



## Food and Drug Administration

### **COVID-19 Vaccines**

IDSAs and HIVMA have repeatedly [advocated](#) that COVID-19 vaccines only be licensed or authorized when they meet either existing U.S. Food and Drug Administration (FDA) licensure standards or the recommendations set forth in the 2020 guidance for industry on Emergency Use Authorization (EUA) for vaccines for COVID-19, and when independent experts on the Vaccines and Related Biological Products Advisory Committee give a positive recommendation. Thorough, transparent review of safety and efficacy data are critical to building the confidence necessary to ensure the high levels of vaccine uptake needed to control the pandemic. Prematurely authorizing a COVID-19 vaccine without adequate randomized clinical trials demonstrating safety and effectiveness in preventing disease could cause harm by eroding public confidence in all vaccines and in public health authorities. Thus far, the FDA has followed through with these key recommendations.

### **We recommend continuing to:**

- **Ensure data from Phase 3 studies include a median follow up duration of at least two months after the completion of a full vaccination regimen;**
- **Require sponsors to present a compelling case regarding their ability to continue studies following an EUA. FDA has stated that an EUA is *not* a compelling reason to unblind current trial participants, and we support this statement;**
- **Make trial data available to clinicians and other vaccine providers to increase their confidence in a COVID-19 vaccine and best position them to boost vaccine uptake by educating and counseling their patients;**
- **Ensure that COVID-19 vaccines are adequately studied in populations that have been disproportionately impacted by the pandemic and who face disparities in care, including the elderly; individuals with chronic conditions; and Black/African American, Indigenous, Latinx and other communities of color. Additionally, studies in children, pregnant women and other populations in whom vaccines may perform differently should be a priority;**
- **Collaborate with sponsors on post-market surveillance to gather additional safety data on COVID-19 vaccines made available via an EUA. Ensure a coordinated and transparent process for collection of adverse events associated with COVID-19 vaccines (in coordination with other agencies as appropriate). This process and resulting data can help build vaccine confidence.**

## **COVID-19 Therapeutics**

In the understandable effort to promote timely access to potentially beneficial treatments, FDA has in some instances, issued EUAs before evidence supported routine use of the drugs as standard of care. In addition to potentially promoting widespread use of ineffective or even harmful therapies, issuance of an EUA may lead to difficulties in completing ongoing trials as well as undermine the generation of evidence needed to develop safe and effective therapies. It is important to note that the challenges within the current EUA process are due, in part, to systemic deficiencies upstream — within the clinical trials infrastructure — that limit the speed of rapid innovation in times of need. Within this system, attempting to introduce and systematically study experimental treatments outside of tertiary care academic medical settings is extremely challenging. Efforts need to be made to restructure rapid evaluation trials to address this issue for future disasters.

### **We recommend:**

- **Establishing and publicly communicating benchmarks for COVID-19 therapeutics to receive an EUA, as the agency has done for COVID-19 vaccines. Specifically, before issuing an EUA for a COVID-19 therapeutic, FDA should work with the sponsor and clinical research community to develop a plan to ensure a mechanism for the collection and publication of data necessary to inform optimal use;**
- **Promoting efforts to restructure and improve the conduct of rapid evaluation trials by improving clinical trial infrastructure, funding mechanisms, and better analytical tools so that the EUA mechanism can be used when strong data are available, and trials can be performed on larger populations, in more settings, to increase access to treatments and the ability to gather data.**

## **Diagnostic Tests**

**COVID-19 Testing:** The COVID-19 pandemic has demanded a real-time assessment of the current diagnostics regulatory framework and illustrated the consequences of not having rapidly available, adequate testing to manage infectious diseases. We are seeing firsthand the impact that delayed testing has on transmission, reporting, resource utilization and management, and above all, patient and public health. As illustrated by the ongoing COVID-19 outbreak, tens of thousands of tests are needed to identify and isolate a relatively modest number of positive patients. It is also essential in cases of localized outbreaks which may not necessarily meet the criteria for an EUA, that well-validated tests make their way to public health officials as expeditiously as possible. The inability to modify test elements without triggering additional oversight was one of the major impediments to implementation of the CDC SARS-COV-2 assay in the early days of the COVID-19 pandemic, as any parts of the testing protocol, including instrumentation, that differed from those used in the Centers for Disease Control and Prevention's (CDC) validation were considered outside the EUA.

The COVID-19 pandemic has also illustrated that rare and “orphan” infectious diseases with no FDA-approved *in vitro* diagnostic tests must often rely on laboratory developed tests (LDTs).

Rare diseases with multiple commercial tests available can also require LDTs for effective management. Speed of test results is a key issue unique to ID, and infectious diseases LDTs, developed by high-complexity CLIA-certified academic medical centers and public health laboratories, have high sensitivity and specificity (sometimes even higher than their FDA-approved counterpart, when one exists). These tests are designed for in-house use to fill critical gaps, unlike many of the EUA test kits that were marketed commercially but later found to be deficient by FDA. ID physicians rely on both commercial tests and LDTs to manage complex patients, and the COVID-19 pandemic has illustrated the need for a regulatory system that maintains patient access to and promotes innovation for both.

