U.S. FOOD & DRUG ADMINISTRATION

FY2023

MCMi Program Update

FDA MEDICAL COUNTERMEASURES INITIATIVE

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Background

FDA plays a critical role in protecting the U.S. from chemical, biological, radiological, and nuclear threats; emerging infectious diseases; and outbreaks. This report provides updates on FY 2023 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) threats; emerging infectious diseases, 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 biological products, 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 certain available candidate MCMs to respond to public health and military emergencies, even when products are still investigational or not 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

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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 webpage 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 U.S.C. § 247d–6a(a))(2)(A); qualified pandemic or epidemic products as defined in section 319F–3(i)(7) of the PHS Act (42 U.S.C. § 247d–6d(i)(7)); and security countermeasures as defined in section 319F-2(c)(1)(B) of the PHS Act (42 U.S.C. § 247d–6b(c)(1)(B)). Some medical products (e.g., traumatic brain injury (TBI) diagnostics) and some activities (e.g., combatting antimicrobial resistance [AMR]) 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 FDA's Medical Countermeasures Initiative (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, cleared, or granted marketing authorization under sections 505, 510(k), 512, 513(f)(2), 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 authorization for marketing under a premarket approval (PMA) application, 510(k) notification, or De Novo classification request.

What are medical countermeasures?

Medical countermeasures, or MCMs, are FDA-regulated products, including biological products, 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.

substantive MCM work ongoing at FDA. The Program 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) 2023 (October 1, 2022 – September 30, 2023).[7]

FY 2023 Resources for MCM Activities

Table 1: FY 2023 resources obligated to MCM activities (dollars in millions)

	FY 23 Enacted	FY 23 FTE Enacted
CBRN Base Funding	$96.9	266.5
Pandemic Influenza Base Funding	$39.7	110
MCMi Base Funding	$36.5	110.5
Subtotal	**$173.1**	**487**
COVID-19 Supplemental Funding	$298.5	160
Total	**$471.6**	**647**

FDA obligated an estimated $472 million in FY 2023 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 647 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 2011-2022 can be found at: **https://www.fda.gov/emergency-preparedness-and-response/about-mcmi/publications-and-reports**

Objectives, Activities and 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 2023 with respect to these activities.

Box 1: Key FDA activities to facilitate development of and access to MCMs
Advising 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 submissions and approving those that meet applicable standards for approval
Supporting the establishment and sustainment of an adequate supply of MCMs, including interagency collaboration on efforts to advance MCM supply chains
Facilitating access to certain available candidate MCMs that are not approved for the proposed use—when necessary—through an appropriate regulatory mechanism, for example via reviewing and taking appropriate action on proposals for clinical trials, expanded access, and EUAs
Responding to emerging and re-emerging public health threats
Establishing and sustaining teams and working groups 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

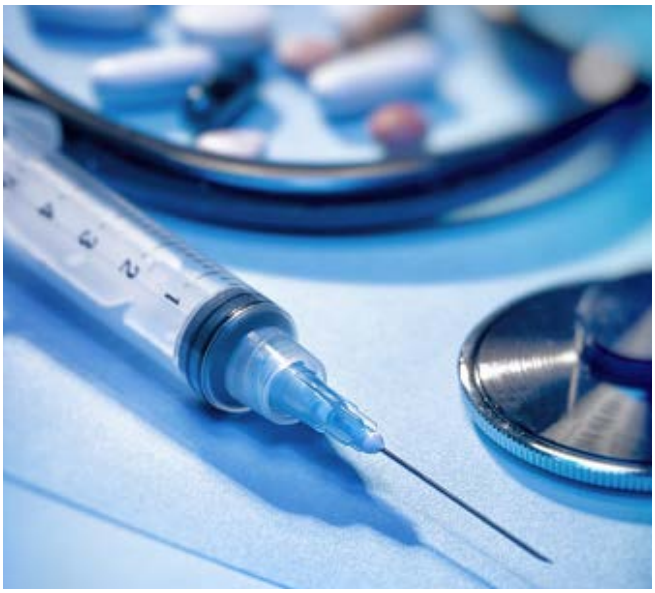
[8] A publicly available list of high-priority threats identified by the Enterprise for which MCMs are needed can be found in the **PHEMCE Strategy and Implementation Plan 2022** (see **Appendix B**), published in October 2022.

Medical Countermeasure Approvals

During FY 2023, FDA continued to review marketing submissions for MCMs against CBRN and emerging infectious disease threats and approve safe and effective MCMs. FDA approved the majority of MCM marketing submissions under review[9] in FY 2023 (see ***Appendixes 1 and 2*** for lists of FY 2023 MCM approvals). The agency also issued and amended numerous EUAs (see: ***Enabling Access to Medical Countermeasures Under FDA's Emergency Use Authorization Authority***).

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

Supporting anthrax preparedness, in February 2023, FDA granted marketing authorization of an *in vitro* immunochromatographic device for use as an aid in the diagnosis of inhalation anthrax, intended for use by military personnel, medical, or health care professionals only. The Active Anthrax Detect Plus Rapid Test (**DEN220044**) is the first point-of-care diagnostic test indicated for testing samples from individuals who have signs and symptoms consistent with inhalation anthrax and a likelihood of exposure; it provides results in about 20 minutes, and does not require a fully equipped lab to process. **Inhalation anthrax** is considered the deadliest form of anthrax and is almost always fatal without treatment. This approach facilitates the triage of infected and non-exposed individuals, allows for earlier treatment, and simplifies subsequent repeat testing should an individual persist with signs of infection. The De Novo classification for this test was **supported** in whole or in part with federal funds from the Biomedical Advanced Research and Development Authority (BARDA). In July 2023,



FDA **approved** Cyfendus (Anthrax Vaccine Adsorbed, Adjuvanted), a vaccine for post-exposure prophylaxis of disease following suspected or confirmed exposure to *Bacillus anthracis* (anthrax) in persons 18 through 65 years of age when administered in conjunction with recommended antibacterial drugs.

Supporting chemical threat preparedness, in May 2023, FDA **approved** Opvee (nalmefene) nasal spray for the emergency treatment of known or suspected overdose induced by natural or synthetic opioids in adults and pediatric patients aged 12 years and older, as manifested by respiratory and/or central nervous system depression. Pharmaceutical-based agents (PBAs), including opioids, are considered a high-priority threat by PHEMCE.[10] Nalmefene is an opioid receptor antagonist which is used to treat acute opioid overdose. If nalmefene is administered quickly, it can reverse the effects of opioid overdose, including respiratory depression, sedation and low blood pressure (i.e., hypotension). The newly approved product, which delivers 2.7 milligrams (mg) of nalmefene into the nasal cavity, is available by prescription and is intended for use in health care and community settings.

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

10 PHEMCE Strategy and Implementation Plan, 2022, Appendix B, available at: **https://aspr.hhs.gov/PHEMCE/2022-SIP/Pages/default.aspx**

Supporting radiological/nuclear agent preparedness, FDA **approved a new indication** for Udenyca (pegfilgrastim-cbqv) and a **new indication** for Stimufend (pegfilgrastim-fpgk) to increase survival of adult and pediatric patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome, or **H-ARS**) as could occur after a radiological or nuclear event. Udenyca and Stimufend are, respectively, the fifth and sixth FDA-approved MCMs and first and second biosimilars that are indicated to increase survival in patients exposed to myelosuppressive doses of radiation. In March 2023, FDA also **approved** a new single-dose prefilled auto-injector presentation of Udenyca (pegfilgrastim-cbqv) for the same indication.

To help rapidly identify a variety of potential threats, in March 2023, FDA cleared the BioFire Global Fever Special Pathogens Panel (**K213362**) for the simultaneous qualitative detection and identification of multiple bacterial, viral, and protozoan nucleic acids directly from ethylenediaminetetraacetic acid (EDTA)[11] whole blood collected from individuals with signs and/or symptoms of acute febrile illness or recent acute febrile illness and known or suspected exposure to the target pathogens described in the **decision summary**. Pathogens identified by this test are: chikungunya virus, dengue virus (serotypes 1, 2, 3 and 4), *Leishmania* spp. that cause visceral leishmaniasis (e.g., *L. donovani* and *L. infantum*), *Leptospira* spp. *Plasmodium* spp. (including species differentiation of *P. falciparum* and *P. vivax/ovale*), and West Nile virus. Pathogens presumptively identified (requiring additional testing and confirmation procedures) are: *B. anthracis*, Crimean-Congo hemorrhagic fever virus, *Ebolavirus* spp., *Francisella tularensis*, Lassa virus, *Marburgvirus*, yellow fever virus, and *Yersinia pestis*.[12] Additionally, in September 2023, FDA cleared the T2 Biothreat Panel (**K231336**) for the qualitative, multiplex detection of nucleic acids from *B. anthracis*, *F. tularensis*, *Burkholderia* spp. (*B. mallei*/B. *pseudomallei*), *Y. pestis*, and *Rickettsia prowazekii* directly from K2EDTA whole blood samples, as described in the **decision summary**. These tests must be used in laboratories that have appropriate biosafety equipment, personal protective equipment (PPE), containment facilities, and personnel trained in the safe handling of diagnostic clinical specimens potentially containing any of the pathogens detected by this panel. Laboratories must also follow public health guidelines that address appropriate biosafety conditions, interpretation of test results, and coordination of findings with public health authorities.

MCMs to diagnose, treat, or prevent COVID-19

In addition to activities noted in other sections of this report to enable access to unapproved MCMs, or unapproved uses of approved MCMs, to diagnose, prevent, or treat COVID-19, FDA approved COVID-19 vaccines, therapeutics, and diagnostic tests in FY 2023.

Vaccines

In FY 2023, FDA approved Biologics License Application (BLA) supplements for two previously approved COVID-19 mRNA vaccines to revise the Package Inserts to update information about side effects reported in post-marketing and post-EUA experience. In September 2023, FDA **took action** approving updated **COVID-19 vaccines** formulated to more closely target circulating variants and to provide better protection against serious consequences of COVID-19, including hospitalization and death. These approvals of updated mRNA vaccines for 2023-2024 manufactured by ModernaTx Inc. and BioNTech Manufacturing GmbH (with Pfizer) were consistent with the **totality of the evidence** and input from FDA's expert advisors to update COVID-19 vaccines to include a monovalent (single) component that corresponds to the omicron variant XBB.1.5.

Therapeutics

In May 2023, FDA **approved** the oral antiviral Paxlovid (nirmatrelvir tablets and ritonavir tablets,

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[11] EDTA is used in blood collection to keep the sample from clotting. Specific anticoagulants or collection tube types (e.g., K2EDTA) may also be noted in medical product indications or instructions for use.

[12] *Y. pestis* is the bacterium that causes **plague**.

co-packaged for oral use) for the treatment of mild-to-moderate COVID-19 in adults who are at high risk for progression to severe COVID-19, including hospitalization or death. Paxlovid was the fourth drug—and **first oral antiviral** pill—approved by FDA to treat COVID-19 in certain adults. In FY 2023, for the intravenous antiviral drug Veklury (remdesivir, approved for certain inpatients in 2020 and outpatients in 2022), FDA approved several New Drug Application (NDA) supplements, including supplements approved on July 13 and August 23, 2023, to facilitate appropriate usage for patients with renal or hepatic impairment respectively.

In December 2022, FDA **approved** a new indication for Actemra (tocilizumab) injection for the treatment of hospitalized adult patients with COVID-19 who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO). FDA first issued an EUA for tocilizumab in hospitalized adult and pediatric patients (2 years of age and older) for the same use on June 24, 2021. Tocilizumab remains authorized for emergency use for hospitalized pediatric patients 2 to less than 18 years of age who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO.

Diagnostic tests – De Novo

De Novo **requests** provide a marketing pathway to classify novel medical devices for which **general controls** alone, or general and **special controls**, provide reasonable assurance of safety and effectiveness for the intended use, but for which there is no legally marketed **predicate device**.

In March 2023, FDA permitted marketing of the first COVID-19 antigen test using one of the traditional premarket review processes. FDA granted marketing authorization of the Sofia 2 SARS Antigen+ FIA, Sofia SARS Antigen FIA Control Swab Set (**DEN220039**), intended for prescription use only for the detection of the COVID-19 virus within six days of symptom onset and which can be used in a point-of-care setting. The test aids in the diagnosis of COVID-19 for people experiencing symptoms and is to be repeated twice over three days with at least 48 hours between tests.

In May 2023, FDA permitted marketing of the first COVID-19 serology tests through the De Novo pathway. FDA granted marketing authorization of the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Reagent Pack (**DEN210038**) for use with the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Calibrator and the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack (**DEN210040**) for use with the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Calibrator. These tests are intended for prescription use only for the qualitative detection of antibodies to SARS-CoV-2 in human serum and plasma samples collected on or after 15 days post-symptom onset as an aid in identifying individuals who have an adaptive immune response to SARS-CoV-2 from either a recent or prior infection. Serology tests detect the presence of antibodies to SARS-CoV-2 and do not detect the virus itself. This is one reason that serology tests should not be used to diagnose or exclude acute COVID-19 infection. The sensitivity of the tests in early infection is unknown. Negative results do not mean that the tested individual is free from an acute SARS-CoV-2 infection. If acute infection is suspected, diagnostic testing, such as a polymerase chain reaction (PCR) or antigen test for COVID-19, is necessary. BARDA and DoD **supported** development of these tests.

In June 2023, FDA granted marketing authorization for the Cue COVID-19 Molecular Test (**DEN220028**). The product is a molecular nucleic acid amplification test (NAAT) that is intended to detect genetic material from SARS-CoV-2 virus present in nasal swabs from adults with signs and

symptoms of upper respiratory infection. This test is the **first at-home over the counter (OTC) test** for COVID-19 to be granted marketing authorization using a traditional premarket review pathway and the first ever at-home test authorized using a traditional premarket review pathway for any respiratory illness. Development of this test was **supported** by BARDA.

> FDA clears first ever at-home test for any respiratory illness using a traditional premarket review pathway

Diagnostic tests – 510(k)

The ability for health care providers to distinguish between the pathogens causing respiratory infections, which often present similar symptoms, is crucial for making more informed decisions about patient health management, as well as the management of health care resources. Adaptable, highly sensitive and specific diagnostic testing technologies are needed to quickly detect a respiratory pathogen, inform earlier treatment, improve equitable diagnostic access, reduce burdens on the health care system, and help mitigate the impacts of outbreaks.

In February 2023, FDA cleared the BioFire SPOTFIRE Respiratory (R) Panel (**K213954**), an *in vitro* diagnostic (IVD) test used for the simultaneous detection and identification of multiple respiratory viral and bacterial infections in individuals suspected of having COVID-19 or other respiratory tract infections. This test was cleared through the Dual 510(k) and Clinical Laboratory Improvement Amendments (CLIA) waiver pathway, making it the first COVID-19 test to be given a CLIA waiver. In April 2023, FDA also cleared the BioFire SPOTFIRE Respiratory (R) Panel Mini (**K230719**), a similar multiplexed PCR test for the simultaneous, qualitative detection and identification of multiple respiratory viral nucleic acids.

In March 2023, FDA cleared the Simplexa COVID-19 & Flu A/B Direct (**K220963**), a SARS-CoV-2 and influenza molecular diagnostic test. **Supported** by BARDA, this test is designed for use on the LIAISON MDX platform and is run using the direct amplification disc, enabling rapid results for up to eight samples in a little over an hour. Enabling faster turnaround times can help improve patient management and prevent future transmission within the community.

In May 2023, FDA cleared the Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay (**K222736**), a fully automated multiplexed respiratory test for SARS-CoV-2, influenza, and respiratory syncytial virus (RSV).[13] The assay uses nasopharyngeal swab (NPS) specimens obtained from individuals exhibiting signs and symptoms of a respiratory tract infection. The Panther Fusion SARS-CoV-2/Flu A/B/RSV assay is a cartridge-based assay which runs on the fully automated, high-throughput, sample-to-result Panther Fusion system. This system is widely used in the U.S., with Panther instruments installed across all 50 states. Each system can provide initial results in less than 3 hours and process more than 1,000 tests in a 24-hour period. This assay was **supported** by BARDA. Additionally, in October 2022 and June 2023, FDA cleared the cobas SARS-CoV-2 Qualitative for use on the cobas 5800/6800/8800 Systems (**K231306** and **K213804**) for the qualitative detection of nucleic acids from SARS-CoV-2.

In July 2023, FDA cleared the BD Respiratory Viral Panel for BD MAX System (**K230956**) for the simultaneous, qualitative detection and differentiation of SARS-CoV-2, influenza A, influenza B, and/or RSV nucleic acid, and the cobas SARS-CoV-2 & Influenza A/B for use on the cobas Liat System (**K223591**) for the simultaneous qualitative detection and differentiation of SARS-CoV-2, influenza A, and/or influenza B virus nucleic acid. In August 2023, FDA cleared the ID NOW COVID-19 2.0 (**K221925**) and the Xpert Xpress CoV-2/Flu/RSV plus (**K231481**) for the simultaneous *in vitro* qualitative detection and differentiation of SARS-CoV-2, influenza A, influenza B, and/or RSV.

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[13] SARS-CoV-2, influenza, and RSV are major respiratory viruses that have the potential to circulate at the same time and may cause similar symptoms. In FY 2023, in addition to diagnostics noted in this report, FDA **approved** two new RSV vaccines and a monoclonal antibody for RSV prophylaxis. More information about these approvals can be found in the report section, ***Other examples of approvals related to public health preparedness***.

Monkeypox virus, the virus that causes mpox

MCMs to prevent smallpox and mpox

Supporting smallpox and mpox preparedness, in March 2023, FDA approved two BLA supplements for Jynneos (Smallpox and Monkeypox Vaccine, Live, Non-Replicating) to **add a new finishing site** for Liquid Frozen MVA-BN Drug Product manufacture, to **increase** the product storage time at 2-8°C from 12 hours to 4 weeks when thawed from -20°C, and to remove the word "deltoid" from the administration instructions. These actions helped increase availability of this vaccine during mpox vaccination campaigns.

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.

Other examples of approvals related to public health preparedness

Supporting Ebola preparedness, in July 2023, FDA **approved** a BLA supplement for the Ervebo (Ebola Zaire Vaccine, Live) to extend the indication for use to include individuals 12 months of age and older.

Supporting sepsis preparedness, in December 2022, FDA cleared the IntelliSep test (**K220991**), designed to determine, in under 10 minutes, the probability that a patient will develop sepsis with organ dysfunction within the next three days, quickly providing health care providers with actionable results. Using high-speed imaging, microfluidics, and a proprietary algorithm, the IntelliSep test analyzes sepsis-specific biophysical properties of white blood cells from a blood draw that informs on host immune response to infection. The short turn-around time (STAT) assay runs on the Cytovale system and is indicated for use in adult patients with signs and symptoms of infection who present to hospital emergency departments. This test was developed with **support** from BARDA. In April 2023, FDA cleared the Access PCT test (**K222996**), designed for the quantitative determination of procalcitonin (PCT) levels in human serum and plasma (lithium heparin and EDTA). Measurement of PCT in conjunction with other laboratory findings and clinical assessments can be used as an aid in the risk assessment of critically ill patients on their first day of Intensive Care Unit (ICU) admission for progression to severe sepsis and septic shock, as described in the decision summary.

Sepsis is a life-threatening complication that occurs when the body has an extreme response to a pathogen and can be caused by any infection. According to the CDC, each year **sepsis** affects 1.7 million Americans and is associated with one in three hospital deaths. Identifying sepsis early is crucial to saving lives. Sepsis can be caused by any infection or injury—whether it originates from a natural disaster, a chemical, biological, radiological, or nuclear event, or an emerging infectious disease like COVID-19. To be fully prepared against severe outcomes of any threat, better solutions for diagnosis and treatment of sepsis are needed.

Improving respiratory virus preparedness, in May 2023, FDA approved **Arexvy** (Respiratory Syncytial Virus Vaccine, Adjuvanted), the first RSV vaccine approved for use in the U.S. Arexvy is approved for the prevention of lower respiratory tract disease caused by RSV in individuals 60 years of age and older. FDA also approved a second vaccine, **Abrysvo**, for active immunization for the prevention of lower respiratory tract disease (LRTD) caused by RSV in individuals 60 years and older in May 2023 and for active immunization of pregnant individuals 32 through 36 weeks gestational age for the prevention of LRTD and severe LRTD in infants from birth through 6 months of age in August 2023. Additionally, in July 2023, FDA **approved** Beyfortus (nirsevimab-alip), a monoclonal antibody with activity against RSV, for the prevention of RSV lower respiratory tract disease in neonates and infants born during or entering their first RSV season, and in children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV

season. One dose of Beyfortus, administered as a single intramuscular injection prior to or during RSV season, may provide protection during the RSV season.

As discussed in the previous ***MCMs to diagnose, treat, or prevent COVID-19*** section, FDA has cleared several multi-analyte diagnostic tests for qualitative detection and differentiation of various respiratory pathogens, including RSV. In March 2023, FDA also cleared an update to the Lyra RSV + hMPV [human metapneumovirus] Assay (**K230349**). While **RSV** is not generally considered a material threat in the context of MCM preparedness, a confluence of respiratory illnesses can increase strain on health care and hospital systems, as happened in late 2022 with **COVID-19, influenza, and RSV cases surging at the same time**. RSV is a highly contagious virus that causes infections of the lungs and breathing passages in individuals of all age groups. RSV is a common cause of respiratory infections including bronchiolitis (inflammation of small airways in the lung) in young children, but is also a common cause of lower respiratory disease in older adults, potentially including pneumonia that can be serious or life-threatening. RSV circulation is seasonal, typically starting during the fall and peaking in the winter. According to the CDC, each year in the U.S., RSV leads to approximately 60,000-120,000 hospitalizations and 6,000-10,000 deaths among adults 65 years of age and older.

