announcement of the MOU on the FDA website, visits to the NIH **3DPX** increased by 709%, and, within one month, 488 designs were uploaded to the site. The NIH 3DPX COVID 3D TRUST collection included 625 designs, with more than 2 million views from nearly every country around the globe. The most popular downloads were face masks, face shields, and ear savers—favorites of small groups with desktop 3D printers responding to the urgent needs of frontline workers. An FDA-funded impact report by America Makes **published in July 2021** identified the number of devices 3D-printed in the beginning of the pandemic. They estimated 38 million face shield parts, 12 million nasal swabs, 2.5 million ear savers, 241,000 mask parts, and 116,000 ventilator parts were 3D-printed in the U.S. between February 15 and July 15, 2020.[104]

NASA

In FY 2018, FDA and the National Aeronautics and Space Administration (NASA) signed an **MOU** to provide mutual support to biomedical research on drugs, biologics, and medical devices and for MCM development.[105] This partnership continues. In 2021, NASA solicited science investigations for **Extended Longevity of 3D Tissues and Microphysiological Systems for Modeling of Acute and Chronic**

Exposures to Stressors (3DTANDMPS).[106] This multi-agency solicitation was sponsored by NASA's Human Exploration and Operations Mission Directorate (HEOMD)'s Human Research Program (HRP), the NIH National Center for Advancing Translational Sciences (NCATS), NIH/NIAID, NCI, HHS/BARDA, and FDA, to solicit for research in support of common cross-organizational goals. This solicitation is focused on adapting existing 3D tissues and microphysiological systems (MPS), also known as "tissue chips" or "organs-on-chips," to **extend the current longevity** of the 3D tissues and MPS to at least 6 months.[107]

NASEM-HMD Board on Global Health, Form on Microbial Threats

FDA participated in three NASEM-HMD **Forum on Microbial Threats** workshops in 2021 to solicit stakeholder discussion and debate on critical scientific and policy issues impacting response to infectious diseases: a February 2021 workshop titled **Systematizing the One Health Approach in Preparedness and Response Efforts for Infectious Disease Outbreaks**; a two-part virtual workshop held in March and September 2021 titled **Towards a Post-Pandemic World: Lessons from COVID-19 for Now and the Future**; and a two-part virtual workshop held in July and September 2021 titled **Innovations for Tackling Tuberculosis in the Time of COVID-19**.

NASEM, Division on Earth and Life Studies, Institute of Laboratory Animal Research (ILAR)

FDA actively participated in planning and presenting topics at the **NASEM ILAR**-hosted **Micro-Physiological Systems for Efficacy and Safety Studies: A Workshop on Advances in Organs-On-Chip Technologies for Animals** held in January 2021. The purpose of the workshop was to promote discussion and understanding of progress made toward developing more physiologically realistic organs-on-chips, particularly regarding developing animal MPSs and sustainable animal chip banks.

Additionally, FDA actively participated in planning ILAR's workshop titled, **Rapid Response by Laboratory Animal Research Institutions During the COVID-19 Pandemic: Lessons Learned**, held in March 2021. The aim of this workshop was to discuss institutional challenges and strategies for addressing them to provide guidance to the broader community for the ongoing pandemic and inform a rapid and sustainable response framework for future pandemics. FDA provided expert input on the content of the workshop, provided or recommended subject matter experts and presented topics, facilitated workshop sessions, and provided input on manuscripts of workshop sessions for publication.

International collaborations

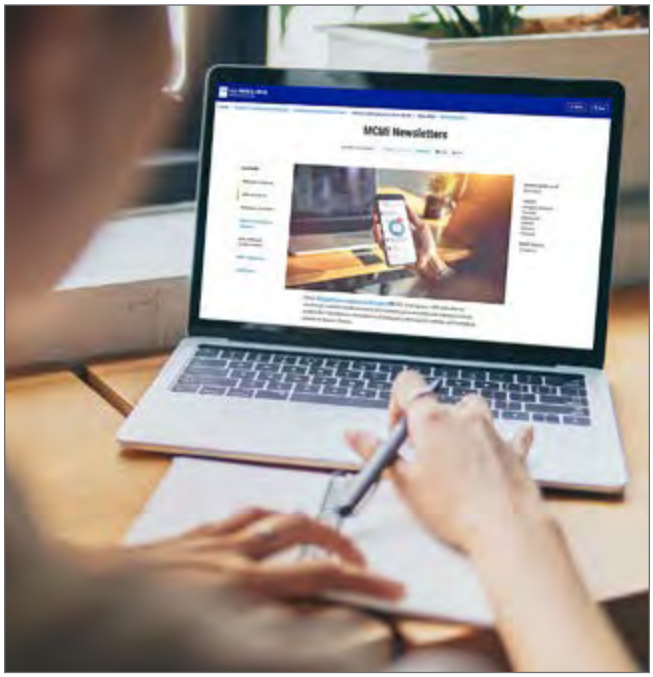
In addition to working with federal and SLTT governments and NGOs, FDA continued to work with international partners such as WHO to foster the development and availability of MCMs.

Agreements between FDA and its international counterparts established in previous fiscal years have continued to support information-sharing and collaboration and have better prepared the international regulatory community to respond to COVID-19 and future public health emergencies.

Examples of FDA's key international MCM collaborations include:

- Working with HHS to help establish an international framework for sharing MCMs during an international public health emergency.
- Supporting and participating in the U.S. government's GHSA and strategy,[108] as well as other HHS-led efforts related to global MCM legal and policy frameworks, including through JEE efforts.[109]
- Implementing CBER-WHO Cooperative Agreements[110] to advance global access to safe and effective vaccines and build capacities for the import, registration, and emergency use of pre-qualified MCM vaccines.
- Participating in international consultations to advance efforts to conduct research, pharmacovigilance, and product development during public health emergencies. For example, FDA is an active participant in:

- **WHO's R&D Blueprint** - The R&D Blueprint is a global strategy and preparedness plan intended to allow the rapid activation of research and development activities during epidemics. Its aim is to fast-track the availability of effective tests, vaccines and medicines that can be used to save lives and avert large-scale crisis.
- **Coalition for Epidemic Preparedness Innovations (CEPI)** - CEPI is an innovative partnership between public, private, philanthropic, and civil organizations that aims to stop future epidemics by developing new vaccines.
- **Global Research Collaboration for Infectious Diseases Preparedness (GloPID-R)** - GloPID-R is the only network of major research funding organizations working on a global scale. Together, these organizations strive to facilitate an effective research response within 48 hours of an infectious disease outbreak.
- **International Coalition of Medicines Regulatory Authorities (ICMRA)** - The ICMRA is comprised of medicines regulators worldwide who have committed to enhanced cooperation with the WHO and among regulatory agencies to encourage submission of regulatory dossiers and evaluation of the submitted information on potential new medicines to address emerging public health threats.
- **Foundation for Innovative New Diagnostics (FIND)** - A WHO Collaborating Centre for Laboratory Strengthening and Diagnostic Technology Evaluation, FIND is a global non-profit organization driving innovation in the development and delivery of diagnostics to combat major diseases affecting the world's poorest populations.



Enhancing communication

In addition to extensive COVID-19-related communication, as noted previously, in FY 2021, FDA continued ongoing work to enhance communication related to MCM preparedness and response through a variety of outreach activities (e.g., MCMi **email newsletter**, social media,[111] and various presentations).

MEDICAL COUNTERMEASURE REGULATORY SCIENCE

In FY 2021, FDA continued to implement the **MCMi Regulatory Science Program** through both intra- and extramural collaborative research, as well as through partnerships with U.S. government agencies, academia, and industry.[x]

MCMs often present unique and complex challenges with respect to developing the data necessary to support public health, clinical, and regulatory decision-making. For example, many of the high-priority threats for which MCMs are being developed do not occur naturally to an extent that would support the conduct of field efficacy studies in humans, and it is not ethical to conduct human challenge studies with threat agents that would pose unacceptable risks to study volunteers. In these situations, efficacy data from adequate and well-controlled animal studies may be used if the results can reasonably be extrapolated to expected human use.

The challenges are even more complex when it comes to developing MCMs for use in specific populations, such as children or pregnant women. For example, ethical evaluation of the participation of children in clinical trials depends on both the level of risk and the prospect of direct benefit to the participant. Thus, in some circumstances it may not be ethical to conduct certain types of clinical trials in the pediatric population to obtain data that can be used for approving pediatric indications for MCMs—such as safety or dosing information—and FDA may rely on the extrapolation of efficacy data from adult populations, along with information and experience the agency has with the use of a particular class of product (e.g., monoclonal antibodies for use in the pediatric population) to the extent permitted by law.[112]

> The MCMi Regulatory Science Program helps translate cutting-edge technologies into innovative, safe, and effective MCMs.

The goal of the MCMi Regulatory Science Program is to develop tools, standards, and approaches to assess MCM safety, efficacy, quality, and performance, and to help translate cutting-edge science and technology into innovative, safe, and effective MCMs, including for specific populations.

FDA has established a broad and robust intra- and extramural research portfolio under the MCMi Regulatory Science Program to meet its goals in these priority research areas.[113] In a 2021 report, **Advancing Regulatory Science at FDA: Focus Areas of Regulatory Science (FARS)**, FDA identified public health preparedness and response as a key area

[x] Many projects described in this section are preliminary and/or exploratory in nature. Listing a project does not imply any determination with regard to utility in public health, clinical, or regulatory decision-making.

Box 3: MCM regulatory science research areas
Priority research areas sustained under the MCMi Regulatory Science Program to support preparedness for high-priority threats include:
Identifying, developing, and qualifying drug development tools, such as animal models and immune biomarkers, to assess safety and efficacy of MCMs
Developing and evaluating novel assays and models to study emerging infectious diseases
Developing and qualifying *in silico* predictive models (e.g., computational models) and *in vitro* assays (e.g., microphysiological systems) to complement the use of *in vivo* animal models to assess safety and efficacy of MCMs
Developing tools to support validation of next-generation *in vitro* diagnostic platforms
Developing reference materials related to CBRN threat agents and emerging infectious diseases to facilitate development of MCMs
Assessing the performance of emergency medical equipment including PPE
Enhancing emergency preparedness and response capabilities, and tracking and evaluating the safety and clinical benefit of MCMs used during public health emergencies
Advancing broadly applicable, commercially ready tools, technologies, and platforms that can improve the manufacturing efficiency, consistency, and quality of MCMs

needing continued, targeted investment in regulatory science research to facilitate development of innovative products, provide data and methods to inform regulatory decision-making, and improve guidance to sponsors.[114] To ensure that the MCMi Regulatory Science Program is appropriately targeted and coordinated with USG MCM priorities, FDA coordinates with interagency partners including representatives from NIH, CDC, BARDA, and DoD to evaluate MCMi Regulatory Science Program research proposals for scientific/technical merit, feasibility, and for alignment with PHEMCE priorities. FDA continually engages with USG stakeholders to maintain an MCMi Regulatory Science Program that actively addresses current regulatory science gaps.

MCM-related **regulatory science research tools** funded (or partially funded) by FDA are available at no charge to help MCM researchers advance their products, and help FDA reviewers evaluate MCM products for approval.[115]

Since late January 2020, and continuing into FY 2021, FDA has initiated a number of regulatory science projects to support development and evaluation of MCMs that would prevent, treat, or diagnose COVID-19. Some notable activities since these efforts began include:

- Developing a **reference panel** to aid in the evaluation of diagnostic tests for SARS-CoV-2. The reference panel provided test developers with well characterized reagents to compare the sensitivity and specificity of different molecular diagnostic tests.
  - From February through mid-May 2020, FDA issued a total of 59 EUAs for IVDs for the qualitative detection of nucleic acid from SARS-CoV-2 based on validation data using contrived specimens derived from SARS-CoV-2 viral RNA.
  - As the pandemic progressed and more patient specimens became available, on May 11, 2020, the FDA recommended in the **Policy for Coronavirus Disease-2019 Tests** that developers obtain and use patient specimens to validate their tests.
  - FDA began distribution of the FDA SARS-CoV-2 Reference Panel in May 2020. As of November 14, 2020, the FDA had sent the reference panel to developers of 190 authorized assays, and reported sensitivity mean estimates for more than 125 authorized tests.[116]
- Participating in evaluation of antibody and RNA reference materials that are being developed by the National Institute of Biological Standards and Control under the auspices of the WHO, as candidate international standards for assays used for SARS-CoV-2/COVID-19.
- Supporting animal models that might help to evaluate COVID-19 vaccines and therapeutics.
- Supporting development of *in vitro* models (including MPS) that might be relevant to exploration of infectious processes and potential countermeasure activity.
- Developing assays that might be useful in evaluation of vaccine and therapeutic responses.

- Characterizing coronavirus variants and host/pathogen responses.
- Describing responses (e.g., MCM efficacy and pathogenicity) in nonclinical and clinical samples of SARS-CoV-2 including variants of concern.
- Developing computational models for PPE integrity to support supply chain resiliency.

As detailed in the ***COVID-19 Response*** section, in FY 2021, the MCMi Regulatory Science Program awarded two new contracts, and revised several previously awarded extramural research contracts to expand efforts supporting COVID-19 MCM development. Additionally, an extramural project with the **University of California Los Angeles** was expanded to develop a Marburg clinical biobank to support vaccine development. This work was co-funded by DTRA.

FDA intramural research supported by MCMi includes 12 new intramural research projects performed by FDA scientists, including development of assays and models (e.g., computational, *in vitro*, and nonclinical) to facilitate development and evaluation of MCMs for nerve agents and infectious diseases including influenza, SARS-CoV-2, Marburg, and Zika.

In FY 2020, FDA posted to our website a **catalog of regulatory science tools to help assess new medical devices**. This catalog, which continues to be updated, collates a variety of regulatory science tools that the FDA's CDRH Office of Science and Engineering Labs (OSEL) developed and plans to expand as new tools become available. FDA also updated its **Regulatory Science Research Tools** web page with additional information about regulatory science tools funded, at least in part, by FDA, and freely available to researchers, including the FDA SARS-CoV-2 reference panel.[117] Funded by MCMi, the FDA SARS-CoV-2 Reference Panel allows for a more precise comparison of the analytical performance of different molecular IVD assays intended to detect SARS-CoV-2. The Reference Panel contains common, independent, and well-characterized reference material that is available to developers of SARS-CoV-2 nucleic acid-based amplification tests (NAATs) for which EUA was requested. FDA has made **SARS-CoV-2 Reference Panel comparative data** publicly available.[118]

FDA also continued work to build and maintain a national capability to **monitor and assess MCMs** after they are dispensed or administered in response to a CBRN threat or emerging infectious disease. In FY 2021, FDA continued collaboration with Harvard Pilgrim Health Care to explore how the Sentinel System—an active surveillance system that uses routine querying tools and pre-existing electronic health care data from multiple sources to monitor the safety of regulated medical products—may inform study protocols for MCM safety and effectiveness and to provide a valuable baseline for comparison during a public health emergency. The FDA Sentinel System is conducting a number of **activities in support of the COVID-19 response**.[119] Additionally, FDA is participating in the Systemic Harmonization and Interoperability Enhancement for Laboratory Data **(SHIELD) collaborative**,[120] in partnership with the COVID-19 **Diagnostics Evidence Accelerator**,[121] to harmonize COVID-19 test data referenced in the HHS COVID-19 laboratory data reporting requirements,[y] to support evaluation of real-world performance of SARS-CoV-2 diagnostic tests and antibody tests.

FY 2021 MCMi Regulatory Science Program activities are included in ***Table 7***.

