



**Center for Biologics Evaluation and
Research (CBER)
2021–2025**

Strategic Plan



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A MESSAGE FROM THE CBER CENTER DIRECTOR

On behalf of the Center for Biologics Evaluation and Research (CBER), I am pleased to present the Center’s strategic plan for the years 2021 through 2025, which outlines the direction that we will take to support and achieve our mission and vision over the next five years. This is an exciting time to be CBER’s Director, with science and technology advancing at an unprecedented rate. Evidence is emerging that we can evaluate and incorporate into our work to streamline our regulatory processes with the ultimate goal of accelerating the approval of safe and effective innovative medical products.

CBER’s strategic plan is based on our mission and vision, and outlines the goals, objectives, and strategies designed to further our mission and vision during the term of the strategic plan. Our plan aligns with HHS and FDA priorities and new authorities provided through the 21st Century Cures Act. It reflects the contributions of all Offices and Divisions, and sets forth the Center’s four goals:



- Goal 1:** Facilitate the development and availability of safe and effective medical products through the integration of advances in science and technology
- Goal 2:** Conduct research to address challenges in the development and regulatory evaluation of medical products
- Goal 3:** Increase preparedness for emerging threats and promote global public health
- Goal 4:** Manage for strategic excellence and organizational accountability

Furthermore, the strategic plan reflects CBER’s current priorities for the near term:

- Priority 1: Addressing the COVID-19 outbreak
- Priority 2: Developing a regulatory program for individualized or bespoke therapies
- Priority 3: Facilitating compliance with human cells, tissues, and cellular and tissue-based product regulations
- Priority 4: Advancing manufacturing technologies for biologic products

New scientific advances give us the opportunity to reduce the burden of disease by bringing patients safe and effective novel products to prevent and treat diseases. At CBER, a fundamental part of our mission and vision is helping to provide the scientific foundations and the regulatory framework that will maximally expedite the translation of new scientific advances into such benefits for individuals and for the public health.

We view this strategic plan as a living document that will allow us to modify our direction and approach in order to address new regulatory challenges and obligations as the need arises, such as in the case of the current pandemic. Together, these goals, objectives, and strategies put CBER in the position to contribute to improving public health in the years to come. We have a clear direction and look forward to rising to the challenge of building on our successes to serve the American public.

With Best Regards,

Peter Marks, MD, PhD
 Director, Center for Biologics Evaluation and Research

OVERVIEW

MISSION

The mission of the Center for Biologics Evaluation and Research (CBER) is to ensure the safety, purity, potency, and effectiveness of biological products including vaccines, allergenics, blood and blood products, and cells, tissues, and gene therapies for the prevention, diagnosis, and treatment of human diseases, conditions, or injury. Through CBER's mission, the Center also seeks to protect the public against the threats of emerging infectious diseases and bioterrorism.

VISION

CBER uses sound science and regulatory expertise to:

- Protect and improve public and individual health in the United States and, where feasible, globally;
- Facilitate the development, approval of, and access to safe and effective biological products and promising new technologies; and
- Strengthen CBER as a preeminent regulatory organization for biological products.

ORGANIZATION

CBER is comprised of the Office of the Director and seven program offices. Three of the program offices are responsible for regulatory oversight of biological products—vaccines and allergenics; blood and blood products; and tissues and advanced therapies. The four remaining offices provide cross-cutting support in the areas of compliance; surveillance, epidemiology and biostatistics; communication, outreach and development; and management, budget and administrative services. The Office of the Director provides leadership and policy direction to the program offices and coordinates Center activities and resource management.

INTRODUCTION

CBER's portfolio encompasses many complex medical products that can positively impact people's lives. The Center's diverse regulatory portfolio includes blood components and derivatives, vaccines, allergenics, cellular and gene therapies, and tissues for transplantation. It also includes certain devices, including *in vitro* diagnostic tests for screening the blood supply and devices for the manufacturing of blood and tissue products. These include numerous products that are living microorganisms, cells or tissues from humans or animals, and products that are derived from them, such as stem cells and genetically engineered immune cells. Biologics are often not easily identified or characterized, and many are manufactured using biotechnology. These products frequently represent cutting-edge biomedical research and, in time, may offer the most effective means to treat a variety of medical illnesses and conditions that presently have few or no other treatment options.

The *CBER 2021–2025 Strategic Plan* outlines the Center's strategic direction for supporting CBER's mission and striving toward CBER's vision over the next five years. Since the last plan (*CBER Interim Strategic Plan FY 2017–2019*) was published, new legislation to help accelerate medical product development and bring new innovations and advances to patients who need them faster and more efficiently has been enacted. These laws include:

1. **The 21st Century Cures Act (Cures Act)** was signed into law on December 13, 2016 and is designed to help accelerate medical product development and bring new innovations and advances faster and more efficiently to patients who need them.
2. **The Food and Drug Administration Reauthorization Act of 2017 (FDARA)** was signed into law on August 18, 2017, amending the Federal Food, Drug, and Cosmetic Act and reauthorizing the user-fee programs for drugs, medical devices, generic drugs, and biosimilar biological products through the end of FY2022.
3. **The Pandemic and All-Hazards Preparedness and Advancing Innovation Act (PAHPAIA) of 2019** reauthorizes and strengthens efforts to respond to disasters and threats from emerging infectious diseases. The PAHPAIA furthers FDA’s mission of fostering the development and availability of medical countermeasures (MCMs).

Over the last several years, CBER has engaged in groundbreaking work involving the regulation of vaccines, blood products, innovative cellular and gene therapies, and other complex biological products. Those areas include the rapid progress in cellular and gene therapies, advances in advanced manufacturing technologies, and the ability to effectively leverage information from large databases by using artificial intelligence tools.

CBER’s 2021–2025 Strategic Plan offers a path forward to help the Center advance product development to increase access to safe and effective products to improve the lives of patients. The updated strategic plan contains four goals which provide the structural framework of the plan, objectives which will help define how the Center will make advances in critical mission-oriented focus areas, and strategies which lay out activities to achieve the goals.

CBER STRATEGIC PLAN GOALS

1. Facilitate the development and availability of safe and effective medical products through the integration of advances in science and technology.
2. Conduct research to address challenges in the development and regulatory evaluation of medical products.
3. Increase preparedness for emerging threats and promote global public health.
4. Manage for strategic excellence and organizational accountability.

This plan provides a comprehensive overview of the Center’s current and planned portfolio and considers legislative mandates, a commitment to advancing the development of complex biological products through applied scientific research, recent innovations in regulatory science and technology, global health needs, and expanded opportunities for collaboration and partnership.

To ensure the CBER 2021–2025 Strategic Plan captured CBER’s direction for the next five years, each employee was afforded a chance to review and comment on the revised goals and objectives for the 2021 to 2025 Strategic Plan. The revised goals and objectives were developed by subject matter experts representing each organizational unit in CBER and crosscutting areas such as counterterrorism, international affairs, review management, policy and regulatory science. The plan represents a coordinated Center-wide effort to guide CBER’s direction over the next five years.

GOAL 1 | Facilitate the development and availability of safe and effective medical products through the integration of advances in science and technology.

CBER incorporates advances in science and technology into the full product life cycle from concept to marketed product. This focus on integration facilitates access to safe and effective products that improve how patients feel, function, and survive. The development of innovative products presents unique challenges, and CBER must balance timely patient access to novel (new) products with meeting key standards for safety and efficacy, such as the current [Good Manufacturing Practice \(cGMP\)](#) regulations for human pharmaceuticals.

To achieve this goal, CBER actively engages with stakeholders, including patients, to inform and support product development. CBER also advises sponsors at an early stage to enable product development. CBER supports the expedited development and review of medical products to treat serious conditions for a broad range of complex and life-threatening diseases, including many that fill unmet medical needs, through accelerated approval programs when appropriate.

CBER conducts a wide range of compliance and surveillance activities to ensure the quality of products through their entire lifecycle. These activities range from premarket approval inspections to inspections of FDA approved products that are on the market. Through these inspections, CBER helps to ensure compliance with human subject protection in clinical trials, good manufacturing procedures and, as necessary, support appropriate enforcement actions on marketed products that are not approved by FDA, with a focus on those that are manufactured with significant deviations from cGMP requirements that may harm the public.

The following objectives define how CBER will progress on this goal.

OBJECTIVE 1.1 | Integrate emerging science and technology in policy development for regulatory oversight to expedite the availability of safe and effective medical products.

The increasing diversity, complexity, and technological sophistication of CBER-regulated products requires the Center develop and adapt innovative approaches to evaluate these products, such as gene therapies, vaccines, and regenerative medicine therapies, and ensure their safety and efficacy. Recent breakthroughs in science and technology, such as tools to mine [Real-World Data](#) (RWD), are transforming CBER's ability to bring safe and effective new products to market more efficiently.

To help these new scientific advances and technologies reach their full potential, CBER will continue to develop policies and guidance to keep pace with them. CBER's policy and guidance documents help ensure the regulatory process is predictable, transparent, and scientifically modern. CBER's goal is to create clear recommendations, frameworks, and pathways that allow beneficial new technologies to more efficiently reach patients while maintaining standards for product safety and effectiveness.

CBER will continue to solicit public input in guidance development and build on its comprehensive policy framework to address how the agency plans to support and expedite the development of novel biological products. For example, building on the regulations governing human cells, tissues, and cellular and tissue-based products (HCT/Ps) and key provisions in the 21st Century Cures Act, CBER has established a comprehensive regenerative medicine framework that will help to drive forward an efficient, science-based process to ensure the safety and effectiveness of regenerative medicine products, including HCT/Ps. Innovators can use this framework to bring new, effective therapies to patients as quickly and safely as possible. CBER has also developed [Gene Therapy Guidances](#) to keep pace with new scientific advances and technologies in gene therapy.

Recent advances in technology have permitted the development of biological products, including vector-based gene therapies, genetically modified cellular therapies, and bacteriophage, designed for one or a small number of patients (so-called individualized or bespoke therapies). While these products have the potential to make a difference in the lives of many patients with rare and very rare diseases, there are challenges associated with their development, including limited numbers of patients available to participate in clinical trials, manufacturing challenges and expense, and, ultimately, commercial viability of these products. CBER remains committed to working with researchers and developers to address the challenges and exploring how best to apply its existing regulatory framework to these innovative products. To further facilitate the development and sustainable access to these promising, novel products, CBER has established an Individualized Therapeutics Council, hosted a workshop, and collaborated with the Foundation for the National Institutes of Health and the National Center for Advancing Translational Sciences to establish the Bespoke Gene Therapy Consortium to advance access to adenovirus-associated virus technologies and vectors to help facilitate end-to-end development of vector-based bespoke gene therapies.

To provide independent expert advice on scientific, technical, and policy matters related to medical products, CBER consults with its Advisory Committees.¹ Advisory Committees review and evaluate data concerning the safety, effectiveness, and appropriate use of biological products that are intended for use in the prevention, treatment, or diagnosis of human diseases, and, as required, any other products for which the FDA has regulatory responsibility. CBER will continue to leverage its Advisory Committees to access expert advice on challenges going forward, such as the continued evolution of blood safety policies through identification of additional information that could support alternative procedures to FDA’s current time-based donor deferral policies and the use of pathogen reduction technologies.

Interactions with stakeholders, both internal and external, are essential to help CBER identify issues of regulatory and scientific concern that can be addressed through policy updates. CBER will continue to convene public workshops to bring together government agencies, academia, industry, and other stakeholders to discuss the scientific and regulatory challenges. These discussions about the challenges in product development and surveillance will help to create new perspectives on how CBER can most effectively respond to scientific and technological innovations in a manner that results in improved practices and, ultimately, more efficient development of safe and effective biologics products.



To achieve Objective 1.1, CBER will employ the strategies below.

Strategy 1.1.1 | Continue to promote interactions between CBER policy and scientific experts to support regulatory oversight of medical products involving emerging science and technology.

Strategy 1.1.2 | Engage with external stakeholders to identify issues of regulatory and scientific relevance concerning emerging science and technology.

Strategy 1.1.3 | Issue guidance and other policy documents that help clarify regulatory and scientific expectations of emerging science and technology and help expedite availability of medical products.