Antimicrobial resistance (AMR) also continues to be a challenging and evolving issue for public health.[14] **Gram-negative bacteria** are considered a high-priority health security threat due to their growing resistance to multiple antibiotics. They can cause infections including pneumonia, bloodstream infections, wound or surgical site infections, and meningitis in health care settings. Quickly determining antibiotic susceptibility can help enable early and efficient infectious disease management and improve patient outcomes.

In April 2023, FDA cleared the Selux AST System; Model AST Gen 1.0 (**K211748**) for use with the Selux Gram-Negative Comprehensive Panel; this followed clearance of the system in January 2023 for use with the Selux Gram-Positive Comprehensive Panel (**K211759**). The Selux AST System is an IVD test system used for antimicrobial susceptibility testing (AST). This testing is performed to determine whether an organism is susceptible or resistant to an antimicrobial drug to help physicians select the appropriate drug to treat an infection. The Selux AST System allows for simultaneous testing of a larger number of drugs and drug concentrations than previous systems. The two panels also have the ability to expand to incorporate new drugs in the future. Susceptibility testing systems use FDA-recognized cut-off values (referred to as susceptibility test interpretive criteria or breakpoints), to indicate whether the drug is likely to be effective (drug concentrations below the cut-off are likely to be effective, and drug concentrations above the cut-off are not likely to be effective). Because breakpoints are updated to maintain accurate interpretations of the susceptibility test results, the Selux AST System was also cleared with a predetermined change protocol, allowing the developer to update breakpoints without an additional premarket submission to the FDA. Development of both panels was **supported** by BARDA.

In FY 2023, FDA cleared a number of AMR-related diagnostic devices, including clearing several additions and updates to the VITEK 2 Gram-Negative Susceptibility Cards and VITEK 2 Gram-Positive Susceptibility Cards used with the VITEK 2 Systems in clinical laboratories to determine the susceptibility of various clinically significant microorganisms to antimicrobial agents. In October 2022 and March 2023, FDA cleared the Colibrí System (**K220546**) and Colibrí (**K223245**) as semi-automated and automated, respectively, pre-analytical processors that pick isolated colonies designated by the operator and

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[14] As noted in footnote 2, some medical products and activities 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 these examples is not intended as comprehensive reporting on agency activities related to these topics, including AMR. For additional AMR information from FDA, see: **https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/antimicrobial-resistance-information-fda**

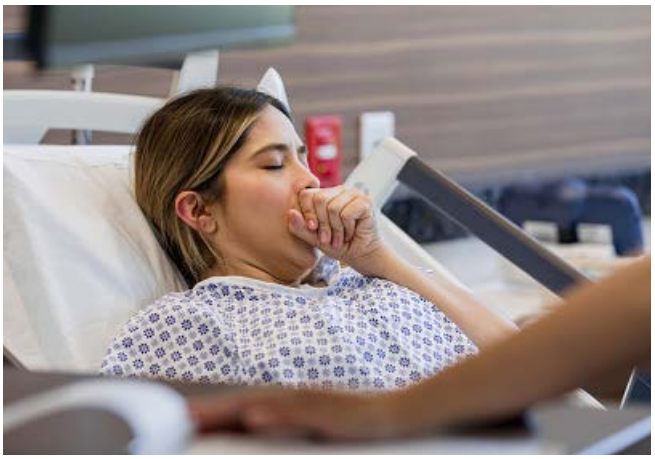
use a pipetting system to prepare matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF MS), target slides for bacterial identification and microbial suspension at known concentration for AST and purity assessment for use with the VITEK 2. In May 2023, FDA cleared the ComASP Cefiderocol 0.008-128 test (**K230479**), a quantitative broth microdilution method intended for the *in vitro* determination of antimicrobial susceptibility of bacteria to cefiderocol. In FY 2023, FDA also cleared several additions and updates regarding the Sensititre 20-24-hour *Haemophilus influenzae/Streptococcus pneumoniae* MIC or Breakpoint Susceptibility System to include additional antimicrobial agents and/or test microorganisms and breakpoint updates and also cleared several additions to the Sensititre YeastOne Susceptibility System to add new antifungal agents for clinical susceptibility testing of various *Candida* spp. FDA also cleared several AST discs used for semi-quantitative *in vitro* susceptibility testing by the agar diffusion test procedure for Rezafungin (**K230827**), Cefiderocol (**K221826**), and Lefamulin (**K230651**).

In May 2023, FDA **approved** Xacduro (sulbactam for injection; durlobactam for injection), a new **treatment** for hospital-acquired bacterial pneumonia (HABP) and ventilator-associated bacterial pneumonia (VABP) caused by susceptible strains of bacteria called *Acinetobacter baumannii-calcoaceticus* complex, for patients 18 years of age and older. *Acinetobacter* species are gram-negative bacteria that can be associated with serious multi-drug-resistant infections especially in health care settings. According to the World Health Organization (WHO), carbapenem-resistant *A. baumannii* are among the bacterial pathogens with the most critical urgent need for new antimicrobial treatments, highlighting the high level of need for additional treatment options amid growing global resistance to antimicrobial medicines.[15] In addition to approval of the new antimicrobial, in July 2023, FDA cleared the HardyDisk AST Sulbactam/Durlobactam 10/10µg (SUD20) (**K231568**) for semi-quantitative *in vitro* susceptibility testing by the agar diffusion test procedure (Kirby-Bauer) and in August 2023, FDA cleared addition of Sulbactam-durlobactam in the dilution range of 0.015/4-32/4 µg/mL to the automated Sensititre 18-24 hour MIC or Breakpoint Susceptibility System (**K231994**).

Symptoms from acute bacterial and viral infections are similar and distinguishing between a bacterial and viral infection early in patient diagnosis can be crucial in providing the correct patient management and reducing the risk of antibiotic-associated adverse events, such as allergic reactions or neurological complications, antibiotic resistance, and other potentially confounding problems, such as delayed diagnosis. In March 2023 (**K222332**) and June 2023 (**K230944**), FDA cleared updates and additions to the previously cleared MeMed BV device that is designed to measure three non-microbial (host) proteins (TRAIL, IP-10, and CRP) in adult and pediatric serum and venous whole blood samples and intended for use in conjunction with clinical assessments and other laboratory findings as an aid to differentiate bacterial from viral infection.

Pandemic influenza preparedness

Supporting pandemic influenza preparedness, in addition to combination COVID-19/flu and other multiplex tests as noted above, FDA also cleared two updates and additions to existing influenza diagnostic tests (BD VeritorTM System for Rapid Detection of Flu



[15] See, from WHO, WHO publishes list of bacteria for which new antibiotics are urgently needed, at: **https://www.who.int/news/item/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed**

A+B CLIA-Waived Kit [**K223016**] and Lyra Influenza A+B Assay [**K230236**]) in FY 2023. These clearances may help facilitate additional preparedness for both seasonal and pandemic influenza, including through potential reference as predicates for subsequent tests.

All-hazards preparedness

Triaging quickly and accurately is key to saving lives in the wake of a public health emergency, such as a mass casualty incident or an infectious disease outbreak, and in routine care settings. In March 2023, FDA cleared the Butterfly iQ/iQ+ Ultrasound System (**K220068**), a handheld ultrasound tool that may help accelerate assessment of suspected lung function abnormality in patients with conditions ranging from chronic obstructive pulmonary disease (COPD) to COVID-19. In contrast to traditional manual processes for counting **B-lines** from lung ultrasound scans, the Auto B-line Counter utilizes deep learning (artificial intelligence [AI]) technology that can provide a B-line count from a six-second ultrasound clip.

In May 2023, FDA also cleared the automated merged B-lines imaging feature on the Lumify Diagnostic Ultrasound System (**K223771**), an app-based ultrasound system with predictive machine learning (ML) algorithms under development to provide real-time decision-assist capabilities that can aid health care providers in quickly evaluating internal organ injuries from a range of causative agents from smoke inhalation; illness or infectious diseases; or as a result of blast trauma. This ultrasound device is handheld, improving access by enabling point of care assessment of lung injury which allows for quicker triage and clinical decision-making. Development was **supported** by BARDA.

Helping with preparedness of U.S. military personnel, in March 2023, FDA cleared the Alinity i TBI lab test (**K223602**), a commercially available laboratory traumatic brain injury (TBI) blood test, which will provide clinicians with an objective way to quickly assess individuals with mild TBIs, also known as concussions. The test measures two biomarkers in the blood that, in elevated concentrations, are tightly correlated to brain injury. The DoD, through the U.S. Army Medical Research and Development Command (USAMRDC) U.S. Army Medical Materiel Development Activity (USAMMDA), played a critical role in developing this test run on the i-STAT Alinity platform. The Alinity i TBI lab test (**K223602**) offers results in 18 minutes, as compared to the previously approved Banyan BTI (**DEN170045**) test which takes 4 hours, to help health care providers quickly assess concussion and triage patients. For those with negative results, it rules out the need for a CT scan. The test measures two biomarkers in the blood that, in elevated concentrations, are tightly correlated to brain injury. Previously, in January 2021, the DoD **announced** FDA clearance of a field-deployable rapid, handheld TBI blood test, the i-STAT TBI Plasma cartridge (**K201778**), which runs on the same platform.

Supporting preparedness in the event of a large-scale event involving thermal burns (e.g., radiation-induced skin injuries), in October 2022, FDA cleared a new indication for Silverlon Wound Contact, Burn Contact Dressings, for use up to seven days for radiation dermatitis and cutaneous radiation injury through dry desquamation (peeling of dry, scaly skin) (**K221218**). Silverlon is a sterile, non-adherent, knitted nylon plated with 99% elemental silver, and 1% silver oxide that delivers antimicrobial silver ions in the dressing when activated by moisture. Silverlon is a non-adherent wound contact layer that reduces pain during dressing changes, allows evaporation of moisture in the dressing, and reduces wound infections because it contains silver, which has antimicrobial properties. Silverlon was previously approved for other cutaneous syndromes including first- and second-degree thermal burns, and was also cleared (**K190343**) in 2019 as the **first MCM to treat sulfur mustard-induced cutaneous injuries**. Sulfur mustard is commonly known as mustard gas. This product is also important to military combat medics in the management of battlefield burn injuries. Development of this product was **supported** by BARDA.

In December 2022, FDA **approved** a BLA for NexoBrid (anacaulase-bcdb) gel, developed as part of a **partnership** with BARDA, the American Burn Association, and the sponsor. NexoBrid is indicated for eschar removal in adults with deep partial thickness and/or full thickness thermal burns. Removal of eschar is a required and critical early step in the burn

care continuum. NexoBrid is a debridement agent composed of proteolytic enzymes extracted from pineapple stems which, when applied topically as a paste, selectively dissolves eschar while preserving viable tissue. Surgically removing burn eschar may result in blood loss. Non-surgical eschar removal using products such as NexoBrid can alleviate the known risks associated with surgical removal. BARDA procured NexoBrid in 2020 to build national preparedness and make it available for use during mass casualty incidents.

In February 2023, FDA cleared S.E.A.L. Hemostatic Wound Spray (**K210751**), an aerosolized chitosan intended to be used to achieve hemostasis in emergency situations for the temporary control of severe topical bleeding. When sprayed on a bleeding wound, the spray quickly forms a barrier that helps stop bleeding within seconds. The product may be applied under windy and wet conditions and in low-light, and can be administered by first responders, patients, professional medical staff, or caregivers. It is also available in an over-the-counter (OTC) version for local management of minor bleeding.

Additional marketing submissions in progress

Thirty-four additional marketing submissions for new MCMs or new MCM indications were pending before FDA in FY 2023; 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 submission for a medical product under applicable statutory and regulatory provisions unless the submission 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 2023.

Preventing and mitigating shortages

FDA helps to ensure an adequate supply of MCMs for potential emergencies, in part, by working to resolve MCM shortages[16] as quickly as possible when they occur. In FY 2023, FDA continued its extensive COVID-19-related and other supply chain monitoring and mitigation activities to help address and mitigate shortages. For additional information, see ***Box 7: Strengthening the MCM Supply Chain***.

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[16] Information in this report is specific to MCM-related shortage prevention and mitigation. For more general information from FDA regarding medical product shortages, see: Drug Shortages (**https://www.fda.gov/drugs/drug-safety-and-availability/drug-shortages**), CBER-Regulated Products: Current Shortages (**https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/cber-regulated-products-current-shortages**), and Medical Device Supply Chain and Shortages (**https://www.fda.gov/medical-devices/medical-device-safety/medical-device-supply-chain-and-shortages**).

Extending expiration dates

Another way FDA may help ensure adequate supplies of MCMs is by extending the expiration dating of MCMs based on FDA's review of scientific data. FDA continues to review applicable data through the Shelf-Life Extension Program (**SLEP**), to assess whether, if properly stored, certain lots of MCMs 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. For example, in 2019, FDA issued final **guidance** to support government public health and emergency response stakeholder testing to support FDA extensions of the expiration date of **specific lots** of doxycycline hyclate 100 mg capsules held in strategic stockpiles for anthrax emergency preparedness and response purposes. 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. FDA also reviewed scientific data to assess whether certain lots are no longer useable and, therefore, should be properly disposed of. For example, FDA responded to numerous stakeholder inquiries on nerve agent autoinjector **expiry dating extensions** to assist in determinations about whether stockpiled autoinjector products should be retained. FDA continues to work with the applicant on manufacturing issues.

> To help ensure an adequate supply of MCMs for potential emergencies, FDA may extend the expiration dating of MCMs based on FDA's review of scientific data.

Vaccines and therapeutic biological products authorized for emergency use—as products that are not approved under a BLA and are still being studied under Investigational New Drug applications (INDs)—may not have fixed expiry dates. For doses of vaccines and therapeutic biological products that are close to expiry, if those doses are being held under appropriate conditions for ensuring their integrity for use, they could 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 2023, FDA **extended the expiration dates** of several lots of Pfizer-BioNTech COVID-19 Vaccine, Moderna COVID-19 Vaccine, and several COVID-19 therapeutics including Paxlovid, Lagevrio (molnupiravir), and monoclonal antibodies (mAbs).

Reagent stability studies are needed to support shelf-life expiration dates for 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 may be 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 2023, FDA extended the shelf life of 27 at-home 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 2023, as a result of SLEP testing that ensured drug stability and quality, FDA granted shelf-life extensions for approximately 830 lots (batches) of MCM drugs.

Enabling Access to Medical Countermeasures Under FDA's Emergency Use Authorization Authority

During FY 2023, FDA continued to work with USG partners, including DoD and other PHEMCE partners, and product sponsors to facilitate access to certain unapproved candidate MCMs when circumstances are appropriate, including availability of appropriate supporting data for review.[17] One way FDA does this is by issuing EUAs. The EUA authority[18] 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.[19] Lists of **current EUAs** are published on the FDA website.

Table 2: COVID-19 EUA recap

Product type	New EUAs issued in FY 2023	Total EUAs issued since 2020*
In vitro diagnostics	44	531
Drugs and biological therapeutics	2	21
Vaccines	0	4
Other devices**	1	63
Total	**47**	**619**

**This total includes 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 2023, additional products (e.g., surgical masks) were made available under such EUAs issued in previous years.*

New COVID-19 EUAs issued in FY 2023 include:

- A new EUA for **Kineret (anakinra)** for the treatment of COVID-19 in hospitalized adults with pneumonia requiring supplemental oxygen (low- or high-flow oxygen) who are at risk of progressing to severe respiratory failure and likely to have an elevated plasma soluble urokinase plasminogen activator receptor (suPAR).

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17 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.

18 Section 564 of the FD&C Act (21 USCS § 360bbb-3).

19 The Project BioShield Act of 2004 [Public Law 108-276] added section 564 to 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 [Public Law 114-255], Public Law 115-92 in 2017, and section 2504 of the Consolidated Appropriations Act of 2023 [Public Law 117-328].

- A new EUA for the use of **Gohibic (vilobelimab) injection** for the **treatment** of COVID-19 in hospitalized adults when initiated within 48 hours of receiving invasive mechanical ventilation or ECMO (artificial life support).
- A new EUA for the **first at-home OTC diagnostic test** that can differentiate and detect influenza A and B, commonly known as the flu, and SARS-CoV-2. The **Lucira by Pfizer COVID-19 & Flu Home Test** is a single-use at-home test kit that provides results from self-collected nasal swab samples in roughly 30 minutes.
- A new EUA for the **Lucira by Pfizer COVID-19 and Flu Test** for use in a point-of-care (POC) setting, following collaboration with the National Institutes of Health (NIH) Independent Test Assessment Program (**ITAP**).
- The first over-the-counter saliva-based molecular test, **Metrix COVID-19 Test**, a single-use molecular diagnostic test for the detection of SARS-CoV-2.
- A new EUA for the **Diazyme SARS-CoV-2 Neutralizing Antibody CLIA Kit**, a test kit supported by BARDA. The Diazyme SARS-CoV-2 Neutralizing Antibody CLIA Kit is intended for use as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating a recent or prior infection, and should not be used to diagnose or exclude an acute SARS-CoV-2 infection.
- Seven new EUAs for COVID-19 IVDs, including at-home tests, and additional tests supported by the NIH ITAP program.
- A new EUA for the **Anumara Electrocardiogram (ECG) Low Ejection Fraction Tool** (ELEFT) for use as a diagnostic to screen for potential cardiac complications associated with COVID-19 or underlying cardiac conditions that may affect clinical management of COVID-19.

FDA modifies or amends EUAs as appropriate, including revisions to fact sheets and instructions for use. Multiple revisions were made to COVID-19 vaccine,

therapeutic, and device EUAs in FY 2023—a substantial and ongoing effort. The latest information is available on the FDA website. For example, FDA:

- In November 2022, revised the EUAs of all **COVID-19 antigen tests** to revise the authorized uses and require updates to product labeling regarding repeat, or serial, testing. This action was in response to available data about the performance of COVID-19 antigen tests showing that repeat testing after a negative COVID-19 antigen test result increases the chance of an accurate result in people with and without symptoms and could help prevent people from unknowingly spreading the SARS-CoV-2 virus to others.
- Made several amendments to the EUAs of the Moderna COVID-19 Vaccine, Bivalent and the Pfizer-BioNTech COVID-19 Vaccine, Bivalent including the following:
  - In October 2022, to authorize their use as a single booster dose in in children down to six years of age for administration at least two months following completion of primary vaccination or their most recent booster dose with an FDA authorized or approved monovalent COVID-19 vaccine.
  - In December 2022, to **authorize** use of these bivalent mRNA COVID-19 vaccines for certain children down to six months of age.
  - In March 2023 to **authorize** the Pfizer-BioN-

Tech COVID-19 Vaccine, Bivalent as a single booster dose for certain children six months through four years of age.

  - In April 2023, to **authorize changes to simplify** the use of the bivalent mRNA COVID-19 vaccines.

- In October 2022, **amended** the EUA of the Novavax COVID-19 Vaccine, Adjuvanted to authorize its use as a first booster dose to certain individuals 18 years of age and older at least six months after completion of primary vaccination with an authorized or approved COVID-19 vaccine.[20]
- Revised the EUA for Evusheld (tixagevimab co-packaged with cilgavimab) to limit the use of Evusheld for pre-exposure prophylaxis of COVID-19 in the U.S. only when, based on information including variant susceptibility to Evusheld and national variant frequencies, the combined frequency of non-susceptible variants nationally is less than or equal to 90%. Consistent with this limitation, FDA later **announced** that Evusheld is not currently authorized for emergency use in the U.S. due to the high frequency of circulating SARS-CoV-2 variants that are not susceptible to this treatment at this time. In following national variant frequencies and treatment susceptibility, FDA announced that **several** mAbs were not currently authorized for use in the U.S.
- Reviewed variant circulation and newly available clinical trial data to revise the EUA for bebtelovimab to change the EUA status to not currently authorized for emergency use in the U.S. because the product is not expected to neutralize omicron subvariants BQ.1 and BQ.1.1. This change to the EUA was later **announced** by FDA.
- In **September** and **October** 2023, took action authorizing for emergency use three updated COVID-19 vaccines for 2023-2024 that were formulated to more closely target circulating variants and to provide better protection against serious consequences of COVID-19, including hospitalization and death.
- Continued to monitor appropriateness and circumstances of authorized EUAs, taking action when appropriate. For example, in December 2022, FDA announced a voluntary **recall** of three Detect COVID-19 Test lots due to an increased chance that the tests from certain lot numbers may give false negative results. In addition, in May 2023, FDA issued a **safety communication** and a subsequent **recall notice** related to certain lots of SD Biosensor, Inc.'s Pilot COVID-19 At-Home Tests due to concerns of bacterial contamination in the Pilot COVID-19 At-Home Test liquid solution, provided in the test kit.
- Authorized 1,436 revisions to **COVID-19 IVD EUAs** from March 2020 through September 2023.

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.[21]

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 2023, FDA revoked EUAs including a COVID-19 therapeutic, and 29 IVDs. FDA also delisted three IVDs from various COVID-19 umbrella EUAs in FY 2023. Information about revoked and terminated EUAs is available on the FDA webpage **Emergency Use Authorization--Archived Infor-**

[20] Development of this vaccine was supported in part with federal funds from BARDA, through the DoD Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense (JPEO-CBRND).