Digital generated image of COVID-19 vaccine bottles standing on robotic production line

[y] COVID-19 Pandemic Response, Laboratory Data Reporting: CARES Act Section 18115, available at: **https://www.hhs.gov/sites/default/files/covid-19-laboratory-data-reporting-guidance.pdf**

Table 7: MCMi Regulatory Science Program activities in FY 2021
CBRN
Developing models of radiation damage in lung, gut, and bone marrow **organs-on-chips** and then using these models to test candidate MCMs to treat such damage. In FY 2021, the project continued to characterize the interplay between human bone marrow organs-on-chips and intestine organs-on-chips that include a complex human gut microbiome in response to radiation exposure.
Developing novel reagents to support MCMs for organophosphate nerve agents
Working with the Reagan-Udall Foundation to hold stakeholder meetings on EUA processes and the use of MCM master files to advance use of platform technologies to support development of MCMs
Emerging threats (e.g., SARS-CoV-2, Ebola, and Zika)
Expanding a **database of reference-grade nucleic acid sequences** for emerging threats, to include viruses such as Ebola and Zika, and antimicrobial-resistant pathogens. In April 2020, **SARS-CoV-2 reference-grade sequence data** was added to the FDA-ARGOS database.[122]
Initiating a project to develop quality metric tools for next-generation sequencing databases to support SARS-CoV-2 and influenza diagnostics. This project will also complement the MCMi-supported FDA-ARGOS database.
Distributing **Zika virus RNA reference materials** to manufacturers of nucleic acid-based diagnostic tests for Zika virus, which **supported product testing for EUA and 510(k) submissions**[123]
Distributing **Zika serological reference panel** to manufacturers seeking EUA for serological diagnostic tests specific for detection of recent Zika virus infection
Providing Zika test developers with study recommendations for Zika nucleic acid-based diagnostic tests and Zika serological assay premarket submissions
Continuing to support improvement of small and large animal models for emerging threats (e.g. SARS-CoV-2, Ebola, and Zika)
Conducting survivor studies to better understand Ebola's after-effects, to help find new treatments
Identifying target peptide sequences for a Zika IgM immunoglobulin M (IgM) diagnostic device
Exploring antibody responses following Zika virus infection or vaccination in humans, to help support development of effective vaccines and serodiagnostics
Developing MPS models for emerging threats (including Zika and SARS-CoV-2) as tools to support MCM development
Applying advanced transcriptomic analysis (the study of all messenger RNA from the genes of an organism) to **compare responses to Ebola virus disease in humans and in animals**, to help identify biomarkers of Ebola, and expected disease outcomes
Studying **antibody responses** in Ebola survivors and in vaccinated individuals, and evaluation of potential countermeasures
In collaboration with DoD, working to better understand the **microbial pathogenesis** of Ebola, Marburg, Rift Valley fever, Crimean Congo hemorrhagic fever, Chikungunya, and Zika viruses
Establishing the largest Ebola virus and host gene expression (i.e., transcriptomics) study to date, using the latest sequencing technologies, including single-cell sequencing methods, to **assess how Ebola virus evolves and spreads** within the body. In FY 2021, this project was expanded to better understand viral infection, pathogenesis, and immune response to SARS-CoV-2 to inform development and review of MCMs for COVID-19.
Developing a **unique biobank** of clinical Ebola samples from over 2,500 participants, including investigational Ebola vaccinees and Ebola survivors, to characterize the durability and correlates of vaccine-induced and natural immunity to Ebola virus disease (EVD). In FY 2021, the project was expanded, in collaboration with DTRA, to develop a Marburg clinical biobank to support vaccine development.

Analyzing SARS-CoV-2, SARS-CoV, and Middle East Respiratory Syndrome coronavirus (MERS)-CoV clinical samples, collected through global partnerships, to better understand coronavirus evolution and virulence, characterize host-pathogen interactions and immunity, and identify biomarkers of disease progression and severity. In FY 2021, this project was expanded to study variants of concern, such as the delta variant, and potential impacts on MCM efficacy.
Profiling circulating immune signatures of coronavirus infection and completing COVID-19 pathology tissue imaging, leveraging novel tools to define the characteristics of tissue viral reservoirs (cell types or areas of the body where the virus persists), and learning more about how SARS-CoV-2 affects different systems in the body. In FY 2021, FDA expanded this contract to identify biomarkers and immune correlates of protection to further understanding of responses across diverse populations, including race, ethnicity, sex, and age to aid the development and evaluation of MCMs for all.
Developing and distributing a **reference panel to aid in the evaluation of diagnostic tests for SARS-CoV-2**. The reference panel provides test developers with well characterized reagents to compare the sensitivity and specificity of different molecular diagnostic tests.[124]
Participating in evaluation of antibody and RNA reference materials that are being developed by the National Institute of Biological Standards and Control under the auspices of the WHO, as candidate international standards for assays used for SARS-CoV-2/COVID-19
Developing tools and assays that support evaluation of COVID-19 MCMs
Collaborating with NIH to design a study of SARS-CoV-2 hyperimmune globulin to be conducted by NIAID/NIH
Developing models of emerging infectious diseases (such as Ebola, Zika, and SARS-CoV-2) in organ chips for potential testing of MCMs
Supporting development of COVID-19 MCMs, including a **contract** awarded in FY 2021 to CSIRO, Australia's scientific research agency, to strengthen coronavirus models through systems biology, AI, and machine learning
Coordinating with USG partners to ensure that USG-supported candidate MCMs could be independently evaluated for activity against SARS-CoV-2 variants of concern
Developing and validating methods to detect viral pathogens (e.g., African swine fever) that pose a significant threat to animal health and the food supply
Pandemic influenza
Demonstrating the ability of a universal influenza vaccine candidate to **reduce the transmission of influenza virus** in mice, even though this vaccine does not completely block infection by the virus[125]
Characterizing immune responses against influenza virus proteins to support development of pandemic and universal influenza vaccine
Evaluating the impact of influenza polymerase mutations on influenza replication and sensitivity to anti-influenza drugs
Public health emergency preparedness and response
Continuing support of the **CDC & FDA Antibiotic Resistance Isolate Bank**
Establishing new methods to test PPE to help mitigate shortages during a public health emergency

FDA also expanded and sustained MCM regulatory science collaborations in FY 2021. For example, FDA:

- Continued collaborations with the Defense Advanced Research Projects Agency (DARPA) and DTRA on regulatory science research for the development of innovative regulatory tools, such as biomimetic models.
- Expanded collaboration with DTRA to develop a Marburg clinical biobank.
- Continued work with the National Interagency Confederation for Biological Research (NICBR) to collaborate and share technical expertise and scientific services in the pursuit of a healthier and more secure nation.
- Continued to support a three-year interagency agreement with USAMRIID to **establish a better understanding of the microbial pathogenesis of several viruses**: Ebola, Marburg, Rift Valley fever, Crimean Congo hemorrhagic fever, Chikungunya virus, and Zika. This project leverages the U.S. Army's Joint Mobile Emerging Disease Intervention Clinical Capability (JMEDICC) project.
- Continued collaborations with NIAID to support innovative analytical technologies for emerging infectious diseases through co-sponsorship of Stanford University's **Survivor Studies: Better Understanding Ebola's After-Effects to Help Find New Treatments** and University of Liverpool's **FDA and Global Partners to Analyze Coronavirus Samples** projects. In FY 2021, FDA established a partnership with NIAID to expand a project developing human organ chips for radiation countermeasure development to develop new organs-on-chips to aid development and testing of MCMs for COVID-19.
- Continued collaborations with the **Bill and Melinda Gates Foundation** on the development and evaluation of home-use influenza diagnostic tests and other common goals to improve public health by stimulating and fostering medical product innovation and enabling medical product development, including MCMs.
- Continued collaborations with NASA on regulatory science research to develop and provide MCMs to support human space exploration.
- Continued serving as one of 14 voting representatives on the HHS Tick-Borne Disease Working Group, established under Section 2062 of the Cures Act [PL 114-255]. The working group is developing recommendations on how to address the growing incidences of diseases transmitted by ticks.[126]
- Continued collaborating and meeting with CDC, BARDA, NIH, DoD, the U.S. Department of Agriculture (USDA), EPA, the U.S. Geological Survey (USGS), and DHS to help develop a national strategy on vector-borne diseases to develop a comprehensive national system to detect, prevent, and respond to these threats. This is a sustained effort to address significant challenges and reverse the upward trends in illness, suffering, and death from vector-borne diseases.

FDA also continues to create and support programs to advance the development and review of MCMs that will be regulated under the Animal Rule. For example, in FY 2021 FDA:

- **Posted** information about FDA's support of and the requirement to use the Clinical Data Interchange Standards Consortium (**CDISC**) for Study Data Tabulation Model version 1.8 (SDTM v1.8) and CDISC Standard for Exchange of Nonclinical Data Implementation Guide–Animal Rule version 1.0 (**SENDIG–AR v1.0**). FDA's support of these new electronic data standards began on March 15, 2020. SEND data sets **will be required** in Animal Rule submissions to CDER for studies initiated after either March 15, 2022, or March 15, 2023, depending on the type of regulatory submission.[127]
- Continued to support the **Animal Model Qualification Program**, which provides a mechanism for the evaluation of product-independent animal models for use in drug and biological product development under the Animal Rule.

ADVANCED MANUFACTURING

Advanced manufacturing can accelerate therapy development, rapidly scale manufacturing capabilities for vaccines and other MCMs, as well as shorten supply chains to increase manufacturing resilience. The potential public health value of advanced manufacturing is even greater in the context of the ongoing COVID-19 pandemic, which has highlighted the strain on supply chains and the need for adaptive manufacturing systems to accelerate the production of MCMs. FDA has established a strong regulatory foundation to support the uptake of advanced manufacturing, and COVID-19 provides the unique impetus to spur further advancement of medical manufacturing.[128]

FDA continues to take creative and flexible approaches to address availability of critical medical products in response to the COVID-19 pandemic. In addition, non-traditional manufacturers and community responders have helped address shortages and gaps in medical supplies during the COVID-19 pandemic, and yielded millions of pieces of equipment and supplies, such as masks, face shields, and other 3D-printed medical devices. In September 2020, FDA funded a study, conducted by **America Makes**, to summarize the impact of 3D printing on the overall COVID-19 response. FDA made this report on the use of additive manufacturing by non-traditional producers public in July 2021. The study shows successes, challenges, and key lessons learned to build on and improve future crisis response. FDA is reviewing the report to assess gaps in the response and potential mitigations for future public health emergencies.[129] Based on data collected during this project, the following were estimated to have been additively manufactured in the U.S. between February 15 and July 15, 2020:

> Advanced manufacturing is a collective term for new medical product manufacturing technologies that can improve drug quality, address shortages of medicines, and speed time-to-market.

- 38 million face shield parts
- 12 million nasal swabs
- 2.5 million ear savers
- 241,000 mask parts
- 116,000 ventilator parts

FDA also funded a **study** to increase the agency's understanding of factors that impact a manufacturer's decision to invest in and adopt digital technologies by identifying both perceived and demonstrated barriers. The project team performed evaluations of nine manufacturers, interviewed representatives, collated the responses, and created a perspective that will allow the agency to assess areas where it can foster greater manufacturing resilience.[130]

In FY 2021, the FDA Office of Counterterrorism and Emerging Threats (**OCET**) acquired a smart manufacturing demonstration system to use as a shared resource FDA-wide. The system is intended to increase FDA capabilities in developing metrics, inspectional guidelines, guidance documents, and policy for supply chain resilience and will help facilitate increased adoption of innovative technologies.[131]

As noted under ***Collaboration and Communication***, a new MOU between FDA and NIST signed in FY 2021 is promoting use of advanced manufacturing methods including real-time analytics and process control to support supply chain resilience and domestic manufacturing.

In September 2021, CBER **funded new grants** to enhance innovations in advanced manufacturing technologies for vaccines against influenza and emerging infectious diseases (four grants), and to support vector manufacturing for diseases affecting very small populations (five grants). Such technologies and processes may increase the domestic production of critical MCMs and other medical products needed for pan-

> A new FDA & NIST collaboration is enabling real-time analytics to support supply chain resilience and domestic manufacturing.

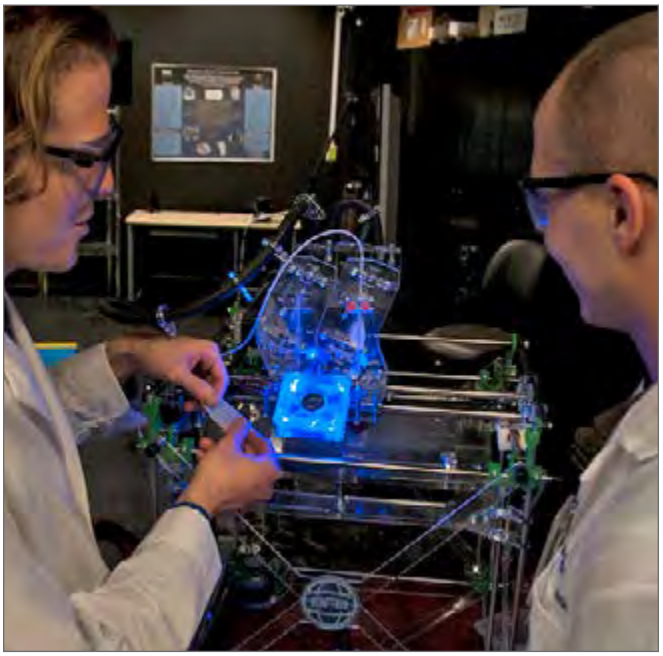
demic or other response activities.

Collaborations begun in previous years also continue. In March 2020, FDA **entered an MOU** with the VA Innovation Ecosystem and the NIH 3D Print Exchange to share data, and coordinate on open-source medical products for the COVID-19 response. As noted under ***Collaboration and Communication***, this project resulted in millions of pieces of PPE and other medical devices being 3D-printed to support front-line COVID-19 response efforts. FDA and the U.S. Army Medical Logistics Command also continue information-sharing begun in previous years on additive manufacturing of medical devices and medical device components.

In FY 2019, FDA signed a Cooperative Research and Development Agreement (CRADA) with the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL). NIIMBL is a **Manufacturing USA** public private partnership (PPP) dedicated to advancing biopharmaceutical manufacturing innovation and workforce development. The CRADA allows FDA to collaborate with biotech stakeholder NIIMBL members, accelerating agency and industry adoption of biotech innovations. FDA actively engages with other PPPs, many of which are **Manufacturing USA Institutes**, including America Makes, **BioFabUSA**, and **NextFlex**, to proactively address regulatory challenges presented by advanced manufacturing technologies, including continuous manufacturing. In addition to PPPs, FDA is engaging with industry and government consortia, such as the **4D Bio^3** consortium of the Uniformed Services University, Naval Research Laboratory, and Walter Reed National Military Medical Center, dedicated to bringing advanced technologies and therapies to military personnel. This work continues and is bolstered by changing needs.

Since 2015, FDA has been working with BARDA to advance innovations in manufacturing for BARDA-supported MCMs, including those manufactured in HHS Centers for Innovation in Advanced Development and Manufacturing (**HHS-CIADM**) facilities. In addition, FDA coordinated with DoD on the opening of its DoD Medical Countermeasures Advanced Development and Manufacturing (MCM ADM) facility, and continues to support ongoing operations. These innovations in manufacturing technology will help enable rapid ramp-up of manufacturing capabilities for vaccines and other MCMs to respond to emerging threats and other public health emergencies, such as pandemic influenza. These technologies could also accelerate the development of therapies for orphan diseases by improving the cost-efficiency of small-scale manufacturing processes, and enable manufacturing process and standards development for emerging therapies including cell and gene therapies, supporting goals of the Cures Act.