¹ CBER Advisory Committees include: [Allergenic Products Advisory Committee](#); [Blood Products Advisory Committee](#); [Cellular, Tissue, and Gene Therapies Advisory Committee](#); and the [Vaccines and Related Products Advisory Committee](#).

OBJECTIVE 1.2 | Interact with stakeholders to facilitate the development of innovative medical products.

The American public are the ones who ultimately experience the benefits, risks, and daily impact of diseases and medical products for their prevention and treatment. They have diverse circumstances and experiences that shape their preferences and their willingness to accept risks. As CBER considers biological products for approval, it is important to understand how different patient populations view the benefits and risks of different options. CBER will continue to interact with patients and stakeholders to facilitate the development of innovative medical products that best fit patient needs.

To better understand the patients' perspective, and incorporate patient engagement into the regulatory process, CBER is committed to creating opportunities for communication and collaboration with patients and caregivers, within the Center and among other FDA Centers, among government agencies, and with external stakeholders. Enhanced communication and coordination facilitate the development of innovative medical products that meet patient needs.

CBER is bridging patient engagement efforts across the agency through workgroups to advance more systematic, sound approaches to collecting patient and caregiver input. Workgroups allow for collaboration with FDA Offices and patient engagement teams on patient engagement meetings, workshops, and activities to coordinate patient engagement activities and [Patient-Focused Drug Development](#) (PFDD) efforts.

PFDD meetings give FDA a deeper appreciation for the expertise that patients and caregivers can bring to the drug development process. FDA enhances its direct communication with patients through a [patient portal website](#) that gives patients and caregivers a common entry point to the Agency for questions and meeting requests. CBER wants patients and those who advocate on their behalf to know that CBER's door is open, and CBER is committed to developing programs that clarify patient values and advance the science of patient input.



CBER will continue to develop its targeted early engagement programs where product development challenges exist, to promote early interactions prior to filing a regulatory submission. Through these meetings CBER supports dialogue, education, and input from prospective innovators and developers of new products and technologies. These medical products introduce unique challenges: unknown safety profiles, complex manufacturing technologies and issues, incorporation of innovative devices, and the use of cutting-edge testing practices. To address these challenges in the development of innovative products, CBER developed the CBER [Initial Targeted Engagement for Regulatory Advice on CBER products](#) (INTERACT) program.

The INTERACT program fosters industry engagement with CBER on issues critical to early product development. INTERACT meetings help innovators meet the FDA's science-based requirements more effectively. These meetings help to streamline development by avoiding unnecessary pre-clinical studies. They also provide an opportunity to collaboratively plan initial clinical development tactics. These meetings are especially critical as advances in science and technology complicate the development process. For example, CBER is witnessing a surge of cell and gene therapy products entering early development, and this program has been heavily used by the sponsors of these products. These meetings can also help move forward the development of vaccines and therapeutics for emerging infectious diseases.

CBER also encourages the development and adoption of advanced technologies to modernize manufacturing. This modernization effort aims to create a more robust manufacturing process with fewer interruptions in production, fewer product failures before or after distribution, and greater assurance that the medical products manufactured will provide the expected clinical performance. An example of a pathway to provide early interaction with developers

of advanced manufacturing technologies is the CBER Advanced Technologies Team (CATT) meeting program, where interested parties have access to early interactions with CBER prior to filing a regulatory submission.

To achieve Objective 1.2, CBER will employ the strategies below.

Strategy 1.2.1 | Engage with patients and their caregivers to obtain their input.

Strategy 1.2.2 | Facilitate early interactions with developers of innovative technologies and manufacturing methods intended to be utilized or applied by regulated medical products to enhance dialogue and clearly communicate regulatory expectations.

Strategy 1.2.3 | Engage with internal stakeholders to increase awareness of and obtain feedback about patient engagement programs and activities.

Strategy 1.2.4 | Leverage external expertise to enable application of innovative approaches to advance manufacturing technologies.

OBJECTIVE 1.3 | Advance the evaluation of product safety and efficacy with innovative statistical and epidemiological approaches, analysis of patient input, and bioinformatics.

CBER works to expand the utility of RWD and Real-World Evidence (RWE) to inform the discovery, development, and delivery of new biological products for patients, provide high-quality evidence about risks and benefits in practice, and inform which products are most appropriate for which patients. As new technologies and scientific methods emerge, CBER will implement new approaches to the use of RWD to evaluate safety and efficacy where feasible. By accessing existing data sources, such as electronic health records (EHRs), claims and billing data sources, product and disease registries, patient-generated data including in home-use settings, and data gathered from other sources that can inform on health status, such as mobile devices, CBER can expand the RWD available to make more informed regulatory decisions.

CBER will promote the use of RWE in regulatory submissions by encouraging sponsors and applicants who are using RWD to use a simple, uniform format. This approach allows CBER to more effectively track how RWE is used in product applications. This information can also be used to assess effectiveness or safety outcomes in randomized clinical trials or in observational studies.

After a product has been approved, AI and machine learning techniques allow CBER to leverage the vast amount of available RWD to improve approaches to monitoring post-market safety and adverse events. CBER's RWE priority is to improve product surveillance by using large databases and new analytical tools to continuously monitor approved products once they are on the market. These techniques allow CBER to gain a deeper understanding of a medical product's safety, benefits, and limitations. Increased surveillance is also important during a pandemic to track vaccine adverse events for new products or products that have been expanded to a larger or different population. For example, CBER's use of Medicare databases and the development of specialized tools has already provided key information regarding the effectiveness of high dose influenza vaccines in the elderly.

The Biologics Effectiveness and Safety (BEST) System was launched in October 2017 to expand and enhance CBER access to new and better data sources, methods, tools, expertise and infrastructure to conduct surveillance and epidemiologic studies. The surveillance of biologics is slightly different from that of drugs, therefore the BEST Initiative was built with those requirements integrated into its building blocks. It leverages RWD from multiple electronic healthcare sources and provides evidence for regulatory decisions. The system consists of large-scale administrative claims, EHRs, and linked claims-EHR data sources with a short data lag. It also has access to on-demand

sophisticated analytic capabilities to interrogate the data sources with simple or complex studies. The BEST Initiative collaborates with multiple partner organizations that provide access to healthcare data and scientific expertise.

CBER uses patient preference information (PPI), a promising strategy, and will continue to advance the science of identifying, collecting, and evaluating patient input to inform regulatory decision making. CBER continues to explore existing and new ways to effectively integrate patient input data into its regulatory framework. CBER's [Science of Patient Input](#) (SPI) initiative and CBER's Rare Disease program support the advancement of patient engagement and PFDD. SPI activities include supporting studies on methods and tools to obtain patient input and providing CBER reviewers with assistance in the regulatory review of patient input and patient-reported outcomes data. CBER's Rare Disease program facilitates the incorporation of the patient perspective in regulatory decision making for biologics that treat rare diseases.

CBER also encourages stakeholder development of [Patient-Reported Outcome](#) (PRO) instruments. A PRO is any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else. PRO is a tool that can be used in trials to directly measure the effect of a medical treatment by how the patient feels and functions. Integrating these measures into the design of a clinical study is one way to enhance a patient's assessment of a medical product's effects.

To achieve Objective 1.3, CBER will employ the strategies below.

Strategy 1.3.1 | Advance the CBER Biologics Effectiveness and Safety (BEST) Initiative for conducting active biologic product safety and effectiveness studies that inform regulatory decisions.

Strategy 1.3.2 | Apply new, innovative methods such as machine learning to automate reporting of adverse event (AE) information.

Strategy 1.3.3 | Leverage technologies, knowledge, infrastructure and external expertise to develop the tools, standards, and approaches required to assess safety and efficacy of innovative products.

Strategy 1.3.4 | Develop and implement scientific methods to obtain and analyze patient input to incorporate into the work performed at CBER.

OBJECTIVE 1.4 | Provide risk-based oversight of product compliance in keeping with regulatory policy to help ensure that approved products are safe, effective, and available, and that unapproved treatments are not on the market.

CBER ensures the quality of the products it regulates over their entire lifecycle through pre-market review and inspection, and post-market review, surveillance, inspection, outreach, and compliance actions. CBER develops regulatory policies and compliance standards that apply a risk-based approach to protect patients from poor quality, unsafe, and ineffective medical products.

Products that are marketed without FDA approval or have significant deviations from cGMP requirements can put patients at risk. CBER monitors the quality of marketed medical products through surveillance, inspections, and compliance procedures and takes appropriate action when patients are put at risk. In addition to putting patients at risk, innovative products that are reliably and carefully developed will be harder to advance if bad actors are able to make hollow claims and market unsafe products. To ensure the safety of patients and confidence in future products

approved by FDA, CBER will continue to take regulatory and compliance action against companies and individuals that market potentially unsafe therapies to patients.

Oversight activities are also conducted before a biologic is approved for the market or to evaluate changes in manufacturing processes submitted by industry. As part of the CBER-managed review process, CBER leads pre-approval and pre-license inspections supporting [Biologics License Application](#) (BLA) submissions and supplements, evaluates proposed proprietary names and other factors that contribute to medication errors, conducts lot release testing for vaccines and develops protocols, and directs CBER's bioresearch monitoring program with oversight of clinical investigators, institutional review boards, and sponsors of clinical research for biological products.

Shortages of biologic medical products pose a significant public health threat, delaying, and in some cases even denying, critically needed care for patients. Quality problems at the manufacturing facility are the most common causes of CBER-regulated product shortages, though other causes may include increased demand, corporate delays, production changes, unavailability of materials, new indications, decisions to discontinue the product, or natural disasters. CBER understands the importance of access to CBER-regulated products that patients and healthcare providers need and works with manufacturers to monitor and mitigate product shortages. CBER encourages early and open dialogue between FDA and manufacturers, which is critical to the success in mitigating shortages. When appropriate, CBER will use regulatory flexibility, such as expedited reviews, lot releases, and expiration date reviews to prevent or mitigate shortages.

To achieve Objective 1.4, CBER will employ the strategies below.

Strategy 1.4.1 | Develop regulations, policies, and procedures for CBER-regulated products and work to ensure their uniform application.

Strategy 1.4.2 | Monitor the quality of marketed CBER-regulated products through surveillance, inspections, and other mechanisms; and review, evaluate and take appropriate regulatory and compliance action.

Strategy 1.4.3 | Take compliance action where appropriate to protect the public health.

Strategy 1.4.4 | Monitor, evaluate, and mitigate product shortages, when possible.

GOAL 2 | Conduct research to address challenges in the development and regulatory evaluation of medical products.

CBER's goal is to conduct scientific research of the highest quality and relevance that is integral to the Center's regulatory mission and public health portfolio. To fulfill this goal, CBER must continually enhance the knowledge of staff to ensure they are integrating and applying relevant knowledge when evaluating the benefits and risks of products. The research CBER performs is proactive, anticipating regulatory and public health needs. Additionally, CBER's research directly supports CBER's regulatory decision-making and policy development responsibilities.

CBER continues to identify the best available science to advance product development and review so that progress and innovation in science can benefit patients and the public. CBER research efforts are important because they typically address a need for an entire class of medical products, whereas sponsors and industry experts only conduct research on a specific product for development. By broadening the scope of CBER's research and publishing the outcomes in peer-reviewed scientific journals, CBER makes innovative models and methods easily available to all stakeholders.

CBER engages its leadership team in decision-making and leverages unique internal knowledge and external expert input to support a balanced approach to developing and evaluating CBER's research programs in order to ensure the research is supporting CBER's regulatory mission and of the highest scientific quality.

The following objectives define how CBER will progress on this goal.

OBJECTIVE 2.1 | Develop and evaluate technology and tools to support non-clinical evaluation of medical products.

Non-clinical studies provide critical proof-of-concept and safety data to support "first-in-human" clinical trials. Oftentimes, phase one clinical trials include specialized safety monitoring informed by data from non-clinical studies. As clinical evaluation progresses from phase one to later phases, non-clinical studies support clinical dose selection and may also be used to evaluate product effectiveness.