[21] Section 564(g)(2) of the FD&C Act.

mation, and published in the Federal Register.

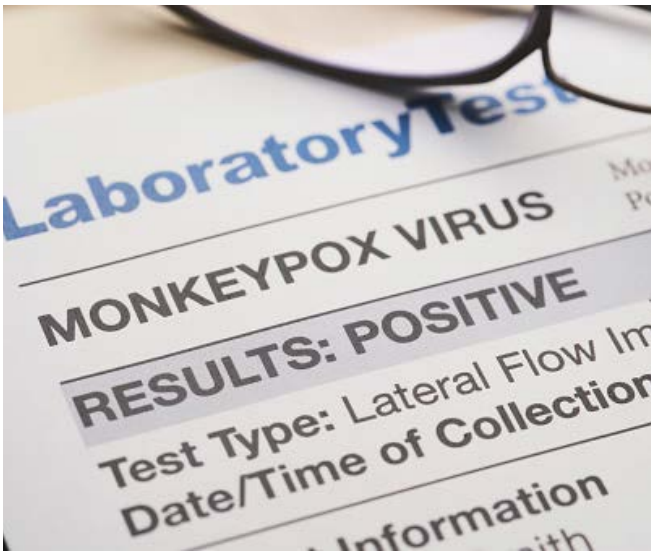
On May 22, 2023, Janssen Biotech, Inc. requested the voluntary withdrawal of the EUA of the Janssen COVID-19 Vaccine. Janssen Biotech, Inc. informed the FDA that the last lots of the vaccine purchased by the USG have expired, there is no demand for new lots of the vaccine in the U.S., and they do not intend to update the strain composition of this vaccine to address emerging variants. On June 1, 2023, FDA **revoked** the EUA for this vaccine.

In 2023, FDA's Center for Devices and Radiological Health (CDRH) issued two final guidance documents to assist with transition plans for **medical devices that were issued EUAs** or fall within **certain enforcement policies** issued to support the response to COVID-19. Since the beginning of the COVID-19 pandemic, CDRH has taken a number of proactive steps to help facilitate the availability of critical medical devices, including IVDs, PPE, and ventilators. Given the magnitude of the response to the COVID-19 pandemic, CDRH is taking steps to assist stakeholders, including industry, health care professionals, and patients, who may need time to transition from certain temporary emergency measures. CDRH developed these transition guidances to help avoid disruption in device supply and facilitate compliance with applicable requirements, while providing stakeholders with recommendations and an appropriate transition period to ensure an orderly and transparent transition to normal operations.

- CDRH has received 71 marketing submissions for transitioning EUA devices, including 28 for IVDs.
- To date, 43 submissions have been authorized for medical devices that were issued EUAs or **fall within certain enforcement policies issued to support COVID-19 response**.

Mpox EUAs

In addition to the extensive EUA work ongoing in response to COVID-19, in October 2022, following the September 7, 2022 Secretary of HHS declaration that circumstances exist justifying the authorization of emergency use of IVDs for the detection and/or diagnosis of infection with the monkeypox [mpox] virus, including IVDs that detect and/or diagnose infection



with non-variola *Orthopoxvirus*, FDA **authorized** the **first commercial test kit** for detection of the virus that causes mpox. The Alinity m MPXV is a real-time PCR test intended to detect monkeypox deoxyribonucleic acid (DNA) using lesion swab specimens from individuals suspected of monkeypox virus infection.

In FY 2023, FDA also **authorized** seven additional IVDs to detect the virus that causes mpox, including two point-of-care tests, in addition to the **first** such authorization in September 2022. In addition, at the sponsors' request, FDA revoked two of the mpox EUA IVDs in April and May 2023.

In November 2022, FDA posted two mpox EUA **templates** for mpox antigen tests, in addition to two molecular diagnostic test EUA templates posted in FY 2022. These templates offer recommendations on what to include in EUA requests or Pre-EUA submissions. The templates are intended to help test developers provide validation data and other information to the FDA, but alternative approaches may be used.

Other EUAs

On February 6, 2023, pursuant to section 564 of the FD&C Act, the Secretary of HHS determined that there is no longer a significant potential for a public health emergency that has a significant potential to affect national security or the health and security of U.S. citizens living abroad and that involves enterovirus D68 (EV-D68). Also, on February 6, 2023, the Secretary of HHS determined that circumstances justifying the authorization of emergency use of new IVDs for

detection of EV-D68 no longer exist. Based on these determinations, the Secretary of HHS terminated, effective **February 20, 2023**, the declaration that circumstances justifying the authorization of emergency use of new IVDs for detection of EV-D68 exist. As a result, the EUA for CDC Enterovirus D68 2014 Real-time RT-PCR Assay (EV-D68 2014 rRT-PCR) was **terminated**.

In addition, FDA authorized one update to an **Ebola IVD EUA** and at the sponsors' request revoked two **Ebola IVD EUAs**. FDA authorized updates to two **Zika IVD EUAs** and a minor labeling update to a Middle East respiratory syndrome coronavirus (MERS-CoV) **IVD EUA**.

Pre-EUAs

In addition to issuing EUAs when appropriate, FDA engages in ongoing pre-EUA interactions 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 2023, 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 2023, CDRH received 134 new pre-EUA requests for IVDs, 34 for COVID-19, and 100 for mpox. The same team closed a total of 227 pre-EUA requests in the same period, including some received in previous fiscal years: 96 COVID-19 IVDs, and 131 mpox IVDs. In FY 2023, CDRH did not receive any pre-EUA requests for non-IVD devices.

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, such as **vaccines**, including EUAs related to our response to COVID-19 and 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.

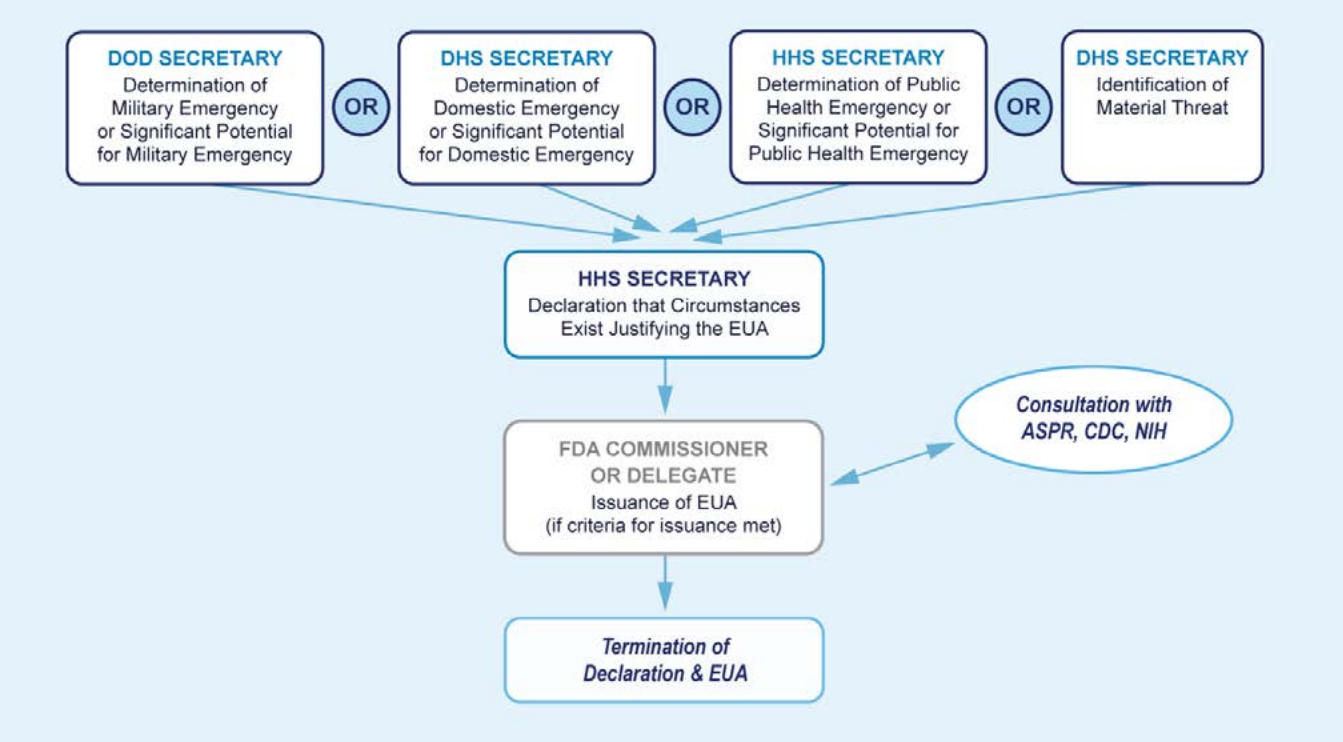
Data and information supporting EUA issuance of IVDs is included in the Instructions for Use or EUA Summary documents, which are **published** for every IVD EUA.

What is a pre-EUA?

To help prepare for potential and current emergencies, FDA works with MCM developers to advise them on preparation of 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 and reviews 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. Existence of a pre-EUA does not necessarily mean that sufficient information is available to support issuance of an EUA. Learn more in the guidance **Emergency Use Authorization of Medical Products and Related Authorities**.

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?***

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 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***.

In addition to preparedness and response activities noted in Box 2, FDA engaged in emerging infectious disease-specific response activities in FY 2023, 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** under section 319 of the PHS Act 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 2020-2023—and beyond—thousands of FDA scientists, clinicians, lawyers, and other experts have worked tirelessly to respond to COVID-19.

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 when appropriate 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
Facilitating access to investigational MCMs—when necessary—through an appropriate mechanism, for example via reviewing and taking appropriate action regarding proposals for clinical trials, expanded access, or EUAs
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 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 addressing misinformation
Addressing health disparities and promoting health equity in preparedness and response to public health emergencies

SARS-CoV-2, the virus that causes COVID-19

On May 11, 2023, the COVID-19 public health emergency (PHE) declared under the PHS Act **expired**. Since the start of the COVID-19 PHE, FDA has been committed to providing timely recommendations and regulatory information to support response efforts, and important tools and flexibilities to manufacturers, health care facilities, providers, patients, and other stakeholders. FDA remains committed to providing appropriate notice and information to impacted stakeholders to help ensure a smooth transition. Importantly, the ending of the PHE declared by HHS under the PHS Act **will not impact** FDA's ability to authorize devices (including tests), treatments or vaccines for emergency use. Existing EUAs for products will remain in effect and the agency may continue to issue new EUAs while there is an applicable declaration under section 564 of the FD&C Act in effect.

While a wide range of work continues across FDA to support COVID-19 response, this report offers a snapshot of MCM-related COVID-19 response activities during the FY 2023 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. *(See previous section:* ***MCMs to diagnose, treat, or prevent COVID-19****)*
- Facilitating access to unapproved MCMs or to approved MCMs for unapproved uses, including certain appropriately accurate and reliable diagnostics through an appropriate mechanism, such as EUAs or INDs. *(See* ***Table 2: COVID-19 EUA recap****)*. For example, in FY 2023, FDA:
  - Received nine new INDs and three pre-INDs for Center for Drug Evaluation and Research (CDER)-regulated COVID-19 biological products, and authorized one Emergency Investigational New Drugs Application (EIND) for a biological product.
  - Received 26 new pre-INDs and 58 new INDs for COVID-19 drugs, and authorized 37 EINDs for COVID-19 drugs.
  - Approved more than 2,000 COVID-19-related Abbreviated New Drug Applications (ANDAs) (since 2020), including critical medications that have been in shortage due to their use in treating patients with COVID-19.
  - To date, 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.
  - Received 15 new INDs for Center for Biologics Evaluation and Research (CBER)-regulated biological products intended for prevention of COVID-19, received 15 pre-INDs for biological products to treat or prevent COVID-19, and authorized 1 EIND for treatment of severe disease associated with COVID-19.
  - Issued 44 new EUAs and 311 revisions to current EUAs for COVID-19 IVD devices.
- 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** or **recalls,**

market withdrawals, and safety alerts 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 COVID-19 MCMs, and to help diagnostic test manufacturers 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, and on November 1, 2022, a **Repeat Testing Revision Letter** was issued revising the authorized uses and requiring updates to product labeling regarding repeat, or serial, testing, for all currently authorized SARS-CoV-2 antigen tests.

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 outbreak.[22] Before the 2022 mpox outbreak, Jynneos vaccine had been 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, based, in part, on immunogenicity in a human clinical study (including comparison to a previously approved smallpox vaccine) and on animal study data. Two antiviral drugs, TPOXX (tecovirimat) and Tembexa (brincidofovir), had been approved for smallpox under the **Animal Rule**; but mpox treatment was not considered eligible for Animal Rule approval because of ongoing occurrence of human mpox disease such that clinical trials would be ethical and feasible. No clinical trial data are currently available to assess whether any treatment interventions are safe and effective in humans with mpox. However, FDA continues to work closely with sponsors interested in developing and implementing protocols to generate safety and efficacy information while facilitating access. Because tecovirimat and brincidofovir were FDA-approved for treatment of smallpox, there has been substantial interest in uses of these drugs for mpox. FDA has strongly encouraged development and implementation of appropriate clinical trials to provide interpretable information on whether such products are safe and effective for treatment of mpox in the clinical setting, while also facilitating opportunities for expanded-access usage if needed. For example, FDA worked with the Reagan-Udall Foundation to facilitate addition of brincidofovir to a web-based application for single-patient emergency IND requests. The NIH Study of Tecovirimat for Human Monkeypox Virus (**STOMP**) trial remains ongoing.

In January 2023, FDA announced the availability of a draft guidance, **Mpox: Development of Drugs and Biological Products**. When finalized, the draft

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[22] The PHE declared under section 319 of the PHS Act Section for mpox **expired** on January 31, 2023, but FDA continues MCM-related preparedness and response efforts. Expiration of the Section 319 PHE did not impact the FD&C Act Section 564 declarations for mpox vaccines (effective August 9, 2022), and mpox diagnostics (effective September 7, 2022), which enable FDA to issue EUAs. For more information, see FAQs: What happens to EUAs when a public health emergency ends? at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/faqs-what-happens-euas-when-public-health-emergency-ends**

[23] See 21 Code of Federal Regulations (CFR) 314 Subpart I for drugs and 21 CFR 601 Subpart H for biological products.

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.[23]

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.

guidance will provide FDA's current thinking regarding nonclinical, virology, and clinical considerations for mpox drug development programs. The purpose of this guidance is to assist sponsors in the clinical development of drugs for the treatment of mpox.

In addition to the FY 2023 mpox IVD EUAs issued, updated, and revoked as discussed above, in October 2022, FDA updated its **Mpox and Medical Devices** webpage to provide lists of certain laboratories that have notified FDA of their laboratory developed mpox diagnostic test, modification to an FDA-cleared or EUA-authorized mpox diagnostic test, or laboratory developed mpox serology test, as described in Sections IV.A.2, IV.A.3, and IV.C, respectively, of the **Policy for Monkeypox Tests to Address the Public Health Emergency**. While

Ebola virus

FDA has not reviewed the laboratory's validation of the listed tests and has not issued EUAs for these tests, the agency is providing this information to promote transparency.

Ebola virus disease

FDA continues to work with sponsors whenever appropriate to facilitate product development targeting filoviruses including ebolaviruses and related viruses, such as Marburg virus. FDA continued to support the international response to outbreaks of Ebola virus disease (EVD), including follow-up activities related to the 2014-2016 West Africa EVD outbreak and more recent EVD outbreaks in Guinea, the Democratic Republic of the Congo (DRC), and Uganda. In FY 2023, 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 mAb therapies for *Zaire ebolavirus* disease. Based

on this NIH trial and other experience with clinical 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 other filoviruses implicated in recent outbreaks such as *Sudan ebolavirus* or Marburg virus, because these are 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 to encourage traditional marketing submissions for these products.
- 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.

Action Teams

Under the MCMi Program, FDA established multidisciplinary 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 2023.

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 2023 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 IVDs.
- Continuing to facilitate the population of a publicly available **database** for reference-grade microbial genomic sequences, **FDA-ARGOS**. In FY 2023, FDA continued to seek SARS-CoV-2 reference-grade sequence data for the FDA-ARGOS database and develop and deploy a software pipeline to expand the current ARGOS database.
- Continuing collaboration with the National Institute of Standards and Technology (NIST) for suitability assessment of standards for NGS platform-based emerging pathogen detection.

Photo credit: DoD

- 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 2023 activities included:

- Working with DoD partners to support COVID-19 response efforts, including:
  - The use of EUA diagnostic tests.
  - With the 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.[24]
- 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.
- 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 2023 included:

- Continuing to coordinate FDA rad/nuc preparedness activities and working with scientific and

[24] 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 experts across the FDA to enhance development of MCMs for gastrointestinal acute radiation syndrome (GI-ARS), lung-ARS, and biodosimetry medical devices.

- Continuing to facilitate cross-agency rad/nuc collaboration and participation in HHS Administration for Strategic Preparedness and Response (ASPR) activities.
- 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 certain pre-submissions relating to radiation biodosimetry devices.
- Supporting draft guidance published in April 2023, **Acute Radiation Syndrome: Developing Drugs for Prevention and Treatment**.
- Continuing to work with USG partners to address the challenges and gaps in the development of pediatric rad/nuc MCMs.
- Continuing to provide regulatory input on the draft HHS ASPR and Global Health Security Initiative (GHSI) Nuclear Detonation Playbook.
- Continuing to provide regulatory updates on HHS Radiation Emergency Medical Management (**REMM**) guidance.
- Providing FDA reviewers with training including: seminars on nuclear fallout-related health consequences; participating in a CDC tabletop exercise simulation on how to respond to a radiation incident; and participating in an International Atomic Energy Agency (IAEA) program to help reviewers better understand development challenges of biodosimetry medical devices.

Regulatory Advice and Guidance

During FY 2023, 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

After the public health emergency declared under section 319 of the PHS Act ended in May 2023, FDA remains committed to providing timely recommendations, regulatory information, scientific advice, guidance, and technical assistance to impacted stakeholders to help ensure a smooth transition. In the Federal Register of March 13, 2023, FDA **published a notice** addressing the agency's COVID-19-related guidance documents, including which of those guidance documents would no longer be in effect after the expiration of the PHE, and which of those guidance documents FDA was revising to temporarily continue in effect for 180 days after the PHE expired to provide a period for stakeholder transition. The notice also addressed guidances that FDA intended to retain, with appropriate changes, after the PHE expired. FDA continues to foster MCM development by engaging with a variety of stakeholders through webinars, workshops, town hall meetings, and other formats.

As noted previously, in 2023, CDRH issued two final guidance documents to assist with transition plans for medical devices that were issued EUAs or fall within certain enforcement policies issued to support COVID-19 response. FDA continues to take steps to assist stakeholders, including industry, health care professionals, and patients, who may need time to transition from certain temporary emergency measures.

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

Engaging with product sponsors

FDA medical product review centers engage with MCM sponsors and applicants throughout the product life cycle. For example, FDA reviews INDs and Investigational Device Exemption applications (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 submission. FDA also continues to engage with sponsors and applicants to address any issues that arise during regulatory review as well as during the post-marketing phase for these MCMs.

FDA has established policies and procedures for conducting formal meetings with product sponsors or applicants. For detailed information on meetings about product development, please see the **Search for FDA Guidance Documents** webpage, 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 as described in FDA guidance.

Types and numbers of drug and biologic product meetings

Under the Prescription Drug User Fee Act (PDUFA), CBER and CDER categorize formal meetings with product sponsors and applicants of NDAs and BLAs as Type A, B, C, D and Initial Targeted Engagement for Regulatory Advice on CDER and CBER ProducTs (INTERACT).[25] Type A meetings are meetings to help an otherwise stalled product development program proceed or to address an important safety issue (such as a dispute resolution meeting, a meeting to discuss a clinical hold,[26] and an FDA Nonagreement Special Protocol Assessment (SPA) meeting).[27]

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 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 PDUFA regarding the development and review of a product other than a Type A, Type B, Type D, or INTERACT 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.).

Type D meetings are focused on a narrow set of

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25 For more information, see the September 2023 draft guidance, Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products, available at: **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/formal-meetings-between-fda-and-sponsors-or-applicants-pdufa-products**.

26 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 CFR 312.42.

27 Meetings that are requested after receipt of an FDA Nonagreement Special Protocol Assessment letter in response to protocols submitted under the special protocol assessment procedures as described in the guidance for industry, Special Protocol Assessment (April 2018), available at: **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/special-protocol-assessment-guidance-industry**.

issues that are used to discuss issues at key decision points to provide timely feedback critical to move the program forward. Type D meeting requests could include follow-up questions that raise a new issue after a formal meeting, a narrow issue on which the sponsor is seeking FDA input with only a few associated questions (e.g., three to five questions total), or a general question about an innovative development approach that does not require extensive, detailed advice.

INTERACT meetings are intended for novel products and development programs that present unique challenges in early development (i.e., before filing of an IND or before having a pre-IND meeting). The issues typically relate to IND requirements, for example, questions about design of IND-enabling toxicity studies (e.g., species, endpoints), complex manufacturing technologies or processes, development of innovative devices used with a drug or biological product, or the use of New Approach Methodologies. INTERACT meetings are intended to facilitate IND-enabling efforts when the sponsor is facing a novel, challenging issue that might otherwise delay progress of the product toward entry into the clinic in the absence of this early FDA input. Questions and topics within the scope of an INTERACT meeting include questions for novel products and development programs that present unique challenges in early development for all CDER and CBER products (i.e., questions for which there is no existing guidance or other information in writing that the company could reference from FDA), and a variety of issues that a sponsor needs to address before a pre-IND meeting.

