U.S. FOOD & DRUG ADMINISTRATION

FY 2022
MCMi Program Update

FDA MEDICAL COUNTERMEASURES INITIATIVE

Contents

List of Tables

List of Boxes

List of Figures

BACKGROUND

FDA plays a critical role in protecting the U.S. from chemical, biological, radiological, and nuclear threats, and emerging infectious diseases, like COVID-19 and mpox. This report provides updates on FY 2022 activities agency-wide to support medical countermeasure-related public health emergency preparedness and response.

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), and outbreaks including Ebola and mpox.[1] 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.[2]

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.[3] This includes the agency's unprecedented COVID-19 pandemic response efforts that began in December 2019, and continue today. 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.[4,5]

In 2010, FDA launched its Medical Countermeasures Initiative (**MCMi**) Program, building on the substantive MCM work ongoing at FDA. The Program

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[1] In November 2022, the World Health Organization **announced**, and the USG **supported**, renaming monkeypox disease to mpox. This report refers to the disease as mpox, except where the term "monkeypox" is part of a product name, indication, guidance or policy title, or other proper name (such as web page titles) that had not yet been updated at the time of report compilation.

[2] 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 their connection to public health preparedness. Inclusion of such examples is not intended as comprehensive reporting on agency activities related to these topics.

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

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

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

focuses 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 the agency to more effectively support preparedness and response efforts. The Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (**PAHPRA**)[6] requires FDA to issue an annual report detailing its MCM activities. This report responds to that requirement for fiscal year (FY) 2022 (October 1, 2021 – September 30, 2022).[7]

What are medical countermeasures?

Medical countermeasures, or MCMs, are FDA-regulated products, including biologics, drugs, and devices, that may be used in the event of a potential public health emergency stemming from a terrorist attack with a biological, chemical, or radiological/nuclear material, or a naturally occurring emerging disease. MCMs can be used to diagnose, prevent, protect from, or treat conditions associated with chemical, biological, radiological, or nuclear threats, or emerging infectious diseases.

FY 2022 RESOURCES FOR MCM ACTIVITIES

Table 1: FY 2022 resources for MCM activities (dollars in millions)

	FY 22 Estimate	FY 22 FTE Estimate
CBRN Base Funding	$126.06	474.7
Pandemic Influenza Base Funding	$28.83	93.1
MCMi Base Funding	$36.55	110.5
Subtotal	**$191.44**	**678.3**
COVID-19 Supplemental Funding	$306.71	178.0
Total	**$498.15**	**856.3**

FDA obligated an estimated $498.15 million in FY 2022 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 856.3 full-time equivalents (FTEs).

[6] Public Law 113-5, 127 Stat. 161 (2014).

[7] Detailed information on FDA's MCM development and review activities covering FY 2011-2021 can be found at: **https://www.fda.gov/emergency-preparedness-and-response/about-mcmi/publications-and-reports**

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.[8]

The following sections provide detail on achievements in FY 2022 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 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 that may include an expedited approval pathway 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 legal, 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

[8] An updated publicly available list of high-priority threats identified by the Enterprise for which MCMs are needed can be found in the ***PHEMCE Strategy and Implementation Plan 2022*** *(see* **Appendix B**), published in October 2022.

MEDICAL COUNTERMEASURE APPROVALS

During FY 2022, 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[9] in FY 2022 (***see Appendixes 1 and 2*** for lists of FY 2022 MCM approvals). The agency also issued and amended numerous EUAs (see: ***Enabling Access to MCMs Under FDA's Emergency Use Authorization Authority***).

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

To help with preparedness of U.S. military personnel, in February 2022, FDA **approved** a New Drug Application (NDA) for a naloxone hydrochloride autoinjector for use by military personnel and chemical incident responders for emergency treatment of patients 12 years of age and older where use of high-potency opioids, such as fentanyl analogues, as a chemical weapon is suspected, and for temporary prophylaxis of respiratory and/or central nervous system depression in military personnel and chemical incident responders entering an area contaminated with high-potency opioids such as fentanyl analogues.

In addition, in August 2022, FDA **approved** an NDA for the use of Midazolam Injection, 10 mg/0.7 mL, autoinjector, indicated for the treatment of status epilepticus in adults. This indication could include seizures resulting from nerve agent exposure. DoD developed the product with Rafa Laboratories, Ltd. **According to JPEO-CBRND** (the U.S. Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense), the autoinjector "improves upon and will replace the currently fielded convulsant antidote for nerve agent (CANA) diazepam

autoinjector." The DoD's Chemical and Biological Defense Program also supported this effort.

MCMs to diagnose, treat, or prevent COVID-19

In addition to activities noted in other sections of this report to enable access to investigational MCMs to diagnose, prevent, or treat COVID-19, FDA approved additional COVID-19 vaccines, therapeutics, and diagnostic tests in FY 2022.

Vaccines

In January 2022, FDA **approved** the second COVID-19 vaccine, **Spikevax** (COVID-19 Vaccine, mRNA) from ModernaTX, Inc., a monovalent COVID-19 vaccine for the prevention of COVID-19 in individuals 18 years of age and older as a two-dose series. Also known as the **Moderna COVID-19 Vaccine**, this vaccine has been available under EUA since December 18, 2020.

In July 2022, FDA approved **Comirnaty** (COVID-19 Vaccine, mRNA) for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 12 through 15 years of age as a two-dose series. Also known as the **Pfizer-BioNTech COVID-19 Vaccine**, this vaccine has been authorized for emergency use in this age group since May 2021. Comirnaty has been approved for use in individuals 16 years of age and older since August 2021. The Pfizer-BioNTech COVID-19 Vaccine has been available under EUA since December 2020. In December 2021, FDA **approved** a manufacturing change for Comirnaty to include a

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

formulation that uses a different buffer. Buffers help maintain a vaccine's pH (a measure of how acidic or alkaline a solution is) and stability. This new formulation is more stable at refrigerated temperatures for longer periods of time, permitting greater flexibility for vaccination providers.

Therapeutics

In April 2022, FDA **approved** the expanded use of the first COVID-19 treatment, Veklury (remdesivir), to include young children. FDA approved the expanded use of Veklury to include pediatric patients 28 days of age and older weighing at least 3 kilograms (kg) (about 7 pounds) with positive results of direct SARS-CoV-2 viral testing, who are hospitalized, or not hospitalized and have mild-to-moderate COVID-19 and are at high risk for progression to severe COVID-19, including hospitalization or death. Previously, Veklury was only approved to treat certain adults and pediatric patients (12 years of age and older who weigh at least 40 kg, which is about 88 pounds) with COVID-19. The April 2022 action made Veklury the first approved COVID-19 treatment for children less than 12 years of age. Previously, in January 2022, FDA **approved** Veklury for a three-day dosing regimen for the treatment of coronavirus disease 2019 (COVID-19) in adults and pediatric patients (12 years of age and older and weighing at least 40 kg) with positive results of direct severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral testing, who are not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death.

In May 2022, FDA **approved** Olumiant (baricitinib) for the treatment of COVID-19 in hospitalized adults requiring supplemental oxygen, noninvasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).

Diagnostic tests

In November 2021, FDA cleared a 510(k) for a SARS-CoV-2 test. The **BioFire COVID-19 Test** offered under an **EUA** since March 2020, is the second SARS-CoV-2 diagnostic test granted marketing authorization that permits the test to be marketed beyond the public health emergency.[10] In July 2022, FDA cleared an **additional 510(k)** for the BioFire COVID-19 Test 2 to display results for four additional SARS-CoV-2 assays which were present on the test, but for which results were masked through software. The assays were unmasked as a mitigation against the risk of future SARS-CoV-2 variants affecting the sensitivity of the test due to mutations in assay primer regions.

In September 2022, FDA cleared a 510(k) for a SARS-CoV-2 test, the **Simplexa COVID-19 Direct, Simplexa COVID-19 Positive Control Gen II Pack**. Development of this test, which has been **offered** under an EUA since March 2020, was **supported** by the Biomedical Advanced Research and Development Authority (BARDA).

MCMs to diagnose, treat, or prevent smallpox and mpox

Following reports of mpox in the U.S. in late May 2022, FDA worked with BARDA to expedite the submission of a manufacturing supplement to FDA to facilitate production of an FDA-licensed vaccine at an additional site that was originally planned for Fall 2022. In September 2022, FDA **approved** a BLA supplement for the **Jynneos Smallpox and Monkeypox Vaccine, Live, Non-Replicating**, which allowed additional doses manufactured at a

[10] The first FDA-cleared SARS-CoV-2 diagnostic test was **granted marketing authorization** in March 2021, using the De Novo premarket review pathway, a regulatory pathway for low- to moderate-risk devices of a new type.

facility in Europe to be further distributed and administered in the U.S. to help address the mpox outbreak. The expedited inspection and approval of Bavarian Nordic's fill-and-finish capabilities enabled an **additional 786,000 doses** of vaccine to be made available for use in the U.S. Given the emerging public health need, FDA facilitated advance shipments of manufactured doses to the U.S. for prepositioning so that they would be onshore and ready to be distributed once FDA completed inspection and approved the manufacturing changes.

Also supporting smallpox and mpox preparedness, in May 2022, FDA **approved** an intravenous (IV) formulation of TPOXX (tecovirimat) for the treatment of human smallpox disease caused by the variola virus in adults and pediatric patients weighing at least 3 kg. The oral formulation of the drug was **originally approved** in 2018. The IV formulation is an option for those who are unable to swallow the oral capsule, and this approval expanded the eligible population from patients weighing at least 13 kg down to patients weighing at least 3 kg. Like the original NDA, this approval was granted under the Animal Rule.

Since the first case of mpox was detected in the U.S., FDA has been working closely with the Centers for Disease Control and Prevention (CDC), laboratories, and commercial manufacturers to support test development and help make tests more readily available to consumers who need them. The CDC also has an FDA-cleared real-time polymerase chain reaction (PCR) test that detects non-variola Orthopoxvirus DNA, including the virus that causes mpox. The CDC test was cleared in 2018 (**K181205**) for *in vitro* qualitative presumptive detection of non-variola Orthopoxvirus DNA extracted from human pustular or vesicular rash specimens and viral cell culture lysates submitted to a CDC Laboratory Response Network (LRN) reference laboratory. In 2022, FDA cleared additional 510(k)s from CDC, which expanded testing capacity through use:

- of additional reagents and automation (**K221658**; cleared on June 10, 2022),
- in CDC-designated laboratories outside the LRN (**K221834**; cleared on June 24, 2022), and
- of new extraction platform options, among other changes (**K222558**; cleared on August 30, 2022).

About the Animal Rule

Before a medical product can be approved by FDA, the sponsor must prove the product's safety and effectiveness for its intended use. FDA has regulations, commonly known collectively as the Animal Rule, that allow, under very limited circumstances, FDA to rely on evidence of effectiveness from adequate and well-controlled studies conducted in animal models of the disease or condition of interest when human efficacy studies are not ethical or feasible and when the results of those animal 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.

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

To support Ebola preparedness, in September 2022, FDA **approved** a Biologics License Application (BLA) supplement for **Ervebo** (Ebola Zaire Vaccine, Live), to revise the package insert based upon Study V920-018 conducted in frontline workers.

Pandemic influenza preparedness

To support pandemic influenza preparedness, FDA extended the eligible population for certain vaccines and therapeutics. In October 2021, FDA **approved** a

BLA supplement for **Flucelvax Quadrivalent** influenza vaccine to extend its use to individuals down to 6 months of age for the prevention of influenza disease. In August 2022, FDA **approved** a supplemental NDA for Xofluza (baloxavir marboxil) for the treatment of influenza and for post-exposure prophylaxis of influenza in a new population, pediatric patients ≥ 5 to less than 12 years of age.

FDA also cleared two new influenza diagnostic tests in FY 2022. 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 pandemic influenza strains once approved for seasonal influenza use.

All-hazards preparedness

For preparedness in the event of a large-scale event involving thermal burns, FDA cleared two products. In February 2022, FDA **cleared** Zeolite Hemostatic Gauze, intended to be used for temporary external use to control traumatic bleeding. In May 2022, FDA **cleared** the MYO1 Continuous Compartmental Pressure Monitor. This monitor is used for real-time measurement of the muscle compartment pressure to aid in the diagnosis of **compartment syndrome** (acute and chronic).

Additional marketing applications in progress

Sixteen additional marketing applications for new MCMs or new MCM indications were under review in FY 2022; 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.

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 2022.

Preventing and mitigating shortages

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, in FY 2022, FDA continued to collaborate with USG partners and manufacturers of autoinjector products used for the treatment of nerve agent and insecticide poisoning to help prevent shortages of these products. FDA continues to review applicable scientific data, including through the Shelf-Life Extension Program (**SLEP**), to assess whether, if properly stored, **certain lots** of autoinjector 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.

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

Extending expiration dates

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. For example, in 2019, FDA issued final **guidance** to support government public health and emergency

> 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.

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. 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 BLA and are still being studied under Investigational New Drug applications (INDs)—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 2022, FDA **extended the expiration date** of several lots of Pfizer-BioNTech COVID-19 Vaccine, Janssen COVID-19 Vaccine, and several COVID-19 therapeutics including Paxlovid and five monoclonal antibodies (mAbs).

Reagent stability studies are needed to support shelf-life expiration dates for *in vitro* diagnostics (IVDs) authorized under an EUA for emergency use during the COVID-19 pandemic; however, they generally do not need to be completed at the time of initial review of the EUA request and/or EUA issuance, but should be initiated immediately following authorization, if not before. In the absence of real-time stability data, initial reagent stability claims typically do not exceed a four-to-six-month expiration date. Following initial FDA authorization, FDA has extended and authorized shelf-life expiration dates after reviewing real-time data generated by the IVD manufacturer. Shelf-life expiration dates have been extended multiple times as additional data becomes available. When shelf-life expiration dates are extended for devices that have already been distributed, the IVD manufacturer typically sends a notice to customers to

inform them of the extension so they are aware of how long they can continue to use in-stock devices. In FY 2022, FDA extended the shelf life of 13 at-home over-the-counter (OTC) COVID-19 diagnostic tests, and continually updates the **list** for easy reference by consumers.

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 ensure stability and quality before an expiry dating extension is granted. In FY 2022, as a result of SLEP testing that ensured drug stability and quality, FDA granted shelf-life extensions for approximately 1,085 lots (batches) of MCM drugs.

ENABLING ACCESS TO MCMs UNDER FDA'S EMERGENCY USE AUTHORIZATION AUTHORITY

During FY 2022, FDA continued to work with USG partners, including DoD and other PHEMCE partners, and product sponsors to enable access to unapproved MCMs when necessary.[11] One way FDA does this is by issuing EUAs. The EUA authority[12] 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.[13] Lists of **current EUAs** are published on the FDA website.