In December 2017, FDA became the first regulator worldwide to provide a comprehensive technical framework to advise manufacturers creating medical products on 3D printers, by issuing the guidance **Technical Considerations for Additive Manufactured Medical Devices**. To date, FDA has cleared more than 150 3D-printed medical devices and has approved a **3D-printed drug**, finished dosage forms, an active



3-D printing at FDA

pharmaceutical ingredient, and biological molecules produced using advanced manufacturing technologies. Since releasing this guidance, FDA has worked closely with America Makes on a Standards Roadmap for 3D printing. FDA's continued interaction with stakeholder groups, including the Department of Veterans Affairs Innovation Network, is facilitating advanced 3D-printed solutions that are reaching civilian and military patients.

To support innovation in this field, FDA has led the world in advancing efforts to provide a comprehensive regulatory framework to manufacturers and a more effective pathway to getting state-of-the-art medical products into the hands of patients and health care providers. Examples include CDER's **Emerging Technology Program**, which provides opportunities for early engagement regarding innovative approaches to pharmaceutical product design or manufacturing.[132]

Under this program, FDA has approved 13 applications involving advanced manufacturing, including 11 that used continuous manufacturing. For example, to support COVID-19 response, FDA approved two supplemental applications that used advanced manufacturing in a U.S. facility to address the potential shortage of two critical drug products. The new **CBER Advanced Technology Team** was also started to promote communication between CBER and prospective innovators/developers of advanced manufacturing technologies.

MEDICAL COUNTERMEASURE REGULATORY POLICY

During FY 2021, FDA continued efforts to ensure that the FDA **legal, regulatory and policy framework** enables the application of advances in regulatory science to the regulatory review process and adequately supports preparedness for and response to CBRN and emerging infectious disease threats by facilitating the development and availability of MCMs. In addition to addressing policy aspects of those activities described generally throughout this document (see ***Box 1***, and ***COVID-19 Response***), examples of FDA advancing policy-specific efforts in FY 2021, as discussed in more detail in other sections, include:

- Advancing efforts to create a national capability to track, collect, analyze, and evaluate information related to MCMs used during public health emergencies, including the COVID-19 countermeasures, to inform real-time decisions about the safety and effectiveness of these MCMs.
- Addressing issues related to use of expanded access mechanisms and EUAs to make available unapproved MCMs for CBRN and other emerging infectious disease threats and for certain DoD-related threat agents.
- Supporting efforts to advance FDA capacities to monitor the MCM supply chain to identify product shortages and distribution of misbranded/counterfeit products.
- Supporting an adequate supply of MCMs through efforts to extend the shelf life of certain MCMs outside of SLEP, utilizing authorities under section 564A(b) of the FD&C Act.
- Leading or providing policy subject matter input to FDA MCM-related collaborations, including with DoD under PL 115-92.
- Maintaining a surveillance program that routinely monitors online sources for fraudulent products,

especially during public health emergencies, such as COVID-19 and Ebola.

- Updating regulatory policy to improve availability of blood and blood components, ensure adequate protections for donor health and maintain a safe blood supply for patients.
- Clarifying regulatory issues around building frameworks for conducting clinical trials during public health emergencies.
- Participating in interagency emergency preparedness exercises and follow up activities.
- Publishing a **list of essential medicines, MCMs, and critical inputs** on October 30, 2020, required by an Executive Order issued on August 6, 2020.[133] The goal of the Executive Order is to ensure that the U.S. is able to protect patients and our military forces against emerging infectious diseases, such as COVID-19 as well as CBRN threats. To accomplish this goal, the Executive Order seeks to ensure sufficient and reliable, long-term domestic production of these products, and to minimize potential shortages by reducing our dependence on foreign manufacturers of these products.[134]
- During the COVID-19 pandemic, section 506J of the FD&C Act (21 U.S.C. 356j) was added giving FDA certain authorities related to device shortages and potential device shortages occurring during or in advance of a public health emergency. This authority requires manufacturers to notify FDA of a permanent discontinuance in the manufacture of certain devices or an interruption in the manufacture of certain devices that is likely to lead to a meaningful disruption in supply of that device in the U.S. This provides the FDA with better visibility of the medical devices supply chain. FDA issued an immediately in effect guidance document, **Notifying CDRH of a Permanent Discontinuance or Interruption in Manufacturing of a Device Under Section 506J of the FD&C Act During the COVID-19 Public Health Emergency**, to implement section 506J of the FD&C Act. In FY 2021, FDA published a **list of medical device types to help determine Section 506J notification obligations**.[135]

FDA also continued to develop and propose new approaches for addressing legal, regulatory, and policy challenges associated with the development and use of MCMs. For example, FDA is:

- Continuing work to harmonize the multi-jurisdictional regulation of certain PPE that may be used during public health emergencies, such as COVID-19 and pandemic influenza.

- Continuing to address issues related to information disclosure, including related to COVID-19 interagency activities, and liability protections related to MCM products.
- Identifying and developing new legislative proposals, providing technical assistance on others' MCM-related legislative proposals, and supporting MCM-related congressional testimony.
- Implementing MCM-related provisions of the Pandemic and All-Hazards Preparedness and Advancing Innovation Act of 2019 (PAHPAIA) (**PL 116-22**), which reauthorizes and modifies programs related to public health emergency preparedness and response[136] and the CARES Act (PL 116-136).
- Established templates for notifying master file holders of reliance upon information held in the master file in accordance with section 603 of the FD&C Act as provided for in PAHPAIA.[137]
- Developing MCM-related guidance documents issued in FY 2021 (***Appendix 3: MCM-Related Guidance Issued in FY 2021***), key meetings and workshops (***Appendix 4: Key MCM-Related Meetings Held in FY 2021***), and information for stakeholders about key MCM-related authorities.
- Supporting efforts to modernize the legal framework for regulating laboratory developed tests (LDTs) and other IVD tests made available during emergency circumstances, and working with CDC and CMS to leverage the expertise of each agency to collaborate on and address issues related to the implementation of EUA diagnostic tests in clinical and public health laboratories during public health emergencies.
- Continuing to support development of the State Party Annual Report as required under the International Health Regulations and **U.S. Health Security National Action Plan: Strengthening Implementation of the International Health Regulations** based on the 2016 JEE, containing hundreds of cross-sectoral activities to better prepare the U.S. to prevent, detect, and respond to public health emergencies.
- Supporting HHS's GHSA through participation in the Research and Development and Legal Preparedness Action Packages.
- Drafting **MOUs** to provide frameworks for FDA collaborations.

During FY 2021, FDA continued working to implement several additional MCM-related provisions of the **Cures Act**, which was signed into law in December 2016. Specifically, the Cures Act amended the FD&C Act to allow FDA to establish a new priority review voucher (PRV) program for material threat MCMs. FDA developed a **draft guidance**[138] that provides to internal and external stakeholders answers to questions FDA has received on material threat MCM PRVs and established a material threat **MCM PRV** web page where awards are publicly posted. FDA issued this draft guidance in January 2018, to explain to internal and external stakeholders how FDA intends to implement the material threat MCM PRV program. FDA is working to issue a comprehensive draft guidance on all FDA PRV programs, and intends to incorporate this draft guidance into it. On September 30, 2021, FDA issued a notice establishing the fee rate for using a material threat MCM PRV in FY 2022.[139] FDA issued four material threat MCM PRVs in FY 2021.[140]

In addition, throughout FY 2021, FDA continued work to implement Public Law 115-92, enacted in December 2017, which amended FDA's EUA authorities to allow for emergency uses of medical products for threats in addition to CBRN agents, to include other agents that may cause or are otherwise associated with, an imminently life-threatening and specific risk to U.S. military forces.

FDA also continues to work with DoD to implement Public Law 115-92's provisions for enhanced engagements to expedite development and FDA's review of products to diagnose, treat, or prevent serious or life-threatening diseases or conditions facing American military personnel.

PROFESSIONAL DEVELOPMENT

FDA launched the **MCMi professional development program** during FY 2011 to ensure that FDA scientists are informed about CBRN threats and associated health impacts as they conduct benefit-risk analyses on MCMs, and that FDA scientists can meet the regulatory challenges posed by new areas of science and technology in the area of MCM development.

Due to the COVID-19 pandemic, the MCMi professional development program held fewer training sessions than in previous years. Activities in FY 2021 included:

MCMi Lecture Series

These lectures, presented by highly respected leaders in their fields, broaden understanding of the policies, procedures, and U.S. governmental preparedness and response framework for FDA reviewers who are assessing MCM applications. FDA held four virtual lectures in this series during FY 2021 with a total of 288 attendees.

Foundations for Preclinical Review Lecture Series

These lectures focus on preclinical scientific and technical issues of importance to MCM reviewers, since many MCMs are developed under the Animal Rule. Presentations cover topics that address a new procedure or infrastructure change and are targeted to FDA staff reviewing preclinical information in medical product applications. FDA held one virtual lecture in this series during FY 2021 with 82 attendees.

MCMi Intramural Research and Collaborative Lecture Series

This lecture series, initiated in FY 2019, brings together the FDA research community to engage with FDA scientists supported by the MCMi Intramural Regulatory Science Program to share ideas and knowledge, and inspire continued advancement in MCM regulatory science. These sessions are designed for an FDA audience, including scientists involved in the review of medical product applications. FDA held two virtual lectures in this series during FY 2021 with a total 96 attendees.

Data quality and integrity training for high-consequence pathogens

FDA also sponsored the ninth installment of a **week-long training course** with the University of Texas Medical Branch (UTMB) to provide training on best practices to ensure the quality and integrity of data generated in maximum-containment (i.e., biosafety level (BSL)-3 and -4) laboratories used to support product approval under the Animal Rule. This course was held virtually June 14-18, 2021, with 69 participants.

Building on the success of a 2019 pilot course, FDA and UTMB also held the second annual clinical course, **Achieving Data Quality and Integrity in Clinical Trials Involving High-Consequence Pathogens** on August 2-4, 2021, with 63 participants.[z] This course is designed to provide a learning environment that cultivates collaboration of ideas; yields tools for clinical study conduct; enhances mutual understanding of clinical, scientific, and regulatory complexities; and promotes the data quality and integrity derived from these regulated studies according to good clinical practice (GCP) principles.

[z] Though planned for one week, including a full-day hands on clinical practicum, the COVID-19 pandemic limited the 2020 clinical course to three days of virtual lectures, including two separate expert panel discussions, which were held October 26-28, 2020 (FY 2021). The 2021 course, held in August 2021, followed a similar virtual format.

APPENDIX 1: FY 2021 MEDICAL COUNTERMEASURE APPROVALS – BIOLOGICS AND DRUGS[aa,ab]

Medical Countermeasure	Applicant	Key Dates	Indication
cobas Zika nucleic acid test	Roche Molecular Systems, Inc.	• Submitted September 16, 2020 • Approved February 25, 2021	BLA supplement to update hazard information on the product labeling for products used on the cobas 6800 and 8800 systems, including Zika.
Comirnaty (COVID-19 Vaccine, mRNA)	BioNTech Manufacturing GmbH	• Submitted May 18, 2021 • Approved August 23, 2021	To prevent COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older.
Ebanga (ansuvimab-zykl)	Ridgeback Biotherapeutics	• Submitted May 29, 2020 • Approved December 21, 2020	To treat *Zaire ebolavirus* (Ebola virus) infection in adults and children. Ebanga is a human monoclonal antibody.
Flucelvax Quadrivalent (influenza vaccine)	Seqirus, Inc.	• Submitted March 31, 2020 • Approved March 3, 2021	BLA supplement to extend the use of this vaccine, when manufactured at two specific facilities, to persons 2 years of age and older.
Inmazeb (atoltivimab, maftivimab, and odesivimab-ebgn)	Regeneron Pharmaceuticals, Inc.	• Submitted February 25, 2020 • Approved October 14, 2020	To treat *Zaire ebolavirus* infection in adult and pediatric patients. Inmazeb is a mixture of three monoclonal antibodies.
NPLATE (romiplostim)	Amgen Inc.	• Submitted July 28, 2020 • Approved January 28, 2021	BLA supplement for the indication to increase survival in adults and pediatric patients (including term neonates) acutely exposed to myelosuppressive doses of radiation (H-ARS).
StrataGraft (allogeneic cultured keratinocytes and dermal fibroblasts in murine collagen- dsat)	Stratatech Corporation	• Submitted June 5, 2020 • Approved June 15, 2021	To treat adults with thermal burns containing intact dermal elements for which surgical intervention is clinically indicated (deep partial-thickness burns).

[aa] Includes MCMs approved, licensed, or cleared by FDA in FY 2021 (October 1, 2020 - September 30, 2021).

[ab] For products (biologics) regulated by CBER, additional information can be found at: **https://www.fda.gov/vaccines-blood-biologics/biologics-products-establishments**; for products (drugs and biologics) regulated by CDER, additional information can be found at: **http://www.accessdata.fda.gov/scripts/cder/daf/**. The Purple Book Database of Licensed Biological Products is available at: **https://purplebooksearch.fda.gov/**

Medical Countermeasure	Applicant	Key Dates	Indication
Tembexa (brincidofovir)	Chimerix, Inc.	• Submitted October 7, 2020 • Approved June 4, 2021	To treat smallpox in adult and pediatric patients, including neonates.
Ticovac (Tick-Borne Encephalitis Vaccine)	Pfizer Ireland Pharmaceuticals	• Submitted December 15, 2020 • Approved August 13, 2021	For active immunization to prevent tick-borne encephalitis in individuals 1 year of age and older.
Veklury (remdesivir)	Gilead Sciences, Inc.	• Submitted August 7, 2020 • Approved October 22, 2020	To treat COVID-19 requiring hospitalization in adult and pediatric patients 12 years of age and older and weighing at least 40 kilograms (about 88 pounds).
Xofluza (baloxavir marboxil)	Genentech, Inc.	• Submitted January 23, 2020 • Approved November 23, 2020	New indication to include post-exposure prevention of influenza (flu) for patients 12 years of age and older after contact with an individual who has the flu. Xofluza, previously available only in tablet form, is also now available as granules for mixing in water.

APPENDIX 2: FY 2021 MEDICAL COUNTERMEASURE APPROVALS – DEVICES[ac,ad]

Diagnostic Tests

Medical Countermeasure	Applicant	Key Dates	Indication
BioFire Respiratory Panel 2.1 (RP2.1)	BioFire Diagnostics, LLC	• Received May 19, 2020 • Cleared March 17, 2021	For the simultaneous qualitative detection and identification of multiple respiratory viral and bacterial nucleic acids in NPS obtained from individuals suspected of respiratory tract infections, including COVID-19.
Cobas Influenza A/B & RSV Nucleic Acid Test For Use On The Cobas Liat System	Roche Molecular Systems, Inc.	• Received January 28, 2021 • Cleared February 16, 2021	For the rapid *in vitro* qualitative detection and discrimination of Influenza A virus, Influenza B virus and respiratory syncytial virus (RSV) RNA in NPS specimens from patients with signs and symptoms of respiratory infection in conjunction with clinical and epidemiological risk factors.
I-STAT TBI Plasma Cartridge With The I-STAT Alinity System	Abbott Laboratories	• Received June 30, 2020 • Cleared January 8, 2021	The i-STAT TBI Plasma test is a panel of IVD immunoassays for the quantitative measurements of glial fibrillary acidic protein (GFAP) and ubiquitin carboxyl-terminal hydrolase L1 (UCH-L1) in plasma and a semiquantitative interpretation of test results derived from these measurements, using the i-STAT Alinity Instrument. This is a rapid handheld TBI blood test.
MeMed BV	MeMed Diagnostics Ltd.	• Received January 29, 2021 • Cleared September 9, 2021	An automated semi-quantitative immunoassay that measures three non-microbial (host) proteins (TRAIL, IP-10, and CRP) in adult and pediatric serum samples and is intended for use in conjunction with clinical assessments and other laboratory findings as an aid to differentiate bacterial from viral infection.
Merit Medical Systems, Inc	Cultura Collection and Transport System	• Received June 19, 2020 • Cleared March 3, 2021	The Merit Cultura Collection and Transport System is intended for collection and transport of clinical specimens to the laboratory for standard diagnostic/identification techniques. The Merit Cultura Collection and Transport System is a culture-based media that can be used for upper respiratory viral diagnostic assays including SARS-CoV-2, Influenza A, Influenza B, RSV, and Rhinovirus.