Meetings that are not categorized under the types listed above are non-PDUFA meetings, such as meetings on a sponsor's compliance status or follow-up on post-marketing commitments.

In FY 2023, CBER provided written responses or held 51 formal meetings with MCM sponsors or applicants, and CDER held 25 formal meetings (***Table 3***) and 73 other (non-PDUFA) meetings.

Table 3: FY 2023 formal meetings between CBER/CDER and MCM sponsors or applicants

Meeting Type	CBER	CDER
Type A	0	1
Type B	34	9
Type C	16	12
Type D	0	1
INTERACT	1	2
Total	**51**	**25**

Types and numbers of medical device meetings

CDRH generally categorizes its meetings with product sponsors as Pre-Submission (Pre-sub) and Submission Issue Request (SIR) meetings.[28] 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 132 Pre-subs and 6 SIR meeting requests (related to marketing submissions) for MCM medical devices in FY 2023. 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 feedback, a Pre-sub meeting was held. SIR meetings are sometimes held to discuss deficiencies identified during premarket review of device marketing submissions and to provide clarification of FDA's questions or to discuss an approach to address any complex issues identified. In FY 2023, CDRH provided written feedback for 105 MCM Pre-subs or SIRs and held 29 Pre-sub and 3 SIR meetings with MCM sponsors or submitters (***Table 4***).

[28] For more information on Pre-subs and SIR meetings, along with other mechanisms for requesting feedback on medical device submissions see the FDA guidance, Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program (June 2023), available at: **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/requests-feedback-and-meetings-medical-device-submissions-q-submission-program**.

Table 4: FY 2023 meetings between CDRH and MCM sponsors or submitters	
Meeting Type	**CDRH**
Pre-Submission	29
Submission issue meetings	3
Total	**32**

In addition to the meetings 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.[29] In FY 2023, 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 2023.

FDA also conducted enhanced inspection and compliance activities to support early identification of any problems that might impede MCM product development. FDA conducted activities and 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 submission 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.[30] Guidance documents issued during FY 2023 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 2023 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.

What are guidance documents?

Guidance documents are documents prepared for FDA staff, applicants/sponsors, and the public that describe the agency's interpretation of or policy on a regulatory issue.

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[29] 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**.

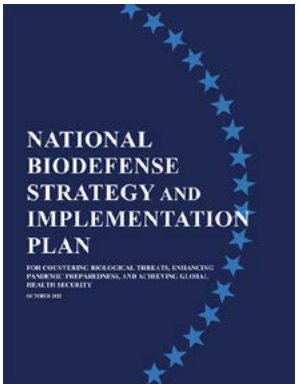
[30] Guidance documents include, but are not limited to, documents that relate to the design, production, labeling, promotion, manufacturing, and testing of regulated products; the processing, content, and evaluation or approval of submissions; and inspection and enforcement policies. (21 CFR § 10.115(b)(2)).

Collaboration and Communication

During FY 2023, 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 83 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-annual, 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.

In FY 2023, FDA signed agreements with other federal agencies that directly or indirectly further joint efforts to support development, safety, and availability of MCMs. In January 2023, FDA and the National Center for Advancing Translational Sciences (NCATS) at NIH signed an **MOU** to provide a framework between NCATS and FDA for coordination and collaborative efforts towards widespread use of microphysiological systems (**MPS**) in advancing novel therapies that are safe and effective, and in biomedical research for understanding pathophysiology and modeling of human diseases/conditions. In April 2023, FDA's CDRH, the CDC National Institute for Occupational Safety and Health (NIOSH), and the Occupational and Safety Health Administration (OSHA) signed an **MOU** to provide a framework for continued collaboration, including the sharing of certain information to facilitate coordination, decision-making, law enforcement activities, and guidance or regulation development through the agencies' respective authorities and overlapping missions to ensure safe and effective devices for a broad range of PPE, including respiratory protective devices. In May 2023, FDA and the Veterans Health Administration (VHA) signed an **MOU** to provide a framework for collaboration to facilitate the development of requirements for trusted networks needed to help enable the use of distributed manufacturing and digital stockpiles to protect public health by promoting supply chain resilience during emergencies, shortages, and pandemics. *(Also see the section: **Advanced Manufacturing**.)*

FDA also continues to support implementation of the **National Biodefense Strategy and Implementation Plan**.



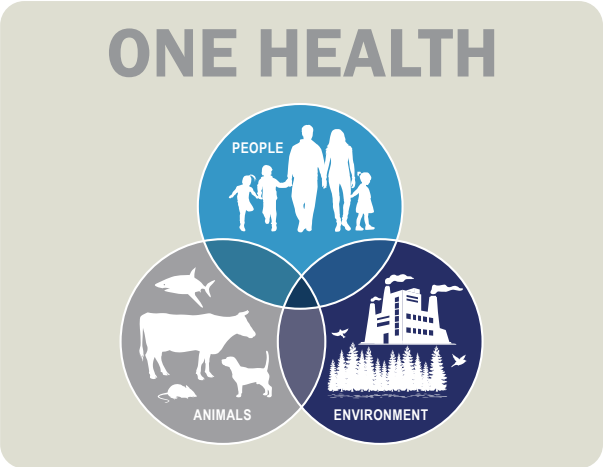
In October 2022, HHS **announced actions** the department—including FDA—will take following **National Security Memorandum 15**, signed by President Biden, directing implementation of the plan. The strategy and implementation plan detail a coordinated approach to address the challenges from naturally occurring, deliberate, and accidental biological threats. These threats are among the most serious threats facing the U.S. and the international community. The 2022 strategy builds on the 2018 National Biodefense Strategy, incorporating lessons learned during the COVID-19 pandemic, and laying out a comprehensive implementation plan with bold, concrete actions to transform our health security.

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 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 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**), 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.
- The **Sepsis Innovation Collaborative**, to help accelerate the development, availability, and adoption of safe and effective medical devices, digital health, and other medical technologies to prevent, diagnose, manage infection, and support sepsis patients and survivors through precompetitive collaboration. CDRH participates in the Infection Management/Sepsis Collaborative Community (IMSCC).

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 our shared environment. FDA continues to leverage relationships with other agency partners to identify further opportunities to improve health outcomes utilizing a One Health approach. In FY 2023, FDA's agency-wide One Health Steering Committee participated in activities including:



- Presenting at FDA's **2023 Broad Agency Announcement (BAA) Day**, which shared information with stakeholders about FDA funding to support public health preparedness and response, and other priority areas for FDA regulatory science.
- Collaborating with federal partners on the development of a **National One Health Research Framework** aligned with the National Biodefense Strategy and Implementation Plan supporting a One Health research agenda for biological incidents.
- Participating in One Health outreach conferences including the 2023 **FDA Science Forum**, the Military Health Research Symposium, and the Army Public Health Forum.

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 future public health emergencies.

Examples of FDA's key international MCM collaborations include:

- Serving in leadership roles in the leading international regulatory organizations working toward greater regulatory harmonization worldwide and helping to shape and build global regulatory capacities.[31]
- Supporting HHS's efforts to advance the global MCM architecture through amendments to the International Health Regulations and Pandemic Treaty negotiations.
- Supporting and participating in the U.S. government's Global Health Security Agenda (**GHSA**) and strategy, working to help establish legal frameworks and tools to advance global legal preparedness and equitable access MCMs to MCMs during international public health emergency. 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, such as WHO's **R&D Blueprint** and the **Access to COVID-19 Tools (ACT) Accelerator**.
- Participating in collaborations such as: **Coalition for Epidemic Preparedness Innovations (CEPI)**, a 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)**, a network of major research funding organizations working on a global scale; and **Foundation for Innovative New Diagnostics (FIND)**, a global nonprofit organization driving innovation in the development and delivery of diagnostics to combat major diseases affecting the world's poorest populations.

Enhancing communication

FDA continued extensive agency-wide efforts to communicate openly and often about its response to the COVID-19 pandemic and mpox public health emergency, including press releases, email updates, web updates, videos, and social media, to help promote confidence in the public health response. Intensive

[31] The following are examples of organizations for which FDA serves as leadership: International Coalition of Medicines Regulatory Authorities (ICMRA) (**https://www.icmra.info/drupal/en**); the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) (**https://www.ich.org/**); and the International Medical Device Regulators Forum (IMDRF) (**https://www.imdrf.org/**).

stakeholder outreach also continued, including town hall meetings, webinars, workshops, email alerts, and individual outreach. Examples of FDA communications in FY 2023 include:

- A new webpage to help consumers **understand** at-home OTC COVID-19 antigen diagnostic test results
- A new webpage to help consumers and health care professionals easily **find a list** of COVID-19 tests that have undergone traditional marketing authorization by FDA
- A new webpage to help consumers understand the dangers of **illegally sold mpox products**
- An updated webpage answering **frequently asked questions** about what happens to EUAs when a public health emergency ends
- An FDA Voices post by FDA Commissioner Dr. Robert Califf and Chief Medical Officer Dr. Hilary Marston on how lessons learned from COVID-19 are **informing preparation** for future public health emergencies

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 2023, 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.[32]

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, if the requirements outlined in the Animal Rule regulations are met, 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 certain populations, such as children or pregnant individuals. For example, ethical evaluation of the participation of

[32] 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.

children in clinical trials under FDA's regulations[33] involves considering, among other things, the level of risk and the prospect of direct benefit to the participant. Thus, in some circumstances it may not be ethical to conduct certain types of clinical trials in the pediatric population to obtain data that can be used for approving pediatric indications for MCMs—such as safety or dosing information. 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) may be appropriately leveraged to support approval of an indication for pediatric use in certain situations. 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 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 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 **BAA**, "Food and Drug Administration 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.

BOX 3: MCM regulatory science research areas

Priority research areas sustained under the MCMi Regulatory Science Program to support preparedness for high-priority threats include:
Identifying, developing, and qualifying drug development tools, such as animal models and immune biomarkers to assess safety and efficacy of MCMs
Developing, qualifying, and facilitating innovative analytical technology of tissues/cells to advance characterization and further scientific understanding of pathophysiological mechanisms of infection, disease progression, susceptibility, or virulence
Developing and qualifying *in silico* predictive models (e.g., computational models) and *in vitro* assays (e.g., MPS) to complement—and help reduce—the use of *in vivo* animal models to assess potential toxicity and activity of MCMs
Enhancing the agility, quality, and utility of diagnostics and diagnostic data
Developing tools to support validation of next-generation IVD platforms
Developing reference materials related to CBRN threat agents and emerging infectious diseases to facilitate development of MCMs
Assessing the performance of emergency medical equipment including PPE
Enhancing emergency preparedness and response capabilities, and tracking and evaluating the safety and clinical benefit of MCMs used during public health emergencies
Advancing broadly applicable, commercially ready tools, technologies, and platforms that can improve the manufacturing efficiency, consistency, and quality of MCMs
Modernizing tools to evaluate MCM product safety, efficacy, and quality, and secure the MCM supply chain

Supporting COVID-19 response with regulatory science

Beginning in 2020, and continuing through FY 2023 and beyond, 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.

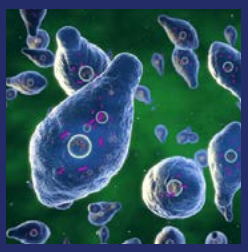
[33] 21 CFR part 50, subpart D.

The reference panel provided test developers with well characterized reagents to compare the sensitivity and specificity of different molecular diagnostic tests.

- 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.
- 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 ML 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.

BOX 4: FEATURED MCMI-FUNDED EXTRAMURAL PROJECTS

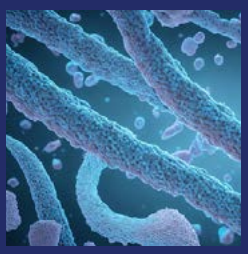
Alternative models for MCM research



Clostridium botulinum bacteria, which causes botulism

In FY 2023, FDA's MCMi Regulatory Science Program initiated two projects with Battelle Memorial Institute to explore the viability of alternative nonclinical models to develop MCMs for chemical- and toxin-based threats. Nerve agents are highly poisonous chemicals that prevent the nervous system from working properly. One project aims to create a well-characterized model that will accurately recapitulate physiological responses of human **organophosphorus nerve agent** exposure, including efficacy of candidate MCMs.

Botulinum neurotoxin (BoNT)—the toxin that causes **botulism**—is one of the most deadly toxins known, and a CDC **Category A** threat agent. FDA and Battelle also initiated a study to establish a new nonclinical parenteral challenge model of systemic BoNT intoxication, to support the advancement of candidate therapeutic MCMs. Data from this study could result in new models for evaluating efficacy of MCMs to botulinum toxicity from BoNT serotypes A, B, and E.



Marburg virus

Provision of Marburg virus control serum

Building on current initiatives in the international research community to develop MCMs for Marburg virus disease, the MCMi Regulatory Science Program awarded a contract to Oxford University in 2023 for continued research. Under this contract, researchers are identifying and collecting biological samples from individuals previously identified (via a lab test: enzyme-linked immunosorbent assay, or ELISA) as having been exposed to or infected with Marburg virus. The goal of this project is to collect biological material and data that can be used as reference (control) to help evaluate the effectiveness of novel MCMs for Marburg virus.

Regulatory science to support public health emergency preparedness and response

In FY 2023, the FDA Office of Counterterrorism and Emerging Threats (OCET), in the Office of the Chief Scientist (OCS), supported three extramural contract awards under the FDA BAA:

- Development of a parenteral challenge model of systemic botulinum neurotoxin intoxication to support the advancement of candidate therapeutic MCMs (Battelle)
- Development of a nerve agent exposure model for chemical warfare agent countermeasure evaluation (Battelle)
- Collection of Marburg virus control serum (Oxford University)

In FY 2023, OCET supported five contract extensions to existing research projects:

- **Human organ chips for radiation countermeasure development** (Wyss Institute)
- **Cellular signaling and immune correlates for SARS-CoV-2 infection** (Stanford University)
- **Development and maintenance of FDA-ARGOS** containing regulatory grade reference genomes for diagnostic use and regulatory science study (Embleema, Inc.)
- **Development of a model** that integrates inflammation and tissue injury to predict and mitigate the post-acute sequelae of COVID-19, or long COVID (Children's Hospital of Los Angeles/ University of Southern California)
- **Characterizing immunity to Ebola and Marburg to support MCM development** (University of California Los Angeles)

In coordination with NASA, in FY 2023, OCET supported one interagency agreement (IAA) with the National Aeronautics and Space Administration (NASA), BARDA, and NIH to continue research on extended longevity of 3D tissues and MPS for modeling of acute and chronic exposures to stressors.

FDA intramural research supported by the OCET MCMi Regulatory Science Program in FY 2023 includes 11 new research projects performed by FDA scientists, including PPE decontamination, advanced manufacturing, development of assays and models (e.g., nonclinical models including computational and *in vitro* models) to facilitate development and evaluation of MCMs for rad/nuc threats, nerve agents and infectious diseases including influenza, COVID-19, and botulinum neurotoxin.

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 2023, FDA continued collaboration with Harvard Pilgrim Health Care to explore how the Sentinel System—an active surveillance system that uses routine querying tools and pre-existing electronic health care data from multiple sources to monitor the safety of regulated medical products—may inform study protocols for MCM safety and effectiveness and to provide a valuable baseline for comparison during a public health emergency. The FDA Sentinel System is conducting a number of **activities in support of the COVID-19 response**. Additionally, FDA continues to participate 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,[34] to support evaluation of real-world performance of SARS-CoV-2 diagnostic tests and antibody tests.

FY 2023 MCMi Regulatory Science program activities are included in ***Table 5***.

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34 COVID-19 Pandemic Response, **Laboratory Data Reporting**: Coronavirus Aid, Relief, and Economic Security Act (CARES) Act Section 18115.

Table 5: MCMi Regulatory Science Program activities in FY 2023
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 2023, researchers worked to complete analysis and characterization of lung, gut, and bone marrow chips and implemented testing of selected MCMs in chips.
Developing novel reagents and MCM models to support MCMs for organophosphate nerve agents and biological toxins (e.g., BoNT)
Emerging threats (e.g., SARS-CoV-2, Ebola, Marburg, and mpox)
Continuing a project that is creating disease models for pediatric long COVID. In FY 2023, the project also collected and integrated data for adult long COVID.
Expanding a project to develop quality metric tools for next-generation sequencing databases to support emerging threat MCM products. This project complements the MCMi-supported FDA-ARGOS database.
Continuing to support improvement of small and large animal models for CBRN (e.g. chemical/toxin) and emerging (e.g., SARS-CoV-2, Ebola, Marburg, and pandemic influenza) threats
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 EVD and Marburg diseases. Collection of samples was completed in 2023, and samples are being shared with interagency partners for continued research.
Analyzing SARS-CoV-2, SARS-CoV, and 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
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
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 the National Institute of Allergy and Infectious Diseases (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 by **strengthening 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
Along with interagency partners, funding a research project that aims to extend tissue viability and physiological function to a minimum of six months using automated engineering capabilities for real-time online readouts in complex human *in vitro* models, such as tissue chips or MPS
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
Collaborating internally (CDRH and CBER) to re-establish and produce the annual influenza reactivity panel to support manufacturers of FDA-cleared antigen-based influenza detection tests to assess their test reactivity with contemporary influenza strains and to comply with special controls established in a 2017 final order reclassifying influenza virus antigen detection test systems.[35] Information about this panel was announced at an FDA-Industry IVD **Roundtable** on May 22, 2023.
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 PHE
Collaborating with USG partners and academia to assess at-home COVID-19 antigen IVD test performance, evaluate the benefits of serial testing, and develop methods to predict SARS-CoV-2 mutation impacts on antigen and molecular IVD performance

BOX 5: FEATURED REGULATORY SCIENCE COLLABORATIONS

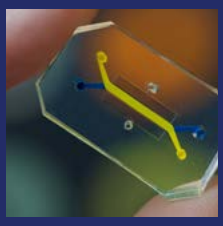
Credit: NASA

NASA: 3D tissue chips

In FY 2022, 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. In FY 2023, FDA and NASA entered a new agreement to provide additional funding for the continuation of the projects, working to extend tissue viability and physiological function to a minimum of six months using automated engineering capabilities for real-time online readouts in complex human *in vitro* models, such as tissue chips or MPS.

DoD: Innovative regulatory tools

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



Credit: Wyss Institute

NIAID/NIH: MPS

FDA is collaborating with NIAID on several projects to conduct alternative methods research. An alternative method generally refers to a testing strategy that reduces or replaces the use of animal testing to support benefit-risk assessment for FDA-regulated products. This collaborative research specifically explores the use of human MPS for ARS and COVID-19, and development of nonhuman primate (NHP) organ chip models. FDA is conducting 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 (UKHSA, formerly Public Health England). The COVID-19 MPS models, including NHP models, are being used to investigate MCM efficacy and to provide a bridge from these models to clinical and animal model data.

35 By regulation 21 CFR 866.3328, annual reactivity testing for influenza virus antigen detection test systems must be performed with contemporary influenza strains. This panel is the source for appropriate 2023 strains.

FDA continues agency-wide efforts and external collaborations to advance the use of **alternative methods** to replace, reduce, or refine the use of animals for certain aspects of product development such as toxicological testing. In addition, FDA continues to create and support programs to advance the development and review of MCMs that may be proposed for development under the Animal Rule. A variety of ongoing collaborations, including MCMi regulatory science collaborations, are **listed** on the FDA website.

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 help 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 help accelerate the production of MCMs. These innovations in manufacturing technology can help support goals of the 21st Century Cures Act, including by:

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

Advanced manufacturing innovation hub

In September 2022, HHS **announced actions** the Department will take following the **Executive Order on Advancing Biotechnology and Biomanufac-**

The I-TEAM Hub open house

turing 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 OCET, 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

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**). Increased use of emerging technologies and advanced manufacturing can help improve supply chain resilience. As part of FDA's overall program to understand and address these technologies, the I-TEAM Hub fills a specific role as an agency-wide resource for collaborative projects. Upon its opening in January 2024 (FY 2024), the I-TEAM Hub will facilitate:

- Training and demonstrations of advanced manufacturing and emerging technologies to give 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.
- Internal FDA collaborations on cross-cutting technologies, processes, and platforms that affect multiple product areas.
- 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 management metrics, and by supplying real-world data streams to FDA and partner information systems.

The I-TEAM Hub includes research and collaboration spaces, remodeled from existing FDA facilities. It will contain state-of-the-art manufacturing, sensing, AI/ML, and other cross-cutting technology platforms that enable the manufacture of medical products. The first pilot project on digital and smart manufacturing is already installed and operational. 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 will be cycled into the Innovation facility.

The I-TEAM Hub is part of OCET's **Advanced Manufacturing Program**, which 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.

Advanced Manufacturing Landscape Analysis

To support keeping FDA up-to-date with best practices for advanced manufacturing across industries, OCET commissioned a report detailing the practices and challenges that have occurred in non-medical industries when implementing different technologies that are advanced or disruptive to their status quo. Some of the technologies will eventually be used for medical products and some of the regulatory questions that have been asked in other industries will eventually be asked of the FDA. The agency will use the lessons learned and best practices to inform its regulatory science and policy-making as appropriate.

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, and policies for supply chain resilience. When it becomes operational in FY 2024, it will help facilitate increased adoption of innovative technologies and predictability for emerging smart manufacturing use cases. The full suite of design and manufacturing lifecycle products that have been implemented in the I-TEAM Hub include:

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

The software modules are 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.