For example, CBER conducted non-clinical studies to support the development of a COVID-19 vaccine. CBER scientists identified specific areas on the so-called 'spike protein' of SARS-CoV-2, the virus that causes COVID-19. In order to better understand the various antibody responses triggered by spike-protein-based vaccines, scientists evaluated the quality of antibody responses in rabbits triggered by various SARS-CoV-2 spike antigens that are similar to those being used to develop vaccines to prevent COVID-19. These insights into the immune responses to specific areas of the spike protein could help scientists predict and evaluate whether vaccines under development will offer clinical benefit.

For some biological products, little is known about the mechanism of action or what would be a good *in vitro* or *in vivo* model to evaluate their safety and potential effectiveness. CBER research aims to fill those gaps by developing and evaluating methods and models to ensure quality, consistency, and performance of regulated products. In the development of new methods and models, CBER is applying the principles of refinement, reduction, and replacement of animals where possible. For example, past research efforts have led to replacement of lot release safety testing of

the oral poliovirus vaccine in non-human primates with a combination of newly developed in vitro assay and a neurovirulence test in transgenic mice.^{2 3 4}.

Regulatory evaluation of modeling and simulation is advancing alongside the power and sophistication of information technology (IT). Therefore, FDA formed an Agency-wide working group on modeling and simulation with objectives that include advancing the Agency's ability to facilitate modeling and simulation in product development and FDA's regulatory processes.

For example, CBER is actively engaged in research on the use of *in silico* approaches for predicting immune responses to therapeutic proteins, which is the fastest growing class of medical products. Immune responses reduce the efficacy of these medications and can cause severe adverse effects, which can lead to companies abandoning development during or after clinical trials. CBER worked with one such company, whose drug development was stopped during clinical trials due to immunogenicity issues. Together, they provided a validation of the *in silico* and other non-clinical approaches and used a CBER-developed algorithm to correctly identify all patients in the clinical trial who had developed anti-drug antibodies. Their work is now in the public domain for all companies and clinicians to use.



CBER will support the application of novel technologies for advanced manufacturing. Modernization of manufacturing processes improves the agility, flexibility, cost, and reliability of manufacturing products such as vaccines and cell- and gene-based therapies to improve the health of patients. FDA will continue to build its intramural regulatory science program and leverage outside knowledge to foster innovation in the development and creation of more modern, domestically-based manufacturing. For example, CBER will facilitate the development of technologies that may enable rapid, reliable scale-up of cellular therapies and viral vectors typically used for delivery of therapeutic genes. These improvements could enable more people living with rare diseases in the United States and around the world to benefit from such treatments.

To achieve Objective 2.1, CBER will employ the strategies below.

Strategy 2.1.1 | Develop and evaluate methods and models to ensure quality, consistency, and performance of regulated medical products.

Strategy 2.1.2 | Support development of methods and approaches based on advanced computational approaches to include artificial intelligence.

² Chumakov KM, Powers LB, Noonan KE, Roninson IB, Levenbook IS. Correlation between amount of virus with altered nucleotide sequence and the monkey test for acceptability of oral poliovirus vaccine. *Proc. Natl. Acad. Sci. USA* 1991; 88:199-203.

³ Neverov A, Chumakov K. Massively parallel sequencing for monitoring genetic consistency and quality control of live viral vaccines. *Proc. Natl. Acad. Sci. USA* 2010; 107:20063-8.

⁴ Dragunsky E, Chernokhvostova, Y., Taffs, R., Chumakov, K., Gardner, D., Asher, D., Nomura, T., Hioki, K., Levenbook, I. TgRVR21 mice for testing type-3 oral poliovirus vaccines: role of clinical observation and histological examination. *Vaccine* 1997; 15:1863-6

Strategy 2.1.3 | Support the application of novel technologies for advanced manufacturing of complex biologic products and innovative analytical approaches to improve product manufacturing and quality.

OBJECTIVE 2.2 | Enhance the validity and efficiency of clinical evaluation through use of innovative statistical, analytical, and modeling approaches.

CBER will improve clinical evaluation of product efficacy and safety through research on biomarkers⁵ and bioassays⁶. Biomarkers can provide researchers interim evidence about the safety and efficacy of treatments and can allow researchers to stop interventions that may be harmful to patients before the associated clinical data would be available. In other cases, biomarkers may allow researchers to design smaller, more efficient studies, reducing the number of patients exposed to a given experimental treatment. In addition, to keep trial participants safe, the use of biomarkers, and their qualification under the process, can help to accelerate the development and availability of safe and effective products.

Novel products can require new tools and techniques for evaluation and review. CBER will work to improve product safety and efficacy in both pre- and post-market settings through use of decision tools to support drug development and review. CBER will continue working to develop and promote the use of Drug Development Tools (DDTs), which are methods, materials, or measures that have the potential to facilitate drug development. Examples of DDTs may include but are not limited to: a biomarker used for clinical trial enrichment, a bioassay used to determine the potency of a biological product, or clinical outcome assessments.

In addition to conducting its own research to improve the use of biomarkers, CBER will continue to convene government agencies, academia, industry, and other stakeholders to discuss the scientific, clinical, and regulatory challenges encountered in the identification, characterization, and qualification of biomarkers for preventive vaccines. For example, FDA, in collaboration with the [National Institutes of Health](#) (NIH) and [Coalition for Epidemic Preparedness Innovations](#) (CEPI), convened a [public workshop](#) titled "Identification and Use of Biomarkers to Advance Development of Preventive Vaccines" to actively exchange information with stakeholders.

CBER conducts research to develop and evaluate bioassays that are faster and more versatile than those being currently used. For example, FDA developed a poliovirus assay that is the first to measure the amount of several different strains simultaneously in a mixture of polioviruses, enabling the assay to rapidly process the large number of fecal samples collected from subjects during clinical trials, thereby facilitating public health surveillance of the vaccine virus in the environment. The assay thus offers a better way to track poliovirus by simplifying and speeding [high-throughput processing](#) of samples, which will be useful for achieving the [Global Polio Eradication Initiative](#) (GPEI) goal of eradicating polio worldwide.

While CBER continues to improve clinical evaluation of product efficacy and safety through research on biomarkers and bioassays, CBER also encourages sponsors to explore the relationship between exposure and effectiveness and safety endpoints during development. Exposure-response relationships using biomarkers from early dose-finding studies can help identify dose and dosing regimens for controlled effectiveness studies. Importantly, assessment of

⁵ Biomarkers are objective indications of the patient's medical state that can be measured accurately and reproducibly. In contrast, clinical endpoints are variables that reflect how a subject in a study or clinical trial "feels, functions, or survives." Clinical endpoints, such as survival or cardiovascular events, occur so infrequently that their use in clinical trials can be impractical, or even unethical.

⁶ Bioassays provide a measure of potency by evaluating a product's active ingredient(s) within a living biological system.

exposure-response can also contribute to interpretation of evidence of effectiveness from controlled studies. The exposure-response relationship can determine the need for dose adjustment for various extrinsic and intrinsic factors, such as drug interactions and organ impairment.

The science of patient input refers to scientific methods to quantitatively measure patient perspectives to inform clinical evaluation of medical products and assessment of their post-market safety. CBER uses these methods for two main purposes: measuring patients' perceptions of their own health status (e.g., patient-reported outcome measures or PROMs) and quantifying their benefit-risk tradeoff preferences between outcomes associated with treatments of interest or PPI. CBER is conducting multiple studies to solicit and leverage PPI from external patient groups for the assessment of post-market safety data. One such study is a collaboration with National Organization for Rare Disorders (NORD) on the design and conduct of a pilot national history study, which will serve as a potential source of external control that can provide additional power for the future Random Clinical Trials (RCTs) of CBER-regulated therapies of metachromatic leukodystrophy. In addition, the aforementioned BEST Initiative is being used to provide technical support to implement a mobile application to collect PROMs as measurement tools to capture specific patients' health status (e.g., pain intensity) that cannot be measured physiologically. CBER has applied PROMs to clinically evaluate medical products by including study endpoints in confirmatory trials and measuring product burdens on patients (e.g., side effects) for post-market safety assessment.

CBER will promote the use of these approaches to facilitate the development of more efficient strategies to assess the safety and efficacy of medical products, including techniques such as Model-Informed Drug Development (MIDD). MIDD approaches use a variety of quantitative methods to balance the risks and benefits of drug products in development. When successfully applied, MIDD approaches can improve clinical trial efficiency, increase the probability of regulatory success, and optimize drug dosing/therapeutic individualization in the absence of dedicated trials. CBER participates in FDA's [MIDD Pilot Program](#), which allows selected sponsors or applicants to meet with Agency staff to discuss the development and application of exposure-based, biological, and statistical models derived from pre-clinical and clinical data sources.

Because clinical trials are typically designed to assess efficacy, single studies rarely have enough power to provide reliable information regarding adverse effects, especially when these adverse events are rare. Meta-analysis provides a useful framework for combining information across related studies and has been widely utilized to combine data from clinical studies in order to evaluate treatment efficacy. More recently, meta-analysis has also been used to assess drug safety.

In recent years, there has been an increased scientific demand for more systematic and quantitative approaches to incorporate RWD and patient input throughout the medical product lifecycle, including to inform regulatory benefit-risk assessments. CBER is exploring how RWD can improve benefit-risk assessment processes through enhanced statistical methods, mathematical modeling, computer simulation, and patient input.

Benefit-risk assessment is the foundation of FDA's review process. CBER will continue to advance benefit-risk assessment, including improvements in qualitative, and quantitative methods and development of benefit-risk assessment tools. This strategy will be implemented through internal training, engagement with external experts and organizations, methods development through pilot projects, and improved internal processes to integrate appropriate benefit-risk assessment at all stages of the review process. The efforts will also include integration of patient preference information and real world evidence and application of novel individual-level benefit-risk assessment methodology.

As new sources and methods for collecting healthcare data become available, CBER applies tools and techniques to review for biological products to assess the safety and effectiveness of licensed medical products on the market. For example, the Transfusion-Transmissible Infections Monitoring System (TTIMS) tracks HIV, HBV, and HCV infections in

donors for approximately 60% of the US blood supply. The intent is to track whether significant changes are present in the frequency of donor TTI markers attributable to changes in donor characteristics including demographics or geographic distribution, or impact of changes in national blood program policies. Further, CBER will employ machine learning and natural language processing to refine detected potential safety cases and to improve the quality and specificity of the adverse event (AEs) reported to the FDA. CBER will utilize artificial intelligence, to learn from annotated cases and reports, and to develop exposure and outcomes detection phenotypes that are highly scalable and sensitive, and that leverage structured healthcare data, which will facilitate the deployment of these phenotypes on a national scale.

To achieve Objective 2.2, CBER will employ the strategies below.

Strategy 2.2.1 | Improve clinical evaluation of product efficacy and safety in pre- and post-market settings through research on biomarkers and bioassays.

Strategy 2.2.2 | Promote the use of decision tools to support drug development and review, including complex clinical innovative trial designs, model informed drug development, and the drug development tools qualification program.

Strategy 2.2.3 | Improve benefit-risk assessments of regulated products by applying mathematical modeling, computer simulation, preference elicitation, and decision analysis techniques.

Strategy 2.2.4 | Develop and apply best practices for causal inferences and meta-analyses to investigate product safety.

Strategy 2.2.5 | Apply real-world evidence and patient input methods to clinical evaluation and into the assessment of post-market safety data.

Strategy 2.2.6 | Develop and implement methods, including the use of artificial intelligence, to improve the use of healthcare data to enhance monitoring of the safety and effectiveness of licensed biological products.

OBJECTIVE 2.3 | Proactively address public health challenges and emerging infectious diseases.

A robust intramural research program with diverse expertise and experience positions CBER to proactively facilitate development of innovative medical products addressing a variety of public health challenges from rare genetic disorders to cancer while also providing rapid responses to emerging infectious diseases (EIDs). CBER's overall approach is to create a collaborative research environment to ensure synergies, avoid duplication, support data and reagent sharing, and to effectively manage resources. The research program is led by intramural research scientists who proactively develop and evaluate assays and models that may be easily adapted to study emerging threats.