[ac] Includes MCMs approved, licensed, or cleared by FDA in FY 2021 (October 1, 2020 - September 30, 2021).

[ad] Additional information about device approvals can be found in Medical Devices Databases: **https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/medical-device-databases**, including the 510(k) Premarket Notification Database: **https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm**

Personal Protective Equipment (PPE)

FDA cleared more than 400 items of PPE in FY 2021, including gloves, surgical masks, and gowns.

Additional information about these device approvals can be found in the FDA **Medical Devices Databases**, including the **510(k) Premarket Notification Database**. To locate records for a particular type of product (vs. specific product by name), use the **Product Classification Database** to find the product code assigned to that type of device,[ae] and search FDA medical device databases for that product code.

Product codes for PPE include:

- LZA - Polymer patient examination glove
- LZC - Patient examination glove, specialty
- QDO - Fentanyl and other opioid protection glove
- FYA - Gown, surgical
- KGO - Surgeon's gloves
- LYY - Latex patient examination glove
- OPJ - Medical gloves with chemotherapy labeling claims - test for use with chemotherapy drugs
- FRF - Cleaner, air, medical recirculating
- FRA - Purifier, air, ultraviolet, medical
- FXX - Mask, surgical
- PEM - Dental barriers and sleeves
- FYC - Gown, isolation, surgical
- LYZ - Vinyl patient examination glove
- CAH - Filter, bacterial, breathing-circuit
- OXZ - Pediatric/child facemask

[ae] Product codes are assigned based upon the medical device product classification designated under 21 CFR Parts 862-892. For more information, see Product Code Classification Database at: **https://www.fda.gov/medical-devices/classify-your-medical-device/product-code-classification-database**

Other Devices

FDA also cleared other types of devices to support COVID-19 pandemic response, and other public health emergency preparedness priorities. These include respiratory support devices (e.g., oxygen concentrators, ventilators/accessories, and sensors including pulse oximeters), and wound care devices.

Additional information about these device approvals can be found in the FDA **Medical Devices Databases**, including the **510(k) Premarket Notification Database**. To locate records for a particular type of product (vs. specific product by name), use the **Product Classification Database** to find the product code assigned to that type of device, and search FDA medical device databases for that product code.

Medical Countermeasure	Applicant	Key Dates	Indication
A8, A9 Anesthesia System	Shenzhen Mindray Bio-Medical Electronics Co., LTD.	• Received July 14, 2020 • Cleared March 26, 2021	A device used to administer to a patient, continuously or intermittently, a general inhalation anesthetic and to maintain a patient's ventilation.
Axiostat Patch	Advamedica Inc.	• Received September 25, 2020 • Cleared April 15, 2021	Axiostat Patch is intended for local management of bleeding wounds and to provide a barrier to bacterial penetration of the dressing for patients and for the rapid control of moderate to severe bleeding. The dressing is indicated for the following wounds: lacerations, abrasions, surgical debridement sites, skin surface puncture sites, vascular procedure sites, and sites involving percutaneous catheters, tubes and pins.
Biomonitor III, Biomonitor IIIm	Biotronik, Inc	• Received July 6, 2020 • Cleared December 8, 2020	The Biomonitor III, Biomonitor IIIm is indicated to detect cardiac arrhythmias. It is indicated for use in patients with clinical syndromes or situation at increased risk of cardiac arrythmias and patients who experience transient symptoms that may suggest cardiac arrythmias.
CLEWICU System (ClewICUServer And ClewICUnitor)	CLEW Medical Ltd.	• Received March 18, 2020 • Cleared January 9, 2021	CLEWICU provides the clinician with physiological insight into a patient's likelihood of future hemodynamic instability. CLEWICU is intended for use with intensive care unit (ICU) patients 18 years and over. CLEWICU is considered to provide additional information regarding the patient's predicted future risk for clinical deterioration, as well as identifying patients at low risk for deterioration.
Dreamwear Silicone Pillows Mask	Respironics, Inc.	• Received March 22, 2021 • Cleared August 24, 2021	The DreamWear Silicone Pillows Mask is intended to provide an interface for application of continuous positive airway pressure (CPAP) or bi-level therapy to patients. The mask is for single patient use in the home or multi-patient use in the hospital/institutional environment.

Medical Countermeasure	Applicant	Key Dates	Indication
F&P Optiflow Nasal Oxygen Cannula With Co2 Sampling	Fisher & Paykel Healthcare Ltd.	• Received June 23, 2020 • Cleared March 16, 2021	This product is a single-patient-use device that delivers respiratory gases to adult patients in hospitals and long-term care facilities. This product is indicated for the delivery of Nasal High Flow (NHF) and Low Flow Oxygen to spontaneously breathing patients by appropriately qualified health care professionals.
F&P Visairo Niv Mask Range	Fisher & Paykel Healthcare Ltd	• Received November 23, 2020 • Cleared April 14, 2021	The Fisher & Paykel Healthcare Visairo masks are single patient use masks intended for use as an accessory to ventilators to enable non-invasive positive pressure ventilation (NPPV) therapy (CPAP or bi-level) to be delivered to spontaneously breathing adult patients (> 30 kg) with respiratory insufficiency or respiratory failure who have been prescribed NPPV. The masks are to be fitted and therapy maintained by trained medical practitioners in a hospital/institutional environment with patient monitoring in place.
Fingertip Pulse Oximeter	Shenzhen BSX Technology Electronics Co., Ltd.	• Received August 18, 2020 • Cleared December 14, 2020	The Fingertip Pulse Oximeter is intended for spot-checking of oxygen saturation and pulse rate for use with the finger of adult patients in health care environments. It is not intended to be used under motion or low perfusion scenarios.
Fingertip Pulse Oximeter	Shenzhen LEPU Intelligent Medical Equipment Co., Ltd.	• Received September 21, 2020 • Cleared March 1, 2021	The Fingertip pulse oximeter is a handheld non-invasive device intended for spot-checking of oxygen saturation of arterial hemoglobin (SpO2) and pulse rate (PR) of adult, adolescent and child patients in hospitals, hospital-type facilities, and homecare.
Fingertip Pulse Oximeter	Zhuhai Linte Medical Instrument Co., Ltd.	• Received February 1, 2021 • Cleared July 30, 2021	The Fingertip Pulse Oximeter is a non-invasive device intended for spot checking of functional SpO2 and PR. This portable device is indicated for use in adult patients in clinical institution and home environments.
Galapogos	ResMed Corp	• Received March 4, 2020 • Cleared January 17, 2021	The Galapagos app is intended for patients who are prescribed a compatible ResMed S10 platform device to simulate therapy prior to using their device with their prescribed settings. It is an optional software accessory to allow patients to acclimate to their therapy device.
Gospiro	Monitored Therapeutics, Inc.	• Received September 25, 2020 • Cleared December 4, 2020	The GoSpiro is intended to be used by adults and children over 5 years old in physician's offices, clinics, and home settings to conduct basic lung function and spirometry testing.
Hamilton-C3	Hamilton Medical AG	• Received May 15, 2020 • Cleared February 5, 2021	The Hamilton C3 ventilator is intended to provide positive pressure ventilatory support to adults and pediatrics and optionally infants and neonates.

Medical Countermeasure	Applicant	Key Dates	Indication
Hamilton-C6	Hamilton Medical AG	• Received June 18,2020 • Cleared December 11, 2020	The Hamilton C6 ventilator is intended to provide positive pressure ventilatory support to adults and pediatrics and optionally infants and neonates.
Hill-Rom Heart And Respiration Rate Monitoring System: Single Sensor, Hill-Rom Heart And Respiration Rate Monitoring System: Sensor Packs, Hill-Rom Heart And Respiration Rate Monitoring System: Sensor Activation	Hill-Rom Inc.	• Received July 21, 2020 • Cleared March 4, 2021	The Hillrom Heart and Respiration Rate Monitoring System powered by Earlysense is used with compatible bed system models and is intended for continuous measurement of respiratory rate (RR) and heart rate (HR) in an automatic contact-less manner.
Hvt 2.0	Vapotherm Inc.	• Received November 16, 2020 • Cleared August 25, 2021	The HVT 2.0 system is intended to deliver warmed and humidified high-flow respiratory gases to spontaneously breathing adult patients and pediatric patients (5 kg and up). The device is intended to be used in hospital, sub-acute facility, and home-use settings.
Innova Nasal Non-Vented Mask	Sleepnet Corporation	• Received December 9, 2020 • Cleared April 30, 2021	The Innova Nasal Non-Vented Mask is intended to be used as an accessory to CPAP/bi-level positive pressure systems containing exhalation valves.
Invacare Platinum 5nxg Oxygen Concentrator	Invacare Corporation	• Received October 30, 2020 • Cleared April 12, 2021	The Invacare Platinum 5NXG Oxygen Concentrator is indicated for patients with respiratory disorders requiring supplemental oxygen at flow rates of 1 to 5 liters per minute. For flow rates below 1 liter per minute use with Invacare Pediatric Flowmeter accessory. It is not intended to sustain or support life.
Leadtek Fingertip Pulse Oximeter (Wireless), Leadtek Fingertip Pulse Oximeter (Wireless)	Leadtek Research Inc.	• Received January 5, 2021 • Cleared September 1, 2021	The Fingertip Pulse Oximeter (Wireless) is intended for measuring functional Sp02 and pulse rate for both adults and adolescent as non-invasive spot checking in home and professional caring environment.
Luna G3 Bpap 25a	3B Medical, Inc.	• Received June 15, 2020 • Cleared January 29, 2021	The Luna G3 BPAP 25A is a Bi-level PAP (Bi-level Positive Airway Pressure) device designed for the treatment of adult obstructive sleep apnea (OSA). The integrated humidifier is indicated for the humidification and warming of air from the flow generator device. These devices are intended for single-patient use by prescription in the home or hospital/institutional environment on adult patients. It is to be used on patients >66lbs/30kg for whom CPAP therapy has been prescribed. The system can deliver bi-level therapy or auto bi-level therapy.

Medical Countermeasure	Applicant	Key Dates	Indication
Magneto Nasal Mask	Respironics, Inc.	• Received February 9, 2021 • Cleared July 12, 2021	This mask is intended to provide an interface for application of CPAP or bi-level therapy to patients. The mask is for single patient use in the home and multipatient use in the hospital/institutional environment.
Maxxi Flow Sensor	Neurovirtual USA, INC.	• Received June 5, 2020 • Cleared December 14, 2020	The Maxxi Flow sensor is a respiratory sensor. It is placed under the patient's nostrils and produce a signal that is directly proportional to the temperature changes in the air inhaled and exhaled during respiration. Maxxi Flow sensors generate a small analog electrical signal that provides clear, reliable indication of respiration airflow.
Med-Link Temp-Pulse Oximeter	Shenzhen Med-Link Electronics Tech Co., Ltd	• Received September 18, 2020 • Cleared March 1, 2021	Med-link Pulse Oximeter is intended for spot checking in measuring and displaying functional SpO2 and pulse rate of patients in hospitals, physician's office, clinical settings and home care environment. It's a reusable device intended for adults and pediatrics who are well or poorly perfused.
Medumat Easy Cpr, Medumat Easy Cpr With Bag	Weinmann Emergency Medical Technology GmbH + Co. KG	• Received November 19, 2019 • Cleared November 20, 2020	MEDUMAT Easy CPR is an electrical, pneumatically operated emergency and transport ventilator used for ventilation and oxygen inhalation with either a mask or tube.
O2asis Personal Oxygen Humidifier	Perma Pure LLC	• Received December 9, 2019 • Cleared November 12, 2020	The O2asis Personal Oxygen Humidifier is indicated to add moisture and may warm breathing gases for administration to infant, pediatric and adult patients in the home, hospital, and clinical settings. It is used with an external gas source of up to 6 Lpm via nasal cannula.
Pulse Oximeter	Guangdong Long Yao Electronic Technology Co., Ltd.	• Received March 20, 2020 • Cleared November 27, 2020	The Pulse Oximeter is a non-invasive device intended for spot checking of functional SpO2 and PR. This portable device is indicated for use in adult patients in clinical institutions and home environments.
Pulse Oximeter	Shenzhen AOJ Medical Technology Co., Ltd.	• Received August 3, 2020 • Cleared December 7, 2020	The pulse oximeter is a reusable device intended for spot-checking of oxygen saturation and pulse rate for use with the finger of adult patients in health care environments. It is not intended to be used under motion or low perfusion scenarios.
Pulse Oximeter	Shenzhen Hexin ZONDAN Medical Equipment Co., Ltd.	• Received December 31, 2020 • Cleared April 23, 2021	The pulse oximeter is non-invasive device intended for spot-checking of functional Sp02 and PR.

Medical Countermeasure	Applicant	Key Dates	Indication
Pulse Oximeter	Shenzhen Raysintone Technology CO., Ltd	• Received May 26, 2020 • Cleared December 7, 2020	The Fingertip Pulse Oximeter is a reusable non-invasive device intended for the spot checking of SpO2 and PR of adult patients in hospital and other health care environments. It is not intended to be used under motion or low perfusion scenarios.
Pulse Oximeter	Shenzhen Creative Industry Co., Ltd.	• Received June 2, 2020 • Cleared January 25, 2021	This Pulse Oximeter is intended for measuring and recording the functional SpO2 and PR. It is intended for spot check and continuous recording of SpO2, PR of adult or pediatric patients in hospitals, clinics, or home. This device is not intended for continuous monitoring.
Puritan Bennett 980 Series Ventilator System	Covidien LLC	• Received November 1, 2019 • Cleared November 20, 2020	The Puritan Bennett 980 Series Ventilator System is designed for use on patient population sizes from neonatal (neonatal intensive care unit (NICU)) through adult who require respiratory support or mechanical ventilation and weigh a minimum of 0.3kg (0.66lb).
S10 Kirra	ResMed Pty Ltd	• Received October 19, 2020 • Cleared December 18, 2020	The S10 Kirra is indicated to provide CPAP and bi-level therapy for the treatment of OSA in patients (female patients with mild to moderate OSA when using AfH treatment mode) weighing more than 66 lb (30 kg). ASV and ASVAuto modes are also indicated for the treatment of central and/or mixed apneas, or periodic breathing. It is intended for home and hospital use.
Servo-U Ventilator System 4.1, Servo-N Ventilator System 4.1, Servo-U Mr Ventilator System 4.1	Maquet Critical Care AB	• Received July 7, 2020 • Cleared April 20, 2021	The Servo Series Ventilator System is intended for respiratory support, monitoring and treatment of neonatal, pediatric and adult patients, be used only by health care providers, and only in professional health care facilities and for transport within these facilities.
Sleep Apnea Breathing Therapy Mask: Yf-01 Full Face Mask, Yf-02 Full Face Mask, Yf-03 Full Face Mask, Yn-02 Nasal Mask, Yn-03 Nasal Mask, Yp-01 Nasal Pillow Mask	Suzhou Yuyue Medical Technology Co., Ltd.	• Received November 13, 2020 • Cleared July 2, 2021	The sleep apnea breathing therapy mask is a non-invasive accessory used for channeling airflow to a patient from a positive airway pressure (PAP) device such as a CPAP or bi-level system.
Spirometer	MeHow Innovative Ltd	• Received June 4, 2020 • Cleared June 10, 2021	The spirometer (LA104, LA105) is a diagnostic tool to measure volume and flow of air that can be moved in and out of a patient's lungs.
Spirotrac	Vitalograph Ireland Ltd.	• Received June 10, 2020 • Cleared October 14, 2020	The Vitalograph Spirotrac Model 7000 is a PC-based software application intended to be used as a spirometer or connect to compatible Vitalograph or third party devices to acquire, view, store and print the device output.