VHA

In May 2023, building on an innovative partnership during the COVID-19 pandemic to fill supply chain gaps in certain medical devices and accessories, FDA and VHA signed a new **MOU** to jointly develop emergency preparedness and response tools and protocols intended to help increase medical product manufacturing capacity and flexibility, and improve resilience of domestic supply chains during emergencies, shortages, and pandemics. This collaboration will help facilitate the development of requirements for trusted networks needed to help enable the use of distributed manufacturing and digital stockpiles, which could ultimately enable veterans and civilians to more rapidly access innovative medical products to support their care. This MOU is specific to medical devices and accessories that

Digital stockpile

A digital stockpile does not store physical goods and products. Instead, it stores the electronic plans, instructions, and methods to make and test medical products. Using digital stockpiles relies on one or more trusted suppliers that can make the product from the digital information, either by using manufacturing capacity typically allotted for other purposes or through methods like 3D printing or self-contained distributed manufacturing lines. Ensuring the quality of these products and instilling trust in patients and clinicians is paramount to successful implementation of a digital stockpile.

Distributed manufacturing

Distributed manufacturing is a manufacturing strategy that allows products to be made at or near the point of use. For example, medical products such as PPE, nasal swabs, or even drugs and saline could be made near the point of care to help ameliorate or prevent shortages caused by supply chain disruptions.

may be made using advanced and distributed manufacturing methods.

In September 2023, the White House Office of Science and Technology Policy (OSTP) hosted a roundtable on digital stockpiles and distributed manufacturing in partnership with FDA and VHA. The results of these discussion have launched interagency working groups for medical device digital stockpiles and digital infrastructures for distributed manufacturing.

Advanced manufacturing innovation around FDA

To support innovation in this field, FDA has led the world in advancing efforts to develop a comprehensive regulatory framework to help facilitate advanced manufacturing and provide a more predictable pathway to getting state-of-the-art medical products into the hands of patients and health care providers, while maintaining the Agency's high standards for ensuring that regulated medical products are safe, effective, and of high quality. To date, FDA has cleared more than 350 3D-printed medical devices and has approved a 3D-printed drug. In addition to medical devices, small molecule drug products, active pharmaceutical ingredients, biological molecules, and vaccine products

BOX 6: FEATURED ADVANCED MANUFACTURING PROJECT

NIST/FDA Collaboration

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.

In FY 2023, NIST and FDA worked together to design a comprehensive set of experiments using NIST's own mAb (**NIST mAb**)— one of the most characterized and consistent mAbs available—and several other mAbs. The team was able to set up online resources that will not only be used by collaborators on this project, but will also be extended to future projects characterizing large biomolecules such as antibodies, proteins, and mRNA. Data from thousands of samples from the current project will be initially stored in this system. The ability to share data streams around the world will greatly enhance the capabilities of U.S. researchers and collaborators.

Overall, this effort will provide a framework to support development and harmonization of accelerated methods and models to predict long term stability. This will help researchers understand molecule stability at different temperatures, simplify test design and reduce testing to more quickly alleviate the burden on cold storage supply chains and help facilitate the distribution of mAbs and other biomolecules during public health emergencies.

are being developed and produced using an array of 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 21 regulatory submissions involving advanced manufacturing, including 16 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.

In October 2023, CDER issued a discussion paper, **Distributed Manufacturing and Point-of-Care Manufacturing of Drugs**. This discussion paper presents areas associated with distributed manufacturing (DM) and POC manufacturing that FDA has identified for consideration as FDA evaluates our existing risk-based regulatory framework as it applies to these technologies. The discussion paper does not constitute guidance; instead, its purpose is to gather feedback from the public to inform future policy development. The discussion paper considers relevant background, including terminology, to the FDA's regulation of DM and POC, identifies challenges presented by DM and POC, and poses key questions to facilitate public comment.

In FY 2023, FDA also **released two discussion papers** to spur conversation about AI and ML in drug development and manufacturing. As with other evolving fields of science and technology, there are challenges associated with AI/ML in drug development, such as ethical and security considerations like improper data sharing or cybersecurity risks. There are also concerns with using algorithms that have a degree of opacity, or algorithms that may have internal operations that are not visible to users or other interested parties. This can lead to amplification of errors or preexisting biases in the data. We aim to prevent and remedy discrimination—including algorithmic discrimination, which occurs when automated systems favor one category of people over other(s)—to advance equity when using AI/ML techniques.

CBER

The CBER Advanced Technologies Team (**CATT**) also provides an interactive mechanism to promote dialogue, education, and input between CBER and prospective innovators/developers of advanced manufacturing and testing technologies. CATT facilitates discussions to promote the implementation of these technologies in the development of CBER-regulated biological products. Another activity under this program is funding of extramural research and development projects to study and identify potential improvements for the advanced manufacturing of biological products, including the investigation and development of innovative monitoring and control techniques. The funded research addresses knowledge and experience gaps identified for emerging manufacturing technologies and supports the development and adoption of such technologies in the biological product sector. As an example of this effort, CBER recently awarded a contract to the Massachusetts Institute of Technology (MIT) for the development of a fully integrated production line in a facility for the continuous manufacturing of mRNA therapeutics and cutting-edge mRNA research technologies. 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, 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

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.

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 help 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.

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 and discussed in more detail in other sections, examples of FDA

advancing policy-specific efforts and developing new approaches to addressing legal, regulatory, and policy challenges associated with the development and use of MCMs in FY 2023 include:

- Working with interagency partners to implement national strategies such as the National Biodefense Strategy and Implementation Plan, the National Health Security Strategy, Pandemic Influenza Preparedness Strategy, and the Global Health Security Strategy, as well as Executive Orders for supply chain resilience.

- 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 facilitate access to unapproved MCMs and unapproved uses of approved products 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, adulterated, or unapproved 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 Public Law 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.
- Continuing to address issues related to information disclosure, including related to COVID-19 interagency activities, and liability protections related to MCM products.
- Continuing to implement **MCM-related legislation** and identify and develop new legislative proposals, providing technical assistance on others' MCM-related legislative proposals, and supporting MCM-related congressional testimony.
- Implementing the material threat MCM priority review voucher (PRV) **program** (codified in section 565A of the FD&C Act), including 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 2023; no material threat PRVs were **redeemed** in FY 2023.[36]
- Developing MCM-related guidance documents issued in FY 2023 (***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 IVDs made available during emergency circumstances, and working with CDC and the Centers for Medicare and Medicaid Services (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**

[36] Section 565A of the FD&C Act contains a sunset provision. Unless this program is re-authorized in subsequent legislation, after October 1, 2023, FDA is no longer authorized to award any material threat MCM PRVs. Material threat MCM PRVs that have already been awarded do not expire and may continue to be redeemed after October 1, 2023.

BOX 7: 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, counterfeit, adulterated, or unapproved products.

In May 2023, in an effort to transition after the end of the COVID-19 PHE and to avoid potential supply chain disruptions that could harm the COVID-19 response and recovery, FDA has granted **exemptions** from certain requirements under section 582 of the FD&C Act, as added by the Drug Supply Chain Security Act (DSCSA). FDA has determined that these exemptions are appropriate to maintain public health and has determined that these exemptions address prescription drug products approved or authorized by FDA to diagnose, cure, mitigate, treat, or prevent COVID-19.

FDA contributed to the HHS-led **Public Health Supply Chain and Industrial Base One-Year Report**, published in February 2022, identifying practical strategies the U.S. Government 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 2023, FDA joined the **Drug Supply Chain Resilience and Advanced Manufacturing Consortium** convened by the Duke Margolis Center for Health Policy. The Consortium's mission is to identify effective policy solutions that promote a resilient drug supply chain with advanced manufacturing capabilities and, ultimately, reduce the frequency and severity of drug shortages.

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 declared by the HHS Secretary under section 319 of the PHS Act. 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, which expired[37] on May 12, 2023, 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.

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37 FDA maintains a list of withdrawn or expired CDRH guidance documents at: **https://www.fda.gov/medical-devices/guidance-documents-medical-devices-and-radiation-emitting-products/withdrawn-or-expired-guidance**

Health Regulations based on the 2016 Joint External Evaluation (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. Activities in FY 2023 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 submissions. FDA held two virtual lectures, and one in-person/virtual hybrid lecture in this series during FY 2023 with a total of 239 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 submissions. FDA held three virtual lectures in this series during FY 2023 with a total of 170 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 submissions. FDA held one virtual lecture in this series during FY 2023 with a total of 36 attendees.

Data quality and integrity training for high-consequence pathogens

FDA also sponsored the 11th annual installment of a week-long training course, **Achieving Data Quality and Integrity in Maximum Containment Laboratories**, 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; One Health sessions were also included in this training. This course was held with virtual and in-person options April 24-28, 2023, with 154 total participants.

In FY 2023, FDA and UTMB also planned the fourth annual clinical course, **Achieving Data Quality and Integrity in Clinical Trials Involving High-Consequence Pathogens** with virtual and in-person options, which was held in October 2023 (FY 2024). 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 2023 Medical Countermeasure Approvals – Biological Products and Drugs

This list includes MCMs approved or licensed by FDA in FY 2023 (October 1, 2022 - September 30, 2023). Additional information can be found on our website at:

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

Medical Countermeasure	Applicant	Key Dates	Indication and/or Change Approved
Abrysvo Respiratory Syncytial Virus Vaccine	Pfizer Inc.	• Submitted September 30, 2022 • Approved May 31, 2023 • Submitted December 21, 2022 • Approved August 21, 2023	For active immunization for the prevention of LRTD caused by RSV in individuals 60 years of age and older. (May 2023) For active immunization of pregnant individuals at 32 through 36 weeks gestational age for the prevention of LRTD and severe LRTD caused by RSV in infants from birth through 6 months of age. (August 2023)
Actemra (tocilizumab) injection	Genentech, Inc.	• Submitted January 29, 2022 • Approved December 21, 2022	BLA supplement for a new indication for the treatment of hospitalized adult patients with COVID-19 who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO.
Afluria Influenza Vaccine	Seqirus Pty Ltd.	• Submitted October 28, 2022 • Approved April 7, 2023	To include the addition of syncope and presyncope as potential adverse reactions in Section 6.2 (Postmarketing Experience) of the Afluria and Afluria Quadrivalent package inserts.
Arexvy Respiratory Syncytial Virus Vaccine, Adjuvanted	GlaxoSmith-Kline Biologicals	• Submitted September 2, 2022 • Approved May 23, 2023	For active immunization for the prevention of lower respiratory tract disease caused by RSV in individuals 60 years of age and older.
Beyfortus	AstraZeneca	• Submitted September 26, 2022 • Approved July 17, 2023	Prevention of RSV LRTD in neonates and infants born during or entering their first RSV season, and in children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season.

Medical Countermeasure	Applicant	Key Dates	Indication and/or Change Approved
Comirnaty COVID-19 Vaccine, mRNA	BioNTech Manufacturing GmbH	• Submitted October 18, 2022 • Approved April 20, 2023 • Submitted February 23, 2023 • Approved September 11, 2023	BLA supplement to update the package inserts for the PBS/Sucrose 30 mcg and Tris/Sucrose 30 mcg formulations to include "dizziness" in Section 6.2 Postmarketing Experience. (April 2023) BLA supplement to use as a single dose for individuals 12 years of age and older, the 2023-2024 formula, and all associated labeling revisions. (September 2023)
Cyfendus	Emergent Product Development Gaithersburg Inc.	• Submitted (rolling) December 14, 2021, and April 20, 2022 • Approved July 20, 2023	Post-exposure prophylaxis of disease following suspected or confirmed exposure to *Bacillus anthracis* (anthrax) in persons 18 through 65 years of age when administered in conjunction with recommended antibacterial drugs.
Ervebo Ebola Zaire Vaccine, Live	Merck Sharp & Dohme LLC	• Submitted June 27, 2023 • Approved July 27,2023	BLA supplement to include individuals 12 months of age and older. This submission fulfills postmarketing requirement #1 identified in the December 19, 2019, approval letter for BLA STN BL 125690/0.
Fluad Influenza Vaccine, Adjuvanted	Seqirus Inc.	• Submitted August 29, 2022 • Approved February 24, 2023	BLA supplement to update Section 6.2 Postmarketing Experience of the Package Insert for Fluad Quadrivalent to include adverse events reported from postmarketing surveillance in individuals 65 years of age and older for Fluad Quadrivalent and/or for Fluad (trivalent formulation).
FluMist Influenza Vaccine Live, Intranasal	MedImmune, LLC	• Submitted August 19, 2022 • Approved January 12, 2023	BLA supplement to include minor, non-seasonal editorial changes to the package insert and carton and container labels intended for implementation during the 2023-2024 flu season.
Jynneos Smallpox and Monkeypox Vaccine, Live, Non-replicating	Bavarian Nordic	• Submitted August 19, 2022 and November 14, 2022 • Approved March 14, 2023 and March 16, 2023 • Submitted March 31, 2022 • Approved September 29, 2023	Two BLA supplements to add a new finishing site for Liquid Frozen Modified Vaccinia Ankara-B avarian Nordic (MVA-BN) Drug Product manufacture, and to increase the Jynneos drug product storage time at 2-8ºC from 12 hours to 4 weeks when thawed from -20ºC; and to remove the word "deltoid" from the administration instructions. (March 2023) BLA supplement to include syncope in Section 5 (Warnings and Precautions), and to add Section 6.2 (Postmarketing Experience) to the package insert to include the following adverse reactions: Cardiac Disorders: myocarditis, pericarditis; Immune System Disorders: hypersensitivity reactions, including angioedema, rash, and urticaria; Nervous System Disorders: dizziness, syncope; General disorders and administration site conditions: injection site warmth, injection site vesicles. (September 2023)

Medical Countermeasure	Applicant	Key Dates	Indication and/or Change Approved
NexoBrid (anacaulase-bcdb) gel	Mediwound, Ltd.	• Submitted June 29, 2020 • Approved December 28, 2022	For eschar removal in adults with deep partial thickness and/or full thickness thermal burns.
Opvee (nalmefene) nasal spray	Opiant Pharmaceuticals, Inc.	• Submitted November 22, 2022 • Approved May 22, 2023	For the emergency treatment of known or suspected overdose induced by natural or synthetic opioids in adults and pediatric patients aged 12 years and older, as manifested by respiratory and/or central nervous system depression.
Paxlovid (nirmatrelvir tablets and ritonavir tablets, co-packaged for oral use)	Pfizer, Inc.	• Submitted June 29, 2022 • Approved May 25, 2023	For the treatment of mild-to-moderate COVID-19 in adults who are at high risk for progression to severe COVID-19, including hospitalization or death.
Spikevax COVID-19 Vaccine, mRNA	Moderna Tx Inc.	• Submitted November 8, 2022 • Approved May 9, 2023 • Submitted March 28, 2023 • Approved September 11, 2023	BLA supplement to add urticaria to Section 6.2 (Emergency Authorization Use Experience) of the package insert and to revise the patient package insert to add a section on post-authorization use side effects. (May 2023) BLA supplement to include manufacturing and quality control testing of multiple dose vials (2.5 milliliter [mL] nominal volume) of the 2023-2024 Formula manufactured at Catalent (Bloomington, IN) and Patheon (Greenville, NC) and associated labeling revisions for administration as a single dose to individuals 12 years of age and older. This supplement also fulfills Pediatric Research Equity Act (PREA) post-marketing requirement (PMR) #1 from the January 31, 2022, approval letter for submission tracking number (STN) 125752/0. (September 2023)
Stimufend (pegfilgrastim-fpgk)	Fresenius Kabi USA, LLC	• Submitted March 27, 2020 • Approved September 29, 2023	BLA supplement for a new indication to increase survival of adult and pediatric patients acutely exposed to myelosuppressive doses of radiation (H-ARS).
Udenyca (pegfilgrastim-cbqv)	Coherus Biosciences Inc.	• Submitted May 27, 2022 • Approved November 28, 2022	BLA supplement for a new indication to increase survival of adult and pediatric patients acutely exposed to myelosuppressive doses of radiation (H-ARS).
Udenyca (pegfilgrastim-cbqv)	Coherus BioSciences, Inc.	• Submitted May 4, 2022 • Approved March 3, 2023	BLA supplement to approve a new single-dose prefilled auto-injector presentation, to increase survival of adult and pediatric patients acutely exposed to myelosuppressive doses of radiation (H-ARS).

Medical Countermeasure	Applicant	Key Dates	Indication and/or Change Approved
Veklury (remdesivir) injection/for injection, for intravenous use	Gilead Sciences, Inc.	• Submitted November 30, 2022 • Approved July 13, 2023 • Submitted March 23, 2023 • Approved August 23, 2023	NDA supplement for the use of Veklury for the treatment of COVID-19 in patients with severely reduced renal function (estimated glomerular filtration rate [eGFR] < 30 mL/min) (July 2023) NDA supplement to update the Prescribing Information that no dosage adjustment of Veklury is recommended for the treatment of COVID-19 in patients with mild, moderate or severe hepatic impairment (Child-Pugh Class A, B, or C) (August 2023)
Xacduro (sulbactam for injection; durlobactam for injection), co-packaged for intravenous use	Entasis Therapeutics, Inc.	• Submitted September 29, 2022 • Approved May 23, 2023	For the treatment of HABP and ventilator-associated bacterial pneumonia (VABP), caused by susceptible isolates of *Acinetobacter baumannii-calcoaceticus* complex in patients 18 years of age and older.

Appendix 2: Fy 2023 Medical Countermeasure Approvals – Devices

This list includes MCMs granted or cleared by FDA in FY 2023 (October 1, 2022 - September 30, 2023). Additional information about device approvals can be found on our website at **Medical Devices Databases**, including the **510(k) Premarket Notification Database** and **De Novo Classification Database**.

Diagnostic Tests

Medical Countermeasure	Applicant	Key Dates	Indication
Access PCT	Beckman Coulter, Inc.	• Received September 28, 2022 • Cleared April 26, 2023	A paramagnetic, chemiluminescent immunoassay for *in vitro* quantitative determination of PCT levels in human serum and plasma (lithium heparin and EDTA) using the Access Immunoassay Systems. Measurement of PCT in conjunction with other laboratory findings and clinical assessments aids in the risk assessment of critically ill patients on their first day of intensive care unit (ICU) admission for progression to severe sepsis and septic shock. (**K222996**)
Active Anthrax Detect Plus Rapid Test	InBios International, Inc.	• Received July 8, 2022 • Granted February 3, 2023	Diagnostic test for pulmonary anthrax is an *in vitro* immunochromatographic device for use as an aid in the diagnosis of inhalation anthrax. It provides visual and rapid qualitative detection of lethal factor of *B. anthracis*. The test can be used to test serum and venous whole blood (dipotassium EDTA, sodium citrate, and sodium heparin). The assay is indicated for testing samples from individuals who have signs and symptoms consistent with inhalation anthrax and a likelihood of exposure. The test is intended for use by military personnel, medical, and/or health care professionals only. Distribution of the test is limited to laboratories that follow public health guidelines that address appropriate biosafety conditions, interpretation of test results, and coordination of findings with public health authorities. (**DEN220044**)
BD BBL Sensi-Disc Cefiderocol 30ug (FDC-30)	Becton Dickinson, and Company	• Received June 23, 2022 • Cleared December 21, 2022	BD BBL Sensi-Disc AST Discs are used in the semi-quantitative agar diffusion test method for *in vitro* susceptibility testing. BD BBL Sensi-Disc Cefiderocol Disc 30 µg (FDC30) can be used to determine susceptibility to Cefiderocol against the bacteria described in the **Decision Summary**, as described in the FDA-approved package insert for this antimicrobial agent. (**K221826**)

Medical Countermeasure	Applicant	Key Dates	Indication
BD BBL Sensi-Disc Lefamulin 20µg (LMU-20)	Becton, Dickinson and Company	• Received March 9, 2023 • Cleared June 7, 2023	BD BBL Sensi-Disc AST Discs are used in the semi-quantitative agar diffusion test method for *in vitro* susceptibility testing. BD BBL Sensi-Disc Lefamulin Disc 20 µg (LMU-20) can be used to determine susceptibility to Lefamulin against the bacteria described in the **Decision Summary**, as described in the FDA-approved package insert for this antimicrobial agent. (**K230651**)
BD Respiratory Viral Panel for BD MAX System; BD Respiratory Viral Panel-SCV2 for BD MAX System	BD Integrated Diagnostic Solutions	• Received April 4, 2023 • Cleared July 31, 2023	The BD Respiratory Viral Panel for BD MAX System is an automated multiplexed real-time RT-PCR test intended for the simultaneous, qualitative detection and differentiation of SARS-CoV-2, influenza A, influenza B, and/or RSV nucleic acid in NPS and anterior nasal swab (ANS) specimens from individuals with signs and symptoms of respiratory tract infection. The BD Respiratory Viral Panel-SCV2 for BD MAX System is an automated multiplexed real-time polymerase chain reaction (RT-PCR) test intended for the simultaneous, qualitative detection of SARS-CoV-2 viral nucleic acid in NPS and ANS specimens from individuals with signs and symptoms of respiratory tract infection. (**K230956**)
BD Veritor System for Rapid Detection of Flu A+B CLIA-Waived Kit	Becton, Dickinson and Company	• Received September 29, 2022 • Cleared January 27, 2023	A rapid chromatographic immunoassay for the direct and qualitative detection of influenza A and B viral nucleoprotein antigens from nasal and nasopharyngeal swabs of symptomatic patients. (**K223016**)
BioFire Global Fever Special Pathogens Panel; BIOFIRE SHIELD Control Kit for the BioFire Global Fever Special Pathogens Panel	BioFire Defense, LLC	• Received October 12, 2021 • Cleared March 22, 2023	A qualitative, multiplexed, nucleic acid-based test intended for use with BioFire FilmArray 2.0 and BioFire FilmArray Torch Systems. For the simultaneous qualitative detection and identification of multiple bacterial, viral, and protozoan nucleic acids directly from EDTA whole blood collected from individuals with signs and/or symptoms of acute febrile illness or recent acute febrile illness and known or suspected exposure to the target pathogens described in the **Decision Summary**. (**K213362**)
BioFire SPOTFIRE Respiratory (R) Panel	BioFire Diagnostics, LLC	• Received December 17, 2021 • Cleared February 3, 2023	A multiplexed PCR test intended for use with the BioFire SPOTFIRE System for the simultaneous, qualitative detection and identification of multiple respiratory viral and bacterial nucleic acids (described in the **Decision Summary**) in NPS specimens obtained from individuals with signs and symptoms of respiratory tract infection, including COVID-19. (**K213954**)