As infectious diseases emerge that pose a threat to public health, CBER's variety of expert capabilities furthers its ability to support development of medical products by being able to quickly extend research programs in related scientific problems to address the current challenge. For example, in response to the COVID-19 pandemic, CBER scientists quickly engaged to support CDRH in developing a reference panel for distribution to diagnostic manufacturers to aid in assessing the assay sensitivity and specificity. In addition, CBER scientists developed animal models to evaluate COVID-19 pathogenesis and immune responses to prototype vaccines, and are developing assays

to assess the immune response to vaccines and to improve our understanding of potential COVID-19 targeted therapeutics regulated by CBER.

In addition to responding to infectious disease threats to public health, CBER also provides more proactive support to enable development and availability of novel biological products, such as cell and gene-based therapeutics, to treat a range of diseases from cancer to rare genetic disorders, including those affecting one or a few individuals. CBER’s research program addresses key scientific gaps that need to be studied to improve understanding of how to characterize innovative, promising, yet biologically complex therapeutic products. For example, CBER is developing and evaluating new methods to reliably characterize stem cell-based therapies. Another important area being addressed by CBER’s research program is to develop tools and data to improve evaluation of gene therapies based on genome editing. CBER researchers develop assays, methods, and models to facilitate product characterization that can be adapted by regulated industry to support product development.

CBER’s research program also addresses scientific gaps to improve CBER’s understanding of how to characterize individualized therapies as a path for treatment for patients with rare diseases. CBER’s research to address the challenges and opportunities for individualized therapies spans the development process, including manufacturing and assurance of product quality, preclinical testing, clinical safety and effectiveness evaluation, and sustainability to facilitate novel therapeutic agents for patients with rare diseases.

To effectively respond to emerging infectious diseases, CBER strives to balance the availability of blood for life-saving transfusions and reduction of the risk of transfusion-transmitted infectious diseases (TTID). CBER develops and evaluates reference panels for screening and confirmatory tests for TTID agents and retroviral diagnostics. Additionally, CBER develops and characterizes novel technology for screening assays used to identify donors suitable for donation of tissues, cells, and plasma proteins for therapeutic use. For example, to protect the national blood supply against pathogens, CBER develops ribonucleic acid (RNA) reference standards that sponsors use to evaluate the sensitivity, specificity, and reproducibility of proprietary nucleic acid-based tests intended for clinical diagnosis or blood screening for emerging and reemerging viruses.



CBER also applies enhancements in EID rate and risk assessment protocols to the development and application of new tools or universal pathogen reduction technologies. Pathogen reduction technology has the potential to improve blood safety by reducing or eliminating infectious organisms, including bacteria, viruses, and parasites, from blood components intended for transfusion. Through investments in intramural and extramural research, CBER is evaluating the ability of technology to inactivate a range of pathogens and the functionality of blood components after exposure to pathogen reduction technology.

In addition to protecting the blood supply from infectious disease, CBER facilitates the development of novel vaccines and improves the availability of approved vaccines to immunize the public prior to EID exposure, thereby decreasing the number of infections. To study novel vaccines, CBER often develops assays that are rapid, accurate, and easy to perform to detect neutralizing antibodies. New approaches to measuring neutralizing antibodies use a platform technology that can be quickly adapted to many predicted or unknown threats, thereby enabling readiness for the next unknown pandemic threat.

To support preparedness for potentially pandemic strains of influenza, CBER scientists identify strain prevalence, develop candidate vaccine strains, generate reagents that are distributed to manufacturers for lot release testing, and conduct an independent verification of lot release testing results. CBER is developing and evaluating new methods for determining influenza vaccine potency. In addition, CBER is exploring new manufacturing methods to retain a higher level of neuraminidase in influenza vaccines to increase the potency. CBER scientists are also developing improved

and simplified methods for the manufacturing of polysaccharide conjugate vaccines. In addition, CBER conducts research to develop or use models to identify immune response that may serve as correlates of protection to a vaccine for a variety of infectious diseases, such as tuberculosis, pertussis, and others.

CBER incorporates scientific advancements into its regulatory framework to expedite availability of beneficial innovations to consumers. By adopting advanced science and risk management tools to inform policy, FDA helps to advance science and technology to design better ways of predicting and evaluating the safety, purity, potency, and effectiveness of biological products early in their lifecycle.

To achieve Objective 2.3, CBER will employ the strategies below.

Strategy 2.3.1 | Develop and study approaches to facilitate development and availability of novel biological products, including innovative approaches to advance individualized therapies.

Strategy 2.3.2 | Assess and promote safety and effectiveness of transfusion-transmitted infectious disease agent donor screening and supplemental tests, retroviral diagnostics, transfusion products and related devices.

Strategy 2.3.3 | Develop and facilitate application of innovative technologies toward universal pathogen reduction of the blood supply.

Strategy 2.3.4 | Enhance safety and effectiveness of donor screening tests, devices and technologies used in sourcing, manufacturing, processing, and/or testing of tissues and advanced therapeutics.

OBJECTIVE 2.4 | Advance scientific capabilities to assess novel technologies and innovative medical products to inform regulatory oversight.

CBER's research program must keep pace with the rapid innovation in biologics to ensure that CBER's regulatory decisions and policy-making are informed by the latest science and technology. To achieve this goal, CBER will continue to maintain a robust scientific infrastructure to support key scientific activities by ensuring that CBER's labs and core research facilities remain up to date with emerging technology. CBER will also meet CBER's advanced computational needs through maintaining and evolving the CBER High-performance Integrated Virtual Environment (HIVE).

CBER will engage in effective management of research resources, ensuring transparency to the research community, and accountability to external stakeholders. Finally, results from ongoing research will be shared with all stakeholders through peer-reviewed research publications, external scientific presentations, and internal reviewer training to ensure translation of findings to regulatory decision-making. Through these activities, CBER will increase the impact of applied research by facilitating the development of innovative medical products that contribute to improved care and increased quality of life.

To effectively manage its resources, CBER uses a single-impact framework to plan, evaluate, and communicate its research. The framework evaluates research projects using four broad categories:

1. Prospective evaluation of new research proposals to ensure alignment with scientific and review capability goals and objectives;

2. Retrospective evaluation of scientific productivity as measured by dissemination of research findings through presentations and publications in scientific peer-reviewed journals;
3. Ongoing evaluation of scientific impact measured by scientific community and regulated stakeholder uptake; and
4. Long-term evaluation for contribution to regulatory practice.

CBER employs a Research Program management structure that includes the Resource Committee, the CBER Regulatory Science Council (RSC), and CBER’s research in human subjects protection liaison with oversight from the CBER Center and Deputy Director and Associate Director for Science. Additionally, CBER’s research programs undergo periodic external peer review both at the level of Private Investigator (PI)-led research programs, and broader reviews of the Office and Center research portfolios. Effective use of leadership engagement, unique internal knowledge, and external expert input support a balanced approach to research review and oversight and provides assurance of the relevance, impact, and highest scientific quality.

CBER’s research program relies on the insights of Researcher-Reviewers who are research scientists who perform research while also performing the same regulatory duties as full-time reviewers. These scientists observe the scientific advances they hear about through their research in the regulatory submissions they review. Therefore, they can propose new research projects that uniquely use CBER’s capabilities to address regulatory needs. Thus, the researcher-reviewer model and investigator-initiated projects form the foundation of CBER research.



CBER scientists will continue to support relevant scientific working groups identified by forums such as the Senior Science Council by identifying subject matter experts to participate in discussions on high priority, cross-cutting topics.

CBER will continue to build upon its scientific infrastructure to advance development of complex and innovative medical products, allowing for a rapid and effective response to public health challenges. To enable rapid responses to address EIDs, CBER houses ten biosafety level three (BSL-3) laboratory suites⁷ that give CBER scientists the capacity to be responsive to emerging threats. For example, to enable rapid research responses to COVID-19, CBER quickly implemented use of three BSL-3 suites to support a variety of CBER and Center for Drug Evaluation and Research (CDER) research needs, including evaluation of a new animal model to assess vaccine immune responses. To the extent possible, CBER will also invest in its core facility laboratories including the Facility for Biotechnology Resources (FBR), Flow Cytometry Core (FCC), and Microscopy and Imaging Core Facility, to ensure research tools and equipment keep pace with emerging technologies. Through the FDA’s Shared Resources Program and other Center-specific agreements, CBER supports research in other FDA Centers by allowing investigators to use CBER’s core facilities in a cost-sharing program. Similarly, CBER researchers leverage the access to other cutting-edge technologies that are available to the FDA community through core facilities in other centers, such as the 3D printing core in CDRH, among others.

As CBER invests in physical infrastructure, it must also focus on the improvement of its technological infrastructure to meet the advanced computational needs of large, complex data analysis. CBER plans to use FDA high-performance computing assets such as the CBER HIVE to develop computational tools to expedite analyses. Such tools can be used

⁷ The primary risk criteria used to define the four ascending levels of containment, referred to as Biosafety Levels 1 through 4, are infectivity, severity of disease, transmissibility, and the nature of the work being conducted. The facility safeguards associated with Biosafety Levels 1 through 4 help protect non-laboratory occupants of the facility, the public health, and the environment.

to support the analysis and interpretation of next generation sequencing data from CBER’s intramural research, as well as data submitted by a manufacturer in support of a product development or a licensing application.

CBER is an active contributor to the FDA Technology Transfer Program, whose goal is to transfer FDA technologies to the market in support of public health. This is especially important for critical emerging technologies with an impact on FDA-regulated products, such as advanced manufacturing, artificial intelligence, and next generation sequencing.

CBER is committed to using our research program as a fertile ground for training scientists through a variety of programs available to post-baccalaureate and post-doctoral individuals. In addition, CBER promotes the sharing of information learned from ongoing research and development, and to provide opportunities for scientists at all career stages to participate in scientific and professional meetings and conferences, present their most current research, and develop collaborations and relationships with academic institutions. In turn, these relationships provide FDA with access to cutting-edge science through a collaborative network. CBER scientists also are encouraged to attend courses, workshops, and seminars to accommodate the fast pace of innovation and understand the depth and breadth of regulatory research needed to address novel technologies.



To achieve Objective 2.4, CBER will employ the strategies below.

Strategy 2.4.1 | Develop and improve scientific infrastructure to support scientific core facilities, key technologies, and advanced computational needs.

Strategy 2.4.2 | Manage effective use of research resources through the development of tools and processes to guide governance and research oversight.

Strategy 2.4.3 | Advance impact of CBER-funded research through communication, training, and technology transfer.

Strategy 2.4.4 | Ensure CBER scientists with appropriate expertise participate in and contribute to agency-wide scientific working groups to enable cross-Center communication, collaboration, and education.

GOAL 3 | Increase preparedness for emerging threats and promote global public health.

During public health emergencies, the American public relies on CBER to act quickly and ensure the availability of [medical countermeasures](#)⁸ (MCMs). To proactively enhance preparedness for response, CBER identifies scientific and regulatory issues that challenge MCM development or use during public health emergencies. Concurrently, CBER works interactively with MCM developers during product development and regulatory review to address those issues. Finally, CBER implements strategies to expedite the development, evaluation, and availability of MCMs during a public health emergency.

Many of the products FDA regulates directly address infectious disease threats that are not unique to the U.S. That means the discovery, development, production, and distribution of its regulated products is a globalized enterprise. To continuously improve international convergence on policy and medical product development, CBER carries out its regulatory responsibilities through international engagements that support both national and global public health. These engagements lead to aligned international collaborations that enable a rapid and effective response to public health emergencies using established communication channels, relationships, and partnerships.

CBER participates in meetings of the [International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use](#) (ICH). ICH is a unique harmonization project by which regulator and industry representatives work to improve the efficiency of the new drug development and registration process, promote public health, prevent duplication of clinical trials in humans, and minimize the use of animal testing without compromising safety and effectiveness. To stay aligned with international partners, CBER adopts the technical guidance that ICH harmonizes. CBER also collaborates with other organizations such as the World Health Organization (WHO), International Pharmaceutical Regulators Programme (IPRP), Asia-Pacific Economic Cooperation Regulatory Harmonization Steering Committee (APEC RHSC) and other venues to promote global convergence, facilitate development and access to safe and effective medical products, and strengthen preparedness to respond to public health emergencies of international concern.