Medical Countermeasure	Applicant	Key Dates	Indication
Spo2 Sensor	JKH USA, LLC	• Received September 28, 2020 • Cleared November 27, 2020	SpO2 Sensors are indicated for continuous non-invasive monitoring of functional SpO2 and PR for adult patients weighing greater than 40 kg, pediatric patients weighing 10-50 kg, and neonatal patients weighing no less than 3 kg.
Sysmed S/T	SysMed (China) Co., Ltd	• Received August 12, 2019 • Cleared November 25, 2020	The device provides positive pressure therapy for the treatment of adult obstructive sleep apnea syndrome in self breathing patients weighing over 30kg (66lbs). This product can be used in the home as well as in clinical/hospital environments.
Tenax Laser Resistant Endotracheal Tube	Bryan Medical, Inc.	• Received March 24, 2020 • Cleared November 25, 2020	The Tenax Laser Resistant Endotracheal Tube is intended for endotracheal intubation. It is indicated for use for all types of surgical procedures involving carbon dioxide (10.60 microns) or KTP (532 nm) laser use (normal pulsed or continuous beam delivery in the non-contact mode), when endotracheal intubation is required to administer anesthetic gases or to overcome emergency obstruction of an airway.
Ventway Sparrow	Inovytech Medical Solutions Ltd.	• Received September 30, 2020 • Cleared January 29, 2021	The Ventway Sparrow ventilator is intended to provide continuous or intermittent ventilatory support for the care of individuals who require mechanical ventilation. Specifically, the ventilator is applicable for adult and pediatric patients weighing at least 5 kg (11 lb), who require the following types of ventilatory support: SIMV VC PS, SIMV PC PS, or CPAP. The Ventway Sparrow lung ventilator is intended for emergency use and during transportation. It may be used for invasive (via an endotracheal tube and tracheostomy) or noninvasive (full non-vented ventilation face mask) ventilation presets. It may be used in hospitals, pre-hospital (transport) and field environments.
Vivo 45 Ls	Breas Medical AB	• Received December 23, 2019 • Cleared January 27, 2021	The Vivo 45 LS ventilator (with or without the SpO2 and C02 sensors) is intended to provide continuous or intermittent ventilatory support for the care of individuals who require mechanical ventilation. Specifically, the ventilator is applicable for pediatric through adult patients weighing more than 5 kg (11 lb), however, the mouthpiece ventilation modes are for adult patients only.
Vortran Go2vent With Peep Valve	Vortran Medical Technology 1, Inc.	• Received August 6, 2020 • Cleared February 11, 2021	The VORTRAN G02VENT with PEEP Valve is to be used by properly trained personnel to deliver emergency, short term, constant flow, pressure-cycled ventilatory support on patients weighing 10 kg and above.

Medical Countermeasure	Applicant	Key Dates	Indication
Wizard 510 Nasal Mask	Apex Medical Corp.	• Received November 20, 2019 • Cleared October 29, 2020	The Wizard 510 Nasal Mask is intended to provide an interface for CPAP or bi-level therapy. The nasal mask is intended for single-patient re-use in the home and multi-patient, multi-use in the hospital environment.
X-Plo2r	Belluscura LLC	• Received October 13, 2020 • Cleared March 2, 2021	The X-PLO2R is a transportable, software-monitored device designed to be used by patients as a portable oxygen delivery system requiring high concentrations of oxygen on a supplemental basis. It is small, portable, and is capable of continuous use in home, institutional, and travel/mobile environments.
XSTAT 30 Pouch	RevMedx, Inc.	• Received March 5, 2021 • Cleared August 27, 2021	XSTAT 30 Pouch is a hemostatic device for the control of severe, life-threatening bleeding from junctional wounds in the groin or axilla not amenable to tourniquet application in adults and adolescents. XSTAT 30 Pouch is a hemostatic device for the control of severe, life-threatening bleeding from narrow entrance extremity wounds in the arms or legs in adults and adolescents.

APPENDIX 3: MCM-RELATED GUIDANCE ISSUED IN FY 2021[af]

In FY 2020 and FY 2021, FDA issued more than 75 COVID-19-related guidances, to provide timely recommendations, regulatory information, guidance, and technical assistance necessary to support rapid response efforts to the COVID-19 public health emergency. Only MCM-related guidances are included below; the full list of COVID-19-related guidance documents is available on the **FDA website**.[141] Note that some COVID-19 guidance documents may have been updated once or more since issuance. The date listed in this table for all documents refers to the most recent update available at the end of FY 2021 (September 30, 2021). Some guidances may be temporary, that is, only in effect during the COVID-19 public health emergency, or until further notice. Accordingly, some guidances in the table below have been subsequently modified or revoked in the time period not covered by this report.

Date	Guidance Type	Guidance Name	Purpose
October 6, 2020 *Updated February 22, 2021, and May 25, 2021*	Final	Emergency Use Authorization for Vaccines to Prevent COVID-19 (**link**)	To provide recommendations for vaccine sponsors regarding the scientific data and information that would support the issuance of an EUA for an investigational vaccine intended to prevent COVID-19. This guidance was updated in May 2021 to include a new section that clarifies how the agency intends to prioritize review of EUA requests for the remainder of the COVID-19 public health emergency.
November 9, 2020	Final	Regulatory Considerations for Microneedling Products (**link**)	To assist industry in understanding when a microneedling product is a device as defined in section 201(h) of the FD&C Act, 21 U.S.C. § 321(h), and is, therefore, subject to the device requirements under the FD&C Act and its implementing regulations.
November 25, 2020	Final	Notifying CDRH of a Permanent Discontinuance or Interruption in Manufacturing of a Device Under Section 506J of the FD&C Act During the COVID-19 Public Health Emergency (**link**)	To implement section 506J of the FD&C Act (21 U.S.C. 356j), as added by section 3121 of the CARES Act, as it relates to device shortages and potential device shortages occurring during the COVID-19 pandemic, for the duration of the COVID-19 public health emergency.

[af] This table includes guidance documents designed to address MCM-specific topics and guidance documents that address more general topics considered to have likely relevance to some aspects of MCM development. It is not intended as a comprehensive list of all guidance documents; some product sponsors may find additional relevant documents on the FDA guidance website at **https://www.fda.gov/regulatory-information/search-fda-guidance-documents**

Date	Guidance Type	Guidance Name	Purpose
December 22, 2020	Final	Effects of the COVID-19 Public Health Emergency on Formal Meetings and User Fee Applications for Medical Devices - Questions and Answers (**link**)	To provide answers to frequently asked questions about regulatory and policy issues related to device development for the duration of the COVID-19 public health emergency.
January 13, 2021	Final	COVID-19: Potency Assay Considerations for Monoclonal Antibodies and Other Therapeutic Proteins Targeting SARS-CoV-2 Infectivity (**link**)	To assist sponsors in the development of monoclonal antibodies and other therapeutic proteins for use as COVID-19 therapeutics. A critical quality control measure for these products is the development and implementation of a potency assay(s) adequate to ensure that each lot is consistently produced with the potency necessary to achieve clinical efficacy and that such potency is maintained over the shelf life of the product.
January 19, 2021	Final	Policy for Testing of Alcohol (Ethanol) and Isopropyl Alcohol for Methanol, Including During the Public Health Emergency (COVID-19) (**link**)	To alert pharmaceutical manufacturers and pharmacists in state-licensed pharmacies or Federal facilities who engage in drug compounding to the potential public health hazard of alcohol (ethyl alcohol or ethanol) or isopropyl alcohol contaminated with or substituted with methanol. FDA is aware of reports of fatal methanol poisoning of consumers who ingested alcohol-based hand sanitizers that were manufactured with methanol or methanol-contaminated ethanol. FDA has also received numerous reports of dermal toxicity associated with such products.
January 19, 2021	Final	Manufacturing Considerations for Licensed and Investigational Cellular and Gene Therapy Products During COVID-19 Public Health Emergency (**link**)	To provide manufacturers of licensed and investigational cellular therapy and gene therapy (CGT) products with risk-based recommendations to minimize potential transmission of SARS-CoV-2.
February 10, 2021	Immediately in Effect (IIE)	Policy for Temporary Compounding of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency (Revised)	To communicate FDA's policy for the temporary compounding of certain alcohol-based hand sanitizer products by pharmacists in state-licensed pharmacies or Federal facilities and registered outsourcing facilities for the duration of the public health emergency.

Date	Guidance Type	Guidance Name	Purpose
February 10, 2021	Final	Temporary Policy for Preparation of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency (COVID-19) (Revised)	Issued in response to a number of queries from entities that are not currently licensed or registered drug manufacturers that would like to prepare alcohol-based hand sanitizers, either for public distribution or for their own internal use, to communicate FDA's policy for the temporary preparation of certain alcohol-based hand sanitizer products by firms that register their establishment with FDA as an OTC drug manufacturer, re-packager, or re-labeler to prepare alcohol-based hand sanitizers under the circumstances described in this guidance for the duration of the public health emergency.
February 11, 2021	Final	Temporary Policy for Manufacture of Alcohol for Incorporation Into Alcohol-Based Hand Sanitizer Products During the Public Health Emergency (COVID-19) (Revised)	Issued in response to a number of queries from entities that are not currently licensed or registered drug manufacturers that would like to prepare alcohol-based hand sanitizers, either for public distribution or for their own internal use, to communicate FDA's policy for the temporary manufacture of ethanol products by firms that manufacture alcohol for incorporation into alcohol-based hand sanitizer products under the circumstances described in this guidance (alcohol production firms) for the duration of the public health emergency.
February 11, 2021	Final (revised)	Investigational COVID-19 Convalescent Plasma (**link**)	To provide recommendations to health care providers and investigators on the use of COVID-19 convalescent plasma or investigational convalescent plasma during the public health emergency. The guidance also provides recommendations to blood establishments on collection, and describes FDA's interim compliance and enforcement policy regarding the IND requirements for the use of investigational convalescent plasma. This guidance was originally issued in April 2020, and has been updated several times, most recently in (for FY 2021) February 2021.
February 22, 2021	Final	COVID-19: Developing Drugs and Biological Products for Treatment or Prevention (Updated) (**link**)	To assist sponsors in the clinical development of drugs for the treatment or prevention of COVID-19.
February 22, 2021	Final	Development of Monoclonal Antibody Products Targeting SARS-CoV-2, Including Addressing the Impact of Emerging Variants, During the COVID 19 Public Health Emergency (**link**)	To provide recommendations to sponsors on the development of monoclonal antibody products targeting SARS-CoV-2, including addressing the impact of emerging variants, during the COVID-19 public health emergency.

Date	Guidance Type	Guidance Name	Purpose
February 22, 2021	Final	Policy for Evaluating Impact of Viral Mutations on COVID-19 Tests (**link**)	To provide a policy and recommendations on evaluating the potential impact of emerging and future viral mutations of SARS-CoV-2 on COVID-19 tests for the duration of the COVID-19 public health emergency. This guidance describes a policy for test developers to consider the impact of emerging and future variants on their COVID-19 tests during development and post-authorization.
April 14, 2021	Final	Remote Interactive Evaluations of Drug Manufacturing and Bioresearch Monitoring Facilities During the COVID-19 Public Health Emergency Guidance for Industry (**link**)	To describe how FDA will request and conduct voluntary remote interactive evaluations at facilities where drugs are manufactured, processed, packed, or held; facilities covered under FDA's bioresearch monitoring (BIMO) p rogram; and outsourcing facilities registered under section 503B of the FD&C Act for the duration of the COVID-19 public health emergency.
May 17, 2021	Final	COVID-19: Master Protocols Evaluating Drugs and Biological Products for Treatment or Prevention Guidance for Industry (**link**)	To describe FDA's current recommendations to sponsors of master protocols evaluating drugs for the treatment or prevention of COVID-19. A master protocol is defined as a protocol designed with multiple substudies, which involve coordinated efforts to evaluate one or more investigational drugs, in one or more disease subtypes, with one or more objectives, all within the same overall trial structure. This guidance focuses on the design, conduct, and statistical considerations of master protocols intended to generate or contribute to substantial evidence of effectiveness and adequate characterization of safety of drugs for the treatment or prevention of COVID-19.
May 17, 2021	Final	Manufacturing, Supply Chain, and Drug and Biological Product Inspections During COVID-19 Public Health Emergency Questions and Answers (Updated) (**link**)	To provide answers to frequently asked questions about regulatory and policy issues related to inspections, pending drug applications, and changes in manufacturing facilities for approved pharmaceutical products.
May 25, 2021	Final	Emergency Use Authorization for Vaccines to Prevent COVID-19 (Updated) (**link**)	To provide sponsors of requests for EUA for COVID-19 vaccines with recommendations regarding the data and information needed to support the issuance of an EUA under section 564 of the FD&C Act (21 U.S.C. 360bbb-3) for an investigational vaccine to prevent COVID-19 for the duration of the COVID-19 public health emergency.
June 3, 2021	Final	Product Identifiers Under the Drug Supply Chain Security Act, Questions and Answers (**link**)	To address anticipated questions regarding product identifiers that are required under section 582 of the FD&C Act (21 U.S.C. 360eee-1), as added by the Drug Supply Chain Security Act (DSCSA) (Title II of Public Law 113-54), for packages and homogenous cases of certain drug products.

Date	Guidance Type	Guidance Name	Purpose
June 3, 2021	Final	Drug Supply Chain Security Act Implementation: Identification of Suspect Product and Notification (link)	To aid certain trading partners in identifying a suspect product and specific scenarios that could significantly increase the risk of a suspect product entering the pharmaceutical distribution supply chain. The guidance also describes how trading partners should notify the FDA of illegitimate product and sets forth a process for terminating notifications of illegitimate product in consultation with the FDA.
June 3, 2021	Draft	Definitions of Suspect Product and Illegitimate Product for Verification Obligation under DSCSA (link)	Lays out the FDA's current understanding of terms used to define "suspect" and "illegitimate" products. These include "counterfeit," "diverted," "stolen," "fraudulent transaction" and "unfit for distribution." In response to comments received from stakeholders, this draft guidance revises the March 2018 draft guidance.
June 3, 2021	Draft	Enhanced Drug Distribution Security at the Package Level under DSCS (link)	To assist supply chain stakeholders, particularly trading partners, with requirements for enhanced drug distribution security at the package level that go into effect on November 27, 2023. This guidance provides recommendations on the system attributes necessary for enabling the secure tracing of product at the package level.
August 30, 2021	Final	FDA Guidance on Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency (Updated) (link)	To provide general considerations to assist sponsors in assuring the safety of trial participants, maintaining compliance with GCP, and minimizing risks to trial integrity for the duration of the COVID-19 public health emergency. The appendix to this guidance further explains those general considerations by providing answers to questions that the agency has received about conducting clinical trials during the COVID-19 public health emergency.
September 8, 2021	Final	Development of Abbreviated New Drug Applications During the COVID-19 Pandemic – Questions and Answers Guidance for Industry (link)	To provide general recommendations to prospective applicants and applicants of ANDAs related to generic drug product development and regulatory submissions in the form of questions and answers that have been received and addressed by FDA during the COVID-19 public health emergency.
September 15, 2021	Final	Enforcement Policy for Face Masks and Respirators During the Coronavirus Disease (COVID-19) Public Health Emergency (Revised) (link)	To provide a policy to help expand the availability of face masks, barrier face coverings, and face shields for the general public, including health care providers, and surgical masks and particulate FFRs (including N95 respirators) for health care providers for the duration of the COVID-19 public health emergency.