COVID-19 EUAs

Recognizing the urgent need for safe and effective COVID-19 MCMs, FDA continues to use its authorities and expertise to facilitate the expeditious development and availability of vaccines, therapeutics, and devices that have met the agency's rigorous science-based standards for quality, safety, and effectiveness. As noted in ***Table 2***, in FY 2022, FDA issued 66 new EUAs to support COVID-19 response. Cumulatively, from 2020 through the end of FY 2022, FDA issued 569 EUAs, enabling access to thousands of products.

Table 2: COVID-19 EUA recap

Product type	New EUAs issued in FY 2022	Total EUAs issued since 2020*
In vitro diagnostics	61	486
Drugs and biological therapeutics	4	17
Vaccines	1	4
Other devices**	0	62
Total	**66**	**569**

**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 there were no new umbrella EUAs in FY 2022, additional products (e.g., surgical masks) were made available under such EUAs issued in previous years.*

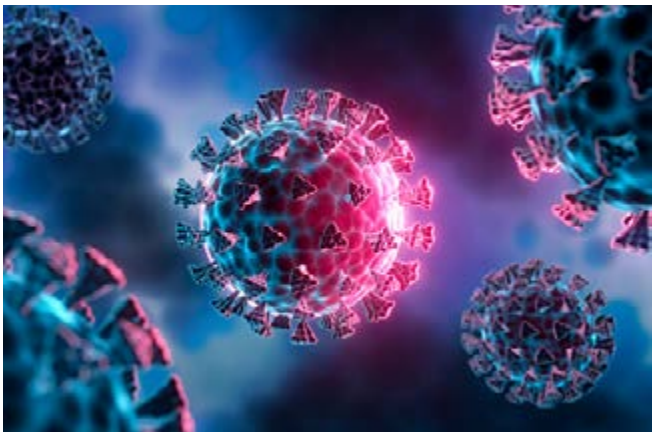
New COVID-19 EUAs issued in FY 2022 include:

- **Evusheld** (tixagevimab co-packaged with cilgavimab and administered together), the first monoclonal antibody for **pre-exposure prevention** of COVID-19 in certain individuals, including those with moderate to severely compromised immune systems
- **Paxlovid** (nirmatrelvir tablets and ritonavir tablets, co-packaged for oral use), the **first oral antiviral** for treatment of mild to moderate COVID-19 in certain adults and pediatric patients who are at high risk for severe COVID-19
- **Lagevrio** (molnupiravir), an **additional oral antiviral** for treatment of mild to moderate

[11] 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.

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

[13] 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.



COVID-19 in certain adult patients who are at high risk for severe COVID-19

- **Bebtelovimab**, a new monoclonal antibody for the treatment of mild to moderate COVID-19 that **retained activity** against a number of variants/subvariants circulating during FY 2022
- **InspectIR COVID-19 Breathalyzer**, the first COVID-19 diagnostic test that detects chemical compounds in **breath samples** associated with a SARS-CoV-2 infection
- **Laboratory Corporation of America (Labcorp) VirSeq SARS-CoV-2 NGS Test**, the first COVID-19 test to identify specific SARS-CoV-2 **lineages**
- **Novavax COVID-19 Vaccine, Adjuvanted**, an additional **vaccine** for the prevention of COVID-19 caused by SARS-CoV-2 in individuals 12 years of age and older (after **initial authorization** for ages 18 and older)

FDA modifies or amends EUAs as needed, including EUA amendments, and revisions to documentation including fact sheets and instructions for use. Multiple revisions were made to COVID-19 vaccine, therapeutic, and device EUAs in FY 2022—a substantial and ongoing effort. The latest information is available on the FDA website. For example, FDA:

- **Authorized use** of Moderna COVID-19 Vaccine as a two-dose series for individuals down to 6 months of age.
- **Authorized use** of Pfizer-BioNTech COVID-19 Vaccine as a two-dose series for children ages 5 through 11.
- **Authorized use** of Pfizer-BioNTech COVID-19 Vaccine as a three-dose series for children 6 months through 4 years of age.
- Authorized **bivalent formulations** of the Moderna and Pfizer-BioNTech COVID-19 Vaccines for use in certain age groups as a single booster dose at least two months following primary or booster vaccination.
- Continued to closely monitor MCM use under EUAs, and when needed, amended EUAs to reflect updated safety information and requirements, and limit use or distribution (for example, due to reduced product activity against circulating variants).
- Continued efforts to communicate with health care providers and consumers important information about products under EUA. Examples include providing information to help prescribers evaluate **potential drug interactions** when using Paxlovid therapy for COVID-19, and helping consumers find extended expiration dates for **at-home OTC COVID-19 diagnostic tests**.
- Authorized 1,125 revisions to **COVID-19 IVD EUAs** from March 2020 through September 2022.

FDA may also revoke an individual EUA prior to the termination of the EUA declaration supporting it if:

1. Circumstances justifying issuance no longer exist,
2. The criteria for its issuance are no longer met, or
3. Other circumstances make revocation appropriate to protect the public health or safety.

Examples of circumstances that may make revocation appropriate to protect the public health or safety are described in the FDA Guidance Document: **Emergency Use Authorization of Medical Products and Related Authorities**. In FY 2022, FDA revoked EUAs for two COVID-19 **therapeutics**, and 30 **IVDs**. In addition, FDA delisted six IVDs from Appendix A of the **EUA for Molecular Diagnostic Tests for**

SARS-CoV-2 Developed And Performed By Laboratories Certified Under CLIA To Perform High Complexity Test.

mpox EUAs

In addition to the extensive EUA work ongoing in response to COVID-19, in August 2022, FDA **authorized** Jynneos (Smallpox and Monkeypox Vaccine, Live, Non-Replicating) for: 1) active immunization by subcutaneous injection (two 0.5 mL doses four weeks apart) for prevention of monkeypox disease in individuals less than 18 years of age determined to be at high risk for monkeypox infection; and 2) active immunization by intradermal injection (two 0.1 mL doses four weeks apart) for prevention of monkeypox disease in individuals 18 years of age and older determined to be at high risk for monkeypox infection. FDA **approved** Jynneos in 2019 for the prevention of smallpox and monkeypox disease in adults 18 years of age and older determined to be at high risk for smallpox or monkeypox infection. Jynneos is approved for administration subcutaneously (beneath the skin), as a two-dose series, four weeks apart. The 2022 EUA was expected to **increase the total number of doses** available for use in these populations by up to five-fold.

In addition, in September 2022, FDA **authorized** the first EUA for an IVD to detect the virus that causes mpox (Quest Diagnostics Monkeypox Virus Qualitative Real-Time PCR), and published **guidance** and **templates** for test developers, among other **actions** to help expand access to testing.

Pre-EUAs

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 2022, 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. For example, in FY 2022, the Center for Devices and Radiological Health (CDRH) received 257 pre-EUA requests for IVDs; 197 for COVID-19; and 60 for mpox. The same team handled a total of 263 pre-EUA requests in the same period: 234 for COVID-19 IVDs, and 29 for mpox IVDs. CDRH also received 49 pre-EUA requests for non-IVD devices.

What is a pre-EUA?

To help prepare for potential and current emergencies, FDA works with MCM developers to prepare pre-EUA packages, when appropriate. A pre-EUA package contains data and information about the safety, quality, and effectiveness of the product, its intended use under a future or current EUA, and information about the emergency or potential emergency situation.

The pre-EUA process allows FDA scientific and technical subject matter experts to begin a review of information and assist in the development of conditions of authorization, fact sheets, and other documentation that would be needed for an EUA in advance of an emergency, and helps facilitate complete EUA requests during a current emergency declaration. A pre-EUA can only transition to an EUA if there is a current applicable emergency determination and declaration under Section 564 of the FD&C Act. Learn more in the guidance **Emergency Use Authorization of Medical Products and Related Authorities**.

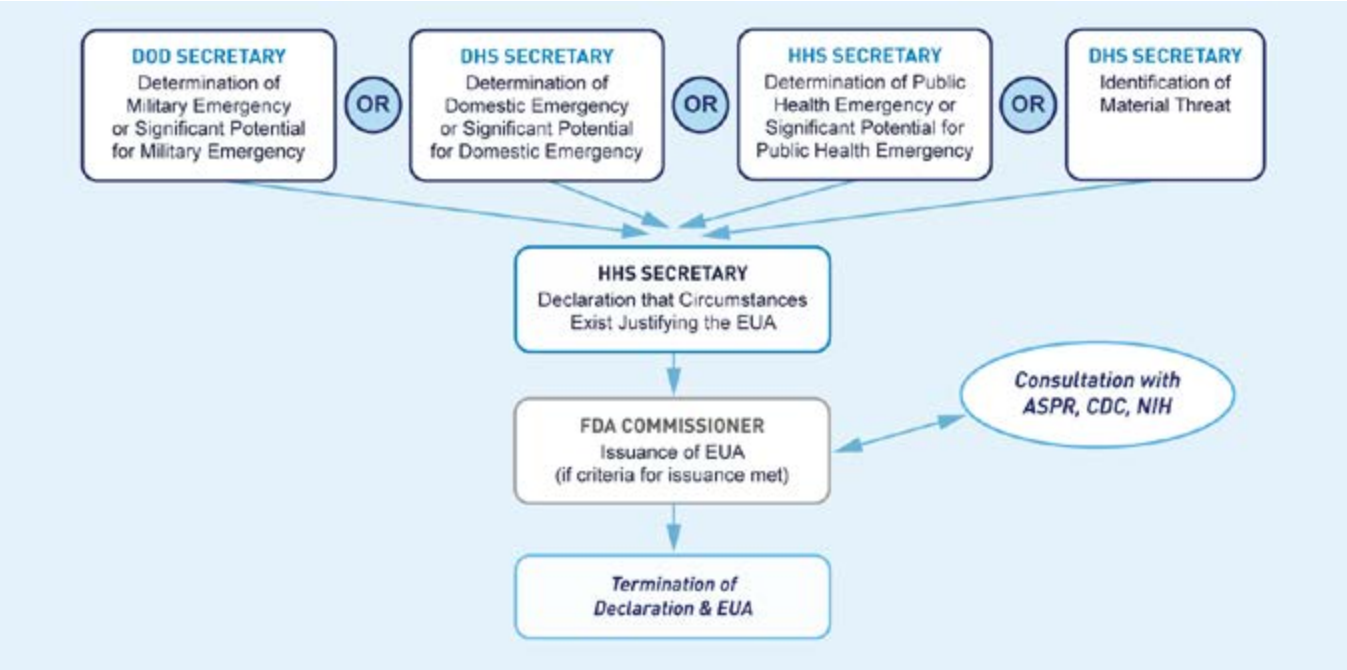
EUA transparency

FDA continues, to the extent appropriate and permitted by law, to publicly post reviews of scientific data and information supporting the issuance, revision or revocation of EUAs for all **drug** and biological products, including **vaccines**, as part of our response to COVID-19 and other public health emergencies, including mpox.

Consistent with FDA's longstanding practice of posting the relevant scientific reviews after new drug and biological product approvals, FDA discloses information from EUA review documents as appropriate after the disclosure review and process is complete. As a part of this process, 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.

Data and information supporting EUA issuance of

Figure 1: Summary of process for EUA issuance



A text description of this chart is available on the FDA website: ***Summary of Process for EUA Issuance***
Note: A determination under section 319 of the PHS Act that a public health emergency exists, such as the ***one issued on January 31, 2020****, does not enable FDA to issue EUAs. A separate determination and declaration are needed under section 564 of the FD&C Act to enable FDA to issue EUAs, provided other statutory criteria are met. For more information, see:* ***FAQs: What happens to EUAs when a public health emergency ends?***

IVDs is included in the Instructions for Use or EUA Summary documents, which are **published** for every IVD EUA. In addition, in October 2021, FDA publicly **posted** information about an independent third-party assessment of the EUA process CDRH implemented to help authorize COVID-19 tests during the public health emergency.

RESPONDING TO EMERGING INFECTIOUS DISEASE PUBLIC HEALTH THREATS

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

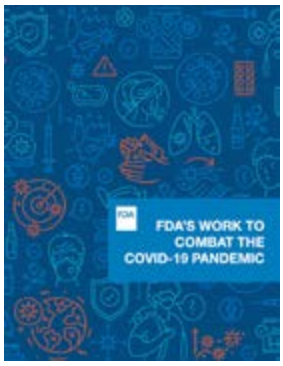
In addition to responding to specific threats, including COVID-19, Ebola, and mpox, FDA also engages in numerous activities to support public health emergency preparedness for a variety of threats; typical activities to support such responses are noted in ***Box 2***.

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 MCM 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 effectiveness 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
Engaging with partners on innovative approaches to respond to public health emergencies as quickly and safely as possible
Communicating proactively and frequently with consumers, health care providers, and other stakeholders, including correcting misinformation whenever possible
Addressing health disparities and promoting health equity in preparedness and response to public health emergencies

In addition to preparedness and response activities noted in ***Box 2***, FDA engaged in emerging infectious disease-specific response activities in FY 2022, including:

COVID-19

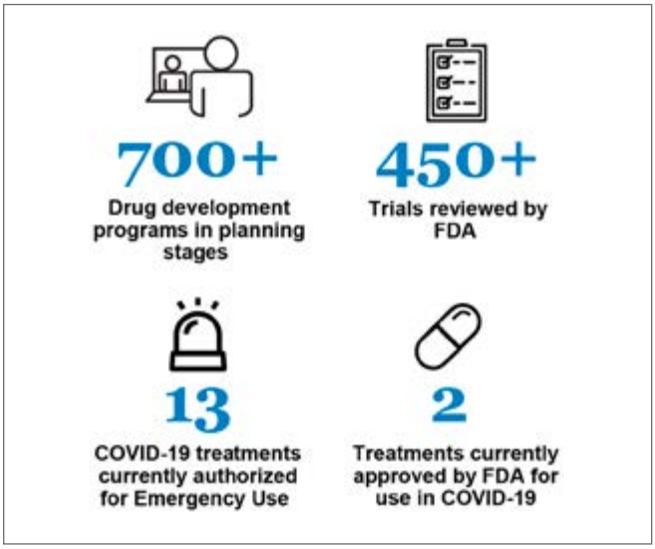
The COVID-19 pandemic is unprecedented in modern history and has required an extraordinary response around the world. On January 31, 2020, the HHS Secretary issued a **determination** that a public health emergency exists, and the WHO **declared** COVID-19 a worldwide pandemic on March 11, 2020. Since December 2019, and throughout the remainder of FY 2020-2022—and beyond—thousands of FDA scientists, clinicians, lawyers, and other experts have worked tirelessly to respond to COVID-19.