The following objectives define how CBER will progress on this goal.

OBJECTIVE 3.1 | Facilitate timely access to safe and effective medical products during public health emergencies.

During public health emergencies, MCMs may be needed to prevent or treat diseases or conditions caused by chemical, biological, radiological and nuclear threats (CBRN) or EID threats, like pandemic influenza. CBER stands ready to employ and adapt existing regulatory tools for maximum effect to make these products readily available in the event of a public health emergency.

When there are no FDA approved products to prevent, treat, or diagnose an emerging threat, CBER's key focus is helping to expedite the development and availability of medical products needed to diagnose, treat, mitigate and prevent a disease. These efforts include facilitating the availability of unapproved products, when appropriate, through Expanded Access Programs (EAP) and Emergency Use Authorization (EUA) of investigational products and unapproved uses of approved MCMs, as well as ongoing work that provides regulatory advice, guidance, and technical assistance to facilitate product development. CBER develops guidance to provide its policy perspectives and

⁸ MCMs are medical products such as drugs, vaccines, diagnostic tests, and other medical equipment and supplies, needed to respond to emergencies.

recommendations on a wide variety of topics that may be of special interest to existing or prospective MCM sponsors, and other stakeholders, including [state, tribal, local and territorial public health preparedness](#) personnel.

During public health emergencies, CBER is forward-thinking, innovative, and responsive, using every available tool to help patients access promising biological products, while also facilitating research to evaluate their safety and efficacy and manufacturing efforts. In response to the COVID-19 pandemic, CBER worked with government partners to help establish the National Expanded Access Treatment Protocol to facilitate access to convalescent plasma for patients with COVID-19. In addition, CBER also worked with industry and government partners to accelerate the development and availability of human SARS-Cov-2 immunoglobulin for investigation into potential COVID-19 treatments, while also providing technical assistance to help establish the Inpatient Treatment with Anti-Coronavirus Immunoglobulin (ITAC) study led by the NIH. Furthermore, CBER launched the Coronavirus Treatment Acceleration Program (CTAP) along with CDER to leverage cross agency resources and expertise to bear on COVID-19 therapeutic development and review. CBER also works with product developers and researchers to help complete regulatory submissions, such as pre-Investigational New Drug (pre-IND) submissions and IND applications which can help to facilitate the timely review of such submissions and the rapid initiation of clinical trials of products being studied for the treatment or prevention of COVID-19, including reviewing and granting original and emergency INDs for COVID-19 convalescent plasma, hyperimmune globulins, and vaccines.

CBER also supports preparedness for and response to CBRN and EID threats by facilitating the availability of MCMs, blood, and tissues. To improve response efforts, CBER works with state and local authorities to support preparedness and response capabilities at the state and community levels. For example, to help the nation prepare for disruptions of blood collection and demand, CBER developed a simulation model to replicate the U.S. blood supply and demand system under various circumstances, including emerging infectious disease outbreaks such as COVID-19. CBER also provides timely guidance to support response efforts during public health emergencies, such as exceptions or alternatives to certain requirements in Title 21 of the Code of Federal Regulations (CFR) regarding blood and blood components. The [Alternative Procedures for Blood and Blood Components During the COVID-19 Public Health Emergency](#) were provided to improve availability of blood and blood components while helping to ensure adequate protections for donor health and maintaining a safe blood supply for patients during the COVID-19 pandemic.



CBER has also approved products, such as vaccines, that are included in the [Strategic National Stockpile \(SNS\)](#); items in the SNS are dispensed or administered to impacted individuals by health care workers and public health responders under official federal, state, and/or local emergency response plans. To avoid a medical product shortage, during a public health emergency, CBER proactively initiates conversations with manufacturers to check on the status of materials that are integral to the manufacturers' supply chains and products produced in the affected areas. CBER's Office of Compliance and Biologics Quality (OCBQ) continues these conversations to understand shortages and/or supply chain issues.

To achieve Objective 3.1, CBER will employ the strategies below.

Strategy 3.1.1 | Stand ready to employ and adapt existing regulatory tools for maximum effect to make products readily available in the event of a public health emergency.

Strategy 3.1.2 | Collaborate with federal partners to identify priorities and facilitate access to available resources.

Strategy 3.1.3 | Collaborate with the WHO, other regulators, manufacturers and NGOs to assure access to safe and effective vaccines, blood and blood products, and other medical products to address public health emergencies.

Strategy 3.1.4 | Anticipate and mitigate shortages of medical products needed in a public health emergency.

OBJECTIVE 3.2 | Facilitate the development and production of critical biological and related products to address public health emergencies.

CBER facilitates the development and production of critical medical products through continued collaboration with the [World Health Organization](#) (WHO), other regulators, manufacturers, non-governmental organizations (NGOs), and [Public Health Emergency Medical Countermeasures Enterprise](#) (PHEMCE)⁹ partners. Together, these stakeholders work to advance development of vaccines, and other medical products for pathogens with epidemic potential.

To support PHEMCE efforts, CBER identifies scientific and regulatory issues that challenge MCM development or use during public health emergencies, assists MCM developers in working interactively with FDA during product development and regulatory review, and establishes and implements strategies to expedite the development and evaluation of MCMs during a public health emergency.

To ensure that information and updates are continuously shared with stakeholders, CBER 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 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 Forum** (NASEM-HMD) 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.



With so many stakeholders, CBER recognizes the importance of internal agility and rapid responses to address public health emergencies. To be prepared for such emergencies, CBER maintains internal expertise through research and strategic organization. This includes CBER's participation in Incident Management Groups (IMGs) to more efficiently interact with stakeholders during a public health emergency when an incident involves multiple FDA organizational components. This structure enables CBER to work more effectively with Agency counterparts in support of a coordinated response with HHS and the U.S. Government (USG) as dynamic, public health threats evolve.

⁹ PHEMCE coordinates Federal efforts to enhance CBRN and EID preparedness from an MCM perspective. The PHEMCE is led by the HHS Office of the ASPR and includes three primary HHS internal agency partners: [Centers for Disease Control and Prevention](#) (CDC), the FDA, and the NIH, as well as several interagency partners: the [Department of Defense](#) (DoD), the U.S. Department of [Veterans Affairs](#) (VA), the [Department of Homeland Security](#) (DHS) and the [U.S. Department of Agriculture](#) (USDA).

The surveillance element of CBER’s response strategy allows CBER to monitor and assess MCMs after they are dispensed or administered in response to a CBRN threat or an EID. Experiences responding to public health emergencies highlight the need for a coordinated plan to leverage every opportunity to learn more about an MCM’s performance. This information is vital to protecting public health, particularly in the case of MCMs that may have limited human efficacy data prior to their use. The emergency may present the only opportunity for clinical assessment. For example, CBER conducts post-authorization/approval surveillance for COVID-19 vaccines as part of CBER’s response strategy to address MCM safety concerns and minimize risk.

FDA and the Centers for Disease Control and Prevention (CDC) recognize the need for an expansive collaborative effort in the pharmacovigilance area. US government agencies including the FDA, CDC, Center for Medicare & Medicaid Services (CMS), the Department of Veterans Affairs (VA), the Department of Defense (DoD), and the Indian Health Service (IHS) are working together in a coordinated effort to monitor the safety of newly authorized or approved COVID-19 vaccines. The Pharmacovigilance Plan (PVP) requires companies to submit PVPs as part of their pre-authorization or pre-licensure submission that detail proposed approaches to safety specifications. The safety profile of each COVID-19 vaccine may be different as will the PVP that is tailored to identify and address the safety specifications, which may include additional safety studies, observational studies, and other areas to address identified safety questions.

Innovations in manufacturing technology help to:

- **Rapidly scale manufacturing capabilities** for vaccines and other MCMs to respond faster to emerging threats and other public health emergencies, such as pandemic influenza.
- **Shorten supply chains and increase manufacturing resilience** to disruption by emerging threats or public health emergencies, such as natural disasters, by creating a distributed network of small manufacturing sites that can provide reserve capacity for centralized manufacturing facilities.
- **Speed availability of emerging therapies** by enabling manufacturing processes and standards development, including cell and gene therapies, thereby supporting goals of the [21st Century Cures Act](#) (Cures Act).
- **Provide new tools to address drug shortages** and other challenges, including pharmaceutical quality.

Innovations in manufacturing technology are particularly important to CBER because, unlike other medicines, biopharmaceuticals require complex manufacturing processes. For example, there is often more than one type of influenza virus circulating each season, so influenza vaccines are designed to target three or four influenza viruses that are most likely to circulate during the season. Since it generally takes several months for influenza vaccines to be produced, flu strains for the next season need to be selected months in advance to ensure the U.S. is prepared with enough supply when flu season hits.



The potential public health value of advanced manufacturing is even greater in the context of a public health emergency such as the COVID-19 pandemic, which has highlighted the need for adaptive manufacturing systems to accelerate the production of MCMs.

Advanced manufacturing technologies could potentially allow CBER to:

- **Make adjustments** to vaccine strains more easily in the event of an unforeseen change;
- **Produce** safe and effective vaccines for mass distribution quickly in the event of a pandemic; and
- **Scale** manufacturing if vaccine supplies run low.

More broadly, CBER continues to invest in advanced domestic manufacturing to ensure new and existing technologies are scalable. Scalable technology would allow manufacturers to more easily meet domestic and global medical

product demands. For example, CBER is working to facilitate the development of more effective cell lines that can be better scaled through advanced manufacturing technologies, while also looking for ways to design a more robust recombinant vaccine manufacturing process to increase the influenza vaccine production.

FDA is taking steps to help realize the potential of advanced manufacturing, including:

- **Issuing guidance** on Chemistry, Manufacturing, and Control (CMC) Information for Human Gene Therapy Investigational New Drug Applications (INDs) to help guide industry to assess manufacturing process controls, manufacturing consistency, and stability as development advances. This is especially important for sponsors of gene therapy products who are pursuing expedited development programs.
- **Reviewing and approving medical products** that are made with advanced manufacturing technologies.
- **Advancing regulatory science** to proactively address regulatory challenges presented by advanced and continuous manufacturing technologies.

CBER representatives actively participate in ongoing public-private partnerships to proactively address regulatory challenges presented by advanced technologies. These partnerships include USG agencies, academia, research institutes, and industry. Examples of these partnerships include federally supported advanced development and manufacturing Centers, the Manufacturing USA Institutes, and America Makes. Through these partnerships, CBER will continue to promote dialogue, education, and input among CBER staff and between CBER and prospective innovators and developers of advanced manufacturing technologies.

To achieve Objective 3.2, CBER will employ the strategies below.

Strategy 3.2.1 | Collaborate with the WHO, other regulators, manufacturers, NGOs, and Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) partners to advance development of vaccines and other medical products for pathogens with epidemic potential.

Strategy 3.2.2 | Assure agility in maintaining internal expertise to support rapid responses to address public health emergencies.

Strategy 3.2.3 | Promote development and adoption of innovative technologies to facilitate production of medical products to address public health emergencies.

OBJECTIVE 3.3 | Promote international harmonization to facilitate development and availability of safe and effective medical products.

The FDA mission includes the mandate to “participate through appropriate processes with representatives of other countries to reduce the burden of regulation, harmonize regulatory requirements, and achieve appropriate reciprocal arrangements.” In support of this mission element, CBER exchanges critical regulatory information on an ongoing basis with foreign regulatory counterparts.

CBER defines “regulatory harmonization” as the process by which technical guidelines are developed to be uniform across participating authorities. To support these efforts, CBER undertakes information exchanges with counterparts in the Americas, Europe, Africa, Asia and Australia, as well as with international organizations such as the WHO and the [Pan American Health Organization](#) (PAHO). These information exchanges enhance CBER’s ability to expand the pool of expertise and information sources it can draw from to make informed decisions. As a result, CBER ensures the safety and effectiveness of the products it regulates and hopes to earn the public’s trust.