APPENDIX 4: KEY MCM-RELATED MEETINGS HELD IN FY 2021[ag]

FDA continued to take steps to ensure the agency was able to continue our vital public health mission in FY 2021. Where possible the agency leveraged technology to host meetings allowing for remote participation. We also continue to explore meeting platforms and formats, including pre-recorded presentations. This continued assessment is necessary as we respond to the challenges presented by the pandemic. The format for any meeting will be based on the discussion, advice, and recommendation that FDA needs from the committee as well as the requirements under the Federal Advisory Committee Act, if applicable.

Date	Type of Event	Event Name	Purpose
Weekly October 2020, biweekly through September 2021	Webinar series	Virtual Town Hall Series – Coronavirus (COVID-19) Test Development and Validation (**link**)	To help answer technical questions about the development and validation of tests for SARS-CoV-2. This series began in April 2020, and continues in FY 2022.
October 2020 – July 2021	Webinar series	Respirators and Other Personal Protective Equipment (PPE) for Health Care Personnel Use During the COVID-19 Pandemic (**link**)	To share information and answer questions from webinar attendees about respirators and other PPE, including decontamination systems for respirators, protective barrier enclosures, sterilizers, disinfectant devices, and air purifiers used during the COVID-19 pandemic. This series began in June 2020.
October 2, 2020	Public meeting	Vaccines and Related Biological Products Advisory Committee (VRBPAC) (**link**)	To discuss and make recommendations on selection of strains to be included in an influenza virus vaccine for the 2021 Southern Hemisphere influenza season.
October 22, 2020	Public meeting	VRBPAC (**link**)	To discuss, in general, the development, authorization and/or licensure of vaccines to prevent COVID-19.
October 22-23, 2020	Public workshop	FDA Public Workshop: Pediatric Dose Selection (**link**)	To discuss the present state of dose selection and how it pertains to pediatric drug development.
November 6, 2020	Webinar	Office of New Drug (OND) Research: Seeking Collaborators, Funding Opportunities Available (**link**)	To educate participants about how FDA's Office of New Drugs (OND) uses regulatory science research to address knowledge gaps that slow down or prevent new drug development, including an overview of OND's Combatting Antibiotic-Resistant Bacteria (CARB) and 21st Century Cures Drug Development Tools Grant programs.

[ag] This table includes FDA-sponsored meetings intended to address MCM-specific topics, or more general FDA-sponsored meetings that may be relevant to some aspects of MCM development. In some cases, FDA may have provided funding to support certain meetings hosted by others (e.g., NASEM).

Date	Type of Event	Event Name	Purpose
November 12, 2020	Webinar	FDA Grand Rounds: Facial Coverings During the COVID-19 Pandemic: How well do they flatten the curve? (**link**)	To provide an overview of FDA's research to evaluate the ability of facial coverings to reduce the spread of infection, and how FDA is developing a comprehensive risk-assessment tool to predict the probability of infection with individuals wearing a non-surgical face mask or cloth face covering.
November 16, 2020	Public meeting	FDA Public Meeting on Potential Approach for Ranking of Antimicrobial Drugs According to Their Importance in Human Medicine: A Risk Management Tool for Antimicrobial Animal Drugs (**link**)	To obtain early public input on a potential revised process and criteria for ranking antimicrobial drugs based on their importance in human medicine. FDA sought public input on a **concept paper** which includes a potential revised process for ranking antimicrobials according to their relative importance in human medicine, the potential criteria for their ranking, and the resulting ranked list of antimicrobial drugs.
December 4, 2020	Webinar	SEND for CBER, What You Need to Know (**link**)	To discuss CBER's support and requirement for the Standard for the Exchange of Nonclinical Data (SEND), which was **published** in the Federal Register on July 14, 2020, and the addition of SEND for CBER to the **FDA Data Standards Catalog**.
December 10, 2020	Public meeting	VRBPAC (**link**)	To discuss the request for EUA of a COVID-19 vaccine from Pfizer, Inc. in partnership with BioNTech Manufacturing GmbH.
December 17, 2020	Public meeting	VRBPAC (**link**)	To discuss the request for EUA of the Moderna, Inc., COVID-19 Vaccine for the prevention of COVID-19 in individuals 18 years and older.
January 14, 2021	Public conference	CDER Compliance Conference (**link**)	To educate participants on a range of drug compliance topics including compounding in cleanrooms, drug importation requirements, DSCSA implementation, and REMS compliance.
February 2-3, 2021	Public workshop	Scientific and Ethical Considerations for the Inclusion of Pregnant Women in Clinical Trials (**link**)	Convened by the Duke-Margolis Center for Health Policy, under a cooperative agreement with FDA, to discuss the need for clinical research in this complex population as well as scientific and ethical considerations for the inclusion of pregnant women in clinical trials.
February 25, 2021	Webinar	Health Equity and COVID-19: What Minority Communities Need To Know (**link**)	To provide the latest COVID-19 response updates from FDA, including information about vaccines and the FDA's approval process.
February 26, 2021	Public meeting	VRBPAC (**link**)	To discuss the request for EUA for a COVID-19 vaccine from Janssen Biotech Inc.

Date	Type of Event	Event Name	Purpose
March 11, 2021	Webinar	FDA Grand Rounds: Studies of SARS-CoV-2 Nonstructural Protein 1 (NSP1) and Envelope Protein (**link**)	To educate participants about FDA research to understand the role of NSP1 and envelope protein in COVID-19 pathogenesis.
May 20, 2021	Webinar	COVID-19 Vaccines & Women (**link**)	To discuss COVID-19 vaccines and their use in women.
May 26-27, 2021	Public workshop	2021 FDA Science Forum: Science as the Foundation for Protecting and Promoting Public Health (**link**)	To discuss FDA research in topic areas including medical countermeasures, infectious diseases, and pathogen reduction technologies. Recordings and a searchable list of more than 300 posters are **available on the FDA website**.[142]
June 1, 2021	Webinar	FDA Drug Topics: Enhanced Drug Distribution Security: 2023 and Beyond (**link**)	To provide updates on implementation of supply chain security requirements under the DSCSA and describe requirements that go into effect in 2023 for enhanced drug distribution security. Enhanced product tracing and verification will help protect patients by improving detection and response to suspect and illegitimate products and prevent the distribution of illegitimate products in the U.S.
June 9, 2021	Public workshop	Model Informed Drug Development Approaches for Immunogenicity Assessments (**link**)	To discuss best practices and future directions of quantitative methods for predicting immunogenicity of biologic products.
June 10, 2021	Public meeting	VRBPAC (**link**)	To provide considerations on data to support licensure and EUA for COVID-19 vaccines intended for use in individuals 12 through 17 years of age, and discuss, in general, the data needed to support an authorization and/or licensure of a COVID-19 vaccine intended for use in pediatric populations.
July 8, 2021	Webinar	FDA Grand Rounds: SARS-CoV-2: Host-pathogen interaction, vaccines & variants of concern (**link**)	To educate participants on MCMi-funded research to better understand how the human body responds to severe SARS-CoV-2 infection, and share results of research on the immunological response to infection and vaccination, including the potential impact of new variants.
July 19-23, 2021	Public workshop	Regulatory Education for Industry (REdI) Annual Conference 2021 (**link**)	To enable participants to learn directly from regulatory experts in FDA's medical product centers. This course is designed to provide participants with a strong, basic foundation in the FDA's regulatory requirements. Keynote speaker, Acting Commissioner Janet Woodcock, MD, reflected on FDA's use of EUAs and other resources in making drug, device, and biological products available to support the public health response to the COVID-19 pandemic.

Date	Type of Event	Event Name	Purpose
August 25, 2021	Webinar	Manufacturing, Supply Chain, and Inspections during the COVID-19 Public Health Emergency (**link**)	To provide the latest updates from CDER regarding policy and approaches toward manufacturing, supply chain, and inspections during the COVID-19 public health emergency.
August 30-September 1, 2021	Public workshop	Science and Regulation of Bacteriophage Therapy (**link**)	Hosted by FDA/CBER and NIH/NIAID to exchange information with the medical and scientific community about the regulatory and scientific issues associated with bacteriophage therapy.
September 1-2, 2021	Public workshop	FDA-M CERSI: Advancing the Development of Pediatric Therapeutics Complex Innovative Trial Design Public Workshop (**link**)	Hosted by FDA's Division of Pediatric and Maternal Health, Complex Innovative Trial Design Pilot Meeting Program (CDER and CBER), and the University of Maryland Center of Excellence in Regulatory Science and Innovation (CERSI) to discuss opportunities for leveraging complex and innovative trial designs, understand the challenges with their applications, and develop solutions on how challenges in the designs can be overcome. The workshop specifically focused on two topics of interest: bridging biomarkers in pediatric extrapolation and Bayesian techniques in pediatric studies.
September 17, 2021	Public meeting	VRBPAC (**link**)	To discuss the matter of additional doses of COVID-19 vaccines and specifically to discuss the Pfizer-BioNTech supplemental BLA for administration of a third ("booster") dose of Comirnaty (COVID-19 Vaccine, mRNA) in individuals 16 years of age and older.
September 20-21, 2021	Public workshop	Pharmacodynamic Biomarkers for Biosimilar Development and Approval (**link**)	Convened by the Duke-Margolis Center for Health Policy, under a cooperative agreement with FDA, to discuss the current and future role of pharmacodynamic biomarkers in improving the efficiency of biosimilar product development and approval.
September 28, 2021	Public workshop	Public Workshop on COVID-19 Lessons Learned: Clinical Evaluation of Therapeutics (**link**)	Convened by the Reagan-Udall Foundation for the FDA, under an FDA contract, to share lessons learned from the Federal COVID-19 Response or Countermeasures Acceleration Groups (formerly known as Operation Warp Speed) to bring relevant therapeutics to use in a public health emergency.
September 30, 2021	Public meeting	VRBPAC (**link**)	To hear an overview of the research programs in the Laboratory of Bacterial Polysaccharides, Division of Bacterial, Parasitic, and Allergenic Products, Office of Vaccines Research and Review, CBER, and to discuss and make recommendations on the selection of strains to be included in the influenza virus vaccines for the 2021 to 2022 southern hemisphere influenza season.

APPENDIX 5: ACRONYMS

3DPX	3D Print Exchange (NIH)
3DTANDMPS	3D Tissues and Microphysiological Systems for Modeling of Acute and Chronic Exposures to Stressors
AI	Artificial intelligence
AMR	Antimicrobial resistance
ANDA	Abbreviated New Drug Application
ATCC	American Type Culture Collection
ARS	Acute radiation syndrome
ASPR	Assistant Secretary for Preparedness and Response (HHS)
BAA	Broad Agency Announcement
BARDA	Biomedical Advanced Research and Development Authority
BE	Bioequivalence
BIMO	Bioresearch monitoring
BLA	Biologics License Application
BSL	Biosafety level
CARB	Combatting Antibiotic-Resistant Bacteria
CARES Act	Coronavirus Aid, Relief, and Economic Security Act
CBRN	Chemical, biological, radiological, and nuclear
CBER	FDA Center for Biologics Evaluation and Research
CCS	Container closure system
CDC	U.S. Centers for Disease Control and Prevention
CDER	FDA Center for Drug Evaluation and Research
CDISC	Clinical Data Interchange Standards Consortium
CDRH	FDA Center for Devices and Radiological Health
CEPI	Coalition for Epidemic Preparedness Innovations
CERSI	Center of Excellence in Regulatory Science and Innovation
CFR	Code of Federal Regulations
CGT	Cellular and gene therapy
CMS	Centers for Medicare and Medicaid Services
COVID-19	Coronavirus disease 2019 (caused by SARS-CoV-2)
CPAP	Continuous positive airway pressure
CR	Complete response
CRADA	Cooperative Research and Development Agreement
CRP	Critical Reagents Program
CSIRO	Commonwealth Scientific and Industrial Research Organization (Australia)
CT	Computed tomography
CTAP	Coronavirus Treatment Acceleration Program
Cures Act	21st Century Cures Act
DARPA	Defense Advanced Research Projects Agency
DHS	U.S. Department of Homeland Security

DNA	Deoxyribonucleic acid
DoD	U.S. Department of Defense
DRC	Democratic Republic of the Congo
DSCSA	Drug Supply Chain Security Act
DTRA	Defense Threat Reduction Agency
EHR	Electronic health records
EPA	Environmental Protection Agency
EUA	Emergency Use Authorization
EVD	Ebola virus disease
FAERS	FDA Adverse Event Reporting System
FAQ	Frequently asked questions
FARS	Focus Areas of Regulatory Science
FD&C Act	Federal Food, Drug, and Cosmetic Act
FDA	U.S. Food and Drug Administration
FDA-ARGOS	FDA Database for Regulatory Grade Microbial Sequences
FEMA	Federal Emergency Management Agency
FIND	Foundation for Innovative New Diagnostics
FFR	Filtering facepiece respirator
FTE	Full-time equivalent
FY	Fiscal year
GCP	Good clinical practice
GFAP	Glial fibrillary acidic protein
GHSA	Global Health Security Agenda
GHSI	Global Health Security Initiative
GI-ARS	Gastrointestinal acute radiation syndrome
GloPID-R	Global Research Collaboration for Infectious Diseases Preparedness
H-ARS	Hematopoietic syndrome of acute radiation syndrome
HCT/P	Human cells, tissues, and cellular and tissue-based products
HEOMD	Human Exploration and Operations Mission Directorate (NASA)
HHS	U.S. Department of Health and Human Services
HHS-CIADM	Department of Health and Human Services Centers for Innovation in Advanced Development and Manufacturing
HR	Heart rate
HRP	Human Research Program (part of NASA's Human Exploration and Operations Mission Directorate)
ICMRA	International Coalition of Medicines Regulatory Authorities
ICU	Intensive care unit
IDE	Investigational Device Exemption
IgM	Immunoglobulin M
IHR	International Health Regulations
IIE	Immediately in effect
ILAR	Institute of Laboratory Animal Research (National Academies of Sciences, Engineering, and Medicine)
IND	Investigational New Drug
IVD	In vitro diagnostic
JEE	Joint External Evaluation
JIC	Joint Information Center

JMEDICC	Joint Mobile Emerging Disease Intervention Clinical Capability
JRAC-SDC	Joint Rapid Acquisition Cell-Screening and Diagnostics Capability
JSTO	Joint Science and Technology Office
kg	Kilogram
lb	Pound
LDT	Laboratory developed test
LLNL	Lawrence Livermore National Laboratory
MCM	Medical countermeasure
MCM ADM	DoD Medical Countermeasures Advanced Development and Manufacturing
MCMi	FDA Medical Countermeasures Initiative
MERS-CoV	Middle East Respiratory Syndrome coronavirus
mg	Milligram
MOU	Memorandum of Understanding
MPS	Microphysiological systems
NAAT	Nucleic acid-based amplification test
NACCHO	National Association of County and City Health Officials
NASA	National Aeronautics and Space Administration
NASEM-HMD	National Academies of Sciences, Engineering, and Medicine, Health and Medicine Division
NCATS	National Center for Advancing Translational Sciences
NCBI	National Center for Biotechnology Information
NCI	National Cancer Institute
NDA	New Drug Application
NETCCN	National Emergency Telecritical Care Network
NGDS	Next-Generation Diagnostic System
NGO	Non-governmental organization
NGS	Next-generation sequencing
NHF	Nasal high flow
NIAID	National Institute of Allergy and Infectious Diseases
NICBR	National Interagency Confederation for Biological Research
NICU	Neonatal intensive care unit
NIH	U.S. National Institutes of Health
NIIMBL	National Institute for Innovation in Manufacturing Biopharmaceuticals
NIST	National Institute of Standards and Technology
NPPV	Non-invasive positive pressure ventilation
NPS	Nasopharyngeal swab
NSP1	SARS-CoV-2 nonstructural protein 1
NSTC	National Science and Technology Council
OCET	FDA Office of Counterterrorism and Emerging Threats
OCS	FDA Office of the Chief Scientist
OMHHE	FDA Office of Minority Health and Health Equity
OND	Office of New Drugs
OSA	Obstructive sleep apnea
OSEL	FDA CDRH Office of Science and Engineering Labs
OSTP	Office of Science and Technology Policy (White House)
OTC	Over-the-counter
PAHPAIA	Pandemic and All-Hazards Preparedness and Advancing Innovation Act of 2019