A July 2022 report issued by FDA, ***FDA's Work to Combat the COVID-19 Pandemic***, outlines much of the broad range of work FDA is undertaking to combat the COVID-19 pandemic and prepare for future emergencies. While a wide range of work continues across FDA to support COVID-19 response, this MCMi report offers a snapshot of MCM-related COVID-19 response activities during the FY 2022 reporting period, including:

- 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 2022, FDA approved a new vaccine and expanded the population eligible for a previously approved vaccine to include individuals ages 12 through 15; approved the first COVID-19 treatment for young children; and cleared two diagnostic tests (see: ***MCMs to diagnose, treat, or prevent COVID-19***).
- Enabling access to emergency use and investigational MCMs including accurate and reliable diagnostics through an appropriate mechanism, such as EUAs or INDs. (See ***Table 2: COVID-19 EUA recap***). For example, in FY 2022, FDA:
  - Received 35 new INDs for COVID-19 biological products, including 13 vaccines; 28 pre-INDs for COVID-19 biologics, including 23 vaccines; and authorized 20 Emergency Investigational New Drug Applications (EINDs) for biological products.
  - Received 40 new pre-INDs and 50 new INDs for COVID-19 drugs, and authorized 453 EINDs for COVID-19 drugs.
  - Approved more than 1,700 COVID-19-related Abbreviated New Drug Application (ANDA) approvals (since 2020), including critical medications that have been in shortage due to their use in treating patients with COVID-19.
  - Reviewed more than 450 clinical trials under the Coronavirus Treatment Acceleration Program (**CTAP**), a special emergency program launched in April 2020 for possible coronavirus therapies.
  - Issued 61 new EUAs and 484 revisions to current EUAs for COVID-19 IVD devices.

Figure 2: Coronavirus Treatment Acceleration Program (CTAP) dashboard

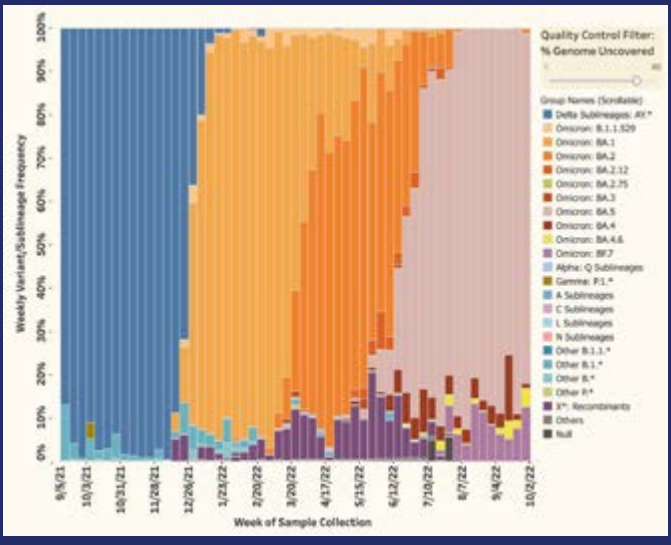


*As of September 30, 2022. The CTAP dashboard is **updated** monthly.*

- 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.
- Protecting consumers against fraudulent products, including issuing **warning letters** to companies selling unapproved and misbranded COVID-19 countermeasures.
- Providing continuous support for the USG **initiative** to distribute COVID-19 OTC test kits to households across the U.S. For example, FDA helped provide established processes for inspection of the test kits received to ensure that products were EUA-authorized, provided up-to-date information to ensure that test kits met specifications, and helped identify and resolve potential program risks.
- 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.
- Collaborating with USG partners and academia to design a comprehensive **study** to assess at-home COVID-19 antigen IVD test performance and evaluate the benefits of serial testing. Results of the study, funded by the NIH Rapid Acceleration of Diagnostics (**RADx**) program, will be made available as a resource to all at-home COVID-19 antigen test manufacturers. This study resulted in an August 2022 **safety communication** to help consumers reduce the risk of false negative results.

mpox

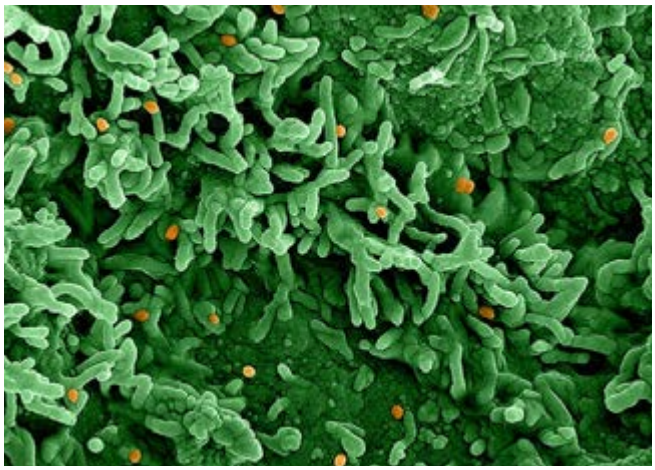
FDA is also closely monitoring the U.S. mpox outbreak that began in 2022, and working to help ensure the development and availability of safe and effective MCMs to address this public health emergency. Although **Jynneos Vaccine** is approved for the prevention of smallpox and monkeypox disease in adults 18 years of age and older determined to be at high risk for smallpox or monkeypox infection, as of September 30, 2022, there are no FDA-approved or authorized therapeutic treatments for mpox disease. However, FDA continues to work closely with sponsors interested in developing and implementing protocols to generate safety and efficacy information while facilitating access. NIAID has opened a randomized,



Wastewater Surveillance for SARS-CoV-2 Variants

Studies have shown that SARS-CoV-2 variants of concern from wastewater can be identified one to two weeks prior to being detected in clinical samples from the same area, making wastewater surveillance useful for detecting and monitoring SARS-CoV-2 in the population.

Through the American Rescue Plan Act of 2021, Congress provided temporary funding for FDA to develop the capacity to **sequence SARS-CoV-2 RNA** from wastewater samples and to conduct a sampling and sequencing project through 2022. By monitoring population-level variants over time, GenomeTrakr labs are providing information about the evolution of the virus, which is critical to evaluating the effectiveness of FDA-regulated COVID-19 vaccines, therapeutics, and diagnostics. The software FDA developed to analyze sequences obtained from wastewater samples has been adopted by other public health partners, including the CDC. Raw sequence data plus a standard suite of metadata is **available for download**.



mpox virus. Credit: NIAID

controlled **clinical trial** to assess the safety and efficacy of TPOXX (tecovirimat), an antiviral medication, for treatment of mpox disease, and CDC has an expanded access protocol available for patients meeting certain specified criteria who are not able to enroll in the randomized trial. In 2018, FDA **approved** TPOXX for treatment of smallpox in adults and children. Because smallpox is eradicated globally, FDA approved TPOXX under the Animal Rule, as it was neither ethical nor feasible to test the efficacy of the drug in humans. **Safety data** was obtained in healthy human volunteers without a smallpox or mpox infection.

Unlike smallpox, mpox was endemic in other parts of the world (e.g., the Democratic Republic of the Congo [DRC]) at the time of TPOXX's initial approval. Consequently, it remained both ethical and feasible to conduct clinical trials in humans to study TPOXX for the treatment of mpox disease. Therefore, TPOXX for the treatment of mpox disease was not appropriate for approval under the Animal Rule.

In May 2022, FDA approved an **IV formulation** of TPOXX for the treatment of smallpox in adults and children. The IV formulation provides a treatment option for individuals who are unable to swallow the oral capsule.

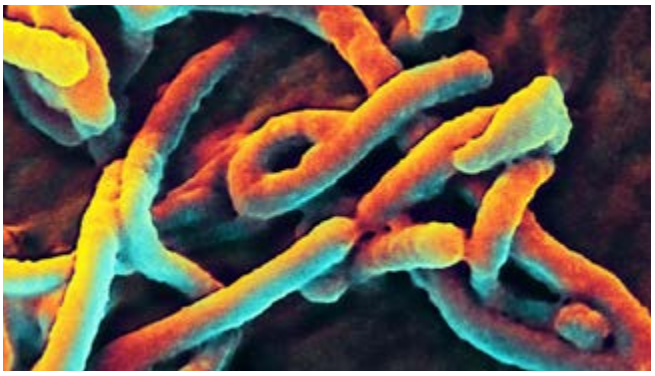
FDA continues to release updated safety information about mpox MCMs as needed, including, in September 2022, **information** for the scientific community on the risk of viral resistance to TPOXX, and a July 2022 **safety communication** advising people to use swab samples taken directly from a lesion (rash or growth) when testing for the monkeypox virus.

In addition to vaccine and diagnostic approvals and EUAs noted earlier, FDA is working closely with the CDC to increase accessibility of its FDA-cleared test (see: ***MCMs to diagnose, treat, or prevent smallpox and mpox***), and with the diagnostic community to augment access to accurate testing to support the response. FDA continues to work closely with product sponsors to clarify regulatory and data requirements necessary to rapidly advance development and availability of additional medical products essential to supporting response efforts.

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, DRC, and Uganda continuing into 2022. In FY 2022, 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—including *Sudan ebolavirus* (SUDV)—forward in development as quickly as possible.
  - For example, FDA had previously participated in discussions of potential clinical trial approaches, including a **trial** comparing several investigational therapeutics against a control arm that began in 2018 and provided information helping to support approval of two monoclonal antibody therapies for *Zaire ebolavirus* disease. Based on this NIH trial and other experience with clinical



Ebola virus. Credit: NIAID

trials in outbreak circumstances, FDA has continued to provide regulatory guidance to product developers. FDA also provided to WHO study recommendations for the evaluation of rapid Ebola antigen-based diagnostic tests to facilitate data collection for future marketing submissions.

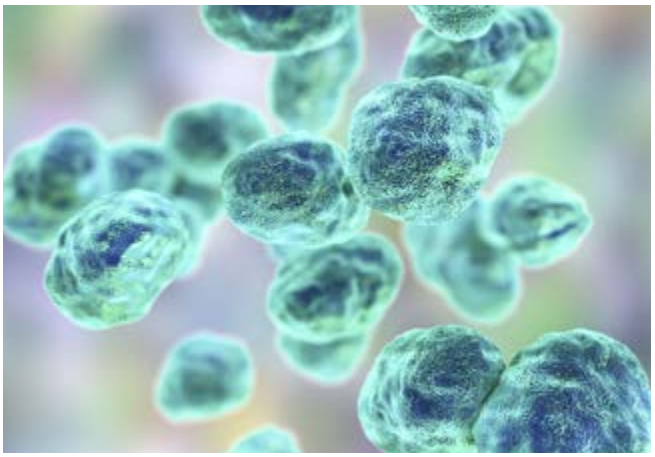
  - Unfortunately the results of therapeutic trials in previous outbreaks caused by *Zaire ebolavirus* cannot be directly applied to the **September 2022** Uganda, Mubende District *Sudan ebolavirus* outbreak because these are two different viral species that cannot be assumed to respond in the same way to the same treatments. FDA continues to discuss clinical trial approaches with potential sponsors to encourage appropriate investigations to assess safety and efficacy of candidate products while facilitating access where needed.

- 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.

Tularemia

Tularemia is a potentially serious illness that occurs naturally in the U.S. It is caused by the bacterium *Francisella tularensis* found in animals (especially rodents, rabbits, and hares). The bacteria that cause tularemia occur widely in nature and could potentially be isolated and grown in quantity in a laboratory, although manufacturing an effective aerosol weapon would require considerable sophistication.

In October 2021, FDA **qualified** a National Institutes of Health (NIH) National Institute of Allergy and Infectious Diseases (NIAID) cynomolgus macaque (*Macaca fascicularis*) animal model of pneumonic tularemia caused by the inhalation of aerosolized *F. tularensis* under the Animal Model Qualification Program (**AMQP**). The qualification of this model may help speed the development and approval of drugs and biological products for the treatment of pneumonic tularemia.



Bacteria Francisella tularensis, 3D illustration

The AMQP is a **Drug Development Tool Qualification Program** specifically established to address the need for publicly available, product-independent animal models intended to support the efficacy testing of multiple investigational drugs or biological products under the regulations commonly known as the Animal Rule. The AMQP provides a framework for early engagement and scientific collaboration with FDA to facilitate animal model development.

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 2022.

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 2022 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**. In FY 2022, FDA continued to seek **SARS-CoV-2 reference-grade sequence data** for the FDA-ARGOS database and develop a software pipeline to expand the current ARGOS database.
- 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).
- Collaborating with DoD to assess the impact of viral mutations on PCR performance.

FDA/DoD Enhanced Engagement Action Team

This Action Team 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 2022 activities included:

- Working with DoD partners to support COVID-19 response efforts, including:
  - The use of EUA diagnostic tests.
  - 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).
- 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:

- Meeting with DoD offices, commands, and programs to discuss regulatory and scientific issues related to developing and providing access to medical products for the warfighter;
- 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.[14]

- 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.
- Facilitating the approval of an improved **midazolam autoinjector** and a **naloxone autoinjector** to protect the warfighter against chemical warfare exposure.
- Providing expert feedback on regulatory considerations for novel CBRN prophylactic approaches identified by the Defense Advanced Research Projects Agency (DARPA).
- Engaging with DoD's JPEO-CBRND to address ongoing nonclinical testing supply chain challenges.
- Strengthening MCM CBRN research and development through partnership and engagement with Australia, Canada, and the United Kingdom to support defense and public health.

Acute Radiation Syndrome (ARS) Action Team

This Action Team continued its efforts to clarify the regulatory requirements for development of MCMs to combat radiological/nuclear (rad/nuc) threats, 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 2022 included:

- Continuing coordinating FDA rad/nuc preparedness activities and working with scientific and regulatory experts across the FDA to enhance development of MCMs for cutaneous radiation injury.
- Continuing to interact with USG partners via Biodosimetry Working Group meetings to engage interagency stakeholders in discussion on regulatory challenges for radiation biodosimetry devices, updating the pre-EUA template for molecular biodosimetry, establishing a draft pre-EUA template for cytogenetic biodosimetry, and supporting biodosimetry review group activities, including review of five pre-submissions relating to three radiation biodosimetry devices.
- Continuing to facilitate cross-agency rad/nuc interaction on MCM development for gastrointestinal acute radiation syndrome (GI-ARS) that includes the FDA Center for Drug Evaluation and Research (CDER) co-sponsoring with NIAID and BARDA a workshop to discuss development of GI-ARS animal models.
- Working with USG partners to address the challenges and gaps in the development of pediatric rad/nuc MCMs.
- Continuing providing regulatory input on the draft Global Health Security Initiative (GHSI) Nuclear Detonation Playbook, and the Administration for Strategic Preparedness and Response (ASPR) Radiation Emergency Medical Management (**REMM**) guidance document for myeloid cytokine treatment of acute exposure to myelosuppressive doses of radiation.
- Providing FDA reviewers with training on national preparedness for medical response to a rad/nuc emergency and ASPR rad/nuc response strategies.

[14] 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** 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.

REGULATORY ADVICE AND GUIDANCE

During FY 2022, FDA continued to provide regulatory advice and scientific 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.