Medical Countermeasure	Applicant	Key Dates	Indication
BioFire SPOTFIRE Respiratory (R) Panel Mini	BioFire Diagnostics, LLC	• Received March 15, 2023 • Cleared April 13, 2023	A Multiplexed PCR test intended for use with the BioFire SPOTFIRE System for the simultaneous, qualitative detection and identification of multiple respiratory viral nucleic acids (described in the **Summary**) in NPS specimens obtained from individuals with signs and symptoms of respiratory tract infection, including COVID-19. This change was for a revision to the device labeling and software to allow use of the device with software-mediated masking of results. (**K230719**)
cobas SARS-CoV-2 & Influenza A/B for use on the cobas Liat System	Roche Molecular Systems, Inc.	• Received December 1, 2022 • Cleared July 27, 2023	An automated rapid multiplex RT-PCR test for use on the cobas Liat System intended for the simultaneous qualitative detection and differentiation of SARS-CoV-2, influenza A, and/or influenza B virus nucleic acid in NPS and ANS specimens from individuals with signs and symptoms of respiratory tract infection. (**K223591**)
cobas SARS-CoV-2 Qualitative PCR test	Roche Molecular Systems, Inc.	K213804 • Received December 6, 2021 • Cleared October 22, 2022 K231306 • Received May 5, 2023 • Cleared June 1, 2023	An RT-PCR test intended for the qualitative detection of nucleic acids from SARS-CoV-2 in nasal and nasopharyngeal specimens collected from symptomatic individuals suspected of COVID-19 by their health care provider. The test is for use on the cobas 6800/8800 Systems. (**K213804**) Subsequent 510(k) was for an update to Assay Specific Analysis Package (ASAP) on the cobas 6800/8800 and cobas 5800. (**K231306**)
Colibrí	Copan WASP S.r.l.	• Received October 20, 2022 • Cleared March 20, 2023	An automated IVD specimen preparation system for use with WASPLab to prepare MALDI-TOF targets for the bioMérieux VITEK MS or Bruker MALDI Biotyper CA mass spectrometry systems for qualitative identification and microbial suspension for the bioMérieux VITEK 2 AST system for qualitative testing of isolated colonies of gram-negative and gram-positive bacterial species grown on solid culture media. The system picks isolated colonies designated by the operator and uses a pipetting system to prepare MALDI-TOF MS target slides for bacterial identification and microbial suspension at known concentration for AST and purity assessment. (**K223245**)

Medical Countermeasure	Applicant	Key Dates	Indication
Colibrí System	Copan WASP S.r.l.	• Received February 25, 2022 • Cleared October 5, 2022	An IVD specimen preparation system comprised of the Colibrí Vision System and Colibrí Preparation Station for use with the bioMérieux VITEK MS or Bruker MALDI Biotyper CA mass spectrometry systems for qualitative identification and with the bioMérieux VITEK AST system for qualitative testing of isolated colonies of gram-negative and gram-positive bacterial species grown on solid culture media. The Colibrí System is a semi-automated pre-analytical processor that picks isolated colonies designated by the operator and uses a pipetting system to prepare MALDI-TOF MS target slides for bacterial identification and microbial suspension at known concentration for AST and purity assessment. (**K220546**)
ComASP Cefiderocol 0.008-128	Liofilchem s.r.l.	• Received February 22, 2023 • Cleared May 18, 2023	A quantitative broth microdilution method intended for the *in vitro* determination of antimicrobial susceptibility of bacteria. Used to determine the minimum inhibitory concentration (MIC) of cefiderocol against microorganisms (described in the **Decision Summary**) for which cefiderocol has been shown to be active clinically and *in vitro* according to the FDA drug approved label (**K230479**)
Cue COVID-19 Molecular Test	Cue Health, Inc.	• Received May 2, 2022 • Granted June 6, 2023	Molecular NAAT intended for the qualitative detection of SARS-CoV-2 nucleic acid directly in anterior nasal swabs from adults with signs and symptoms of COVID-19 (i.e., symptomatic). This test is intended to be sold OTC for testing of individuals 18 years of age and older. (**DEN220028**)
FilmArray Pneumonia Panel plus	BioFire Diagnostics, LLC	• Received August 29, 2022 • Cleared October 27, 2022	A multiplexed nucleic acid test intended for use with FilmArray, FilmArray 2.0, or FilmArray Torch systems for the simultaneous detection and identification of nucleic acids from MERS-CoV and multiple respiratory viral and bacterial nucleic acids (described in the **Summary**), as well as select AMR genes, in sputum-like specimens (induced or expectorated sputum, or endotracheal aspirates) or bronchoalveolar lavage (BAL)-like specimens (BAL or mini-BAL) obtained from individuals meeting MERS-CoV clinical and/or epidemiological criteria. Update was to include additional limitations in the device labeling. (**K222601**)

Medical Countermeasure	Applicant	Key Dates	Indication
HardyDisk AST Rezafungin 5µg (RZF5)	Hardy Diagnostics	• Received May 31, 2023 • Cleared July 6, 2023	Use of HardyDisk AST Rezafungin 5µg (RZF5) for *in vitro* agar diffusion susceptibility testing is indicated when there is the need to determine the susceptibility of microorganisms to Rezafungin. HardyDisk AST Rezafungin at concentration 5µg can be used to determine the zone diameter (mm) of Rezafungin against the following microorganisms for which Rezafungin has been shown to be active both clinically and *in vitro*: *Candida albicans*, *C. glabrata*, *C. parapsilosis*, and *C. tropicalis*. (**K230827**)
HardyDisk AST Sulbactam/Durlobactam 10/10µg (SUD20)	Hardy Diagnostics	• Received May 31, 2023 • Cleared July 6, 2023	For *in vitro* agar diffusion susceptibility testing and is indicated when there is the need to determine the susceptibility of microorganisms to Sulbactam/Durlobactam. HardyDisk AST Sulbactam/Durlobactam at concentration 10/10µg can be used to determine the zone diameter (mm) of Sulbactam/Durlobactam against the following microorganisms for which Sulbactam/Durlobactam has been shown to be active both clinically *and in vitro*: *Acinetobacter baumannii-calcoaceticus* complex (ABC). (**K231568**)
ID NOW COVID-19 2.0	Abbott Diagnostics Scarborough, Inc.	• Received July 1, 2022 • Cleared August 10, 2023	A rapid molecular IVD, preformed on the ID NOW Instrument, utilizing an isothermal nucleic acid amplification technology intended for the qualitative detection of nucleic acid from SARS-CoV-2 in direct anterior nasal (nasal) or NPS from individuals with signs and symptoms of respiratory tract infection. This test is intended for prescription use only and can be used in POC settings. (**K221925**)
IntelliSep test	Cytovale Inc.	• Received April 4, 2022 • Cleared December 20, 2022	A semi-quantitative test that assesses cellular host response via deformability cytometry of leukocyte biophysical properties and is intended for use in conjunction with clinical assessments and laboratory findings to aid in the early detection of sepsis with organ dysfunction manifesting within the first three days after testing. It is indicated for use in adult patients with signs and symptoms of infection who present to the emergency department. The test is performed on an EDTA anticoagulated whole blood sample. (**K220991**)
Lyra Influenza A+B Assay	Quidel Corporation	• Received January 30, 2023 • Cleared March 3, 2023	A multiplex RT-PCR assay for the *in vitro* qualitative detection and differentiation of influenza A and influenza B viral RNA in nasal and nasopharyngeal swabs from patients with signs and symptoms of respiratory infection. Update was for the addition of the bioMérieux EMAG nucleic acid extraction system for use with the test. (**K230236**)

Medical Countermeasure	Applicant	Key Dates	Indication
Lyra RSV+hMPV Assay	Quidel Corporation	• Received February 9, 2023 • Cleared March 10, 2023	A multiplex RT-PCR assay for the qualitative detection and identification of RSV and hMPV RNA extracted from nasal and nasopharyngeal swab specimens from patients with signs and symptoms of respiratory infection. Update was for the addition of the bioMérieux NucliSENS EMAG nucleic acid extraction system for use with the test. (**K230349**)
MeMed BV	MeMed Diagnostics Ltd.	K222332 • Received August 2, 2022 • Cleared March 23, 2023 K230944 • Received April 4, 2023 • Cleared June 30, 2023	An automated semi-quantitative immunoassay that measures three non-microbial (host) proteins (tumor necrosis-factor-related apoptosis-inducing ligand [TRAIL], IP-10, and C-reactive protein [CRP]) in adult and pediatric serum samples and is intended for use in conjunction with clinical assessments and other laboratory findings as an aid to differentiate bacterial from viral infection. (**K222332**) An automated semi-quantitative immunoassay that measures three non-microbial (host) proteins (TRAIL, IP-10, and CRP) in adult and pediatric serum and venous whole blood samples and is intended for use in conjunction with clinical assessments and other laboratory findings as an aid to differentiate bacterial from viral infection. (**K230944**)
MicroScan Prompt Inoculation System-D	Beckman Coulter, Inc.	• Received May 23, 2022 • Cleared April 5, 2023	Used to standardize inocula for microdilution ASTs. The MicroScan Prompt Inoculation System-D is an accessory to the MicroScan Gram Negative and Gram Positive MIC/Combo Panels. Indications for use organisms are specific for each antimicrobial agent on the panel. (**K221493**)
Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay	Hologic, Inc.	• Received September 9, 2022 • Cleared May 16, 2023	Fully automated multiplexed RT-PCR IVD intended for the qualitative detection and differentiation of SARS-CoV-2, influenza A virus, influenza B virus, and RSV. Nucleic acids are isolated and purified from nasopharyngeal specimens obtained from individuals exhibiting signs and symptoms of a respiratory tract infection. This assay is designed for use on the Panther Fusion system. (**K222736**)

Medical Countermeasure	Applicant	Key Dates	Indication
Selux AST System; Model AST Gen 1.0	Selux Diagnostics, Inc.	K211759 • Received June 7, 2021 • Cleared January 18, 2023 K211748 • Received June 7, 2021 • Cleared April 19, 2023	The Selux Gram-Positive Panel is intended for use with the Selux AST System as an *in vitro* test to determine the susceptibility of isolated colonies of specific *Staphylococcus* species and *Enterococcus* species to specific antimicrobial agents when used as instructed. (**K211759**) The Selux Gram-Negative Panel is intended for use with the Selux AST System as an *in vitro* test to determine the susceptibility of isolated colonies of specific gram-negative bacilli to specific antimicrobial agents when used as instructed. (**K211748**) The Selux AST System is intended to be used for the automated quantitative or qualitative susceptibility testing for most clinically significant aerobic microorganisms. The Selux AST System does not provide organism identification.
Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Sulbactam-durlobactam in the dilution range of 0.015/4-32/4 ug/mL	Thermo Fisher Scientific	• Received July 5, 2023 • Cleared August 25, 2023	The Sensititre 18 - 24 hour MIC or Breakpoint Susceptibility System is an in vitro diagnostic product for clinical susceptibility testing of non-fastidious isolates. This 510(k) is for Sulbactam-durlobactam in the dilution range of 0.015/4-32/4 µg/mL for testing non-fastidious Gram negative organisms on the Sensititre 18 - 24 hour MIC panel. Sulbactam-durlobactam has been shown to be active both clinically and *in vitro* against the following organisms according to the FDA drug label: *Acinetobacter baumannii-calcoaceticus* complex. (**K231994**)
Sensititre 20-24 hour Haemophilus influenzae/Streptococcus pneumoniae MIC, or Breakpoint Susceptibility System with Imipenem-relebactam in the dilution, range of 0.03/4-128/4 ug/ml (Haemophilus influenzae)	Thermo Fisher Scientific	• Received April 3, 2023 • Cleared June 30, 2023	The Sensititre 20 - 24 hour *Haemophilus influenzae/Streptococcus pneumoniae* MIC or Breakpoint Susceptibility System is an *in vitro* diagnostic product for clinical susceptibility testing of fastidious isolates. This 510(k) is for Imipenem-relebactam in the dilution range of 0.03/4-128/4 ug/ml for testing *H. influenzae* on the Sensititre 20 - 24 hour *Haemophilus influenzae/Streptococcus pneumoniae* MIC or Breakpoint Susceptibility System. Imipenem-relebactam has been shown to be active both clinically and *in vitro* against the following organisms according to the FDA drug label: *Haemophilus influenzae,* (**K230935**)

Medical Countermeasure	Applicant	Key Dates	Indication
Sensititre 20-24-hour Haemophilus influenzae/Streptococcus pneumoniae MIC or Breakpoint Susceptibility System with Dalbavancin in the dilution range of 0.0005-2µg/ml	Thermo Fisher Scientific	• Received July 5, 2023 • Cleared August 30, 2023	The Sensititre 20-24-hour *Haemophilus influenzae/Streptococcus pneumoniae* MIC or Breakpoint Susceptibility System is an *in vitro* diagnostic product for clinical susceptibility testing of fastidious isolates. This 510(k) is for dalbavancin in the dilution range of 0.0005 - 2µg/ml with new FDA breakpoints for testing fastidious *Streptococcus* spp. on the Sensititre 20 - 24-hour *Haemophilus influenzae/Streptococcus pneumoniae* MIC or Breakpoint Susceptibility System. Dalbavancin has been shown to be active both clinically and *in vitro* against the organisms described in the **Decision Summary** according to the FDA drug label. (**K231988**)
Sensititre 20-24-hour Haemophilus influenzae/Streptococcus pneumoniae MIC or Breakpoint Susceptibility System with Delafloxacin in the dilution range of 0.00025-8ug/ml (Streptococcus species) and 0.000125-8ug/ml (Haemophilus influenzae)	Thermo Fisher Scientific	• Received December 22, 2022 • Cleared March 21, 2023	The Sensititre 20 - 24-hour *Haemophilus influenzae/Streptococcus pneumoniae* MIC or Breakpoint Susceptibility System is an *in vitro* diagnostic product for clinical susceptibility testing of fastidious isolates. This 510(k) is for delafloxacin in the dilution range of 0.00025-8 µg/ml for testing fastidious *Streptococcus* spp., (including *S. pneumoniae*) and delafloxacin in the dilution range of 0.000125 - 8 µg/mL for testing *H. influenzae* on the Sensititre 20 - 24-hour *Haemophilus influenzae/Streptococcus pneumoniae* MIC or Breakpoint Susceptibility System. Delafloxacin has been shown to be active both clinically and *in vitro* against the organisms described in the **Decision Summary** according to the FDA drug label. (**K223844**)
Sensititre YeastOne Susceptibility System with Fluconazole in the dilution range of 0.12-128ug/mL	Thermo Fisher Scientific	• Received April 26, 2022 • Cleared March 10, 2023	The Sensititre YeastOne Susceptibility System is an in vitro diagnostic product for clinical susceptibility testing of *Candida* spp. This 510(k) is for fluconazole with new FDA breakpoints and indications for testing *Candida* spp. on the Sensititre YeastOne Susceptibility System. Fluconazole has been shown to be active both clinically and *in vitro* against the organisms described in the **Decision Summary** according to the FDA drug label. (**K221198**)
Sensititre YeastOne Susceptibility System with Caspofungin in the dilution range of 0.015-16ug/ml	Thermo Fisher Scientific	• Received June 30, 2022 • Cleared January 20, 2023	The Sensititre YeastOne Susceptibility System is an in vitro diagnostic product for clinical susceptibility testing of *Candida* spp. This 510(k) is for caspofungin with new FDA breakpoints and indications for testing *Candida* spp. on the Sensititre YeastOne Susceptibility System. Caspofungin has been shown to be active both clinically and *in vitro* against the organisms described in the **Decision Summary** according to the FDA drug label: *Candida albicans, C. glabrata, C. krusei ,C. parapsilosis,* and *C. tropicalis.* (**K221899**)

Medical Countermeasure	Applicant	Key Dates	Indication
Sensititre YeastOne Susceptibility System with Rezafungin in the dilution range of 0.008-8ug/mL	Thermo Fisher Scientific	• Received May 17, 2023 • Cleared August 31, 2023	The Sensititre YeastOne Susceptibility System is an *in vitro* diagnostic product for clinical susceptibility testing of *Candida* spp. This 510(k) is for rezafungin in the dilution range of 0.008 - 8 ug/mL for testing *Candida* spp. on the Sensititre YeastOne Susceptibility System. Rezafungin has been shown to be active both clinically and *in vitro* against the organisms described in the **Decision Summary** according to the FDA drug label. (**K231433**)
Simplexa COVID-19 & Flu A/B Direct	DiaSorin Molecular LLC	• Received April 1, 2022 • Cleared March 17, 2023	An RT-PCR assay intended for use on the LIAISON MDX instrument for the *in vitro* qualitative detection and differentiation of nucleic acid from SARS-CoV-2, influenza A virus, and influenza B virus in NPS specimens from individuals with signs and symptoms of respiratory tract infection. (**K220963**)
Sofia 2 SARS Antigen+ FIA, Sofia SARS Antigen FIA Control Swab Set	Quidel Corporation	• Received June 16, 2022 • Granted March 8, 2023	A lateral flow immunofluorescent sandwich assay that is used with the Sofia 2 instrument for the rapid, qualitative detection of SARS-Co V-2 nucleocapsid protein antigens directly in ANS specimens from individuals with signs and symptoms of upper respiratory infection (i.e., symptomatic) when testing is started within six days of symptom onset. The test is intended for use as an aid in the diagnosis of SARS-CoV-2 infections in symptomatic individuals when tested at least twice over three days with at least 48 hours between tests. This test is intended for prescription use only and can be used in POC settings. (**DEN220039**)
T2 Biothreat Panel	T2 Biosystems, Inc.	• Received May 8, 2023 • Cleared September 15, 2023	A qualitative, multiplexed, nucleic acid-based IVD intended for use with the T2Dx Instrument. The T2Biothreat Panel detects nucleic acids from organisms described in the **Decision Summary** directly from K2EDTA whole blood samples. Intended to test individuals with signs and symptoms of infection from biothreat agents and/or individuals who are at risk for exposure or may have been exposed to these agents. (**K231336**)

Medical Countermeasure	Applicant	Key Dates	Indication
Traumatic brain injury (TBI) test (Alinity i)	Abbott Laboratories	K223602: • Received December 2, 2022 • Cleared March 2, 2023 K232669: • Received September 1, 2023 • Cleared September 29, 2023	A panel of IVD chemiluminescent microparticle immunoassays (CMIA) used for the quantitative measurements of glial fibrillary acidic protein (GFAP) and ubiquitin carboxyl-terminal hydrolase L1 (UCHL1) in human plasma and serum, and provides a semi-quantitative interpretation of test results derived from these measurements using the Alinity i system. The interpretation of test results is used, in conjunction with other clinical information, to aid in the evaluation of patients, 18 years of age or older, presenting with suspected mild traumatic brain injury (Glasgow Coma Scale score 13-15) within 12 hours of injury, to assist in determining the need for a computed tomography (CT) scan of the head. (**K223602**) Subsequent 510(k) was for an update to add use on the ARCHITECT i1000SR System and include a limitation for use on the ARCHITECT i1000SR System that informs users of a potential risk for false positive TBI results for the GFAP assay when the TBI test is run after the 25-OH Vitamin D assay and provides actions to take to mitigate potential contamination after 25-OH Vitamin D assay testing. (**K232669**)
VITEK 2 AST-Gram Positive Daptomycin (≤0.12 - ≥8 µg/mL), VITEK 2 AST-GP Daptomycin (≤0.12 - ≥8 µg/mL), VITEK 2 AST-GP Daptomycin	BioMérieux, Inc	• Received March 29, 2023 • Cleared July 5, 2023	VITEK 2 AST-Gram Positive Daptomycin is designed for antimicrobial susceptibility testing of gram-positive microorganisms and is intended for use with the VITEK 2 and VITEK 2 Compact Systems as a laboratory aid in the determination of *in vitro* susceptibility to antimicrobial agents. VITEK 2 AST-Gram Positive Daptomycin is a quantitative test. Daptomycin has been shown to be active against most strains of the microorganisms (described in the **Decision Summary**), according to the FDA label for this antimicrobial. (**K230864**)
VITEK 2 AST-Gram Negative Fosfomycin (≤4 - ≥256 µg/mL), VITEK 2 AST-GN Fosfomycin (≤4 - ≥256 µg/mL), VITEK 2 AST-GN Fosfomycin	bioMérieux SA, Inc.	• Received August 11, 2022 • Cleared March 9, 2023	Designed for AST of gram-negative *bacilli* and is intended for use with the VITEK 2 and VITEK 2 Compact Systems as a laboratory aid in the determination of *in vitro* susceptibility to antimicrobial agents. VITEK 2 AST-Gram Negative Fosfomycin is a quantitative test. Fosfomycin has been shown to be active against most strains of the microorganism described in the **Decision Summary**, according to the FDA label for this antimicrobial. (**K222430**)