PAHPRA	Pandemic and All-Hazards Preparedness Reauthorization Act of 2013
PALM trial	Pamoja Tulinde Maisha ("Together Save Lives" in the Kiswahili language)
PAP	Positive airway pressure
PBMC	Peripheral blood mononuclear cell
PDUFA	Prescription Drug User Fee Act
PHEMCE	Public Health Emergency Medical Countermeasures Enterprise
PHS Act	Public Health Service Act
PMA	Premarket Approval
POC	Point of care
PPE	Personal protective equipment
PPP	Public private partnership
PR	Pulse rate
PRV	Priority review voucher
Rad/nuc	Radiological/nuclear
REMS	Risk Evaluation and Mitigation Strategies
RMAT	Regenerative medicine advanced therapy
RMP	Regulatory Management Plan
RNA	Ribonucleic acid
RSCSPP	Resilient Supply Chain and Shortages Prevention Program
RSV	Respiratory syncytial virus
RWD	Real-world data
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SDTM	Study Data Tabulation Model
SEND	Standard for the Exchange of Nonclinical Data
SENDIG	Standard for Exchange of Nonclinical Data Implementation Guide
SHIELD	Systemic Harmonization and Interoperability Enhancement for Laboratory Data
SLEP	Shelf-Life Extension Program
SLTT	State, local, tribal and territorial
SNS	Strategic National Stockpile
SPA	Special Protocol Assessment
Sp02	Oxygen saturation of arterial hemoglobin
TATRC	Telemedicine and Advanced Technology Research Center
TBE	Tick-borne encephalitis
TBI	Traumatic brain injury
TTFED	Tri-Agency Task Force for Emergency Diagnostics
UCH-L1	ubiquitin carboxyl-terminal hydrolase L1
U.S.	United States
USAMRDC	U.S. Army Medical Research and Development Command
USAMRIID	U.S. Army Medical Research Institute of Infectious Diseases
USDA	U.S. Department of Agriculture
USG	United States government
USGS	U.S. Geological Survey
UTMB	University of Texas Medical Branch
VA	U.S. Department of Veterans Affairs
VRBPAC	Vaccines and Related Biological Products Advisory Committee
WHO	World Health Organization

ENDNOTES

[1] For a listing of MCM-related legislation, see: **https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/mcm-related-counterterrorism-legislation**

[2] Detailed information on FDA's MCM development and review activities covering FY 2011-2019 can be found at: **https://www.fda.gov/emergency-preparedness-and-response/about-mcmi/publications-and-reports**

[3] See: **https://www.phe.gov/emergency/news/healthactions/phe/Pages/2019-nCoV.aspx**

[4] WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020, available at: **https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020**

[5] For the latest available snapshot of FDA's response, see FDA COVID-19 Response At-A-Glance Summary, at: **https://www.fda.gov/media/137005/download**

[6] For more information see the FDA news release at: **https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-covid-19** and FDA's approval of Veklury (remdesivir) for the treatment of COVID-19—the science of safety and effectiveness at: **https://www.fda.gov/drugs/news-events-human-drugs/fdas-approval-veklury-remdesivir-treatment-covid-19-science-safety-and-effectiveness**

[7] For more information, see the FDA news release at: **https://www.fda.gov/news-events/press-announcements/fda-permits-marketing-first-sars-cov-2-diagnostic-test-using-traditional-premarket-review-process**

[8] For more information see the FDA news release at: **https://www.fda.gov/news-events/press-announcements/fda-approves-first-covid-19-vaccine**

[9] For more information see Coronavirus Treatment Acceleration Program (CTAP), at: **https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap** and The Path Forward: Coronavirus Treatment Acceleration Program, at: **https://www.fda.gov/news-events/fda-voices/path-forward-coronavirus-treatment-acceleration-program**

[10] See COVID-19-Related Guidance Documents for Industry, FDA Staff, and Other Stakeholders, at: **https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-related-guidance-documents-industry-fda-staff-and-other-stakeholders**

[11] This guidance is available at: **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-vaccines-prevent-covid-19**

[12] This guidance is available at: **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/covid-19-master-protocols-evaluating-drugs-and-biological-products-treatment-or-prevention**

[13] EUA information, and list of current EUAs is available at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization**

[14] For more information see the FDA news release at: **https://www.fda.gov/drugs/drug-safety-and-availability/fda-authorizes-regen-cov-monoclonal-antibody-therapy-post-exposure-prophylaxis-prevention-covid-19**

[15] For more information see the FDA press release FDA Takes Steps to Increase Availability of COVID-19 Vaccine at: **https://www.fda.gov/news-events/press-announcements/fda-takes-steps-increase-availability-covid-19-vaccine**

[16] For more information see Expiration Dating Extension at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/expiration-dating-extension#covidvaccines**

[17] Also see A Closer Look at the FDA's Center for Devices and Radiological Health's Unprecedented Efforts in the COVID-19 Response, at: **https://www.fda.gov/news-events/fda-voices/closer-look-fdas-center-devices-and-radiological-healths-unprecedented-efforts-covid-19-response**

[18] For more information see the FDA news release at: **Coronavirus (COVID-19) Update: FDA takes steps to streamline path for COVID-19 screening tools, provides information to help groups establishing testing programs | FDA**

[19] For more information about FDA's work to address variants, see the FDA news release at: **https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-continues-important-work-support-medical-product-development-address**

[20] For more information see the FDA news release at: **https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-issues-policies-guide-medical-product-developers-addressing-virus**. A list of guidances with links is included in this report in Appendix 3.

[21] For more information see FDA authorizes revisions to fact sheets to address SARS-CoV-2 variants for monoclonal antibody products under emergency use authorization at: **https://www.fda.gov/drugs/drug-safety-and-availability/fda-authorizes-revisions-fact-sheets-address-sars-cov-2-variants-monoclonal-antibody-products-under**

[22] See, for example, Bamlanivimab/etesevimab updates from ASPR at: **https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Bamlanivimab-etesevimab/Pages/default.aspx**

[23] For more information see SARS-CoV-2 Viral Mutations: Impact on COVID-19 Tests at: **https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-viral-mutations-impact-covid-19-tests**

[24] See, for example, a July 2021 FDA Grand Rounds recording describing one such project at: **https://www.fda.gov/science-research/fda-grand-rounds/sars-cov-2-host-pathogen-interaction-vaccines-variants-concern-07082021-07082021**

[25] Also see Coronavirus (COVID-19) Update: FDA takes further steps to help mitigate supply interruptions of food and medical products, at: **https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-takes-further-steps-help-mitigate-supply-interruptions-food-and**

[26] Executive Order on Ensuring Essential Medicines, Medical Countermeasures, and Critical Inputs Are Made in the United

States, available (archived) at: **https://trumpwhitehouse.archives.gov/presidential-actions/executive-order-ensuring-essential-medicines-medical-countermeasures-critical-inputs-made-united-states/** (cited: March 23, 2021)

[27] The list, and additional information is available on the page Executive Order 13944 List of Essential Medicines, Medical Countermeasures, and Critical Inputs at: **https://www.fda.gov/about-fda/reports/executive-order-13944-list-essential-medicines-medical-countermeasures-and-critical-inputs**

[28] Coronavirus Aid, Relief, and Economic Security Act (CARES Act) Drug Shortage Mitigation Efforts at: **https://www.fda.gov/drugs/drug-shortages/coronavirus-aid-relief-and-economic-security-act-cares-act-drug-shortage-mitigation-efforts**

[29] For more information see FDA's Budget: Medical Device Supply Chain and Shortages Prevention Program at: **https://www.fda.gov/news-events/fda-voices/fdas-budget-medical-device-supply-chain-and-shortages-prevention-program**

[30] The final guidance Manufacturing Considerations for Licensed and Investigational Cellular and Gene Therapy Products During COVID-19 Public Health Emergency, issued in January 2021, is available at: **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/manufacturing-considerations-licensed-and-investigational-cellular-and-gene-therapy-products-during**

[31] Also see FDA Protects Patients and Consumers from Fraud During COVID-19, at: **https://www.fda.gov/news-events/fda-voices/fda-protects-patients-and-consumers-fraud-during-covid-19**

[32] See Fraudulent Coronavirus Disease 2019 (COVID-19) Products, at: **https://www.fda.gov/consumers/health-fraud-scams/fraudulent-coronavirus-disease-2019-covid-19-products**

[33] Also see: FDA updates on hand sanitizers consumers should not use, at: **https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-hand-sanitizers-consumers-should-not-use**

[34] For more information, see FDA and global partners to analyze coronavirus samples, at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-regulatory-science/fda-and-global-partners-analyze-coronavirus-samples**

[35] For more information, see Cellular signaling and immune correlates for SARS-CoV-2 infection, at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-regulatory-science/cellular-signaling-and-immune-correlates-sars-cov-2-infection**

[36] For more information, see Human organ chips for radiation countermeasure development at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-regulatory-science/human-organ-chips-radiation-countermeasure-development**

[37] For more information, see A new approach for understanding Ebola virus pathogenesis at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-regulatory-science/new-approach-understanding-ebola-virus-pathogenesis**

[38] For more information, see Expanding next-generation sequencing tools to support pandemic preparedness and response at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-regulatory-science/expanding-next-generation-sequencing-tools-support-pandemic-preparedness-and-response**

[39] For more information, see Innovation to Respond to COVID-19, at: **https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/innovation-respond-covid-19**

[40] For more information, including a poster overview of the COVID-19 Evidence Accelerator presented at the 2021 FDA Science Forum, see COVID-19 Evidence Accelerator at: **https://www.evidenceaccelerator.org/**

[41] For more information about TTFED, see: **https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/information-laboratories-implementing-ivd-tests-under-eua#taskforce**

[42] The challenge was active November 30, 2020 through January 29, 2021. For more information see: **https://precision.fda.gov/challenges/12**

[43] For more information see FDA receives HHS grant to expand CURE ID platform for COVID-19 treatments at: **https://www.fda.gov/drugs/drug-safety-and-availability/fda-receives-hhs-grant-expand-cure-id-platform-covid-19-treatments**

[44] For more information, visit **www.fda.gov/coronavirus**

[45] FDA press announcements are available at: **https://www.fda.gov/news-events/fda-newsroom/press-announcements**

[46] Where available, select speeches by FDA officials are posted at: **https://www.fda.gov/news-events/speeches-fda-officials**

[47] Consumer Updates, including COVID-19 topics, are available at: **https://www.fda.gov/consumers/consumer-updates**

[48] FDA's COVID-19 video playlist is available on YouTube at: **https://www.youtube.com/playlist?list=PLey4Qe-Uxcx-a3152uA5wSC6XRsOK_-9_x**

[49] FDA Voices, including COVID-19 topics, are available at: **https://www.fda.gov/news-events/fda-newsroom/fda-voices**

[50] A list of FDA interactive media accounts is available at: **https://www.fda.gov/news-events/interactive-media**

[51] To subscribe to a variety of FDA email updates, including MCMi updates, visit: **https://public.govdelivery.com/accounts/USFDA/subscriber/new**

[52] FDA Insight podcasts are available on various podcast apps, and at: **https://www.fda.gov/news-events/fda-newsroom/fda-insight**

[53] See COVID-19 Frequently Asked Questions, at: **https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-frequently-asked-questions**

[54] See Multilingual COVID-19 Resources, at: **https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/multilingual-covid-19-resources**

[55] Previous issues of the MCMi email update—one of the two sent weekly during the response—are available at: **https://www.fda.gov/emergency-preparedness-and-response/about-mcmi/mcmi-newsletters**

[56] For more information, see the CDER web page Stakeholder Engagement | COVID-19 at: **https://www.fda.gov/drugs/coronavirus-covid-19-drugs/stakeholder-engagement-covid-19**

[57] Materials from previous events are available at: **https://www.fda.gov/medical-devices/workshops-confer-**

ences-medical-devices/virtual-town-hall-series-coronavirus-covid-19-test-development-and-validation-10142020-10142020

[58] Materials from previous events are available at: https://www.fda.gov/medical-devices/workshops-conferences-medical-devices/webinar-series-respirators-and-other-personal-protective-equipment-ppe-health-care-personnel-use

[59] For more information, see Coronavirus (COVID-19) and Medical Devices, at: https://www.fda.gov/medical-devices/emergency-situations-medical-devices/coronavirus-covid-19-and-medical-devices

[60] This Consumer Update, Know Your Treatment Options for COVID-19, is available at: https://www.fda.gov/consumers/consumer-updates/know-your-treatment-options-covid-19

[61] See, for example, the Consumer Update, Why You Should Not Use Ivermectin to Treat or Prevent COVID-19, at: https://www.fda.gov/consumers/consumer-updates/why-you-should-not-use-ivermectin-treat-or-prevent-covid-19

[62] The Multilingual COVID-19 Vaccines Myths toolkit is available at: https://www.fda.gov/about-fda/fda-en-espanol/multilingual-covid-19-vaccines-myths-social-media-toolkit

[63] FDA In Brief: FDA Advises Against Use of SARS-CoV-2 Antibody Test Results to Evaluate Immunity or Protection From COVID-19, Including After Vaccination | FDA

[64] For more information from FDA's Office of Minority Health and Health Equity, see Vaccine Ready: Addressing COVID-19 Health Disparities among Racial and Ethnic Minority Communities at: https://www.fda.gov/news-events/fda-voices/vaccine-ready-addressing-covid-19-health-disparities-among-racial-and-ethnic-minority-communities

[65] The #VaccineReady toolkit is available at: https://www.fda.gov/consumers/minority-health-and-health-equity/vaccine-ready-social-media-toolkit.