COVID-19

FDA remains committed to providing timely recommendations, regulatory information, scientific advice, 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 - FY 2022, not including revisions, FDA issued 84 new **guidance documents** (63 in FY 2020, 16 in FY 2021, and five in FY 2022) to provide policies, transparency, and regulatory flexibility, as appropriate, to address the vital medical products and public health issues facing the U.S. during this pandemic. The agency continues to update these guidances as relevant needs and circumstances have evolved, and has withdrawn several COVID-19-related guidances after determining that the policies no longer represented the agency's current thinking. The COVID-19 guidances FDA has issued address diagnostics, PPE, ventilators, other medical devices, conduct of clinical trials of medical products, blood supply, development of drugs and biological products to treat or prevent COVID-19, and other topics. FDA also issued 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.

Engaging with product sponsors

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 medical product review centers engage with MCM sponsors and applicants throughout the product life cycle.

FDA has established policies and procedures for conducting formal meetings with product sponsors or applicants. For detailed information on meetings about product development, please see the **Search for FDA Guidance Documents** web page, and enter the desired search criteria, e.g., the term "meetings." 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). When FDA denies a request for a meeting, the sponsor or applicant is provided feedback on steps required to warrant a meeting. Formal meetings may also be rescheduled or canceled based on criteria described in FDA guidance.

Types and numbers of drug and biologic product meetings

Under the Prescription Drug User Fee Act (PDUFA), the Center for Biologics Evaluation and Research (CBER) and CDER categorize formal meetings with product sponsors and applicants of NDAs and BLAs 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,[15] and a **Special Protocol Assessment** (SPA) meeting).

Type B meetings are meetings held at pivotal points during product development to help products move into and through clinical development to marketing application (e.g., pre-IND application meetings, certain end-of-phase 1 meetings, end-of-phase 2/pre-phase 3 meetings, and pre-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 under PDFUA regarding the development and review of a product other than a Type A or Type B meeting, and can address a range of issues (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 Biological Products**. 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 2022, CBER held 28 formal meetings with MCM sponsors or applicants and 94 other (non-PDUFA) meetings, and CDER held 13 formal meetings (***Table 3***) and 96 other (non-PDUFA) meetings.

Table 3: FY 2022 formal meetings between CBER/CDER and MCM sponsors or applicants

Meeting Type	CBER	CDER
Type A	2	1
Type B	23	2
Type C	3	10
Total	**28**	**13**

Types and numbers of medical device meetings

CDRH categorizes its 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 received 109 Pre-subs and nine Submission issue meeting requests (related to marketing submissions) for MCM medical devices in FY 2022. FDA provided extensive written feedback on the Pre-subs, and many of these sponsors elected to cancel meetings after receiving this written feedback, as they did not see the need for the originally requested meeting. If the sponsor wanted to further discuss the written Pre-sub

[15] 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.

feedback, a 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 2022, CDRH provided written feedback for 72 MCM Pre-sub or Submission applications and held 37 Pre-sub and 9 Submission issue meetings with MCM sponsors or applicants (***Table 4***).

Table 4: FY 2022 meetings between CDRH and MCM sponsors or applicants

Meeting Type	CDRH
Pre-Submission	37
Submission issue meetings	9
Total	**46**

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.[16] In FY 2022, 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).

Other regulatory advice and guidance

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. FDA did not receive any written MCM-related RMP requests in FY 2022.

What are guidance documents?

Guidance documents are documents prepared for FDA staff, applicants/sponsors, industry, and the public that describe FDA's non-binding interpretations or recommendations.

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.[17] Guidance documents issued during FY 2022 directly related or applicable to MCM policies or regulatory issues are listed in ***Appendix 3***.

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 2022 are listed in ***Appendix 4***. 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.

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[16] 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**.

[17] 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))

COLLABORATION AND COMMUNICATION

During FY 2022, FDA continued to **collaborate** extensively with other USG partners to foster the development and availability of MCMs. FDA provided subject matter expertise and technical assistance to approximately 71 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 **National Biodefense Strategy**.

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, 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

BOX 3: FEATURED COLLABORATIONS

CDC and public health labs: Enhancing testing surge capacity

In May 2022, FDA, CDC, and several private stakeholders signed a new Memorandum of Understanding (**MOU**) to collaborate on enhancing laboratory testing surge capacity outside of CDC and public health laboratories before and during public health emergencies. Partnerships and engagement between the public and private sector are crucial to supporting a significant increase in demand for diagnostic testing during a public health emergency and to respond to emerging public health threats before reaching the level of a pandemic.

NIST: Supporting supply chain resilience

In 2021, FDA created a new collaboration with NIST through an **MOU** 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 artificial intelligence (AI) and machine learning, and emerging manufacturing processes. Under this MOU, in September 2022, FDA and NIST launched a **new project** to develop new methods to standardize description of the temperature sensitivity and stability of mAbs and other large molecules used for vaccines and therapeutics. This work could help reduce the burden on cold storage supply chains and help facilitate the distribution of mAbs and other biomolecules during public health emergencies.

More MCMi Collaborations

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.

- The Tri-Agency Task Force for Emergency Diagnostics (**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.

FDA also participates in a variety of research and other activities to support **One Health**, a collaborative, multisectoral, and transdisciplinary approach—working at the local, regional, national, and global levels—with the goal of achieving optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment. In FY 2022, FDA's agency-wide One Health Steering Committee reviewed and provided feedback to federal interagency strategic frameworks including:

- U.S. Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS) American Rescue Plan Surveillance Program **Strategic Framework** – To facilitate One Health interagency interactions and needed collaboration to enhance SARS-CoV-2 and other emerging disease surveillance in animals to prevent or limit zoonotic disease outbreaks.
- **CDC National One Health Framework** To address zoonotic diseases in the U.S., including facilitating collaboration across federal agencies.

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 years have continued to support information-sharing and collaboration and have better prepared the international regulatory community to respond to COVID-19 and

FDA is an active participant in numerous MCM-related international collaborations including:

- **WHO's R&D Blueprint** – 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)** - 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)** 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)** 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 nonprofit organization driving innovation in the development and delivery of diagnostics to combat major diseases affecting the world's poorest populations

future public health emergencies. Examples of FDA's key international MCM collaborations include:

- Working with HHS to help establish legal frameworks and tools to facilitate sharing MCMs during an international public health emergency.
- Supporting and participating in the U.S. government's Global Health Security Agenda (**GHSA**) and strategy, as well as other HHS-led efforts related to global MCM legal and policy frameworks, including through Joint External Evaluation (**JEE**) efforts.
- Implementing **CBER-WHO Cooperative Agreements** 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.

Enhancing communication

FDA continued extensive agency-wide efforts to communicate openly and often about its response to the COVID-19 pandemic, including issuing well over 100 press releases, hundreds of email updates, and numerous other communications, including web updates, videos, and social media in FY 2022, to help promote confidence in the public health response. Intensive stakeholder outreach also continued, including town hall meetings, webinars, workshops, email alerts, and individual outreach.

In addition to extensive COVID-19-related communication, 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, and various presentations).

MEDICAL COUNTERMEASURE REGULATORY SCIENCE

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

In FY 2022, FDA continued to implement the **MCMi Regulatory Science Program** through intramural and extramural collaborative research, as well as through partnerships with U.S. government agencies, academia, and industry. 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.[18]

Challenges inherent in reviewing MCMs

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 are reasonably likely to predict clinical benefit in humans.

The challenges are even more complex when it comes to developing MCMs for use in specific populations, such as children or pregnant individuals. 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 partici-

[18] 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.

pant. 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. 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.

> 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.

MCM research portfolio

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. **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**), "FDA Broad Agency Announcement for the Advanced Research and Development of Regulatory Science."

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.

In a 2022 update to the Focus Areas of Regulatory Science (FARS) **report**, FDA identified public health preparedness and response as a key area 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.

Supporting COVID-19 response with regulatory science

Beginning in 2020, and continuing into FY 2022, FDA has initiated a number of regulatory science projects to support development and evaluation of MCMs to 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. Work is ongoing to keep reference materials up to date with respect to circulating variants.
- Participating in evaluation of antibody and RNA reference materials developed by the National Institute of Biological Standards and Control under the auspices of the WHO, as candidate international standards for assays used to detect SARS-CoV-2.
- Supporting development of animal models that might help to evaluate COVID-19 vaccines and therapeutics.

BOX 4: 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 [MPS]) 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 personal protective equipment (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

- 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 activity and pathogenicity) in nonclinical and clinical samples of SARS-CoV-2, including variants of concern.
- Exploring a predictive model in pediatric patients to forecast if a patient is likely to have long-term health effects after COVID-19.
- Establishing next-generation sequencing quality tools to assess SARS-CoV-2 and SARS-CoV-2 variants of concern sequences, adding them to the FDA-ARGOS database to ultimately publish regulatory grade sequence information.
- Using systems biology and machine learning approaches to enable comparison between *in vitro* and *in vivo* models and clinical data of host-pathogen responses, enabling enhanced and host-directed MCM screening methods, and laying the groundwork for extending this approach to emerging pathogens.
- Developing computational models for PPE integrity to support supply chain resiliency.

Regulatory science to support public health emergency preparedness and response

In FY 2022, the MCMi Regulatory Science Program awarded a new **contract** to develop a predictive model in pediatric patients to forecast if a patient is likely to have long-term health effects after COVID-19. The program also revised three previously awarded extramural research contracts to expand efforts supporting COVID-19 response, including enhancing FDA-ARGOS COVID-19 data, furthering COVID-19 organ-on-chip development, and supporting data visualization for immune responses in vaccinated, treated, and infected patients.

Additionally, FDA expanded an existing research project for filovirus MCM development by collecting biological samples from health care workers responding to a 2022 Ebola outbreak in DRC.

FDA intramural research supported by MCMi in FY 2022 includes 12 new research projects performed by FDA scientists, including development of assays and models (e.g., nonclinical models including computational and *in vitro* models) to facilitate development and evaluation of MCMs for nerve agents and infectious diseases including pandemic influenza, COVID-19, Marburg, and Zika.

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 2022, 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

BOX 5: FEATURED MCMI-FUNDED EXTRAMURAL PROJECTS

Understanding long COVID in children

In a **project** begun in June 2022, FDA is working with Children's Hospital Los Angeles (CHLA) on pediatric disease modeling for long COVID-19 (also called post-acute COVID syndrome [PACS], or post-acute sequelae of COVID-19 [PASC]). This project leverages the **NIH RECOVER** initiative to study PASC in children, including researching pediatric cohorts to identify a COVID-19-specific inflammatory and tissue damage disease signature, and determine how obesity may affect the inflammatory response. The project will also identify potential biomarkers that correlate to tissue injury during the disease course and test therapeutics against these targets to discern if modulating target activity improves disease outcomes.

Strengthening coronavirus models with systems biology and machine learning

Australia's national science agency CSIRO (Commonwealth Scientific and Industrial Research Organisation) and global partners will use **systems biology and machine learning approaches** to enhance the understanding of nonclinical model responses to SARS-CoV-2.

They will perform genomic and bioinformatic analysis of the SARS-CoV-2 virus and its key variants, as well as multi-omics analyses (including transcriptomics, metabolomics, lipidomics, and proteomics) on different types of samples collected from a range of nonclinical *in vitro* (organoid/tissue) models and *in vivo* models, as well as from clinical studies on COVID-19 and long COVID-19.

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**. Additionally, FDA is participating in the Systemic Harmonization and Interoperability Enhancement for Laboratory Data (**SHIELD**) **collaborative**, in partnership with the COVID-19 **Diagnostics Evidence Accelerator**, to harmonize COVID-19 test data referenced in the HHS COVID-19 laboratory data reporting requirements,[19] to support evaluation of real-world performance of SARS-CoV-2 diagnostic tests and antibody tests.

FY 2022 MCMi Regulatory Science Program activities are included on the following page in ***Table 5***.

SHIELD collaborative

The SHIELD collaborative is a multi-agency/stakeholder network consisting of FDA, CDC, NIH, HHS Office of the National Coordinator for Health Information Technology (ONC), Centers for Medicare and Medicaid Services (CMS), U.S. Department of Veterans Affairs (VA), IVD manufacturers, electronic health record vendors, laboratories, College of American Pathologists, standards developers, Pew Charitable Trusts, National Evaluation System for health Technology (NEST), and academia.

COVID-19 Evidence Accelerator

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.

[19] COVID-19 Pandemic Response, Laboratory Data Reporting: **CARES Act Section 18115**

Table 5: MCMi Regulatory Science Program activities in FY 2022
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 2022, 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 and biological toxins (e.g., botulinum toxin)
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, Marburg, and mpox)
Creating disease models for pediatric long COVID, in a new **project** begun in June 2022
Expanding a database of reference-grade nucleic acid sequences for emerging threats, to include viruses such as Ebola and Zika, and antimicrobial-resistant pathogens. For example, in April 2020, **SARS-CoV-2 reference-grade sequence data** was added to the FDA-ARGOS database.
Expanding 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.
Continuing to support improvement of small and large animal models for emerging threats (e.g., SARS-CoV-2, Ebola, Marburg, and pandemic influenza)
Conducting survivor studies to better understand Ebola's after-effects, to help find new treatments
Applying advanced transcriptomic analysis (the study of all messenger RNA from the genes of an organism) to **compare** host **responses to Ebola virus disease in humans and in animals**, to help identify biomarkers of Ebola, and expected disease outcomes
Developing a **unique biobank** of clinical Ebola samples from over 2,500 participants, including investigational Ebola vaccinees, Ebola survivors, and Marburg survivors, to characterize the durability and correlates of vaccine-induced and natural immunity to Ebola virus (EVD) and Marburg diseases. In FY 2022, the project was expanded, in collaboration with the Defense Threat Reduction Agency (DTRA), to develop a Marburg clinical biobank to support vaccine development to study Ebola vaccine durability and collection of blood samples in health care workers responding to a 2022 Ebola outbreak.
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 2022, this project was expanded to study variants of concern, such as the SARS-CoV-2 omicron 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 how SARS-CoV-2 affects different systems in the body. In FY 2022, this project continued 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. In FY 2022, FDA identified an external entity to continue the initial FDA efforts on the development and distribution of the FDA SARS-CoV-2 Reference Panel for diagnostic tests, to facilitate long-term availability and maintenance of an up-to-date panel with respect to emerging variants.
Participating in evaluation of antibody and RNA reference materials being developed by the National Institute of Biological Standards and Control under the auspices of the WHO, as candidate international standards for SARS-CoV-2 assays
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 (e.g., Ebola, Zika, and SARS-CoV-2) in MPS, including organ chips, for potential testing of MCMs
Supporting development of COVID-19 MCMs, including a **contract** awarded in FY 2021 and continued in FY 2022, 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
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
Characterizing immune responses against influenza virus proteins to support development of pandemic and universal influenza vaccine
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
Collaborating with USG partners and academia to design a comprehensive study to assess at-home COVID-19 antigen IVD test performance and evaluate the benefits of serial testing

FDA continues to create and support programs to advance the development and review of MCMs that will be regulated under the Animal Rule, and continues agency-wide efforts and external collaborations to advance the use of **alternative methods**. A variety of ongoing collaborations, including MCMi regulatory science collaborations, are listed on the FDA website at: **MCMi Collaborations**.