Medical Countermeasure	Applicant	Key Dates	Indication
VITEK 2 AST-Gram Negative Cefazolin (≤1 - ≥32 ug/mL)	bioMérieux SA, Inc.	• Received July 14, 2022 • Cleared February 9, 2023	Designed for AST of gram-negative *bacilli* and is intended for use with the VITEK 2 and VITEK 2 Compact Systems as a laboratory aid in the determination of *in vitro* susceptibility to antimicrobial agents. VITEK 2 AST-Gram Negative Cefazolin is a quantitative test. Cefazolin has been shown to be active against most strains of the microorganisms listed in the **Decision Summary**, according to the FDA label for this antimicrobial. (**K222073**)
VITEK 2 AST-Gram Positive Cefoxitin Screen	bioMérieux SA, Inc.	• Received March 18, 2022 • Cleared October 13, 2022	Designed to predict mecA-mediated oxacillin resistance in *Staphylococcus* spp. It is intended for use with the VITEK 2 and VITEK 2 Compact Systems as a laboratory aid in the determination of *in vitro* susceptibility to antimicrobial agents. The VITEK 2 Gram-Positive Susceptibility Card is intended for use with the VITEK 2 Systems in clinical laboratories as an *in vitro* test to determine the susceptibility of *Staphylococcus* spp., *Enterococcus* spp., and *Streptococcus agalactiae* to antimicrobial agents when used as instructed. (**K220805**)
VITEK 2 AST-Gram Positive Moxifloxacin (≤ 0.25 - ≥ 8 µg/ml), VITEK 2 AST-GP Moxifloxacin (≤ 0.25 - ≥ 8 µg/mL), VITEK 2 AST-GP Moxifloxacin	bioMérieux SA, Inc.	• Received March 18, 2022 • Cleared January 27, 2023	Designed for AST of gram-positive microorganisms and is intended for use with the VITEK 2 and VITEK 2 Compact Systems as a laboratory aid in the determination of *in vitro* susceptibility to antimicrobial agents. VITEK 2 AST-Gram Positive Moxifloxacin is a quantitative test. Moxifloxacin has been shown to be active against most strains of the microorganisms listed in the **Decision Summary**, according to the FDA label for this antimicrobial. (**K220803**)
VITEK 2 AST-Gram Negative Plazomicin (≤0.5 - ≥16 µg/mL); VITEK 2 AST-GN Plazomicin (≤0.5 - ≥16 µg/mL); VITEK 2 AST-GN Plazomicin	bioMérieux SA, Inc.	• Received November 18, 2022 • Cleared February 16, 2023	Designed for AST of gram-negative *bacilli* and is intended for use with the VITEK 2 and VITEK 2 Compact Systems as a laboratory aid in the determination of *in vitro* susceptibility to antimicrobial agents. VITEK 2 AST-Gram Negative Plazomicin is a quantitative test. Plazomicin has been shown to be active against most strains of the microorganisms listed in the **Decision Summary**, according to the FDA label for this antimicrobial. (**K223478**)
VITEK 2 Streptococcus Tetracycline (≤0.25 - ≥16 µg/mL)	bioMérieux SA, Inc.	• Received November 18, 2022 • Cleared February 03, 2023	Designed for AST of *Streptococcus* species and is intended for use with the VITEK 2 and VITEK 2 COMPACT Systems as a laboratory aid in the determination of *in vitro* susceptibility to antimicrobial agents. VITEK 2 Streptococcus Tetracycline is a quantitative test. Tetracycline has been shown to be active against the microorganisms listed in the **Decision Summary**, according to the FDA label for this antimicrobial. (**K223481**)

Medical Countermeasure	Applicant	Key Dates	Indication
VITEK 2 AST-Gram Negative Levofloxacin (≤0.125 -≥8 ug/mL)	bioMérieux SA, Inc.	• Received August 05, 2022 • Cleared June 26, 2023	Designed for AST of gram-negative bacilli and is intended for use with the VITEK 2 and VITEK 2 Compact Systems as a laboratory aid in the determination of *in vitro* susceptibility to antimicrobial agents. VITEK 2 AST-Gram Negative Levofloxacin is a quantitative test. Levofloxacin has been shown to be active against most strains of the microorganisms listed in the **Decision Summary**, according to the FDA label for this antimicrobial. (**K222378**)
VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Reagent Pack	Ortho-Clinical Diagnostics, Inc.	• Received September 20, 2021 • Cleared May 5, 2023	Intended for prescription use only for the qualitative detection of immunoglobulin G (IgG) antibodies to SARS-CoV-2 in human serum and plasma samples collected on or after 15 days post-symptom onset using the VITROS ECi/ECiQ/3600 Immunodiagnostic Systems and the VITROS 5600/XT 7600 Integrated Systems, as an aid in identifying individuals who have an adaptive immune response to SARS-CoV-2, indicating recent or prior infection. For use with the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Calibrator. (**DEN210038**)
VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack	Ortho-Clinical Diagnostics, Inc.	• Received September 21, 2021 • Granted May 5, 2023	Intended for prescription use only for the qualitative detection of total antibodies to SARS-CoV-2 in human serum and plasma samples collected on or after 15 days post-symptom onset using the VTTROS ECi/ECiQ/3600 Immunodiagnostic Systems and the VITROS 5600/XT 7600 Integrated Systems, as an aid in identifying individuals who have an adaptive immune response to SARS-CoV-2 indicating recent or prior infection. For use with the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Calibrator. (**DEN210040**)
Xpert Xpress CoV-2/Flu/RSV plus	Cepheid	• Received May 23, 2023 • Cleared August 17, 2023	An automated multiplexed real-time RT-PCR test intended for use on the GeneXpert Dx and GeneXpert Infinity Systems for the simultaneous in vitro qualitative detection and differentiation of SARS-CoV-2, influenza A, influenza B, and/or RSV viral RNA in NPS and ANS specimens collected from individuals with signs and symptoms of respiratory tract infection. (**K231481**)

Other MCM Devices (Non-COVID-Related)

Medical Countermeasure	Applicant	Key Dates	Indication
Abdominal Aortic and Junctional Tourniquet - Stabilized (AAJT - S)	Compression Works, Inc.	• Received June 8, 2022 • Cleared March 3, 2023	The Abdominal Aortic and Junctional Tourniquet - Stabilized (AAJT-S) is indicated for use to control bleeding in the pelvis, inguinal area, axilla, and for pelvic fracture stabilization. (**K221661**)
Butterfly iQ/iQ+ Ultrasound System	Butterfly Network, Inc.	• Received January 10, 2022 • Cleared March 31, 2023	Handheld ultrasound tool that may help accelerate assessment of suspected lung function abnormality in patients with conditions ranging from COPD to COVID-19. (**K220068**)
Integrum AB	Opra System	• Received September 28, 2022 • Approved April 21, 2023	Approval for the use of additional instruments for use with the OPRA system (i.e., the Abutment InstallationKit, the Abutment Extraction Kit, the Fixture Removal Kit, and the Fractured Abutment/ Abutment ScrewKit). (**P190009/S003**)
Lumify Diagnostic Ultrasound System	Philips Ultrasound	• Received December 16, 2022 • Cleared May 4, 2023	Automated merged B-lines imaging feature on Lumify POC handheld diagnostic ultrasound system, an app-based ultrasound system with predictive machine-learning algorithms under development to provide real-time decision-assist capabilities that can aid health care providers to quickly evaluate internal organ injuries from a range of causative agents from smoke inhalation, illness or infectious diseases, or as a result of blast trauma (available on all three Lumify transducers). (**K223771**)
S.E.A.L. Hemostatic Wound Spray	BC3 Technologies, Inc.	• Received March 12, 2021 • Cleared February 2, 2023	Prescription use: Intended to be used to achieve hemostasis in emergency situations for the temporary control of severe topical bleeding. OTC use: For the local management of minor bleeding such as minor lacerations, minor cuts, and minor abrasions. (**K210751**)
Silverlon Wound Contact, Burn Contact Dressings	Argentum Medical, Inc.	• Received April 27, 2022 • Cleared October 26, 2022	New indication, for use up to seven days for radiation dermatitis and cutaneous radiation injury through dry desquamation. (**K221218**)

COVID-19 Related Device Clearances

In addition to the diagnostic tests and other devices listed in the previous table, FDA cleared 34 surgical face masks in FY 2023.

Additional information about these device clearances can be found in the FDA **Medical Devices Databases**, including the **510(k) Premarket Notification Database**. To locate records for surgical face masks search FDA medical device databases for product code FXX (Mask, surgical).

Appendix 3: MCM-Related Guidance Issued In FY 2023

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**.

The date listed in this table for all documents refers to the most recent update available at the end of FY 2023 (September 30, 2023). Some guidances may have been intended to be temporary (e.g., only in effect during the COVID-19 public health emergency). Accordingly, some guidances in the table below have been subsequently modified or revoked.

Note that, in March 2023, FDA **issued a notice** addressing the agency's COVID-19-related guidance documents, including which of those guidance documents would no longer be in effect after the expiration of the COVID-19 public health emergency declared under section 319 of the PHS Act, and which of those guidance documents FDA was revising to temporarily continue in effect. FDA remains committed to providing notice and information to impacted stakeholders to help ensure a smooth transition.

Date	Guidance Type	Guidance Name	Purpose
December 16, 2022	Draft	Center for Veterinary Medicine Guidance for Industry (CVM GFI) #152 Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to Their Microbiological Effects on Bacteria of Human Health Concern (**link**)	To provide guidance for industry to evaluate potential microbiological effects of antimicrobial new animal drugs on bacteria of human health concern as part of the new animal drug application process. The scope and purpose of updated GFI #152 remains the same as the initial version of the guidance issued in 2003, but updates better align with current science and clinical practices in human medicine.
January 12, 2023	Final	Policy for Coronavirus Disease-2019 Tests (Revised) (**link**)	To provide FDA's review priorities and enforcement policies regarding COVID-19 tests. Updated in FY 2023 to reflect FDA's intent for this guidance to remain in effect for the duration of the declaration under section 564 of the FD&C Act that circumstances exist justifying EUA of IVDs for the detection of COVID-19, rather than the duration of the PHE determination under section 319 of the PHS Act.

Date	Guidance Type	Guidance Name	Purpose
January 12, 2023	Final	Policy for Evaluating Impact of Viral Mutations on COVID-19 Tests (Revised) (**link**)	To provide a policy and recommendations on evaluating the potential impact of emerging and future viral mutations of SARS-CoV-2 on COVID-19 tests. This guidance describes a policy for test developers to consider the impact of emerging and future variants on their COVID-19 tests during development and post-authorization. Updated in FY 2023 to reflect FDA's intent for this guidance to remain in effect for the duration of the declaration under section 564 of the FD&C Act that circumstances exist justifying EUA of IVDs for the detection of COVID-19, rather than the duration of the PHE determination under section 319 of the PHS Act, and to reflect current information about variants and actions the FDA has taken since the original issuance of this guidance.
January 19, 2023	Draft	Mpox: Development of Drugs and Biological Products; Guidance for Industry (**link**)	To provide FDA's current thinking regarding nonclinical, virology, and clinical considerations for mpox drug development programs, and assist sponsors in the clinical development of drugs for the treatment of mpox.
February 1, 2023	Draft	Considerations for the Design and Conduct of Externally Controlled Trials for Drug and Biological Products (**link**)	To make recommendations to sponsors and investigators considering the use of externally controlled clinical trials to show evidence of the safety and effectiveness of a drug. The guidance provides stakeholders with considerations for designing and conducting externally controlled trials that use patient-level data (i.e., information on individual people, such as medical and treatment history) to study the effectiveness and safety of drugs, including threats to the validity of trial results from sources of potential bias. The external data can include data from other clinical trials or from real-world data sources such as registries, electronic health records, or medical claims. This guidance also describes considerations for communicating with FDA and ensuring the agency has access to data from an externally controlled trial. This draft guidance is part of a series of guidances FDA has already published, or plans to publish, as part of the agency's Real-World Evidence Program and to address, in part, certain requirements of the Cures Act and support PDUFA commitments.

Date	Guidance Type	Guidance Name	Purpose
February 9, 2023	Final	Compounding Certain Ibuprofen Oral Suspension Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act (**link**)	In an effort to **bolster supply** of pediatric ibuprofen amid record high demand, this guidance, issued on January 20, 2023, clarifies FDA's regulatory and enforcement priorities regarding the compounding of certain ibuprofen oral suspension products in outsourcing facilities for administration in hospitals and health systems. A revision on February 9, 2023, addresses outsourcing facilities providing certain ibuprofen oral suspension products to state-licensed pharmacies (including those within hospitals and health systems) and applicable federal facilities to dispense to patients for home use, following receipt of a valid, patient-specific prescription from a health care provider. FDA published this revision to address continual increased demand for fever and pain-reducing medications outside of hospitals and health systems.
March 1, 2023	Final	Q13 Continuous Manufacturing of Drug Substances and Drug Products (**link**)	To describe scientific and regulatory considerations for the development, implementation, operation, and lifecycle management of continuous manufacturing (CM). Building on existing ICH quality guidances, this guidance provides clarification on CM concepts and describes scientific approaches and regulatory considerations specific to CM of drug substances and drug products.
March 2, 2023	Draft	Potency Assay Considerations for Monoclonal Antibodies and Other Therapeutic Proteins Targeting Viral Pathogens (**link**)	To provide drug manufacturers with recommendations for developing and implementing potency assays to ensure each lot of mAbs or other therapeutic proteins is produced consistently with the potency necessary to achieve efficacy and that potency is maintained over the shelf life of the product. In January 2021, FDA published a guidance specific to potency considerations for mAbs and therapeutic proteins targeting SARS-CoV-2. This draft guidance expands the scope of the January 2021 guidance to include all mAbs and other therapeutic proteins targeting viruses, not just mAbs targeting SARS-CoV-2.

Date	Guidance Type	Guidance Name	Purpose
March 15, 2023	Final	Definitions of Suspect Product and Illegitimate Product for Verification Obligations, as part of the agency's implementation of the Drug Supply Chain Security Act (DSCSA) (**link**)	To clarify FDA's interpretation of specific terms used in the definitions of "suspect product" and "illegitimate product" to assist trading partners in meeting verification obligations (including notification). The specific terms discussed in the guidance are counterfeit, diverted, stolen, fraudulent transaction, and unfit for distribution. This guidance replaces the draft guidance of the same name. The DSCSA establishes requirements for product tracing, verification, and product identification for certain drug products that are distributed in the U.S. to enhance FDA's ability to help protect consumers from exposure to drugs that may be counterfeit, stolen, contaminated, or otherwise harmful. These requirements add safeguards to improve detection and removal of potentially dangerous drugs from the drug supply chain to protect U.S. consumers.
March 24, 2023	Final	Transition Plan for Medical Devices That Fall Within Enforcement Policies Issued During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency (**link**)	To provide recommendations and expectations to manufacturers of devices that fall within certain enforcement policies issued during the COVID-19 PHE to transition to normal operations when the PHE declaration related to COVID-19 under section 319 of the PHS Act ends. FDA believes the policy set forth in this guidance will help FDA and other stakeholders transition to normal operations and processes.
March 24, 2023	Final	Transition Plan for Medical Devices Issued Emergency Use Authorizations (EUAs) Related to Coronavirus Disease 2019 (COVID-19) (**link**)	To provide recommendations and expectations to manufacturers of devices that were issued EUAs related to COVID-19 to transition to normal operations when the declarations that allowed for FDA to issue EUAs under section 564 of the FD&C Act end. FDA believes the policy set forth in this guidance will help FDA and other stakeholders transition to normal operations and processes.
March 29, 2023	Final	Cybersecurity in Medical Devices: Refuse to Accept Policy for Cyber Devices Under Section 524B of the FD&C Act	To clarify that FDA generally intends not to issue "refuse to accept" (RTA) decisions for premarket submissions for cyber devices that are submitted before October 1, 2023, based solely on information required by section 524B of the FD&C Act. Instead, FDA intends to work collaboratively with sponsors of such premarket submissions as part of the interactive and/or deficiency review process.

Date	Guidance Type	Guidance Name	Purpose
April 5, 2023	Draft	Notifying FDA of a Discontinuance or Interruption in Manufacturing of Finished Products or Active Pharmaceutical Ingredients (API) Under Section 506C of the FD&C Act (**link**)	To assist applicants and manufacturers in providing FDA timely, informative notifications about changes in the production of certain finished drugs and biological products as well as certain APIs that may, in turn, help the agency in its efforts to prevent and mitigate drug shortages. While some supply disruptions and product shortages cannot be predicted or prevented, early communication and detailed notifications to FDA from manufacturers play a significant role in decreasing the incidence, impact, and duration of supply disruptions and product shortages. These notifications allow the agency to evaluate the situation and determine an appropriate course of action.
April 5, 2023	Draft	Patient-Focused Drug Development: Incorporating Clinical Outcome Assessments Into Endpoints for Regulatory Decision-Making (**link**)	To help clinical trial sponsors in medical product development. The guidance focuses on clinical outcome assessments (COA) issues associated with clinical trial (study) endpoints, design, conduct and analysis and is most relevant to those designing and conducting trials using COAs as well as analyzing and interpreting the trial data. This guidance is the fourth in a series of guidance documents intended to facilitate the advancement and use of systematic approaches to collect and use robust and meaningful patient and caregiver input that can more consistently inform medical product development and regulatory decision-making.
April 19, 2023	Draft	Acute Radiation Syndrome: Developing Drugs for Prevention and Treatment (**link**)	To provide information and recommendations to assist sponsors and other interested parties in the development of drugs to prevent or treat ARS caused by exposure to ionizing radiation from accidental or deliberate events. Generally, drugs developed for such indications will require approval under the regulations commonly referred to as the Animal Rule.
May 2, 2023	Draft	Decentralized Clinical Trials for Drugs, Biological Products, and Devices (**link**)	To provide recommendations for sponsors, investigators, and other stakeholders regarding the implementation of decentralized clinical trials (DCTs) for drugs, biological products, and devices. In this guidance, a DCT refers to a clinical trial where some or all of the trial-related activities occur at locations other than traditional clinical trial sites.

Date	Guidance Type	Guidance Name	Purpose
May 17, 2023	Draft	Pediatric Drug Development: Regulatory Considerations — Complying With the Pediatric Research Equity Act and Qualifying for Pediatric Exclusivity Under the Best Pharmaceuticals for Children Act (**link**)	To assist industry developing drug products to comply with the pediatric study requirements under PREA, and to describe the process for qualifying for pediatric exclusivity and the protections that pediatric exclusivity offers under the Best Pharmaceuticals for Children Act (BPCA). In 2010, the Biologics Price Competition and Innovation Act of 2009 extended provisions of the BPCA to biological products.
May 17, 2023	Draft	Pediatric Drug Development Under the Pediatric Research Equity Act and the Best Pharmaceuticals for Children Act: Scientific Considerations (**link**)	To assist industry in developing data and obtaining information needed to support approval of drug products in pediatric populations. This guidance addresses selected clinical, scientific, and ethical issues regarding the development of drugs for pediatric use when such drugs are subject PREA and/or BPCA.
June 6, 2023	Draft	E6(R3) Good Clinical Practice (GCP) (**link**)	To provide updated recommendations for GCPs aimed at modernizing the design and conduct of clinical trials, making them more agile without compromising data integrity or participant protections. The updates are intended to help pave the way for more efficient clinical trials to facilitate the development of medical products.
July 10, 2023	Final	Temporary Policy Regarding Accredited Third-Party Certification Program Onsite Observation and Certificate Duration Requirements Due to COVID-19 (**link**)	To temporarily provide the Accredited Third-Party Certification Program's currently recognized accreditation bodies and accredited third-party certification bodies flexibility, in certain circumstances.
July 10, 2023	Final	Temporary Policy Regarding Preventive Controls and FSVP Food Supplier Verification Onsite Audit Requirements Due to COVID-19 (**link**)	To state the current intent of the FDA in certain circumstances related to the impact of the COVID-19 not to enforce requirements in three foods regulations to conduct onsite audits of food suppliers if other supplier verification methods are used instead.
September 05, 2023	Final	Enforcement Policy for Face Masks and Barrier Face Coverings for Coronavirus Disease (COVID-19) Response (**link**)	To update and rename the guidance, "Enforcement Policy for Face Masks and Barrier Face Coverings During the Coronavirus Disease (COVID-19) Public Health Emergency" (latest version published March 2023), as "Enforcement Policy for Face Masks and Barrier Face Coverings for the Coronavirus Disease (COVID-19) Response." Updated to reflect FDA's intent for this guidance to remain in effect for the duration of the applicable declaration under section 564 of the FD&C Act, rather than the duration of the PHE determination under section 319 of the PHS Act.