CBER’s information exchanges may consist of publicly available information or may be of a non-public nature when conducted under the Agency’s Confidentiality Commitments, Memoranda of Understanding, and other Cooperative Arrangements. CBER both initiates and responds to ad hoc requests for information exchanges with foreign regulatory counterparts and an international organization such as the WHO on a range of issues, including: product manufacturing issues, potential product shortages, inspectional issues, data interpretation, post-marketing surveillance signals, and preapproval considerations.

CBER also undertakes Parallel Scientific Advice (PSA) with the [European Medicines Agency](#) (EMA). The PSA process is one in which a sponsor seeks joint scientific advice from FDA and EMA on issues related to the development phase of a new product. The benefits of these interactions include: an increased dialogue between the two agencies and sponsors at various points of the lifecycle of a new product, a deeper understanding of the bases of scientific advice, an opportunity to optimize product development, and the avoidance of unnecessary testing replication or unnecessary diverse testing methodologies.

One goal of these regular information exchanges is to build the WHO Member States’ capacity to tackle [Substandard and Falsified](#) (SF) medical products by improving their regulatory capacity in the areas of prevention, detection, and response. To support this effort, CBER’s International Program¹⁰ leads the effort in regulatory capacity building and is involved in information-sharing and training efforts focused on capacity building priorities.



Regulatory capacity building efforts employ multiple modalities, including information sharing, backing initiatives, participating in global engagements and collaborative projects, expert consultation, direct training, hosting foreign counterpart visits, and supporting other organizations’ capacity building and outreach activities. Additionally, CBER continues to offer a web-based capacity building training program that includes an introduction to the U.S. biologics regulatory processes. CBER continues to educate and inform regulators across the globe through its online outreach training.

To assure sustainability of these capacity building efforts, CBER explores partnerships with stakeholders, notably the WHO, to build upon the previous work. CBER’s expansive work with ICH, [International Pharmaceutical Regulators Programme](#) (IPRP), and [Asia-Pacific Economic Cooperation Regulatory Harmonization Steering Committee](#) (APEC RHSC) maximizes collaborative and synergistic activities while harmonizing or converging regulatory ideas and needs of the global community.

CBER is a founding member of the ICH Steering Committee and participates in expert working groups for standardization of technical guidelines. As a regulatory body, CBER works within IPRP to share strategies for harmonizing standards and communicates with other global regulators on priority topics. APEC RHSC plays a primary role in facilitating training mechanisms. To support that effort, CBER contributes to expert working groups in priority areas such as Cell and Gene Therapy product convergence, good clinical practice inspections, consistency and quality of scientific reviews for medical products, and promotion of medical product integrity and supply chain security.

CBER undertakes several structured scientific and policy discussions under confidentiality commitments with foreign regulatory counterparts. “Clusters” are important regulatory discussions that occur throughout the year. These

¹⁰ FDA’s Office of International Programs (OIP) coordinates and facilitates the Agency’s Capacity Building Program which includes technical cooperation and assistance efforts; CBER continues to partner with OIP in many of those activities.

Clusters are established, routine discussions around subject matter areas that involve experts from CBER, other FDA Centers as appropriate, and several international regulatory agencies¹¹. CBER is a principal participant in the Clusters for Blood Products, Advanced Therapy Medicinal Products, and Vaccines. Additionally, CBER participates in the Agency Oncology, Pediatric, Pharmacovigilance, Biosimilar, Rare Disease and Pharmacogenomic Clusters, as appropriate.

In addition to promoting regulatory harmonization and capacity building, CBER strives to achieve “regulatory convergence.” Regulatory convergence represents a process whereby the regulatory requirements across countries or regions become more similar or aligned over time as a result of the gradual adoption of internationally recognized technical guidance documents, standards and scientific principles, common or similar practices and procedures, or adoption of regulatory mechanisms that might be specific to a local legal context but that align with shared principles to achieve a common public health goal.

To achieve Objective 3.3, CBER will employ the strategies below.

Strategy 3.3.1 | Contribute to the development of internationally harmonized standards, both written and physical, that contribute to efficiencies in the development of products that address global public health needs.

Strategy 3.3.2 | Support regulatory convergence through exchanges with regulators at the expert and strategic levels.

OBJECTIVE 3.4 | Enhance interactions with global regulatory authorities and international public health organizations to promote and protect public health.

CBER understands that protection of global public health against infectious disease threats leads to improved public health in the United States. Improving global public health through international collaboration is a CBER strategic priority. By providing scientific and regulatory advice to facilitate development of vaccines and other medical products, CBER contributes to the reduction and spread of infectious diseases globally. Strengthening regulatory systems is key to ensuring increased access to safe and effective biological products, and CBER plays an important leadership role in this effort.

CBER leverages information exchanges to promote and protect public health. To strengthen interaction with global partners, CBER will continue active confidential information exchanges with strategic regulatory counterparts to advance regulatory alignment and joint preparedness. During the COVID-19 pandemic, CBER organizes international meetings to align global regulatory strategies on preclinical and clinical testing requirements for COVID-19 vaccines, in addition to being engaged on a global scale with international partners to provide strategic leadership in the areas of product development, manufacturing, and safety surveillance of high-priority COVID-19 products.

CBER undertakes several structured scientific and policy discussions under confidentiality commitments with foreign regulatory counterparts through Clusters that involve discussions with subject matter experts from FDA and, as appropriate, international regulatory agencies. CBER also engages in technical and policy discussions with the WHO

¹¹ These include the EMA, the [Health Products and Food Branch \(HPFB\)](#) of [Health Canada \(HC\)](#), Government of Japan’s Ministry of Health, Labour and Welfare, and Pharmaceuticals and Medical Devices Agency, and the Therapeutic Goods Administration of Australia.

under confidentiality commitments to prepare for and respond to public health emergencies of international concern, and to support WHO’s vaccine prequalification program.

CBER has a broad range of collaborations with the World Health Organization (WHO). In 2020, CBER reaffirmed its commitment as a WHO Collaborating Center (CC) for Biological Standardization for the term 2020 – 2024. As a WHO CC, CBER experts contribute to development of WHO international reference materials and standards which are used in the U.S. and worldwide to ensure that quality, consistency, and safety of biological products meet the required standards. CBER’s terms of reference as a WHO CC for 2020 – 2024 include:

- Providing technical expertise to support WHO in establishing physical (reference) standards for biologics (vaccines, blood, blood components and derivatives, relevant *in vitro* diagnostic tests, cellular and gene therapy products);
- Providing technical expertise and advice to support WHO in establishing written standards for biologics; and
- Supporting WHO in strengthening regulatory systems, promoting standardization, and enhancing oversight of biologics.

These collaborations also play a central role in preparedness for responding to infectious disease threats. Development of WHO International Standards for infectious diseases with pandemic potential (e.g., pandemic influenza, Ebola, MERS, Zika, SARS-CoV-2 etc.) enhances the ability to respond more quickly with medical countermeasures when these diseases strike the U.S. or global population.

In addition to technical engagement of CBER staff in WHO activities, CBER also has a Cooperative Agreement with WHO to provide funding support to advance projects of mutual interest. Cooperative Agreements support a broad range of activities including benchmarking of national regulatory authorities, training workshops, development of WHO Guideline documents, collaborative studies that support standards development, activities to build pharmacovigilance capacity, and other regulatory capacity building projects. The activities supported by the Cooperative Agreement are responsive to global needs, especially in low-and-middle-income countries and are a means to advance FDA’s goal of strengthening regulatory systems worldwide and preparedness to respond to public health emergencies.

Influenza vaccines play a significant role in protecting the U.S. and global population against influenza disease. The WHO has a central role in coordinating the activities that must be executed so manufacturers have access to the virus strains and standards needed to produce influenza vaccines. CBER is an Essential Regulatory Laboratory (ERL) in WHO’s Global Influenza Surveillance and Response System (GISRS) and plays a critical role in the twice-annual seasonal influenza vaccine strain selection for the Northern and Southern hemispheres. In collaboration with regulatory authorities in the United Kingdom, Australia, and Japan, CBER experts contribute to the following activities each year for manufacture of influenza vaccines:

- Analyze influenza virus surveillance data and issue recommendations on the strain composition of the influenza vaccines;
- Perform serological studies to determine how well current vaccines protect against the most recent circulating strains of influenza virus;
- Analyze influenza virus isolates and prepare virus stocks of candidate strains for use by manufacturers for influenza vaccine production;
- Contribute to the production and calibration of reagents needed for use in the single radial immunodiffusion influenza vaccine potency assay; and
- Provide these reagents to vaccine manufacturers and the global community, as needed.

CBER fulfills these functions each year for seasonal influenza vaccines. CBER also made a commitment to serve as an ERL in WHO's Pandemic Influenza Preparedness Framework, formalizing CBER's role to carry out ERL functions in the case of a pandemic. CBER plays an essential role in ensuring availability of seasonal influenza vaccines, and in national and global preparedness to respond in a timely manner to pandemic influenza threats.

To achieve Objective 3.4, CBER will employ the strategies below.

Strategy 3.4.1 | Continue active confidential information exchanges with strategic regulatory counterparts, to advance regulatory alignment and joint preparedness.

Strategy 3.4.2 | Serve as a WHO Collaborating Center for biological standardization and as an Essential Regulatory Laboratory (ERL) within WHO's Global Influenza Surveillance and Response System (GISRS).

Strategy 3.4.3 | Engage in WHO consultations to share scientific, technical, and regulatory knowledge to facilitate development and access to medical products that address critical global health needs.

Strategy 3.4.4 | Serve as a National Regulatory Authority of reference for WHO's vaccine prequalification program, which United Nations agencies rely on to purchase vaccines of assured quality, safety, and effectiveness for distribution to countries in need.

GOAL 4 | Manage for strategic excellence and organizational accountability.

CBER leadership understands the Center cannot accomplish mission-critical initiatives without an aligned strategy and organizational accountability. To manage for strategic excellence and organizational accountability, CBER relies on the Offices that provide internal program support.

These Offices work collaboratively to advance and maintain a skilled and experienced workforce adaptable to an everchanging environment. At the same time, the internal support staff ensure responsible stewardship and accountability through effective resource management. Finally, they effectively and proactively communicate their strategic priorities and plans with internal and external stakeholders. CBER will continually harmonize and modernize business operations to meet its strategic priorities and prioritize resources.

The following objectives define how CBER will progress on this goal.

OBJECTIVE 4.1 | Advance and maintain a skilled and experienced workforce adaptable to an everchanging environment.

CBER's most valuable resource is its workforce. CBER could not accomplish the mission-critical work of the Center without its highly-qualified employees. CBER prioritizes its ability to recruit, train, and retain these employees in a globally competitive job market, leveraging a data-driven hiring strategy, and a recruiting and retention strategy to realize success.

As CBER attempts to attract the most highly-qualified employees in a competitive market, it focuses on how to get the right people with skills relevant to CBER's mission. To more effectively plan these efforts, CBER aims to rely on data analysis to ensure that recruitment strategies are data-driven and aligned with Center-wide resource needs (e.g., programmatic, management, human resource functions, budget-related, IT-related, scientific). The goal is to equip Center leadership with tools like real-time dashboards that will help them visualize the current state of the workforce and pinpoint areas that should be prioritized. Furthermore, in response to public health emergencies, CBER adapts business processes to enable employees to continue to work.

With data-driven hiring priorities in mind, CBER aims to adapt its hiring culture to shift the focus from filling specific vacancies to identifying talent with the appropriate skills to fill vacant job roles. In FY2020, CBER implemented a next generation hiring and recruiting strategy across the Center. This strategy enables the Offices to make the best data-driven hiring decisions and increases the Center level focus on outreach, recruiting, interviewing, and hiring. This more flexible method brings agility to the hiring process, allowing new staff to be placed in the areas of greatest need and impact.

Recruiters and hiring managers work collaboratively with the Office of Management (OM) to focus on short-, medium-, and long-term workforce needs. Because CBER's hiring decisions are derived from data that prioritize the areas of greatest need, CBER can quickly and effectively make employee placement decisions. By using data, CBER can make targeted, data-driven decisions that support current and future CBER staff. CBER pairs its findings with the FDA workforce analysis, which provides a summary of how many employees are aligned in each grade and series.