BOX 6: FEATURED REGULATORY SCIENCE COLLABORATIONS

Credit: NASA

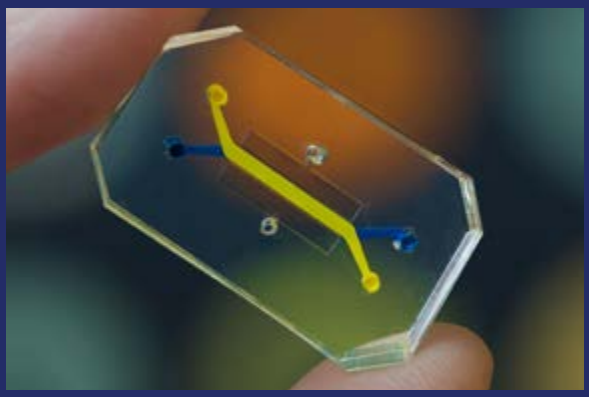
NASA: 3D tissue chips

In March 2022, the National Aeronautics and Space Administration (NASA), NIH, BARDA, and FDA **announced the award** of eight contracts in a multi-agency collaboration to extend longevity of complex *in vitro* (human) models, such as 3D tissue chips and MPS, to at least six months. Currently, such chips are viable for about **one month**, limiting researchers' ability to track longer-term effects of treatments on tissues using these systems. Results from longer studies could be used to better understand disease models, supporting development of and clinical trial design for a **variety** of MCMs.

Credit: DoD

DoD: Innovative regulatory tools

FDA has numerous ongoing DoD collaborations to develop innovative regulatory tools. Examples include work with DARPA and DTRA on biomimetic models, and a collaboration with DTRA to develop a Marburg clinical biobank.



Credit: Wyss Institute

NIAID/NIH: Microphysiological systems

FDA is collaborating with NIAID to conduct alternative methods research, specifically exploring the use of human MPS for Ebola and COVID-19, and development of nonhuman primate (NHP) models. FDA is collaborating on this research with domestic and international academic performers at the Wyss Institute for Biologically Inspired Engineering at Harvard University, the University of Liverpool, and the UK Health Security Agency (formerly Public Health England). The COVID-19 MPS models, including NHPs, are being used to investigate MCM efficacy and to provide a bridge from these models to clinical and animal model data.

ADVANCED MANUFACTURING

Advanced manufacturing

Advanced manufacturing is a collective term for new or innovatively applied medical product manufacturing technologies that can improve medical product quality, address shortages, and speed time-to-market.

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 capabilities to accelerate the production of MCMs. These innovations in manufacturing technology can help support goals of the Cures Act, including by:

- Enabling 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,
- Accelerating the development of therapies for orphan diseases by improving the cost-efficiency of small-scale manufacturing processes, and
- Enabling manufacturing process and standards development for emerging therapies including cell and gene therapies.

MANUFACTURING PROJECT

I-TEAM Hub

FDA has partnered with the HHS ASPR Innovation and Industrial Base Expansion (IBx) program to create the Innovative Technologies and Advanced Manufacturing Hub (**I-TEAM Hub**). The I-TEAM Hub will facilitate:

- Creating a configurable innovation laboratory space to provide FDA reviewers, scientists, and investigators hands-on access to innovative analytic and manufacturing technologies such as digitally enabled manufacturing and deployable manufacturing for critical medicines, devices, and MCMs.
- Bringing technology and manufacturing platforms into FDA and making them available FDA-wide for research, evaluation, and use.
- Supporting technology modernization at FDA by developing manufacturing quality anagement metrics, and by supplying real-world data streams to FDA and partner information systems.

The I-TEAM Hub includes research and collaboration space, remodeled from existing FDA facilities, with work beginning in FY 2023. It will contain state-of-the-art manufacturing, sensing, AI/machine learning, and other cross-cutting technology platforms that enable the manufacture of medical products. FDA and HHS will continue to leverage interactions with industry, academia, and other government agencies to identify technologies that may become part of the next generation in medical products manufacturing. Some of these technologies, that have broad applicability or have the potential to transform an industry, may be cycled into the Innovation facility.

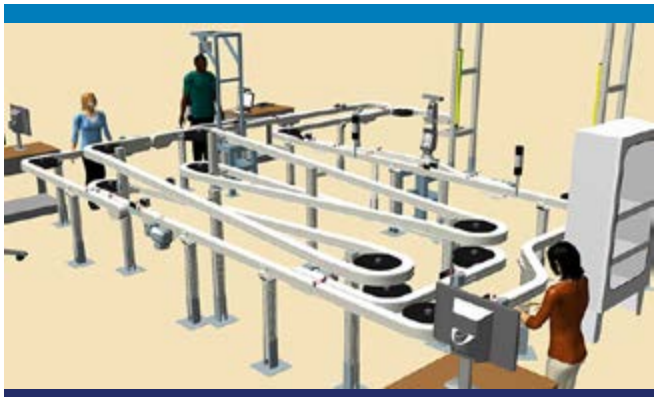
The I-TEAM Hub is part of OCET's **Advanced Manufacturing Program** which supports a growing internal knowledge base of lessons learned, regulatory science, and cross-industry best practices that can be leveraged for FDA-regulated products, especially in the areas of MCMs and supply chain resilience.

Advanced manufacturing innovation hub

In September 2022, HHS **announced actions** the department will take following the **Executive Order on Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy**, which launched a National Biotechnology and Biomanufacturing Initiative (NBBI). In its implementation of the Executive Order, HHS intends to leverage biotechnology and biomanufacturing to achieve medical breakthroughs, reduce the overall burden of disease, and improve health outcomes. HHS will lead the U.S. government in strategically advancing biosafety and biosecurity innovation as part of a growing bioeconomy, to ensure biotechnology research and development and biomanufacturing infrastructure break new ground while reducing risk. This includes supporting development of an **advanced manufacturing innovation hub** in FDA's Office of Counterterrorism and Emerging Threats (**OCET**), in the Office of the Chief Scientist (OCS), to facilitate creation of regulatory science benchmarks and strategies for platform technologies and to drive collaborations that affect multiple product areas (e.g., smart manufacturing, closed loop process controls).

Continued collaborations

Collaborations begun in previous years also continue. An **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 2022, FDA and NIST launched a new **project** to develop new methods to standardize description of the temperature sensitivity and stability of mAbs and other large molecules used for vaccines and therapeutics. When new mAbs and other large biomolecules for drugs and vaccines are developed, they often must be stored in very cold temperatures to ensure their quality and efficacy. This puts a large burden on the supply chain to maintain these freezing temperatures. Testing to reduce cold storage requirements takes time, and there is often not enough information about these biomolecules to predict their temperature sensitivity. This effort will help gain some of that information to understand molecule stability at different temperatures, simplifying test design and reducing testing to more quickly reduce the burden on cold storage supply chains and help facilitate the distribution of mAbs and other biomolecules during public health emergencies.



BOX 8: FEATURED ADVANCED MANUFACTURING PROJECT

Smart Design and Manufacturing Pilot

In FY 2021 OCET, in collaboration with CDRH, acquired a smart manufacturing **demonstration system** to use as a shared resource FDA-wide. The system is intended to increase FDA capabilities to develop metrics, inspectional guidelines, guidance documents, and policy for supply chain resilience and will help facilitate increased adoption of innovative technologies. Implementation activities in FY 2022 and FY 2023 will give FDA access to a full suite of products including:

1. A suite of manufacturing, product lifecycle development, and modeling software,
2. Process design and manufacturing modeling and simulation,
3. Change management and closed loop quality management, and
4. User stories that demonstrate the implementation of a fully digital product lifecycle implementation.

They will be connected to a miniature conveyor line and demonstration system providing a hands-on link to real-world sensors and personnel training opportunities. Internal and external research collaborations on the regulatory science benchmarks, metrics, and the needs of systems using these types of technologies will help create publicly available information and FDA internal expertise to appropriately and transparently review these processes.

FDA also continues to take creative and flexible approaches to address availability of critical medical products in response to the COVID-19 pandemic, and to prepare for future public health emergencies. FDA funded a **study**, completed in 2021, 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. FDA also funded a **study**, completed by America Makes in 2021, to summarize the impact of 3D printing on the overall COVID-19 response. FDA made publicly available this report on the use of additive manufacturing by non-traditional producers in support of the U.S. COVID-19 response.

Under a 2020 **MOU**, FDA is partnering 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. 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. FDA has a number of other active **public-private partnerships** and other industry and government consortia to support advanced manufacturing for emergency preparedness and response.

Advanced manufacturing innovation around FDA

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. To date, FDA has cleared more than 250 3D-printed medical devices and has approved a **3D-printed drug**, finished dosage forms, an active pharmaceutical ingredient, and biological molecules produced using advanced manufacturing technologies.

Programs supporting advanced manufacturing for public health emergency preparedness and response around FDA include:

CDER

CDER's **Emerging Technology Program** provides opportunities for early engagement regarding innovative approaches to pharmaceutical product design or manufacturing. Under this program, FDA has approved 16 regulatory submissions involving advanced manufacturing, including 12 that use continuous manufacturing. For example, to support COVID-19 response, FDA approved two supplemental applications that use advanced manufacturing in a U.S. facility to address the potential shortage of two critical drug products.

CBER

The new **CBER Advanced Technology Team** was also started to promote communication between CBER and prospective innovators/developers of advanced manufacturing technologies. In FY 2022, CBER **funded new research** to enhance innovations in advanced manufacturing technologies for biologics products. Such technologies and processes may increase the domestic production of critical MCMs and other medical products needed for pandemic or other response activities.

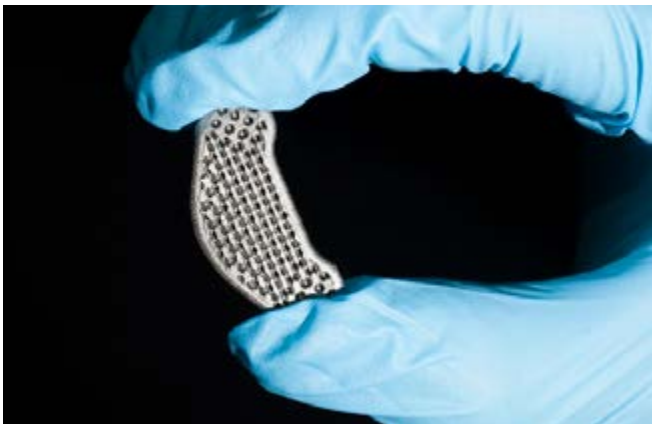
CDRH: 3D Printing of medical devices

The flexibility of 3D printing allows designers to make changes easily without the need to set up additional equipment or tools. It also enables manufacturers to create devices matched to a patient's anatomy (patient-specific devices) or devices with very complex internal structures. These capabilities have sparked huge interest in 3D printing of medical devices and other products, including food, household items,

3D printing and additive manufacturing

3D printing is a process that creates a three-dimensional object by building successive layers of raw material. Each new layer is attached to the previous one until the object is complete. Objects are produced from a digital 3D file, such as a computer-aided design (CAD) drawing or a magnetic resonance image (MRI). 3D printing is a type of additive manufacturing.

There are several types of additive manufacturing, but the terms 3D printing and additive manufacturing are often used interchangeably.



3D-printed titanium spinal disc replacement, similar to those used to treat degenerative disc disease.

automotive parts, and—as noted earlier—producing PPE in response to COVID-19 shortages.

In 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**. 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.

In-house 3D printing: Additive Manufacturing of Medical Products (AMMP)

FDA's Additive Manufacturing of Medical Products (AMMP) core research facility is a multi-center collaboration. It augments center-specific resources and houses high-end, industry-grade 3D printing equipment, software, and expertise that can be used across FDA to perform cutting-edge regulatory research with this advanced technology.

The AMMP Lab will establish a scientific foundation to assist FDA with its assessment of advanced manufacturing, and provide the critical infrastructure the agency will need to meet the regulatory demands of the future. FDA's in-house 3D printing facilities enable FDA scientists to develop standards and metrics for use of 3D printing for medical products; conduct research to determine how the 3D printing of drugs impacts active and inactive drug components; and identify critical quality processes and controls that affect the safety and performance of drugs and devices.

OCET

The **OCET Advanced Manufacturing Program** supports innovative, cross-cutting advanced manufacturing technologies to fill unmet regulatory science needs related to rapidly changing and disruptive needs. Cross-cutting platforms are typically technologies or processes that can be used in two or more FDA-regulated product areas. The program aims to build internal FDA expertise, develop regulatory science tools, and create consistent approaches to regulation, ultimately helping facilitate production of regulated products using these new technologies.

MEDICAL COUNTERMEASURE REGULATORY POLICY

FDA continues efforts to ensure that the FDA MCM **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, examples of FDA advancing policy-specific efforts in FY 2022, 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 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.

Seeking stakeholder input

To gather feedback from key stakeholders, including health care personnel and leadership, FDA and the Reagan-Udall Foundation held two EUA roundtable discussions in November 2021 to solicit input about EUA documentation and processes.

In February 2022, FDA and the Reagan-Udall Foundation held a roundtable to gather stakeholder input on the use of master files for MCM development, and how to best improve the submission and use of master files for MCMs. This activity fulfilled a requirement under Section 603 of the Pandemic All Hazards Preparedness and Advancing Innovations Act of 2019 (**PAHPAIA**).[20]

Developing new approaches

FDA also continued to implement **MCM-related legislation** and 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 informa-

[20] For more information on PAHPAIA, see **MCM-Related Counterterrorism Legislation**.

tion 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 PAHPAIA (**PL 116-22**), which reauthorizes and modifies programs related to public health emergency preparedness and response and the Coronavirus Aid, Relief, and Economic Security Act (CARES Act) (PL 116-136), including identifying approaches for use of master files to facilitate MCM development.
- 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.[21]
- Implementing **MCM-related provisions** of the **Cures Act**, including the material threat MCM priority review voucher (PRV) **program** by working to incorporate the **draft guidance**, issued in January 2018, into a comprehensive draft guidance on all FDA PRV programs. In addition, on October 7, 2022, FDA **issued a notice** establishing the fee rate for using a PRV in FY 2023, including material threat MCM PRVs. FDA **issued** one material threat MCM PRV in FY 2022,

BOX 9: STRENGTHENING THE MCM SUPPLY CHAIN

FDA continues to work 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. FDA monitors the MCM supply chain to identify product shortages and distribution of misbranded or counterfeit products.

FDA contributed to the HHS-led **Public Health Supply Chain and Industrial Base One-Year Report**, published in February 2022, identifying practical strategies the USG can implement to address public health supply chain and industrial base vulnerabilities. The report covers PPE and durable medical equipment, testing and diagnostics, and pharmaceuticals and vaccines, under **Executive Order 14017 on America's Supply Chains**.