Date	Guidance Type	Guidance Name	Purpose
September 29, 2023	Final	Antimicrobial Susceptibility Test (AST) System Devices – Updating Breakpoints in Device Labeling (**link**)	To provide industry and FDA staff with information, recommendations, and describe an enforcement policy regarding updating susceptibility test interpretive criteria (STIC)/breakpoints and associated performance data in device labeling for AST system devices in response to breakpoint changes posted on the FDA-Recognized AST STIC website. This guidance is expected to facilitate the timely adoption of updated breakpoints in AST system devices, which helps to ensure device safety and effectiveness.

Appendix 4: Key MCM-Related Meetings Held In FY 2023

FDA continued to take steps to ensure the agency was able to continue our vital public health mission in FY 2023. 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 March 2023	Webinar series	Virtual Town Hall Series –Test Development and Validation During Public Health Emergencies	To help answer technical questions about the development and validation of tests for SARS-CoV-2. This series began in March 2020, and continued in FY 2023, including COVID-19 and mpox.
October 5, 2022	Webinar	Study Data Standards Update for CBER: Your Guide to a Successful Submission (**link**)	To discuss CBER's support and requirement starting March 15, 2023 for the Standard for the Exchange of Nonclinical Data (SEND), which was **published** in the Federal Register on July 14, 2020, and the addition of SEND for CBER to the **FDA Data Standards Catalog**.
October 6, 2022	Advisory Committee	Vaccines and Related Biological Products Advisory Committee (VRBPAC) (**link**)	To discuss strain selection for influenza virus vaccines for the 2023 Southern Hemisphere influenza season.
October 11, 2022	Webinar	FDA NanoDay Symposium 2022 (**link**)	To address drug development of products that contain nanomaterials in their formulation and how the **guidance for industry** for products that contain nanomaterials finalized in April 2022 can be implemented in filings to the FDA. Discussion included case studies on the development of the COVID mRNA lipid nanoparticle vaccine products.
November 9, 2022	Advisory Committee	Pulmonary-Allergy Drugs Advisory Committee (**link**)	To discuss the request for EUA 113, for sabizabulin oral capsule, a tubulin polymerization inhibitor, submitted by Veru Inc., for the treatment of SARS-CoV-2 infection in moderate to severe COVID-19 infections at high risk of acute respiratory distress syndrome.

Date	Type of Event	Event Name	Purpose
November 14-16, 2022	Public workshop	FDA/PQRI Workshop on the Regulatory Framework for Distributed and Point of Care Pharmaceutical Manufacturing: An Opportunity for DM/POC Stakeholder Engagement (**link**)	To facilitate interaction among DM/POC stakeholders on critical areas for development and implementation of DM and POC technologies including terminology, technical challenges to adoption, operation of Pharmaceutical Quality Systems, good manufacturing practice expectations, and the unique challenges and considerations that apply to complex biological products.
November 15, 2022	Public workshop	CDRH Industry Basics: Understanding Risk with Medical Devices (**link**)	To educate attendees on the basics of risk with medical device use by featuring Risk Basics for Medical Devices and Application of Risk Management Principles for Medical Devices.
December 6, 2022	Industry day[38]	FDA Broad Agency Announcement Day 2022 (**link**)	FDA funds extramural research through an agency-wide BAA for research and development to support regulatory science and innovation. To help prospective applicants and other stakeholders learn more about the FDA BAA, including MCM-related research areas.
December 7-8, 2022	Training course	FDA Clinical Investigator Training Course (CITC) 2022 (**link**)	To promote professionalism in the clinical trial industry for individuals involved with FDA submissions (IND, NDA, BLA, and IDE), and to familiarize stakeholders with the regulatory and scientific issues involved in the development and approval of medical products.
December 7-8, 2022	Public workshop	The DSCSA Implementation and Readiness Efforts for 2023 (**link**)	To provide members of the pharmaceutical distribution supply chain and other interested stakeholders an opportunity to share their perspectives on DSCSA implementation.
December 8, 2022	Advisory Committee	Blood Products Advisory Committee (**link**)	To hear an overview of the research programs of the Laboratory of Emerging Pathogens and the Laboratory of Molecular Virology, Division of Emerging and Transfusion Transmitted Diseases, Office of Blood Research and Review, CBER.
December 8, 2022	FDA Grand Rounds	Wastewater Surveillance for SARS-CoV-2 Variants: a pandemic response project leveraging FDA's GenomeTrakr network (**link**)	With funding from the American Rescue Plan Act, FDA scientists leveraged an existing laboratory network normally tasked for foodborne pathogen surveillance to start sequencing SARS-CoV-2 from **regional wastewater treatment plants** across the US. This event updated attendees on new laboratory and analysis methods, public database structures, and an FDA dashboard summarizing data collected during this project.

[38] The FDA BAA is open to all responsible sources, and small businesses are strongly encouraged to respond. Offerors may include single entities or teams from private sector organizations, Federally Funded Research and Development Centers (FFRDCs), and academic institutions.

Date	Type of Event	Event Name	Purpose
December 15, 2022	Public workshop	Efficacy of Monoclonal Antibodies in the Context of Rapidly Evolving SARS-CoV-2 Variants (**link**)	Hosted by FDA and the European Medicines Agency (EMA) to bring together scientists, clinicians, industry representatives and regulators to discuss alternative strategies to support the development of novel monoclonal antibody therapies including those based on prototype products that have demonstrated safety and efficacy in clinical trials. (**Summary report**)
January 26, 2023	Advisory Committee	VRBPAC (**link**)	To **discuss** the future vaccination regimens addressing COVID-19, including consideration of the composition and schedule of the primary series and booster vaccinations.
February 28-March 1, 2023	Advisory Committee	VRBPAC (**link**)	To discuss and make recommendations on the safety and effectiveness of two RSV vaccine BLAs.
March 7, 2023	Advisory Committee	VRBPAC (**link**)	To discuss and make recommendations on the selection of strains to be included in the influenza virus vaccines for the 2023--2024 influenza season.
March 9, 2023	FDA Grand Rounds	Microphysiological Systems as Novel Disease Models and Drug Development Tools (**link**)	Researchers from FDA's National Center for Toxicological Research (NCTR) presented research evaluating a testicular organoid model for use as an in vitro model of Zika virus infection.
March 14, 2023	Public workshop	FDA CBER Office of Therapeutic Products (OTP) Advanced Manufacturing and Analytical Technol-ogies (AMAT) for Regenerative Medicine Therapies (RMT) Workshop (**link**)	For FDA staff and cell and gene therapy stakeholders to discuss innovative manufacturing technologies and alternative testing methods, and share experiences, challenges, and best practices critical for chemistry, manufacturing, and controls (CMC) of cellular and gene therapies and tissue engineered medical products.
March 16, 2023	Advisory Committee	Antimicrobial Drugs Advisory Committee (**link**)	To discuss an NDA for Paxlovid (nirmatrelvir and ritonavir co-packaged tablets) for oral use. The proposed indication is treatment of mild-to-moder-ate coronavirus disease (COVID-19) in adults who are at high risk for progression to severe COVID-19, including hospitalization or death.
March 30, 2023	Public workshop	Immune Globulin Hypersensitivity Reactions: Root Causes and Mitigation Public Workshop (**link**)	To gain insight and to identify measures to prevent hypersensitivity reactions associated with specific lots of immune globulins.

Date	Type of Event	Event Name	Purpose
April 13, 2023	Webinar	Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence / Machine Learning-Enabled Device Software Functions Draft Guidance (**link**)	To discuss the **draft guidance**, Marketing Submission Recommendations for a Predetermined Change Control Plan for AI/ML-Enabled Device Software Functions. The draft guidance includes proposed recommendations for the content to include in a Predetermined Change Control Plan (PCCP) as part of a marketing submission for an AI/ML-enabled device. A PCCP outlines anticipated device changes and how those changes will be assessed and implemented in accordance with the PCCP, among other things.
April 17, 2023	Advisory Committee	Antimicrobial Drugs Advisory Committee (**link**)	To discuss an NDA for sulbactam-durlobactam for injection. The applicant's proposed indication is for the treatment of infections due to Acinetobacter baumannii-calcoaceticus complex including multidrug-resistant and carbapenem-resistant strains.
April 18, 2023	Webinar	Webinar on Guidances on COVID-19 Transition Plans for Medical Devices (**link**)	To educate stakeholders interested in learning more about the **two final guidances** on the COVID-19 transition plans for medical devices
April 24-28, 2023	Training course	Achieving Data Quality and Integrity in Maximum Containment Laboratories (**link**)	To provide a unique opportunity for the regulatory and scientific communities to discuss complex issues in an interactive environment and identify and share best practices for ensuring data quality and integrity in BSL-4 facilities, including hands-on training for in-person attendees.
April 25, 2023	Public meeting	Public Meeting on Patient-Focused Drug Development for Long COVID (**link**)	To provide FDA the opportunity to obtain initial patient and patient representative input on the aspects of Long COVID, including how Long COVID affects their daily life, symptoms that matter most to patients, their current approaches to treating Long COVID, and what they consider when determining whether to participate in a clinical trial. This virtual public meeting was conducted with live translation in both English and **Spanish**.
April 25-26, 2023	Public workshop	FDA - United States Pharmacopeia (USP) Asia-Pacific Economic Cooperation (APEC) Medical Product Supply Chain Dialogue (**link**)	To bring international medical product regulators, multilateral organization representatives, and industry and academic professionals together, to discuss public health priorities, the impact of the COVID-19 pandemic on supply chains, and why the **APEC Supply Chain Security Toolkit** continues to be a valuable tool to stakeholders.

Date	Type of Event	Event Name	Purpose
April 26, 2023	Webinar	Virtual Town Hall - Test Development and Validation During the COVID-19 Public Health Emergency (**link**)	For COVID-19 test developers, to discuss the two final COVID-19 transition guidances: **Transition Plan for Medical Devices That Fall Within Enforcement Policies Issued During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency**; and **Transition Plan for Medical Devices Issued Emergency Use Authorizations (EUAs) Related to Coronavirus Disease 2019 (COVID-19)**.
April 27, 2023	Public workshop	Recombinant Protein-Based COVID-19 Vaccines Workshop (**link**)	Hosted by BARDA and FDA, to provide: 1) a forum for product sponsors to discuss progress and technical challenges in the manufacturing when changing strain composition to currently circulating variants of SARS-CoV-2; and 2) an open forum for collaborative discussions to facilitate advancement of recombinant protein-based COVID-19 vaccines.
May 8, 2023	International workshop	ICMRA COVID-19 Omicron Variant Workshop (**link**)	Hosted by ICMRA, and co-chaired by FDA, to reach international regulatory alignment on a potential way forward to adapt authorized and new COVID-19 vaccines to emerging SARS-CoV-2 variants. This included identifying the preferred composition for the next updates based on lessons learned from last year's strain changes and considerations for simplification of the product information.
May 18, 2023	Advisory Committee	VRBPAC (**link**)	To discuss and make recommendations on the safety and effectiveness of Abrysvo (Respiratory Syncytial Virus Vaccine), with a requested BLA indication for the prevention of lower respiratory tract disease and severe lower respiratory tract disease caused by RSV in infants from birth through six months of age by active immunization of pregnant individuals.
June 8, 2023	Advisory Committee	Antimicrobial Drugs Advisory Committee (**link**)	To discuss a BLA application for nirsevimab, a long-acting RSV F protein inhibitor monoclonal antibody for intramuscular use, submitted by AstraZeneca AB. The proposed indication is prevention of RSV lower respiratory tract disease in neonates and infants born during or entering their first RSV season, and children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season.

Date	Type of Event	Event Name	Purpose
June 13-14, 2023	Forum	2023 FDA Science Forum (**link**)	To offer an opportunity for the public to view the unique scientific research and collaborative efforts of FDA's 11,000 scientists. Topic areas include medical countermeasures, infectious disease and pathogen reduction technologies, and product development and manufacturing, including advanced manufacturing. In addition to presentations in key topic areas, FDA scientists published more than 200 **posters** as part of this event, including more than 40 MCM-related research posters.
June 15, 2023	Advisory Committee	VRBPAC (**link**)	To discuss and make recommendations on the selection of strain(s) to be included in the periodic updated COVID-19 vaccines for the 2023-2024 vaccination campaign.
June 20, 2023	Webinar	Decentralized Clinical Trials (DCT) Draft Guidance (**link**)	As part of FDA's efforts to be responsive to the rapidly evolving clinical trial landscape and clarify the agency's recommendations on the conduct of DCTs, to provide an overview of the draft guidance, **Decentralized Clinical Trials for Drugs, Biological Products, and Devices**.
September 26-27, 2023	Public workshop	FDA/PQRI Workshop on the Regulatory Framework for the Utilization of Artificial Intelligence in Pharmaceutical Manufacturing (**link**)	Hosted by FDA and the Product Quality Research Institute (PQRI), to facilitate interaction among AI stakeholders on critical areas for development, implementation, and regulatory consideration including uses in process development and control, operation of Pharmaceutical Quality Systems, lifecycle approaches, and Current Good Manufacturing Practice.

Appendix 5: Abbreviations

AAJT-S	Abdominal Aortic and Junctional Tourniquet – Stabilized
ABC	*Acinetobacter baumannii-calcoaceticus* complex
AI	Artificial intelligence
AMAT	Advanced manufacturing and analytical technologies
AMMP	Additive Manufacturing of Medical Products
AMR	Antimicrobial resistance
ANDA	Abbreviated New Drug Application
ANS	Anterior nasal swab
APEC	Asia-Pacific Economic Cooperation
API	Active pharmaceutical ingredients
ARS	Acute radiation syndrome
ASAP	Assay Specific Analysis Package
ASPR	Administration for Strategic Preparedness and Response (HHS)
AST	Antimicrobial susceptibility test
BAA	Broad Agency Announcement
BAL	Bronchoalveolar lavage
BARDA	Biomedical Advanced Research and Development Authority
BLA	Biologics License Application
BPCA	Best Pharmaceuticals for Children Act
BoNT	Botulinum neurotoxin
BSL	Biosafety level
CAD	Computer-aided design
CARES Act	Coronavirus Aid, Relief, and Economic Security Act
CATT	CBER Advanced Technologies Team (FDA Center for Biologics Evaluation and Research)
CBER	FDA Center for Biologics Evaluation and Research
CBRN	Chemical, biological, radiological, and nuclear
CDC	U.S. Centers for Disease Control and Prevention
CDER	FDA Center for Drug Evaluation and Research
CDRH	FDA Center for Devices and Radiological Health
CEPI	Coalition for Epidemic Preparedness Innovations
CFR	Code of Federal Regulations
CITC	Clinical Investigator Training Course
CLIA	Clinical Laboratory Improvement Amendments
CM	Continuous manufacturing
CMC	Chemistry, manufacturing, and controls
CMIA	Chemiluminescent microparticle immunoassays
CMS	Centers for Medicare and Medicaid Services
COA	Clinical outcome assessment
COPD	Chronic obstructive pulmonary disease
COVID-19	Coronavirus disease 2019 (caused by SARS-CoV-2)
CRP	C-reactive protein
CT	Computed tomography
CTAP	Coronavirus Treatment Acceleration Program
Cures Act	21st Century Cures Act
CVM	FDA Center for Veterinary Medicine
DARPA	Defense Advanced Research Projects Agency
DCT	Decentralized clinical trial
DM	Distributed manufacturing
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
ECG	Electrocardiogram
ECMO	Extracorporeal membrane oxygenation
EDTA	Ethylenediaminetetraacetic acid
eGFR	Estimated glomerular filtration rate
EIND	Emergency Investigational New Drug application
ELEFT	Electrocardiogram Low Ejection Fraction Tool

ELISA	Enzyme-linked immunosorbent assay
EMA	European Medicines Agency
EUA	Emergency Use Authorization
EV-D68	Enterovirus D68
EVD	Ebola virus disease
FAQ	Frequently asked questions
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
FFRDC	Federally Funded Research and Development Center
FIND	Foundation for Innovative New Diagnostics
FTE	Full-time equivalent
FY	Fiscal year
GCP	Good clinical practice
GFAP	Glial fibrillary acidic protein
GFI	Guidance for Industry
GHSA	Global Health Security Agenda
GHSI	Global Health Security Initiative
GI-ARS	Gastrointestinal syndrome of acute radiation syndrome
GloPID-R	Global Research Collaboration for Infectious Diseases Preparedness
HABP	Hospital-acquired bacterial pneumonia
H-ARS	Hematopoietic syndrome of acute radiation syndrome
HCT/P	Human cells, tissues, and cellular and tissue-based products
HHS	U.S. Department of Health and Human Services
hMPV	human metapneumovirus
IAA	Interagency agreement
IAEA	International Atomic Energy Agency
IBx	Innovation and Industrial Base Expansion (HHS/ASPR program)
ICMRA	International Coalition of Medicines Regulatory Authorities
ICU	Intensive care unit
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IDE	Investigational Device Exemption
igG	immunoglobulin G
IMDRF	International Medical Device Regulators Forum
IMSCC	Infection Management/Sepsis Collaborative Community
IND	Investigational New Drug
INTERACT	Initial Targeted Engagement for Regulatory Advice on CDER and CBER ProducTs
I-TEAM	Innovative Technologies and Advanced Manufacturing
ITAP	Independent Test Assessment Program (NIH)
IVD	*In vitro* diagnostic
JEE	Joint External Evaluation
JPEO-CBRND	Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense (DoD)
LDT	Laboratory developed test
LLNL	Lawrence Livermore National Laboratory
LRTD	Lower respiratory tract disease
mAb	Monoclonal antibody
MALDI-TOF MS	Matrix-assisted laser desorption/ionization-time of flight mass spectrometry
MCM	Medical countermeasure
MCMi	FDA Medical Countermeasures Initiative
MERS-CoV	Middle East Respiratory Syndrome coronavirus
mg	Milligram
MIC	Minimum inhibitory concentration
MIT	Massachusetts Institute of Technology
mL	Milliliter
ML	Machine learning
MOU	Memorandum of Understanding
mpox	Disease caused by the monkeypox virus
MPS	Microphysiological systems
MRI	Magnetic resonance image
mRNA	Messenger ribonucleic acid
MVA-BN	Modified Vaccinia Ankara-Bavarian Nordic
NAAT	Nucleic acid amplification test

NACCHO	National Association of County and City Health Officials
NASA	National Aeronautics and Space Administration
NASEM-HMD	National Academies of Sciences, Engineering, and Medicine, Health and Medicine Division
NBBI	National Biotechnology and Biomanufacturing Initiative
NCATS	National Center for Advancing Translational Sciences (NIH)
NCTR	National Center for Toxicological Research
NCBI	National Center for Biotechnology Information
NDA	New Drug Application
NETCCN	National Emergency Telecritical Care Network
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
NIOSH	National Institute for Occupational Safety and Health (CDC)
NIST	U.S. National Institute of Standards and Technology
NPS	Nasopharyngeal swab
OCET	FDA Office of Counterterrorism and Emerging Threats
OCS	FDA Office of the Chief Scientist
OSHA	Occupational and Safety Health Administration
OSTP	Office of Science and Technology Policy (White House)
OTC	Over-the-counter
OTP	Office of Therapeutic Products, FDA Center for Biologics Evaluation and Research
PAHPRA	Pandemic and All-Hazards Preparedness Reauthorization Act of 2013
PBMC	Peripheral blood mononuclear cell
PCCP	Predetermined Change Control Plan
PCR	Polymerase chain reaction
PCT	Procalcitonin
PDUFA	Prescription Drug User Fee Act
PHE	Public health emergency
PHEMCE	Public Health Emergency Medical Countermeasures Enterprise
PHS Act	Public Health Service Act
PMA	Premarket Approval
PMR	Post-marketing requirement
POC	Point of care
PPE	Personal protective equipment
PQRI	Product Quality Research Institute
PREA	Pediatric Research Equity Act
PRV	Priority review voucher
rad/nuc	Radiological/nuclear
RADx	Rapid Acceleration of Diagnostics program (NIH)
REMM	Radiation Emergency Medical Management
REMS	Risk Evaluation and Mitigation Strategies
RMP	Regulatory Management Plan
RMT	Regenerative medicine therapies
RNA	Ribonucleic acid
RSV	Respiratory syncytial virus
RT-PCR	Real-time polymerase chain reaction
RTA	Refuse to accept
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SEND	Standard for the Exchange of Nonclinical Data
SHIELD	Systemic Harmonization and Interoperability Enhancement for Laboratory Data
SIR	Submission Issue Request
SLEP	Shelf-Life Extension Program
SLTT	State, local, tribal and territorial
SNS	Strategic National Stockpile
SPA	Special Protocol Assessment
STAT	Short turn-around time
STIC	Susceptibility test interpretive criteria
STN	Submission tracking number
STOMP	Study of Tecovirimat for Human Monkeypox Virus (NIH)
SUDV	*Sudan ebolavirus*

suPAR	Plasma soluble urokinase plasmin ogen activator receptor
TATRC	Telemedicine and Advanced Tech nology Research Center (DoD)
TBI	Traumatic brain injury
TRAIL	Tumor necrosis factor-related apoptosis-inducing ligand
TTFED	Tri-Agency Task Force for Emergency Diagnostics
UCHL1	Ubiquitin carboxyl-terminal hydrolase L1
UKHSA	UK Health Security Agency
U.S.	United States
USAMMDA	U.S. Army Medical Materiel Development Activity
USAMRDC	U.S. Army Medical Research and Development Command
USDA	U.S. Department of Agriculture
USG	United States government
USP	United States Pharmacopeia
UTMB	University of Texas Medical Branch
VABP	Ventilator-associated bacterial pneumonia
VHA	Veterans Health Administration
VRBPAC	Vaccines and Related Biological Products Advisory Committee
WHO	World Health Organization

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