To recruit highly-skilled candidates in a competitive marketplace, it is important to use all recruiting channels and authorities available to attract top talent for scientific and other critical administrative roles. CBER uses all authorities available to bring in new staff and works closely with hiring managers to identify the right candidates. This includes training hiring managers on the best methods and channels for recruiting highly-qualified candidates, both scientific and non-scientific or non-medical, and seeking insight from hiring managers on where best to advertise about CBER roles to reach the right experts. Furthermore, during public health emergencies, as a result of the Direct Hire

authorities, CBER demonstrates increased flexibility in hiring and continues to attract essential talent from the private sector.

To ensure a diverse pool of applicants in its hiring pipeline, CBER attends different conferences throughout the year. CBER plans to modify current conference attendance to targeted participation in panel discussions and tips on the federal application and hiring process. This will allow CBER to increase breadth and scope of reach to potential applicants. Current outreach methods involve advertisements in scientific and medical journals and attendance at large scientific and medical conferences. CBER also plans to create a prospect database to keep potential applicants engaged in future opportunities. CBER will also explore opportunities for non-competitive, inter-agency hires. CBER Human Resources will explore opportunities to plan for advertising positions to existing federal venues and networks.

CBER leverages FDA-wide regulatory science internships, fellowships, and training opportunities for national and international students and postgraduate scientists as well as college and university faculty members. With the intent to educate the next generation of scientists, the [Oak Ridge Institute for Science and Education \(ORISE\) Research Participation Program](#) allows high school, college, and graduate students, recent graduates, post-doctoral scientists and university faculty to actively engage in research experiences with an FDA scientist who serves as a mentor. Additionally, CBER participates in the FDA's Service Fellowship Program, which provides a flexible alternative mechanism for the employment and professional development of promising research or regulatory review scientists for a period of limited duration. Fellowships provide the opportunity to accelerate and enhance scientists' careers through close associations with leading authorities in health-related research.

CBER also works to develop data analyses processes that allow for a more accurate assessment of trends in employee retention and engagement. To retain the employees that CBER hires, CBER prioritizes continuous opportunities for training and career development, promotes a culture of engaged employees, and acknowledges superior contributions. CBER also identifies areas to improve the employee experience, such as expanding the student loan repayment program, to encourage employee retention and recruitment. Even in times of public health emergencies, such as the COVID-19 pandemic, when employees must work under abnormal conditions, CBER remains focused on employee engagement and retention, utilizing a variety of different approaches and initiatives.

To ensure that there are clear paths for employee development after joining CBER's workforce, CBER is developing a comprehensive competency model that aligns with employee individualized development plans, clarifying the knowledge, skills, and abilities that are needed for successful job performance. Competency models and career paths empower employees to take control of their career growth at CBER.



CBER leverages the [Federal Employee Viewpoint Survey \(FEVS\)](#) to get an annual pulse on employee satisfaction and identify areas for growth in employee engagement and retention. CBER analyzes FEVS data to identify growth opportunities and implements programs to address employee concerns. CBER monitors the progress of employee satisfaction programs through surveys and direct feedback and uses these results to understand program effectiveness and adjust as needed. One recurring theme that is monitored in FEVS data is employee engagement and recognition.

To improve employee engagement and recognition, CBER acknowledges superior contributions and accomplishments of employees through awards and other recognition programs. Center-wide award ceremonies provide an opportunity to celebrate the success of top performers and encourage other employees to go above and beyond in pursuit of mission-critical initiatives.

CBER recognizes that continuous employee training and development keep employees engaged, happy, and better equipped to manage their mission-critical work. To ensure that training opportunities keep pace with cutting-edge

developments in science and technology, CBER conducts a training needs assessment and convenes working groups to assess and prepare for upcoming professional development needs. CBER delivers on the training needs requested in the form of formal training, knowledge management programs, science seminars, and public forums.

In addition to partnering with specialists Center-wide to continually develop trainings, CBER's knowledge management team facilitates the official accreditation process for course offerings. CBER stakeholders also meet with Center leadership to determine topics to prioritize for external outreach through the public workshop offerings to external stakeholders.

Finally, CBER fosters a safe, secure, and healthy work environment. The safety team provides manuals for lab safety and works with [Occupational Safety and Health Administration](#) (OSHA) to make sure that all incidents are properly investigated and reported. CBER also works with FDA security personnel to address any issues and ensure that they are properly investigated. The Office of Communication, Outreach and Development (OCOD) supports preventative measures by sharing mandatory safety and security training with all CBER staff.

CBER also partners with the [General Services Administration](#) (GSA) to ensure proper care and maintenance of facilities. Most importantly, all staff in need are offered reasonable accommodations to ensure that people of all abilities feel their contributions are respected and supported in the CBER work environment.

To achieve Objective 4.1, CBER will employ the strategies below.

Strategy 4.1.1 | Ensure efficient processes to identify, attract, hire, and retain diverse and highly qualified candidates.

Strategy 4.1.2 | Utilize targeted, effective outreach and recruitment strategies to attract a pipeline of well-qualified external candidates.

Strategy 4.1.3 | Provide opportunities for updating relevant regulatory, scientific, and technical knowledge.

Strategy 4.1.4 | Facilitate employee career development via a competency model that provides developmental pathways and through individual development plans.

Strategy 4.1.5 | Promote an organizational culture of actively engaged employees through continuous process improvement, increased collaboration, and fostering an empowered work environment.

Strategy 4.1.6 | Acknowledge superior contributions and accomplishments of CBER employees through awards and other recognition programs.

Strategy 4.1.7 | Foster a safe, secure, and healthy work environment.

OBJECTIVE 4.2 | Ensure accountability and responsible stewardship through effective resource management.

CBER could not accomplish the mission-critical work of the Center without its highly-qualified employees. It is an ongoing challenge to recruit, train, and retain these employees in a globally competitive job market with limited funding. As a result, effective resource management involves both planning for CBER’s future workforce needs and managing funding responsibly.

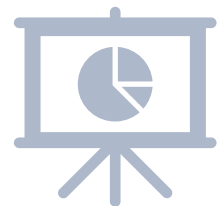
CBER uses resource capacity planning to determine the resources, or employees, needed to address future workload demands. To facilitate effective resource planning, CBER mandates the use of a full-time activity reporting system. CBER’s time tracking system, serves as a platform for all CBER employees to input their daily work activities and the time it takes to accomplish those activities. CBER’s time tracking system helps ensure long-term success by enhancing CBER’s ability to predict and plan for future workload and resource needs.

With all CBER employees reporting time, there is an unprecedented opportunity to track the workload that supports mission-critical work. CBER’s time tracking data is reviewed to determine the total amount of time spent conducting various Center activities. This information is then used, in conjunction with regulatory submission data, to estimate the resources required to achieve CBER’s mission in future years, and to analyze historical trends to predict submission volume.

To effectively manage the Center’s financial resources, CBER uses tools like the Biologics Planning, Execution, and Reporting System (BPERS) to increase transparency and accountability. FDA utilizes the Integrated Budget and Acquisition Planning System (IBAPS), which is a suite of four applications that support the Agency-wide budget formulation, budget execution, acquisition planning, and payroll planning. BPERS is an IBAPS child application at the Center-level that provides budget acquisitions planning, execution, and reporting capabilities across CBER Program Offices, Divisions, and Branches. BPERS allows CBER staff to:

- **Create real-time reports and dashboards** for planning, execution, and status of funds;
- **Manage and report** on the budget and plan data at the Office, Division or Branch level;
- **Maximize use of all funding sources** while maintaining compliance with reporting requirements;
- **Interface on a single platform** to support evolving planning and operational data needs;
- **Plan and report uniformly** to support informed decisions at Program Offices; and
- **Streamline and standardize processes** across CBER Program Offices and the Office of Management.

Additionally, the Resource Committee manages the annual budget and resource planning, including research funding allocation to the Offices. The CBER Regulatory Science Council (RSC) recommends strategic decisions impacting Center-wide research goals to the Center Director for approval, provides oversight of the Center’s research activities to ensure organizational alignment with Center-wide research goals, increases cross-Office awareness and coordination of the research portfolio, and identifies ways to continuously improve the state of CBER’s scientific research. Resource decision-making is informed by transparency into research spend, status, and impact; decision processes and criteria will be openly communicated to the entire Center. Structure, timing, and communication of funding enables prospective planning of the content and direction of research.



As CBER shifts to use real-time data to plan and execute its budget, the Center’s enterprise risk management (ERM) program must keep pace. CBER ERM staff work regularly with subject matter experts or risk owners to identify risks and their likelihood and impact, and then outline what internal controls are or can be put in place to proactively mitigate those risks.

On a broader scale, CBER will measure progress against all its strategic priorities through [FDA TRACK](#), FDA's agency-wide performance management system that monitors FDA Centers and Offices through key performance measures and projects. For enhanced transparency, these measures are shared with the public. The objectives of FDA-TRACK can best be explained through its name:

- **Transparency** – communicate FDA's story to internal and external stakeholders.
- **Results** – highlight office achievements and cross-agency initiatives that align with FDA's public health mission.
- **Accountability** – demonstrate FDA's contributions to office and Agency priorities, plans and results.
- **Credibility** – encourage the sharing of accurate, reliable performance data to FDA stakeholders.
- **Knowledge-sharing** – enhance collaboration across program offices and through the FDA.

To achieve Objective 4.2, CBER will employ the strategies below.

Strategy 4.2.1 | Facilitate effective resource planning in the short-, medium-, long-term, leveraging resource capacity planning capabilities and governance structures to enhance the transparency, effectiveness, and strategic alignment of CBER's resource utilization.

Strategy 4.2.2 | Evaluate enterprise risks and implement mitigation strategies.

Strategy 4.2.3 | Promote accountability to ensure the effective use of resources through the implementation of measurable goals.

OBJECTIVE 4.3 | Communicate effectively and proactively with internal and external stakeholders.

CBER strives to proactively engage with other FDA Centers and Offices to represent interests in crosscutting Agency initiatives. CBER accomplishes this Agency-wide collaboration through review-focused Inter-Center Consult Requests (ICCRs), scientific working groups, enterprise-wide working groups, cross-center training, and unified, crosscutting communication to the public, among others.

CBER will continue to support the ICCR process. ICCR covers inter-Center consults that occur between CBER, CDER, and CDRH. FDA uses the ICCR process to jointly review investigational and marketing applications for combination products. Generally, consults to another Center are requested for combination products. Consults to another Center may also be requested for specific expertise related to non-combination products. The ICCR process and supporting resources are continuously evaluated. Updates are periodically implemented to improve process efficiency and provide necessary resources to staff engaged in inter-Center consults.

While the ICCR is focused primarily on regulatory review, other scientific working groups span reviewers, researchers, and support staff in CBER. Scientific working groups include key employee subject matter experts that gather in Center-wide employee groups to:

1. Communicate and disseminate information among Centers,
2. Coordinate projects, policy, and initiatives, and
3. Collaborate and exchange resources and expertise.

Policy and scientific working groups serve FDA senior management as an information resource, for example, to identify experts at FDA who can help with regulatory decision-making. Many scientific working groups also undertake

educational workshops, seminars, or training activities to ensure the FDA’s scientific staff remain current on a variety of relevant topics to support review activities. A well-trained, well-connected, and well-supported workforce is essential to meet FDA’s challenges of integrating emerging sciences and technologies into the Agency’s research and review processes.

CBER also leads an enterprise-wide working group for consumer complaint processing and handling. The effective communication on consumer product reports are an important part of FDA's monitoring system and help ensure that the products the agency regulates are safe, properly manufactured and stored, and correctly labeled.

Cross center trainings provide a forum for educational collaboration at FDA. CBER participates in programs, lectureships, and scientific exchanges to introduce staff to new concepts and technology to enable them to perform mission-critical work. One example of cross center education is the Committee for the Advancement of Clinical and Scientific Education (CACSE) Lecture Series. The CACSE provides continuing education (CE) to FDA clinical staff and the opportunity to stay current with advances in therapeutics and applied scientific data in various clinical fields, as well as to hear the perspectives of scientists and clinicians on the application of regulatory scientific knowledge.