In 2020, FDA also published a **list of essential medicines, MCMs, and critical inputs**, 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.

Preventing medical device shortages

During the COVID-19 pandemic, Section 506J was added to the FD&C Act (21 U.S.C. 356j) 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**, and continues to update it, including adding new types of devices when circumstances warrant, or removing them when shortages resolve.

[21] **Public Law 116-22**, Jun 24, 2019, 133 Stat. 905.

and posted a notice of one **redeemed** material threat MCM PRV.

- Developing MCM-related guidance documents issued in FY 2022 (***Appendix 3***), key meetings and workshops (***Appendix 4***), 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.
- Continuing to 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.
- Continuing 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.
- Supporting HHS's GHSA through participation in the Research and Development and Legal Preparedness Action Packages.
- Drafting **MOUs** to provide frameworks for FDA collaborations.

PROFESSIONAL DEVELOPMENT

FDA launched the **MCMi professional development program** in 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 2022 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 10 virtual lectures in this series during FY 2022 with a total of 707 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 two virtual lectures in this series during FY 2022 with a total of 101 attendees.

MCMi Intramural Research and Collaborative Lecture Series

This lecture series 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 seven virtual lectures in this series during FY 2022 with a total of 606 attendees.

Data quality and integrity training for high-consequence pathogens

FDA also sponsored the 10th 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 with virtual and in-person options April 25-29, 2022, with 173 total participants.

FDA and UTMB also held the third annual clinical course, **Achieving Data Quality and Integrity in Clinical Trials Involving High-Consequence Pathogens** with virtual and in-person options on July 11-13, 2022, with 183 total participants. 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.

APPENDIX 1: FY 2022 MEDICAL COUNTERMEASURE APPROVALS – BIOLOGICS AND DRUGS

This list includes MCMs approved, licensed, or cleared by FDA in FY 2022 (October 1, 2021 - September 30, 2022). Additional information can be found on our website at:

- For products (biologics) regulated by CBER: **Biologics Products & Establishments**
- For products (drugs and biologics) regulated by CDER: **Drugs@FDA: FDA-Approved Drugs** and **The Purple Book Database of Licensed Biological Products**

Medical Countermeasure	Applicant	Key Dates	Indication
Comirnaty COVID-19 Vaccine, mRNA	BioNTech Manufacturing GmbH	• Submitted December 16, 2021 • Approved July 8, 2022	BLA supplement to include use of this vaccine in adolescents 12 through 15 years of age for active immunization to prevent COVID-19 caused by SARS-CoV-2.
Ervebo Ebola Zaire Vaccine, Live	Merck Sharp & Dohme Corp.	• Submitted March 21, 2022 • Approved September 16, 2022	BLA supplement to revise the package insert based upon Study V920-018 conducted in front-line workers. Ervebo is a vaccine indicated for the prevention of disease caused by *Zaire ebolavirus* in individuals 18 years of age and older.
Flucelvax Quadrivalent Influenza Vaccine	Seqirus, Inc.	• Submitted December 14, 2020 • Approved October 14, 2021	BLA supplement to extend use to persons 6 months of age and older. Flucelvax Quadrivalent is approved for active immunization for the prevention of influenza disease caused by influenza virus subtypes A and types B contained in the vaccine.
Jynneos Smallpox and Monkeypox Vaccine, Live, Non-Replicating	Bavarian Nordic	• Submitted May 6, 2022 • Approved September 2, 2022	BLA supplement to allow additional doses manufactured at a facility in Europe to be further distributed and administered in the U.S.
Midazolam Injection, 10 mg/0.7 mL (autoinjector)	Rafa Laboratories, Ltd.	• Submitted March 28, 2022 • Approved August 8, 2022	Indicated for the treatment of status epilepticus in adults. This could include treatment of seizures resulting from nerve agent exposure.
Naloxone Hydrochloride Injection, 10 mg (autoinjector)	Kaleo, Inc.	• Submitted August 31, 2021 • Approved February 28, 2022	For use by military personnel and chemical incident responders for emergency treatment of patients 12 years of age and older where use of high-potency opioids such as fentanyl analogues as a chemical weapon is suspected, or temporary prophylaxis of respiratory and/or central nervous system depression in military personnel and chemical incident responders entering an area contaminated with high-potency opioids such as fentanyl analogues.

Medical Countermeasure	Applicant	Key Dates	Indication
Olumiant (baricitinib)	Eli Lilly and Co.	• Submitted November 10, 2021 • Approved May 10, 2022	Supplemental NDA for the treatment of COVID-19 in hospitalized adults requiring supplemental oxygen, noninvasive or invasive mechanical ventilation, or ECMO.
Spikevax COVID-19 Vaccine, mRNA	ModernaTx, Inc.	• Submitted August 21, 2021 • Approved January 31, 2022	For active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 18 years of age and older.
TPOXX (tecovirimat) injection	Siga Technologies, Inc.	• Submitted April 30, 2021 • Approved May 18, 2022	Approval of an IV formulation for the treatment of human smallpox disease caused by variola virus in adults and pediatric patients weighing at least 3 kg. The IV formulation is an option for those who are unable to swallow the oral capsule. This approval expanded the eligible population from patients weighing at least 13 kg down to patients weighing at least 3 kg.
TPOXX (tecovirimat capsule, for oral use)	Siga Technologies, Inc.	• Submitted April 18, 2022 • Approved May 18, 2022	Supplemental NDA approval expanding the patient population to include pediatric patients weighing at least 3 kg. The original approval in 2018 was for adult and pediatric patients weighing at least 13 kg.
Veklury (remdesivir) injection	Gilead Sciences, Inc.	• Received October 21, 2021 • Approved January 21, 2022	NDA supplement for use as a 3-day dosing regimen for the treatment of COVID-19 in adults and pediatric patients (12 years of age and older and weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, who are not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death.
Veklury (remdesivir) injection	Gilead Sciences, Inc.	• Received November 30, 2021 • Approved April 25, 2022	NDA supplement for treatment of COVID-19 in pediatric patients (28 days of age and older weighing at least 3 kg [about 7 pounds)] to less than 40 kg) with positive results of direct SARS-CoV-2 viral testing, who are hospitalized, or not hospitalized and have mild-to-moderate COVID-19 and are at high risk for progression to severe COVID-19, including hospitalization or death.
Xofluza (baloxavir marboxil)	Genentech, Inc.	• Received January 23, 2020 • Approved August 11, 2022	NDA supplement for the treatment of influenza and for post-exposure prophylaxis of influenza in in a new population, pediatric patients ≥ 5 to less than 12 years of age.

APPENDIX 2: FY 2022 MEDICAL COUNTERMEASURE APPROVALS – DEVICES

This list includes MCMs approved, licensed, or cleared by FDA in FY 2022 (October 1, 2021 - September 30, 2022). Additional about device approvals can be found on our website at **Medical Devices Databases**, including the **510(k) Premarket Notification Database**.

Diagnostic Tests

Medical Countermeasure	Applicant	Key Dates	Indication
BioFire COVID-19 Test 2	BioFire Diagnostics, LLC	K211079 • Received April 12, 2021 • Cleared November 1, 2021 K221460 • Received May 19, 2022 • Cleared July 25, 2022	For the qualitative detection of nucleic acids (SARS-CoV-2 RNA) in nasopharyngeal swabs (NPS) from symptomatic individuals suspected of COVID-19. (**K211079**) In FY 2022, FDA cleared an additional 510(k) (**K221460**) to display results for four additional SARS-CoV-2 assays which were present on the test, but for which results were masked through software. The assays were unmasked as a mitigation against the risk of future SARS-CoV-2 variants affecting the sensitivity of the test due to mutations in assay primer regions.
cobas Influenza A/B & RSV nucleic acid test for use on the cobas Liat System	Roche Molecular Systems, Inc.	• Received December 8, 2021 • Cleared July 6, 2022	The cobas Influenza A/B & RSV Nucleic acid test was cleared in 2021 (**K210234**) for the qualitative detection of Influenza A, Influenza B, and respiratory syncytial virus (RSV) RNA in NPS specimens. In 2022, FDA cleared (**K213822**) a modification of the negative control and positive control diluent to a functionally equivalent buffer
ID Now Instrument, ID Now Influenza A & B 2, ID NOW Strep A 2	Abbott Diagnostics Scarborough, Inc.	• Received March 18, 2022 • Cleared June 24, 2022	The Alere i Influenza A & B 2 test was cleared in 2017 (**K171792**) for the qualitative detection and discrimination of influenza A and B viral RNA in direct nasal or nasopharyngeal swabs and nasal or nasopharyngeal swabs eluted in viral transport media from patients with signs and symptoms of respiratory infection. In 2022, FDA cleared (**K220801**) a modification of the ID Now Instrument software to mitigate issues with false invalid results due to low baseline values.

Medical Countermeasure	Applicant	Key Dates	Indication
Non-variola Orthopoxvirus Real-time PCR Primer and Probe Set	CDC	K221658 • Received June 8, 2022 • Cleared June 10, 2022 K221834 • Received June 23, 2022 • Cleared June 24, 2022 K222558 • Received August 24, 2022 • Cleared August 30, 2022	A CDC test was cleared in 2018 (**K181205**) for *in vitro* qualitative presumptive detection of non-variola Orthopoxvirus DNA extracted from human pustular or vesicular rash specimens and viral cell culture lysates submitted to an LRN reference laboratory. In 2022, FDA cleared additional 510(k)s from CDC, which expanded testing capacity through use: • of additional reagents and automation (**K221658**; cleared June 10, 2022), • in CDC-designated laboratories outside the LRN (**K221834**; cleared June 24, 2022), and • of new extraction platform options, among other changes (**K222558**; cleared August 30, 2022).
Simplexa COVID-19 Direct, Simplexa COVID-19 Positive Control Gen II Pack	DiaSorin Molecular LLC	• Received July 9, 2021 • Cleared September 13, 2022	For the qualitative detection of nucleic acids (SARS-CoV-2 RNA) in NPS and nasal swabs (NS) from symptomatic individuals suspected of COVID-19.

Other MCM Devices (Non-COVID-Related)

Medical Countermeasure	Applicant	Key Dates	Indication
MY01 Continuous Compartmental Pressure Monitor	MYO1, Inc.	• Received April 1, 2022 • Cleared May 24, 2022	The MY01 Continuous Compartmental Pressure Monitor is used for real-time and continuous measurement of the muscle compartment pressure. The measured muscle compartment pressure can be used as an aid in diagnosis of compartment syndrome (acute and chronic). The MY01 Mobile Application is an application intended for storing and displaying identical pressure values from the MY01 Continuous Compartmental Pressure Monitor device and calculating critical muscle perfusion pressure utilizing diastolic pressure manual entry by the physician. Diagnosis should always be made in conjunction with clinical assessments.
Zeolite Hemostatic Gauze	Hangzhou Zeo-Innov Life Technology Co., Ltd.	• Received May 21, 2021 • Cleared February 10, 2022	The Zeolite Hemostatic Gauze was cleared for prescription use for temporary external use to control traumatic bleeding. It was also cleared for over-the-counter use intended for temporary external use to stop bleeding of superficial wounds, minor cuts, and abrasions.

COVID-19 Related Device Clearances

In addition to the diagnostic tests listed in the previous table, FDA cleared 708 other COVID-19-related medical devices in FY 2022:

- 390 PPE devices, including gloves, surgical masks, and gowns
- 11 dialysis-related products
- 59 general intensive care unit (ICU)/hospital products
- 37 infusion pumps and related accessories
- 55 needles and syringes
- 30 sterilization products
- 26 ventilation-related products
- 100 vital sign monitoring products

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.

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**.

Product codes for PPE include:

- LZA - Polymer patient examination glove
- LZC - Patient examination glove, specialty
- FYA - Gown, surgical
- KGO - Surgeon's gloves
- LYY - Latex patient examination glove
- FXX - Mask, surgical
- FYC - Gown, isolation, surgical
- LYZ - Vinyl patient examination glove
- OXZ - Pediatric/child facemask

Product codes for cleared dialysis related devices:

- FJK - Set, Tubing, Blood, With And Without Anti-Regurgitation Valve
- KDL - Set, Perfusion, Kidney, Disposable
- KDI - Dialyzer, High Permeability With Or Without Sealed Dialysate System

- KDJ - Set, Administration, For Peritoneal Dialysis, Disposable
- KPO - Dialysate Concentrate For Hemodialysis (Liquid Or Powder)

Product codes for cleared general ICU/hospital products:

- PIF - Gastrointestinal Tubes With Enteral Specific Connectors
- EOQ - Bronchoscope (Flexible Or Rigid)
- LHI - Set, I.V. Fluid Transfer
- EZL - Catheter, Retention Type, Balloon
- KNT - Tubes, Gastrointestinal (And Accessories)
- KOD - Catheter, Urological
- KTI - Bronchoscope Accessory
- FRA - Purifier, Air, Ultraviolet, Medical
- FMK - Single Use Only Blood Lancet With An Integral Sharps Injury Prevention Feature
- FRF - Cleaner, Air, Medical Recirculating

Product codes for cleared infusion pumps and related accessories:

- PTI - Non-Coring (Huber) Needle
- FOZ - Catheter, Intravascular, Therapeutic, Short-Term Less Than 30 Days
- FRN - Pump, Infusion
- FPA - Set, Administration, Intravascular
- MRZ - Accessories, Pump, Infusion
- LJS - Catheter, Intravascular, Therapeutic, Long-Term Greater Than 30 Days
- PND - Midline Catheter
- FMG - Stopcock, I.V. Set
- PMS - Peripheral Intravenous (Piv) Infiltration Monitor

Product codes for cleared needles and syringes:

- FMF - Syringe, Piston
- FMI - Needle, Hypodermic, Single Lumen
- MEG - Syringe, Antistick
- QEH - Piston Syringe With Neuraxial Connector – Epidural, Peripheral, And/Or Indirect Cerebral Spinal Fluid Contact

Product codes for cleared sterilization products:

- MLR - Sterilizer, Chemical
- KCT - Sterilization Wrap Containers, Trays, Cassettes & Other Accessories
- FLE - Sterilizer, Steam
- MED - Sterilant, Medical Devices

Product codes for cleared ventilation related products:

- BTR - Tube, Tracheal (W/Wo Connector)
- KFM - Pump, Blood, Cardiopulmonary Bypass, Non-Roller Type
- CBK - Ventilator, Continuous, Facility Use
- DWF - Catheter, Cannula And Tubing, Vascular, Cardiopulmonary Bypass
- CAH - Filter, Bacterial, Breathing-Circuit
- DTZ - Oxygenator, Cardiopulmonary Bypass
- BZD - Ventilator, Non-Continuous (Respirator)
- DTR - Heat-Exchanger, Cardiopulmonary Bypass
- BTT - Humidifier, Respiratory Gas, (Direct Patient Interface)
- CAW - Generator, Oxygen, Portable
- DWC - Controller, Temperature, Cardiopulmonary Bypass
- MNT - Ventilator, Continuous, Minimal Ventilatory Support, Facility Use

Product codes cleared for vital sign monitoring:

- DPS - Electrocardiograph
- DYB - Introducer, Catheter
- MWI - Monitor, Physiological, Patient (Without Arrhythmia Detection Or Alarms)
- MHX - Monitor, Physiological, Patient (With Arrhythmia Detection Or Alarms)
- FLL - Thermometer, Electronic, Clinical
- DQA - Oximeter
- DXT - Injector And Syringe, Angiographic
- DQD - Stethoscope, Electronic
- BZQ - Monitor, Breathing Frequency
- MSX - System, Network And Communication, Physiological Monitors
- DRG - Transmitters And Receivers, Physiological Signal, Radiofrequency
- DRT - Monitor, Cardiac (Incl. Cardiotachometer & Rate Alarm)

APPENDIX 3: MCM-RELATED GUIDANCE ISSUED IN FY 2022

In FY 2020 through FY 2022, 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 current COVID-19-related guidance documents is **available on the FDA website**.[22] 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 2022 (September 30, 2022). 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.