[66] A recording of this webinar, Health Equity and COVID-19: What Minority Communities Need to Know, is available on FDA's YouTube channel at: https://youtube/_TCfqKSf1do?list=PLey4Qe-UxcxbdJTzbekD712YosmrV78uE

[67] See, for example, Cellular signaling and immune correlates for SARS-CoV-2 infection, funded by OCET and OMHHE, at: https://www.fda.gov/emergency-preparedness-and-response/mcm-regulatory-science/cellular-signaling-and-immune-correlates-sars-cov-2-infection

[68] More information is available at: Drugs@FDA: https://www.accessdata.fda.gov/scripts/cder/daf/, Biologics Products & Establishments: https://www.fda.gov/vaccines-blood-biologics/biologics-products-establishments, and Medical Device Databases: https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/medical-device-databases

[69] For more information see: https://www.fda.gov/drugs/drug-safety-and-availability/fda-approves-drug-treat-smallpox

[70] For more information see the FDA news release: https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-covid-19

[71] For more information, see FDA's approval of Veklury (remdesivir) for the treatment of COVID-19—the science of safety and effectiveness at: https://www.fda.gov/drugs/news-events-human-drugs/fdas-approval-veklury-remdesivir-treatment-covid-19-science-safety-and-effectiveness

[72] For the latest information, see the FDA web page Comirnaty and Pfizer-BioNTech COVID-19 Vaccine at: https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/comirnaty-and-pfizer-biontech-covid-19-vaccine

[73] For more information, see the FDA news release at: https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-ebola-virus

[74] For more information, see: https://www.fda.gov/drugs/news-events-human-drugs/fda-approves-treatment-ebola-virus

[75] For more information, see the FDA news release at: https://www.fda.gov/news-events/press-announcements/fda-expands-approval-influenza-treatment-post-exposure-prevention

[76] For more information, see from DTRA: https://www.dvidshub.net/news/405983/memed-key-diagnostic-tool-receives-fda-clearance

[77] For updated information about MCM approvals after the FY 2020 reporting period, see MCMi News and Events at: https://www.fda.gov/emergency-preparedness-and-response/about-mcmi/mcmi-news-and-events

[78] For the latest updates on expiry dating extensions for chemical nerve agent auto-injectors, see FDA alerts health care providers and emergency responders of expiration date extensions of certain auto-injectors manufactured by Meridian Medical Technologies at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-alerts-health-care-providers-and-emergency-responders-expiration-date-extensions-certain-auto

[79] FDA. Extending Expiration Dates of Doxycycline Tablets and Capsules in Strategic Stockpiles: Guidance for Government Public Health and Emergency Response Stakeholders. April 2019. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/extending-expiration-dates-doxycycline-tablets-and-capsules-strategic-stockpiles

[80] For more information, see Expiration date extensions of certain lots of doxycycline hyclate capsules at: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/expiration-date-extensions-certain-lots-doxycycline-hyclate-capsules

[81] The EUA letter of authorization as amended on February 26, 2021, is available at: https://www.fda.gov/media/146320/download

[82] For more information applicable to IVD pre-EUAs, see How to Submit a Pre-EUA for *In vitro* Diagnostics to FDA at: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/how-submit-pre-eua-vitro-diagnostics-fda

[83] For more information, see the FDA news release at: https://www.fda.gov/news-events/press-announcements/covid-19-update-fdas-ongoing-commitment-transparency-covid-19-euas

[84] CDER posts information on the web page CDER Scientific Review Documents Supporting Emergency Use Authorizations

for Drug and Biological Therapeutic Products at: **https://www.fda.gov/drugs/coronavirus-covid-19-drugs/cder-scientific-review-documents-supporting-emergency-use-authorizations-drug-and-biological** and CBER posts information on the EUA web page at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization**

[85] For more information, see NIH Clinical trial of investigational Ebola treatments begins in the Democratic Republic of the Congo at: **https://www.nih.gov/news-events/news-releases/clinical-trial-investigational-ebola-treatments-begins-democratic-republic-congo**

[86] For more information, see Independent Monitoring Board Recommends Early Termination of Ebola Therapeutics Trial in DRC Because of Favorable Results with Two of Four Candidates at: **https://www.niaid.nih.gov/news-events/independent-monitoring-board-recommends-early-termination-ebola-therapeutics-trial-drc**

[87] Also see FDA-ARGOS SARS-CoV-2 Reference Grade Sequence Data, at: **https://www.fda.gov/medical-devices/database-reference-grade-microbial-sequences-fda-argos/fda-argos-sars-cov-2-reference-grade-sequence-data**

[88] In previous reports, accomplishments of this team were listed under Warfighter Action Team. The name was updated in FY 2019 to better reflect FDA/DoD collaborations under PL 115-92, enacted in December 2017, and the subsequent FDA/DoD Memorandum of Understanding, signed in November 2018, available at: **https://www.fda.gov/about-fda/domestic-mous/mou-225-19-001**

[89] A list of COVID-19-related guidance documents for industry, FDA staff, and other stakeholders is available at: **https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-related-guidance-documents-industry-fda-staff-and-other-stakeholders**

[90] See for example, Guidance for Industry - Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA (Prescription Drug User Fee Act) Products (December 2017) available at: **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/formal-meetings-between-fda-and-sponsors-or-applicants-pdufa-products-guidance-industry** and Requests for Feedback on Medical Device Submissions: The Q-Submission Program (May 2019) available at: **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/requests-feedback-and-meetings-medical-device-submissions-q-submission-program**

[91] For more information on Special Protocol Assessments see Guidance for Industry – Special Protocol Assessment (April 2018) available at: **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/special-protocol-assessment-guidance-industry**

[92] Available at: **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/covid-19-public-health-emergency-general-considerations-pre-ind-meeting-requests-covid-19-related**

[93] For more information on the Interactive Review Process see Types of Communication During the Review of Medical Device Submissions - Guidance for Industry and FDA Staff available at: **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/types-communication-during-review-medical-device-submissions**

[94] Available at: **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/effects-covid-19-public-health-emergency-formal-meetings-and-user-fee-applications-questions-and**

[95] Available at: **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/effects-covid-19-public-health-emergency-formal-meetings-and-user-fee-applications-medical-devices**

[96] See Availability of Regulatory Management Plans at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/availability-regulatory-management-plans**

[97] A list of MCM-related events by year is available in the MCMi Events Archive: **https://www.fda.gov/emergency-preparedness-and-response/about-mcmi/mcmi-events-archive**

[98] Where available, MCM-related legal and policy presentations given by FDA staff can be found at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/mcm-related-legal-and-policy-presentations-publications-and-qas** and MCMi regulatory science presentations can be found at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-regulatory-science/mcmi-regulatory-science-presentations**

[99] For more information, see Implementation of the National Biodefense Strategy, published in September 2020 by HHS, at: **https://www.phe.gov/Preparedness/biodefense-strategy/2019-report/Pages/default.aspx**

[100] For more information, see Information for Laboratories Implementing IVD Tests Under EUA at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/information-laboratories-implementing-ivd-tests-under-eua**

[101] MOU 225-21-006 was signed January 15, 2021, and is available at: **https://www.fda.gov/about-fda/domestic-mous/mou-225-21-006**

[102] For more information see Accelerating the Adoption of Advanced Manufacturing Technologies to Strengthen Our Public Health Infrastructure at: **https://www.fda.gov/news-events/fda-voices/accelerating-adoption-advanced-manufacturing-technologies-strengthen-our-public-health**

[103] MOU 225-20-008, available at: **https://www.fda.gov/about-fda/domestic-mous/mou-225-20-008**

[104] Additional findings and best practices were published in November 2021 in *New England Journal of Medicine Catalyst*: Trust in the Time of COVID-19: 3D Printing and Additive Manufacturing as a Solution to Supply Chain Gaps, at: **https://catalyst.nejm.org/doi/full/10.1056/CAT.21.0321**

[105] MOU 225-18-027, available at: **https://www.fda.gov/about-fda/domestic-mous/mou-225-18-027**

[106] For more information see the NASA solicitation at: **https://nspires.nasaprs.com/external/solicitations/summary.do?solId={6CEDD2E4-B3C2-5A70-EB94-01A956BB-D965}&path=&method=init**

[107] For more information, see from NASA 'Chipping' Away at Personalized Medicine at: **https://science.nasa.gov/science-news/biological-physical/chipping-away-at-personalized-medicine**

[108] "Through a growing multisectoral partnership of international organizations, non-governmental stakeholders, and more than 50 countries, GHSA is accelerating efforts to build countries' capacity to prevent, detect, and respond to infectious diseases and achieve the core capacities required by the International Health Regulations (IHR)." HHS. Global Health Security Agenda. **https://www.hhs.gov/about/agencies/oga/global-health-security/agenda/index.html**

[109] For more about JEE efforts, see from HHS, U.S. Health Security National Action Plan: Strengthening Implementation of the International Health Regulations, at: **https://www.phe.gov/Preparedness/international/Pages/JEE.aspx**

[110] For example, CBER-WHO Cooperative Agreement: Supporting Influenza Vaccine Introduction to Low-Middle Income Countries (**https://www.fda.gov/vaccines-blood-biologics/international-activities/cber-who-cooperative-agreement-supporting-influenza-vaccine-introduction-low-middle-income-countries**); for more about CBER's WHO Cooperative Agreements, see: **https://www.fda.gov/vaccines-blood-biologics/who-engagements/who-cooperative-agreements**

[111] Follow MCMi on Twitter at: **https://twitter.com/FDA_MCMi**

[112] For example, pharmacokinetic modeling was the basis for pediatric labeling of the monoclonal antibody raxibacumab, approved in 2012 to treat inhalational anthrax, in combination with appropriate antibacterial drugs, and for prophylaxis of inhalational anthrax when alternative therapies are not available or are not appropriate. Label information is available at: **https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/125349s000lbl.pdf**

[113] Intramural FDA MCM regulatory science is funded through a competitive challenge grant process. Extramural MCM regulatory science is funded primarily through a Broad Agency Announcement (BAA) (Food and Drug Administration Broad Agency Announcement for the Advanced Research and Development of Regulatory Science). More information is available at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-regulatory-science/intramural-research** and **https://www.fda.gov/emergency-preparedness-and-response/mcm-regulatory-science/extramural-research**

[114] For more information see Focus Areas of Regulatory Science at: **https://www.fda.gov/science-research/advancing-regulatory-science/focus-areas-regulatory-science**

[115] A list of tools is available at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-regulatory-science/regulatory-science-research-tools**

[116] For more information, see Coronavirus (COVID-19) Update: FDA Provides New Tool to Aid Development and Evaluation of Diagnostic Tests That Detect SARS-CoV-2 Infection, at: **https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-provides-new-tool-aid-development-and-evaluation-diagnostic-tests**

[117] See Regulatory Science Research Tools, at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-regulatory-science/regulatory-science-research-tools**

[118] Also see SARS-CoV-2 Reference Panel Comparative Data at: **https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-reference-panel-comparative-data**

[119] For more information see FDA Sentinel System's Coronavirus (COVID-19) Activities, at: **https://www.sentinelinitiative.org/assessments/fda-sentinel-systems-coronavirus-covid-19-activities**

[120] The Systemic Harmonization and Interoperability Enhancement for Laboratory Data (SHIELD) collaborative is a multi-agency/stakeholder network consisting of FDA, CDC, NIH, Office of the National Coordinator for Health Information Technology (ONC), CMS, VA, IVD manufacturers, electronic health record vendors, laboratories, College of American Pathologists, standards developers, Pew Charitable Trusts, National Evaluation System for health care Technology, and academia. See, from HHS: **https://aspe.hhs.gov/shield-standardization-lab-data-enhance-patient-centered-outcomes-research-and-value-based-care**

[121] The COVID-19 Evidence Accelerator is an initiative launched by the Reagan-Udall Foundation for the FDA, in collaboration with Friends of Cancer Research, to provide a unique venue for major data organizations, government and academic researchers, and health systems to gather and design quick-turn-around queries and share their results. The project includes a Diagnostics Evidence Accelerator and a Therapeutics Evidence Accelerator. For more information, see: **https://evidenceaccelerator.org/**

[122] For more information, see FDA-ARGOS SARS-CoV-2 Reference Grade Sequence Data, at: **https://www.fda.gov/medical-devices/database-reference-grade-microbial-sequences-fda-argos/fda-argos-sars-cov-2-reference-grade-sequence-data**

[123] Also see FDA Zika virus reference panel for molecular-based diagnostic devices supports product testing for Emergency Use Authorization and 510(k) submissions, at: **https://www.fda.gov/vaccines-blood-biologics/science-research-biologics/fda-zika-virus-reference-panel-molecular-based-diagnostic-devices-supports-product-testing-emergency**

[124] FDA began distribution of the FDA SARS-CoV-2 Reference Panel in May 2020. For more information, see SARS-CoV-2 Reference Panel Comparative Data at: **https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-reference-panel-comparative-data**

[125] These findings are important because they suggest the vaccine could both protect recipients and reduce transmission—even when virus strains emerge with differing envelope proteins, a type of change, that when it occurs, can make existing influenza vaccines less effective. Also see, in *Vaccine*: Reduction of influenza virus transmission from mice immunized against conserved viral antigens is influenced by route of immunization and choice of vaccine antigen, available at: **https://doi.org/10.1016/j.vaccine.2018.06.051**

[126] For additional information, see from HHS, Tick-Borne Disease Working Group, at: **https://www.hhs.gov/ash/advisory-committees/tickbornedisease/index.html**

[127] For more information see Animal Rule Information, Data Standards for Animal Rule Studies at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-regulatory-science/animal-rule-information#datastandards**

[128] Learn more about agency-wide support for advanced manufacturing in Investing in Advanced Manufacturing to Support Public Health Preparedness, at: **https://www.fda.gov/news-events/fda-voices/investing-advanced-manufacturing-support-public-health-preparedness**

[129] *Executive Summary: Assessing the Role of Additive Manufacturing in Support of the U.S. COVID-19* Response is available at: **https://www.fda.gov/media/150615/download**. The full report, *Assessing the Role of Additive Manufacturing in Support of the U.S. COVID-19 Response - An impact survey of interagency 3D Printing response efforts*, covering actions taken between February 15, 2020 and July 15, 2020, is available at: **https://www.fda.gov/media/150614/download**

[130] The project report, *Analysis of the Advantages of and Barriers to Adoption of Smart Manufacturing for Medical Products*, is available at: **https://www.fda.gov/media/152569/download** and an infographic summarizing the results is available at: **https://www.fda.gov/media/152568/download**

[131] For more information see the company press release Siemens awarded $1.78M FDA contract to showcase advanced digital design and manufacturing at: **https://new.siemens.com/us/en/company/press/press-releases/usa/siemens-fda-contract-showcases-advanced-digital-design-manufacturing.html**

[132] On December 15, 2020, Dr. Jeffrey C. Baker, Deputy Director of the FDA's Office of Biotechnology Products, CDER, discussed how FDA's efforts help innovation and implementation of advanced manufacturing technologies regarding food and drug safety. This episode of the FDA Insight podcast also included a discussion of why advanced manufacturing is important to public health, emergency preparedness and response. The recording is available at: **https://www.fda.gov/news-events/fda-insight/fda-insight-advanced-manufacturing**

[133] Executive Order on Ensuring Essential Medicines, Medical Countermeasures, and Critical Inputs Are Made in the United States, available (archived) at: **https://trumpwhitehouse.archives.gov/presidential-actions/executive-order-ensuring-essential-medicines-medical-countermeasures-critical-inputs-made-united-states/**

[134] For more information see Executive Order 13944 List of Essential Medicines, Medical Countermeasures, and Critical Inputs, at: **https://www.fda.gov/about-fda/reports/executive-order-13944-list-essential-medicines-medical-countermeasures-and-critical-inputs**

[135] See Medical Device Types to Help Determine Section 506J Notification Obligations at: **https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/medical-device-types-help-determine-section-506j-notification-obligations**

[136] For more information on PAHPAIA, see MCM-Related Counterterrorism Legislation at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/mcm-related-counterterrorism-legislation**

[137] Public Law 116-22, Jun 24, 2019, 133 Stat. 905. Available at **https://www.congress.gov/116/plaws/publ22/PLAW-116publ22.pdf**

[138] When final, this guidance will represent the agency's current thinking on this subject. The draft guidance is available at: **https://www.fda.gov/media/110193/download**

[139] See Fee for Using a Material Threat Medical Countermeasure Priority Review Voucher in Fiscal Year 2022 (86 FR 54215, September 30, 2021). **https://www.federalregister.gov/documents/2021/09/30/2021-21317/fee-rate-for-using-a-material-threat-medical-countermeasure-priority-review-voucher-in-fiscal-year**

[140] Material threat MCM PRVs issued are listed on FDA website at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/21st-century-cures-act-mcm-related-cures-provisions#prv**

[141] Also see, in the Federal Register, Process for Making Available Guidance Documents Related to Coronavirus Disease 2019, at: **https://www.federalregister.gov/documents/2020/03/25/2020-06222/process-for-making-available-guidance-documents-related-to-coronavirus-disease-2019**

[142] For more information see 2021 FDA Science Forum at: **https://www.fda.gov/science-research/fda-science-forum/2021-fda-science-forum-05262021-05272021**

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