**We recommend that FDA:**

- **Address the ability of laboratories to use an LDT in a Public Health Emergency when EUA tests are unavailable to meet demand. Regulations must ensure safety while limiting hurdles for qualified laboratories.**

**Other ID Diagnostics:** IDSA acknowledges the complexity of diagnostic regulations in a rapidly innovating field. We value FDA's continued work with Congress to create a risk-based framework for *in vitro* diagnostics development and share the agency's goal of advancing an approach consistent with the least burdensome principle for regulation while assuring necessary safeguards for patients. IDSA has long advocated for an approach that avoids introducing new or duplicative regulatory hurdles for LDTs for numerous conditions that are critical in everyday patient care.

We also appreciate FDA's September 2020 [reclassification](#) of cytomegalovirus (CMV) DNA quantitative assay devices intended for transplant patient from class III (general controls and premarket approval) to class II (general and special controls). IDSA has long called for the change from Class III to Class II for CMV, and other transplant virus tests (e.g., BK virus). The reclassification of these tests should help to increase the number of devices submitted to FDA for approval, thus ensuring greater availability of testing.

As FDA continues to provide technical assistance for the *Verifying Accurate Leading-edge IVCT Development (VALID) Act of 2020*, we want to share perspectives from the front lines of infectious diseases testing. Despite the bill's proposed exemptions for grandfathering, modifications, and rare disease testing, this legislation would still have the unintended consequence of preventing clinical laboratories from keeping pace with rapidly changing infectious disease threats, such as those illustrated by the COVID-19 pandemic. Further, the bill's user fee requirements will ultimately hinder the new test development at the local level (i.e., academic clinical laboratories) which is needed for the care of complex, critically ill patients unique to these settings.

**We recommend:**

- **Working with Congress and with all relevant stakeholders, including physicians and academic clinical laboratories, to ensure that new regulatory approaches for LDTs do**

**not inappropriately hinder development of, or patient access to, high quality testing for infectious diseases;**

- **Advising Congress to:**
  - **revise and expand exemptions in the VALID Act.**
  - **adopt a facility-based approach for tests developed by clinical laboratories which ensures that all LDTs are appropriately subject to either Clinical Laboratory Improvement Amendments (CLIA) or FDA requirements.**
  - **In this paradigm, LDTs would be defined as "tests developed by CLIA-certified laboratories meeting the requirements for high-complexity testing to be used in a single laboratory or a network of related laboratories (such as academic medical centers and public health and hospital systems)."**
- **Classifying tests that measure viral loads in transplant patients (e.g., BK Virus, Epstein-Barr Virus) as Class II, following the September 2020 [reclassification](#) of cytomegalovirus (CMV) DNA quantitative assay devices intended for transplant patients.**

### **Antimicrobial Resistance**

Antimicrobial resistance (AMR) is an urgent and growing threat to patient safety and public health with the potential to undermine modern medical advances, including cancer chemotherapy, transplants and other surgeries, and care of immunocompromised patients. While there is still much to learn about the intersection of AMR and the COVID-19 pandemic, secondary bacterial and fungal infections contribute to the mortality of patients seriously ill with COVID-19, particularly those requiring mechanical ventilation. AMR is compromising our ability to effectively treat patients with these infections. In addition, high levels of antibiotic use during the pandemic may be creating new AMR threats that have not yet been identified.

Our antibiotic arsenal is rapidly shrinking. While Congress and other federal agencies must take action to address the significant economic barriers to antibiotic research and development, the FDA must ensure feasible regulatory pathways for the most urgently needed new antibiotics. These critical drugs are typically difficult to study in the patients for whom they are most needed. IDSA strongly supports the Limited Population Antibacterial Drug (LPAD) pathway and the use of novel trial designs. We are pleased that the [National Action Plan for Combating Antibiotic Resistant Bacteria \(CARB\) 2020-2025](#) calls for FDA to develop guidance on trial designs and welcome the opportunity to support this effort. We also support the creation of a clinical trials network, as described in the CARB National Action plan, and look forward to working with FDA to provide input on the network's structure and activities, including platform trial design. We are encouraged by FDA public workshops to discuss opportunities to strengthen antibiotic development, most recently a November 2019 workshop that we were pleased to co-sponsor. We appreciate that the CARB National Action plan calls for FDA to continue advancing this important dialogue.

### **We recommend:**

- **Continuing to work on the clinical trial network and efforts to identify novel trial design;**

- **Increasing efforts to address out of date breakpoints for antimicrobial susceptibility tests (ASTs). While progress has been made in recent years due to implementation of the 21<sup>st</sup> Century Cures Act, important needs remain. Physicians need accurate and up-to-date breakpoints to guide the selection and dosage of antibiotics to maximize patients' chances for positive clinical outcomes;**
- **Supporting the parallel development of antimicrobial susceptibility tests (ASTs) with clinical trials of new drugs to avoid delay in the availability of such testing for new drugs once they are approved;**
- **Supporting the development of novel therapeutics, new and point-of-care diagnostics, and better prevention strategies for AMR;**
- **Speed availability of susceptibility testing for new antimicrobial drugs;**
- **Continuing efforts to reduce inappropriate antibiotic use in animals and agriculture.**

*For questions regarding our recommendations, please contact Amanda Jezek, IDSA Senior Vice President for Public Policy and Government Relations at [ajezek@idsociety.org](mailto:ajezek@idsociety.org) or Andrea Weddle, HIVMA Executive Director at [aweddle@hivma.org](mailto:aweddle@hivma.org).*