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**.

Date	Guidance Type	Guidance Name	Purpose
November 8, 2021	Final	Manufacture of Blood Components Using a Pathogen Reduction Device in Blood Establishments: Questions and Answers (**link**)	To provide blood establishments that collect or process blood and blood components with recommendations for implementing a pathogen reduction device for the manufacture of pathogen-reduced blood components.
November 15, 2021	Final (revised)	Enforcement Policy for Viral Transport Media During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency (Revised) (**link**)	To help facilitate the availability of devices for use in transporting certain clinical specimens, including transport media that can be used to transport certain clinical specimens for use with molecular Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) SARS-CoV-2 assays or antigen-detection diagnostic SARS-CoV-2 assays for the duration of the COVID-19 public health emergency.

[22] Also see, in the Federal Register, **Process for Making Available Guidance Documents Related to Coronavirus Disease 2019**.

Date	Guidance Type	Guidance Name	Purpose
December 10, 2021	Final	Policy for Certain REMS Requirements During the Tocilizumab Shortage Related to the COVID-19 Public Health Emergency	To communicate FDA's temporary policy with respect to certain REMS requirements for tocilizumab due to the shortage related to the COVID-19 public health emergency. This guidance will remain in effect for the duration of the tocilizumab shortage. FDA is continually assessing the needs and circumstances related to this temporary policy. As relevant needs and circumstances evolve, FDA intends to update, modify, or withdraw this policy as appropriate. This product is authorized under EUA for treatment of COVID-19 in hospitalized adults and pediatric patients (2 years of age and older) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO.
December 22, 2021	Draft	Transition Plan for Medical Devices Issued EUAs During the COVID-19 Public Health Emergency (**link**)	To provide recommendations and expectations to manufacturers of devices that were issued EUAs to transition back to normal operations when the emergency use declarations that allowed for FDA to issue EUAs are no longer in effect. FDA believes the policy set forth in this guidance may help FDA and other stakeholders transition from COVID-19 operations and processes to normal operations and processes.
December 22, 2021	Draft	Transition Plan for Medical Devices That Fall Within Enforcement Policies Issued During the COVID-19 Public Health Emergency (**link**)	To provide recommendations and expectations to manufacturers of devices that fell within enforcement policies to transition back to normal operations when the public health emergency expires. FDA believes the policy set forth in this guidance may help FDA and other stakeholders transition from COVID-19 operations and processes to normal operations and processes.
December 23, 2021	Draft	Technical Considerations for Medical Devices with Physiologic Closed-Loop Control Technology (**link**)	To provide FDA's recommendations on design considerations, nonclinical testing, animal studies, and labeling to support premarket submissions for medical devices with physiologic closed-loop control technology.

Date	Guidance Type	Guidance Name	Purpose
January 7, 2022	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, and to provide recommendations to blood establishments on collection. FDA revised the guidance in January 2022, to reflect that the EUA authorizes COVID-19 convalescent plasma with high titers of anti-SARS-CoV-2 antibodies for the treatment of COVID-19 in patients with immunosuppressive disease or receiving immunosuppressive treatment in either the outpatient or inpatient setting, and revise certain recommendations pertaining to COVID-19 convalescent plasma donors.
February 4, 2022	Final	Nonclinical Considerations for Mitigating Nonhuman Primate Supply Constraints Arising from the COVID-19 Pandemic (**link**)	To help sponsors mitigate the challenges related to the constrained supply of NHPs available for conducting nonclinical toxicity assessments, which has arisen as a consequence of the current COVID-19 pandemic.
February 7, 2022	Final	COVID-19 Public Health Emergency Policy on COVID-19-Related Sanitation Tunnels (**link**)	Because of significant concerns for human safety, to discourage sponsors from developing or seeking approval or authorization for the use of sanitation tunnels, also known as disinfection tunnels or sanitizing tunnels. Sanitation tunnels are tunnels, walkways, chambers, and similar systems that use sensor-based nozzles to spray humans (and their clothing) with a mist of disinfectant or aerosolized antiseptic as they walk or ride through these tunnels. First installed in China, these tunnels have been developed in countries outside of the U.S. with the aim of treating or reducing the spread of COVID-19. Sanitation tunnels are generally located outside crowded places such as food markets, shopping malls, hospitals, police stations, airports and train stations, offices, and industrial complexes.
March 31, 2022	Final (revised)	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.
April 8, 2022	Final	Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions (**link**)	To provide recommendations to industry regarding cybersecurity device design, labeling, and the documentation that FDA recommends be included in premarket submissions for devices with cybersecurity risk.

Date	Guidance Type	Guidance Name	Purpose
May 4, 2022	Final (revised)	Supplements for Approved Premarket Approval (PMA) or Humanitarian Device Exemption (HDE) Submissions During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency (Revised) (**link**)	To provide a policy to help address current manufacturing limitations or supply chain issues due to disruptions caused by the COVID-19 public health emergency.
May 20, 2022	Draft	Risk Management Plans to Mitigate the Potential for Drug Shortages (**link**)	To help stakeholders develop, maintain, and implement risk management plans to proactively assist in the prevention of human drug product and biological product shortages. Risk management plans can provide stakeholders with a framework to proactively identify, prioritize, and implement strategies to mitigate hazards that can cause a supply disruption.
September 13, 2022	Final	Policy for Monkeypox Tests to Address the Public Health Emergency (**link**)	To describe FDA's review priorities of EUA requests for monkeypox diagnostic tests and FDA's enforcement policies for certain diagnostic tests that are developed by and performed in a laboratory certified under the Clinical Laboratory Improvement Amendments (CLIA) that meets the requirements to perform tests of high complexity; provide recommendations for diagnostic test validation; describe FDA's enforcement policies for FDA-cleared or authorized monkeypox diagnostic tests that are modified; and describe FDA's enforcement policies for certain serology tests.
September 27, 2022	Final (revised)	Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency (Revised) (**link**)	To provide FDA's review priorities and enforcement policies regarding COVID-19 tests for the duration of the public health emergency.
September 28, 2022	Final	Policy for Device Software Functions and Mobile Medical Applications (**link**)	To communicate how FDA intends to apply its regulatory oversight to certain software, including device software functions and mobile medical applications (MMAs) intended for use on mobile platforms or on general-purpose computing platforms.
September 28, 2022	Final	Medical Device Data Systems, Medical Image Storage Devices, and Medical Image Communications Devices (**link**)	To communicate how FDA intends to apply its regulatory oversight to medical device data systems (MDDS), medical image storage devices, and medical image communication devices.
September 28, 2022	Final	Display Devices for Diagnostic Radiology (**link**)	To provide FDA's recommendations regarding premarket notification (510(k)) submissions for display devices intended for use in diagnostic radiology.

Date	Guidance Type	Guidance Name	Purpose
September 28, 2022	Final	Clinical Performance Assessment: Considerations for Computer-Assisted Detection Devices Applied to Radiology Images and Radiology Device Data in Premarket Notification (510(k)) Submissions (**link**)	To provide FDA's recommendations on clinical performance assessments to support premarket notification (510(k)) submissions for computer-assisted detection (CADe) devices applied to radiology images and radiology device data. This guidance applies to CADe devices, including when a CADe device is part of a combined system, such as the detection portion of combined computer-aided detection and diagnostic devices.
September 28, 2022	Final	Clinical Decision Support Software (**link**)	This final guidance clarifies FDA's thinking expressed in the September 2019 draft guidance and focuses on clarifying the types of clinical decision support (CDS) software functions that are excluded from the definition of device by the criteria in section 520(o)(1)(E) of the FD&C Act ("Non-Device CDS criteria"). The final guidance further clarifies that FDA's existing digital health policies continue to apply to software functions that meet the definition of a device, including those that are intended for use by patients or caregivers.
September 29, 2022	Final	Computer-Assisted Detection Devices Applied to Radiology Images and Radiology Device Data - Premarket Notification [510(k)] Submissions (**link**)	To provide FDA's recommendations regarding premarket notification (510(k)) submissions for CADe devices applied to radiology images and radiology device data.

APPENDIX 4: KEY MCM-RELATED MEETINGS HELD IN FY 2022

FDA continued to take steps to ensure the agency was able to continue our vital public health mission in FY 2022. 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.

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, that are open to the public. 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
Weekly or biweekly March 2020 through September 2022	Webinar series	Virtual Town Hall Series – Test Development and Validation During Public Health Emergencies (**link**)	To help answer technical questions about the development and validation of tests for SARS-CoV-2. This series began in March 2020, and continues in FY 2023, including COVID-19 and mpox.
October 5, 2021	Webinar	Enhanced Drug Distribution Security in 2023 Under the DSCSA (**link**)	To 1) Discuss enhanced drug distribution security requirements that go into effect in 2023 under the Drug Supply Chain Security Act (DSCSA); 2) Explain how enhanced drug distribution security will help protect patients from exposure to drugs that may be counterfeit, stolen, contaminated, or otherwise harmful; and 3) Summarize updates on implementation of supply chain security requirements under the DSCSA.
October 14-15, 2021	Advisory Committee	Vaccines and Related Biological Products Advisory Committee (VRBPAC) (**link**)	To discuss the use of booster doses of the Moderna COVID-19 Vaccine and the Janssen COVID-19 Vaccine, and hear presentations and discuss the available data on the use of a booster of a different vaccine than the one used for the primary series of an authorized or approved COVID-19 vaccine (heterologous or “mix and match” booster).
October 26, 2021	Advisory Committee	VRBPAC (**link**)	To discuss Pfizer Inc.’s request to amend its EUA to allow for the use of the Pfizer-BioNTech COVID-19 vaccine in children 5 through 11 years of age.

Date	Type of Event	Event Name	Purpose
November 8-9, 2021	Public workshop	13th Annual Sentinel Initiative Public Workshop (**link**)	To highlight milestones and strategic initiatives underway to enhance and build a more robust Sentinel Initiative, and discuss opportunities to utilize Sentinel's existing data, infrastructure, and technology. The Sentinel system is a national electronic system for medical product safety surveillance.
November 9, 2021	Webinar	FDA Center of Excellence in Regulatory Science and Innovation (CERSI) Lecture on Long COVID: Risk factors, Symptomology and Patient Reported Outcomes (**link**)	To review the known epidemiology of post-COVID conditions, and describe the methodological approach and data collection strategy of the CDC-funded Innovative Support for Patients with SARS-CoV-2 Infections (**INSPIRE**) study.
November 16, 2021	Webinar	Enhanced Drug Distribution Security at the Package Level Under the DSCSA (**link**)	To provide members of the pharmaceutical distribution supply chain and other interested stakeholders an opportunity to discuss enhanced drug distribution security requirements of the DSCSA related to system attributes necessary to enable secure tracing of product at the package level.
November 30, 2021	Advisory Committee	Antimicrobial Drugs Advisory Committee (AMDAC) meeting (**link**)	To discuss Merck and Ridgeback's request for an EUA for molnupiravir, an investigational antiviral drug to treat COVID-19. The committee discussed available data supporting the use of molnupiravir to treat mild-to-moderate COVID-19 in adults who have tested positive for COVID-19, and who are at high risk for progression to severe COVID-19, including hospitalization or death.
December 7-8, 2021	Webinar	Clinical Investigator Training Course (CITC) Update (**link**)	Update to annual course, including a review of the development and emergency use authorization of medical products for the prevention and treatment of COVID-19, and investigator responsibilities during the pandemic.
December 14, 2021	Webinar	Overview of Expanded Access (EA) Program and EA eRequest Site (**link**)	EA is use of an investigational drug or biologic to treat a patient with a serious disease or condition who does not have comparable or satisfactory alternative therapies. This webinar provided an overview of FDA's EA Program and introduced participants to resources like the **EA eRequest site** hosted by the Reagan-Udall Foundation for the FDA. The EA eRequest site enables physicians to prepare and sign EA requests and submit those requests securely to FDA.
December 14, 2021	Webinar	Webinar on Final Rule for Medical Device De Novo Classification Process (**link**)	To describe background and history of the De Novo Program, and provide updates on new regulations and changes to the De Novo review process, including what is required for acceptance of a De Novo request.

Date	Type of Event	Event Name	Purpose
February 22, 2022	Webinar	Webinar on Draft Guidances on Transition Plans for COVID-19 Related Medical Devices (**link**)	To help prepare manufacturers and other stakeholders for the orderly and transparent transition to normal operations, describe recommendations regarding submitting a marketing submission and the timeline for doing so, provide examples to illustrate the transition policies and exemplify the 180-day transition period timeline, and answer questions about the draft guidance on COVID-19 transition plans.
March 3, 2022	Advisory Committee	VRBPAC (**link**)	To discuss and make recommendations on the selection of strains to be included in the influenza virus vaccines for the 2022-2023 influenza season.
March 7-9, 2022	Public workshop	Good Clinical Practice Workshop: Global Clinical Trials - Considerations and Lessons Learned from the Changing Landscape (**link**)	Hosted by FDA, the UK Medicines and Healthcare products Regulatory Agency (MHRA), and Health Canada, to provide attendees with insight into key topics, compliance trends and the opportunity to hear first-hand from regulators about lessons learned from the changing clinical trial landscape, including the use of innovative tools and approaches to trial design, conduct, and inspections.
March 16-17, 2022	Public workshop	Virtual Public Workshop - 3D Printing in Hospitals: Veteran's Health Administration's Experiences in Point of Care 3D Printing of Device and Implementing a Quality Management System (**link**)	In collaboration with the Veterans Health Administration (VHA), to share VHA's experiences using 3D printing/additive manufacturing in their hospitals, and provide a forum for VHA and other stakeholders to present and discuss their experience that could be useful for health care facilities considering 3D printing medical devices.
March 23-24, 2022	Public workshop	Identification of Concepts and Terminology for Multi-Component Biomarkers (**link**)	To develop multi-component biomarker concepts and terminology, to identify areas of conceptual language development through presentation of use cases, and discuss gaps in terminology for concepts and approaches related to multi-component biomarkers.
April 6, 2022	Advisory Committee	VRBPAC (**link**)	To discuss considerations for future COVID-19 vaccine booster doses and the process for selecting specific strains of the SARS-CoV-2 virus for COVID-19 vaccines to address current and emerging variants.
April 25-29, 2022	Training course	Achieving Data Quality and Integrity in Maximum Containment Laboratories (**link**)	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.