CBER leverages the FEVS to get an annual pulse on employee satisfaction and identify areas for growth in employee engagement and retention. CBER analyzes FEVS data to identify growth opportunities and implements programs to address employee concerns, making sure that all groups (reviewers, researchers, support staff, supervisors, etc.) are engaged. CBER routinely monitors the effectiveness of its internal communications and collaboration efforts to continuously improve.

CBER will continue to explore more efficient ways to share information among its employees. CBER also commits to assessing the effectiveness of its communication practices which include:

- **All Hands Meetings:** All employee meetings where the latest updates are shared with all employees on key CBER initiatives;
- **Brown Bag Sessions:** Employees are asked to meet with key leadership to provide feedback on the progress and impact of key initiatives; and
- **Crowdsourcing:** The Center requests feedback and ideas directly from staff by using crowdsourcing, which allows users to propose their own ideas, see the ideas of others, vote on ideas, and provide feedback.

CBER will also continue to communicate through the Center’s web page about guidance, policy, product approvals, safety issues, shortages, compliance actions, administrative actions, advisory committee information, and workshop information to maintain internal and external stakeholder awareness.

To achieve Objective 4.3, CBER will employ the strategies below.

Strategy 4.3.1 | Leverage available data sources to provide active, timely information to critical stakeholders.

Strategy 4.3.2 | Proactively engage with other FDA Centers and Offices to represent CBER’s interests in cross cutting agency initiatives.

Strategy 4.3.3 | Promote a culture of engagement through proactive communication and information sharing.

OBJECTIVE 4.4 | Continue to harmonize and modernize business operations.

Recent scientific and biomedical advances have brought the promise of significant improvements to public health. To date, however, a gap separates important scientific advances and the technologies needed to translate those advances into new therapies for patients and new ways to protect the public health. To ensure that CBER's reviewers, researchers, and support staff have the tools they need to keep pace with advances in science and technology, CBER will continue to harmonize and modernize business operations.

To support operational harmonization and modernization, CBER will first enhance operational analysis through advanced data analytics and visualization for CBER managers and leaders. Second, CBER will develop highly integrated IT and data platforms to take a lifecycle view across regulatory pathways and leverage commonalities. Finally, CBER will improve business operations through enhancement and implementation of automated business processes.

To enhance CBER's ability to analyze operations, the Center is bringing data to life through data visualization platforms. It is hoped that by making data more accessible through these visualization platforms, CBER will continue to enhance the efficiency of operations through data-driven decision-making. The aim is to develop visualizations that help leaders identify trends that impact Center-wide workload, workforce, and resources. By creating data visualizations, CBER is developing new ways to view and evaluate large data sets.

In making large data sets more easily consumable, CBER can more easily detect areas for improvement or data quality issues when data conflicts with expected outcomes. By sharing discrepancies with leadership and employees, CBER challenges assumptions with actual data, jointly identifies trends that require further review, and develops ways to monitor and improve the integrity of the data. Through visualizations, CBER aims to improve its data-driven decision making by bringing together different data sources to connect information on resources that influence the different parts of the product application lifecycle.

Next, CBER aims to integrate IT and data platforms to take a lifecycle view across regulatory pathways and leverage commonalities. CBER's first step to integrating CBER's IT and data platforms is to align with the FDA's [Technology Modernization Action Plan](#) (TMAP). The plan describes important near-term actions that FDA is taking to modernize use of technology, including computer hardware, software, data, and analytics, to advance FDA's public health mission. TMAP has three elements:

1. Modernization of FDA's technical infrastructure;
2. Enhancing FDA's capabilities to develop technology products to support its regulatory mission; and
3. Communication and collaboration with stakeholders to drive technological progress that is interoperable across the system and delivers value to consumers and patients.

Near-term modernization in computer hardware and software technologies are the focus of the TMAP. Unlocking this potential will require infrastructure to securely receive, store, exchange, link, and analyze data; careful attention to data quality, integrity and security; analyses-at-scale including real-time dashboards, blockchain, appropriate strategies for both structured and unstructured data, and artificial intelligence; and a learning culture that continuously builds on prior knowledge.

Advanced hardware, software and data technologies will allow CBER to deploy its resources more effectively and efficiently. FDA is already beginning to use advanced technology tools to help its scientific and medical reviewers collect the information they need to make regulatory decisions. New tools also allow FDA's investigators in the field to operate more efficiently—maximizing FDA's operational footprint in crucial areas like facility inspections and import operations. Yet, for these new technologies to achieve their full potential, CBER needs to make sure that there is a modern business operation plan in place.



To that end, CBER plans to continuously improve business operations through enhancement and implementation of automated business processes. In order to ensure that we remain prepared to respond effectively to threats, CBER will work to update the Emergency Operations Plan and the Continuity of Operations Plan (COOP), to address changes in duty locations during an emergency, such as COVID-19. CBER will also ensure that employees create and update CBER Standard Operating Procedures in a unified and collaborative manner that organize and clarify the appropriate steps for each business process. To ensure that employees follow the process, CBER will conduct regular audits. These audits will assure data integrity, predictability, and quality of work.

CBER also leverages the Quality Assurance Staff (QAS) as the Center level resource responsible for oversight and management of CBER's laboratory accreditation activities for regulatory testing under the Lot Release Program. Lot release is a mechanism that provides FDA with a real-time system to continuously monitor product quality, through review and testing, of many of the biological products that it regulates. The fully implemented and accredited Laboratory Quality System (LQS) has been accredited to two external International Standards: ISO 17025 for testing activities, and ISO 17034 for Reference Material Producers within the Division of Biological Standards and Quality Control (DBSQC) and the Laboratory of Immunobiochemistry (LIB), respectively. CBER programs promote an adherence to standards and quality.

To achieve Objective 4.4, CBER will employ the strategies below.

Strategy 4.4.1 | Enhance operational analysis through modern data analytics and visualization for CBER managers and leaders.

Strategy 4.4.2 | Develop highly integrated IT and data platforms to take a lifecycle view across regulatory pathways and leverage commonalities.

Strategy 4.4.3 | Improve business operations through enhancement and implementation of automated business processes.

Strategy 4.4.4 | Develop a CBER quality system and foster a culture of continuous process improvement.

APPENDIX A | GLOSSARY OF ACRONYMS

AE – Adverse Event

APEC RHSC – Asia-Pacific Economic Cooperation Regulatory Harmonization Steering Committee

BEST – Biologics Effectiveness and Safety

BLA – Biologics License Application

BPERS – Biologics Planning, Execution, and Reporting System

BSL – biosafety level

CACSE – Committee for the Advancement of Clinical and Scientific Education

CATT – CBER Advanced Technologies Team

CBER – Center for Biologics Evaluation and Research (at FDA)

CBRN – Chemical, Biological, Radiological, and Nuclear threats

CDC – Centers for Disease Control and Prevention

CDER – Center for Drugs Evaluation and Research (at FDA)

CE – continuing education

CEPI – Coalition for Epidemic Preparedness Innovations

cGMP – current Good Manufacturing Practice

CID – Complex Innovative Trial Design

CIs – confidence intervals

CMS – Centers for Medicare & Medicaid Services

COVID-19 – Coronavirus Disease 2019

COOP – Continuity of Operations

CTAP – Coronavirus Treatment Acceleration Program

DBSQC – Division of Biological Standards and Quality Control

DDT – Drug Development Tools

DHHS or HHS – Department of Health and Human Services

DHS – Department of Homeland Security

DoD – Department of Defense

HER – Electronic Health Record

EAP – Expanded Access Program

EID – Emerging Infectious Disease

ERL – Essential Regulatory Laboratory

EMA – European Medicines Agency

ERM – enterprise risk management

EUA – Emergency Use Authorization

FBR – Facility for Biotechnology Resources

FCC – Flow Cytometry Core

FDA – Food and Drug Administration

FDARA – Food and Drug Administration Reauthorization Act of 2017

FDASIA – Food and Drug Administration Safety and Innovation Act

FEVS – Federal Employee Viewpoint Survey

GPEI – Global Polio Eradication Initiative

GISRS – Global Influenza Surveillance and Response System

GSA – General Services Administration

HC – Health Canada

HCT/Ps – human cells, tissues, and cellular and tissue-based products

HIVE – High-performance Integrated Virtual Environment

HPFB – Health Products and Food Branch

IBAPS – Integrated Budget and Acquisition Planning System

ICCRs – Inter-Center Consult Requests

ICH – International Council on Harmonisation

IHS – Indian Health Service

IMG – Incident Management Groups

IND – Investigational New Drug

INTERACT – INitial Targeted Engagement for Regulatory Advice on CBER products program

IPRP – International Pharmaceutical Regulators Programme

IT – Information Technology

ITAC – Inpatient Treatment with Anti-Coronavirus Immunoglobulin study

LIB – Laboratory of Immunobiology

LQS – Laboratory Quality System

MIDD – Model-Informed Drug Development

MCM – Medical Countermeasure

NACCHO – National Association of County and City Health Officials

NASEM-HMD – National Academies of Sciences, Engineering, and Medicine Health and Medicine Division

NGO – Non-Governmental Organization

NIH – National Institutes of Health

NORD – National Organization for Rare Disorders

OCBQ – CBER’s Office of Compliance and Biologics Quality

OCOD – CBER’s Office of Communication, Outreach and Development

OIP – FDA’s Office of International Programs

OM – CBER’s Office of Management

OOPD – Office of Orphan Products Development

ORISE – Oak Ridge Institute for Science and Education

OSHA – Occupational Safety and Health Administration

PAHO – Pan American Health Organization

PAHPAIA – Pandemic and All-Hazards Preparedness and Advancing Innovation Act of 2019

PFDD – Patient-Focused Drug Development

PHEMCE – Public Health Emergency Medical Countermeasures Enterprise

PPI – Patient Preference Information

PRO – Patient-Reported Outcome

PSA – Parallel Scientific Advice

QAS – Quality Assurance Staff

RCTs – Random Clinical Trials

RNA – ribonucleic acid

RSC – CBER Regulatory Science Council

RWE – Real-World Evidence

RWD – Real-World Data

SF – Substandard and Falsified

SNS – Strategic National Stockpile

SPI – Science of Patient Input

TMAP – Technology Modernization Action Plan

TTID – transfusion-transmitted infectious diseases

TTIMS – Transfusion-Transmitted Infections Monitoring System

USDA – U.S. Department of Agriculture

USG – U.S. Government

VA – Department of Veteran’s Affairs

VHA – Veterans Health Administration

WHO – World Health Organization

WHO CC – World Health Organization Collaborating Center

APPENDIX B | CBER CURRENTLY OPERATES UNDER THE LEGAL AUTHORITIES LISTED BELOW.

1. Public Health Service Act (§ 506(g)); (§ 361)
2. Federal Food, Drug, and Cosmetic Act* (21 U.S.C. 321-399) (§ 735-6); (§ 529); (§§ 561, 561A, 561B); (§§ 744A-B)
3. Medical Device Amendments of 1976*
4. Clinical Laboratory Improvement Amendments of 1988 (42 U.S.C. 201)
5. Safe Medical Devices Act of 1990*
6. Medical Device Amendments of 1992*
7. Food and Drug Administration Modernization Act of 1997*
8. Medical Device User Fee and Modernization Act of 2002*
9. Public Health Security and Bioterrorism Preparedness Response Act of 2002*
10. Project BioShield Act of 2004 (21 U.S.C. 360bbb-3)
11. Medical Device User Fee Stabilization Act of 2005*
12. Food and Drug Administration Amendments Act of 2007*
13. Biologics Price Competition and Innovation Act of 2009*
14. Patient Protection and Affordable Care Act, 2010*
15. Food and Drug Administration Safety and Innovation Act, 2012*
16. Drug Quality and Security Act, 2013*
17. Pandemic and All-Hazards Preparedness Reauthorization Act of 2013
18. 21st Century Cures Act, 2016
19. Food and Drug Administration Reauthorization Act of 2017
20. Pandemic and All-Hazards Preparedness and Advancing Innovation Act (PAHPAIA) of 2019
21. Orphan Drug Act (21 U.S.C. 360ee)

* Authorities under this act do not appear in sequence in the U.S. Code. The authorities are codified as amended in scattered sections of 21 U.S.C.