Date	Type of Event	Event Name	Purpose
April 28-29, 2022	Webinar	2022 Sentinel Innovation Day and Public Training	To explore challenges and opportunities in integrating electronic health record-based data in common data models, computable phenotyping to aid medical product safety investigations, advanced analytic approaches to improve confounding adjustments in Sentinel investigations, and a causal inference framework for Sentinel, and discuss Inverse Probability of Treatment Weighting (IPTW), an analytic method that can reduce confounding bias in observational studies of medical treatments.
May 24-25, 2022	Public workshop	Translational Science in Drug Development: Surrogate Endpoints, Biomarkers, and More (**link**)	Hosted by FDA and the Duke-Margolis Center for Health Policy, to present best practices and use cases for successfully bringing forward evidence generated through translational science for regulatory submissions. Stakeholders will discuss ways that translational science can contribute to drug development programs (e.g., surrogate endpoints, enrichment biomarkers, biodynamic/response biomarkers), what some of the challenges are (e.g., validating biomarkers, establishing analytic validation, obtaining biosamples) and strategies to address those challenges (e.g., public-private partnerships, collaborations between industry and academia).
June 6-10, 2022	Conference	Regulatory Education for Industry (REdI) Annual Conference 2022 (**link**)	To provide participants with a strong, basic foundation in the FDA's regulatory requirements, and create awareness of current activities, including a plenary session on some of FDA's noteworthy milestones and landmark accomplishments during the COVID-19 response.
June 7, 2022	Advisory Committee	VRBPAC (**link**)	To discuss an EUA request by Novavax for a vaccine to prevent COVID-19 in individuals 18 years of age and older.
June 7-9, 2022	Public workshop	Building Medical Device Supply Chain Resilience: A Healthcare and Public Health Ecosystem-Wide Collaboration (**link**)	To discuss ways to foster resiliency in the medical device supply chain and to seek input on the new **Resilient Supply Chain Program** (RSCP). The RSCP aims to build upon a foundation of strong partnerships to improve supply chain resiliency through proactive communication, collaboration, and engagement with patient advocates, health care providers, distributors, group purchasing organizations, manufacturers, as well as key component and material suppliers.
June 9, 2022	Webinar	FDA Grand Rounds: Some Perspectives on Data Science and Coronaviruses (**link**)	To present perspectives, illustrated with recent COVID-19 experience and examples, on how in silico modelling and data science techniques could strengthen nonclinical (*in vitro* and animal) models for existing and emerging coronaviral diseases, including updates on some **FDA-funded research**.

Date	Type of Event	Event Name	Purpose
June 14-15, 2022	Advisory Committee	VRBPAC (**link**)	To discuss (Topic I) amending the EUA of the Moderna COVID-19 mRNA vaccine to include the administration of the primary series to children and adolescents 6 years through 17 years of age, and (Topic II) amending the EUA of the Moderna COVID-19 mRNA vaccine to include the administration of the primary series to infants and children 6 months through 5 years of age, and amending the EUA of the Pfizer-BioNTech COVID-19 mRNA vaccine to include the administration of the primary series to infants and children 6 months through 4 years of age.
June 28, 2022	Webinar	FDA Drug Topics: Drug Shortages: Root Causes and Potential Solutions (**link**)	To provide a general overview of CDER's **Drug Shortages** program, current shortage issues, and challenges.
June 28, 2022	Advisory Committee	VRBPAC (**link**)	To discuss whether and how the SARS-CoV-2 strain composition of COVID-19 vaccines should be modified.
July 11-13, 2022	Training course	Achieving Data Quality and Integrity in Clinical Trials Involving High-Consequence Pathogens (**link**)	To enable participants to learn about clinical research protocols for high-consequence pathogens, and help identify and mitigate barriers to data quality and integrity in domestic and international barrier environments involving MCMs. This annual course was presented by FDA and the University of Texas Medical Branch (UTMB), and held at the National Training, Simulation and Quarantine Center (TSQC) at University of Nebraska Medical Center/Nebraska Medicine, a National Ebola Training and Education Center (NETEC) facility.
July 14, 2022	Webinar	FDA Grand Rounds: One Health at FDA: From Concept to Application (**link**)	To describe the One Health concept and how it applies to FDA's regulatory mission and activities.
July 19-20, 2022	Public workshop	Office of Study Integrity and Surveillance (OSIS) Workshop 2022: CDER Inspections of Good Laboratory Practice, Animal Rule, and Bioavailability/ Bioequivalence Study Sites (**link**)	To describe the mission and vision of OSIS; identify the basic elements needed for a bioanalytical lab to successfully undergo an FDA inspection; and to provide an overview of compliance programs dealing with inspections of facilities that perform good laboratory practice (GLP), Animal Rule, *in vivo* clinical bioavailability (BA)-bioequivalence (BE), or *in vivo* analytical BA/ BE; and engage attendees to work through case studies representative of the above programs.

Date	Type of Event	Event Name	Purpose
August 29-30, 2022	Public workshop	Gastrointestinal Acute Radiation Syndrome (GI-ARS) Workshop: Mechanisms, Models, Markers, and Medical Countermeasures	Co-sponsored by NIH, BARDA, and FDA for discussion of gastrointestinal radiation injury with respect to: clinical manifestations; animal models for efficacy studies; mechanisms and biomarkers; regulatory considerations for product development; and industry's experience.
August 30, 2022	Public workshop	Drug Development Considerations for the Prevention of Healthcare-Associated Infections (**link**)	Co-sponsored by FDA and CDC to discuss topics including the current state of development of pathogen-directed products used to prevent health care-associated infections, and antimicrobial resistance threats as potential targets for decolonization and pathogen reduction.
September 13, 2022	Public workshop	Embracing The Future: Regulatory Considerations And Industry Perspectives On Advanced Manufacturing (**link**)	FDA's India Office and the Drug Information Association (DIA) India Office hosted this workshop to discuss regulatory policies, guidance, and support for the adoption of advanced manufacturing technologies.
September 14, 2022	Webinar	An Overview of Sentinel's Publicly Available Analytics Tools	To explore the resources available in Sentinel for individuals unfamiliar with Sentinel's analytics tools and the Sentinel Common Data Model.
September 19, 2022	Public workshop	Increasing the Efficiency of Biosimilar Development Programs (**link**)	To discuss possible innovative ideas that have the potential to streamline and improve the efficiency of biosimilar development, with a focus on comparative clinical studies associated with biosimilar development programs.
September 20-22, 2022	Symposium	2022 CBER Science Symposium (**link**)	To discuss scientific topics related to the regulation of biologics and highlight science conducted at CBER by showcasing how scientific research informs regulatory decision making, and to provide a forum for developing collaborations within FDA and with external organizations.
September 21, 2022	Webinar	Webinar on the Policy for Monkeypox Tests (**link**)	To inform stakeholders about the recently published final guidance, **Policy for Monkeypox Tests to Address the Public Health Emergency**, provide highlights of the final guidance, and answer questions from attendees.
September 22, 2022	Advisory Committee	VRBPAC (**link**)	To discuss BLA #125739 from Rebiotix Inc. for a product, Rebyota (Fecal Microbiota, Live), with a requested indication to reduce the recurrence of *Clostridioides difficile* infection (CDI) in adults following antibiotic treatment for recurrent CDI.

Date	Type of Event	Event Name	Purpose
September 27, 2022	Webinar	FDA Drug Topics: Development and U.S. Regulation of Preventative Vaccines (**link**)	To provide an overview of the development and federal regulations for vaccines in the U.S., including key statutes that grant FDA authority to regulate vaccines, precipitating historical events, and current regulatory requirements for vaccine licensure and marketing approval.

APPENDIX 5: ACRONYMS

AI	Artificial intelligence
AMDAC	Antimicrobial Drugs Advisory Committee
AMMP	Additive Manufacturing of Medical Products
AMQP	Animal Model Qualification Program
ANDA	Abbreviated New Drug Application
APHIS	Animal and Plant Health Inspection Service (USDA)
ARS	Acute radiation syndrome
ASPR	Administration for Strategic Preparedness and Response (HHS)
BA	Bioavailability
BAA	Broad Agency Announcement
BARDA	Biomedical Advanced Research and Development Authority
BE	Bioequivalence
BLA	Biologics License Application
BSL	Biosafety level
CAD	Computer-aided design
CADe	Computer-assisted detection
CANA	Convulsant antidote for nerve agent
CARES Act	Coronavirus Aid, Relief, and Economic Security Act
CBRN	Chemical, biological, radiological, and nuclear
CBER	FDA Center for Biologics Evaluation and Research
CDC	U.S. Centers for Disease Control and Prevention
CDER	FDA Center for Drug Evaluation and Research
CDI	*Clostridioides difficile* infection
CDRH	FDA Center for Devices and Radiological Health
CDS	Clinical decision support
CEPI	Coalition for Epidemic Preparedness Innovations
CERSI	Center of Excellence in Regulatory Science and Innovation
CFR	Code of Federal Regulations
CHLA	Children's Hospital Los Angeles
CITC	Clinical Investigator Training Course
CLIA	Clinical Laboratory Improvement Amendments
CMS	Centers for Medicare and Medicaid Services
COVID-19	Coronavirus disease 2019 (caused by SARS-CoV-2)
CSIRO	Commonwealth Scientific and Industrial Research Organization (Australia)
CTAP	Coronavirus Treatment Acceleration Program
Cures Act	21st Century Cures Act
DARPA	Defense Advanced Research Projects Agency
DIA	Drug Information Association
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
EA	Expanded Access
ECMO	Extracorporeal membrane oxygenation
EIND	Emergency Investigational New Drug application
EUA	Emergency Use Authorization
EVD	Ebola virus disease
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
FIND	Foundation for Innovative New Diagnostics
FTE	Full-time equivalent

FY	Fiscal year
GCP	Good clinical practice
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
GLP	Good laboratory practice
HCT/P	Human cells, tissues, and cellular and tissue-based products
HDE	Humanitarian Device Exemption
HHS	U.S. Department of Health and Human Services
IBx	Innovation and Industrial Base Expansion (HHS/ASPR program)
ICMRA	International Coalition of Medicines Regulatory Authorities
ICU	Intensive care unit
IDE	Investigational Device Exemption
IND	Investigational New Drug
INSPIRE	Innovative Support for Patients with SARS-CoV-2 Infections (a CDC-funded study)
IPTW	Inverse Probability of Treatment Weighting
I-TEAM	Innovative Technologies and Advanced Manufacturing
IV	Intravenous
IVD	*In vitro* diagnostic
JEE	Joint External Evaluation
JPEO-CBRND	Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense (DoD)
kg	Kilogram
LDT	Laboratory developed test
LLNL	Lawrence Livermore National Laboratory
LRN	Laboratory Response Network (CDC)
mAb	Monoclonal antibody
MCM	Medical countermeasure
MCMi	FDA Medical Countermeasures Initiative
MDDS	Medical device data system
MERS-CoV	Middle East Respiratory Syndrome coronavirus
mg	Milligram
MHRA	Medicines and Healthcare products Regulatory Agency (UK)
mL	Milliliter
MMA	Mobile medical application
MOU	Memorandum of Understanding
mpox	Disease caused by the monkeypox virus
MPS	Microphysiological systems
MRI	Magnetic resonance image
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
NBBI	National Biotechnology and Biomanufacturing Initiative
NCBI	National Center for Biotechnology Information
NDA	New Drug Application
NETCCN	National Emergency Telecritical Care Network
NEST	National Evaluation System for health Technology
NETEC	National Ebola Training and Education Center
NGDS	Next-Generation Diagnostic System (DoD)
NGO	Non-governmental organization
NGS	Next-generation sequencing
NHP	Nonhuman primate
NIAID	National Institute of Allergy and Infectious Diseases (NIH)
NIH	U.S. National Institutes of Health
NIST	U.S. National Institute of Standards and Technology
NPS	Nasopharyngeal swab
NS	Nasal swab

NSTC	National Science and Technology Council
OCET	FDA Office of Counterterrorism and Emerging Threats
OCS	FDA Office of the Chief Scientist
ONC	Office of the National Coordinator for Health Information Technology (HHS)
OSIS	Office of Study Integrity and Surveillance
OSTP	Office of Science and Technology Policy (White House)
OTC	Over-the-counter
PACS	Post-acute COVID syndrome (medical term for long COVID-19, also sometimes referred to as post-acute sequelae of COVID-19, or PASC)
PAHPAIA	Pandemic and All-Hazards Preparedness and Advancing Innovation Act of 2019
PAHPRA	Pandemic and All-Hazards Preparedness Reauthorization Act of 2013
PASC	Post-acute sequelae of COVID-19 (also see PACS)
PBMC	Peripheral blood mononuclear cell
PCR	Polymerase chain reaction
PDUFA	Prescription Drug User Fee Act
PHEMCE	Public Health Emergency Medical Countermeasures Enterprise
PHS Act	Public Health Service Act
PMA	Premarket Approval
PPE	Personal protective equipment
PRV	Priority review voucher
rad/nuc	Radiological/nuclear
RADx	Rapid Acceleration of Diagnostics program (NIH)
RECOVER	Researching COVID to Enhance Recovery (NIH)
REdI	Regulatory Education for Industry
REMM	Radiation Emergency Medical Management
REMS	Risk Evaluation and Mitigation Strategies
RMP	Regulatory Management Plan
RNA	Ribonucleic acid
RSCP	Resilient Supply Chain Program (may also be referred to as RSCSPP, the Resilient Supply Chain and Shortages Prevention Program)
RSV	Respiratory syncytial virus
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
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
SUDV	*Sudan ebolavirus*
TATRC	Telemedicine and Advanced Technology Research Center (DoD)
TBI	Traumatic brain injury
TSQC	Training, Simulation and Quarantine Center
TTFED	Tri-Agency Task Force for Emergency Diagnostics
UKHSA	UK Health Security Agency
U.S.	United States
USAMRDC	U.S. Army Medical Research and Development Command
USDA	U.S. Department of Agriculture
USG	United States government
UTMB	University of Texas Medical Branch
VA	U.S. Department of Veterans Affairs
VHA	Veterans Health Administration
VRBPAC	Vaccines and Related Biological Products Advisory Committee
WHO	World Health Organization

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