The Focal Point: Advocacy & Legislative Update

May 26, 2020

COVID-19 Update

The global COVID-19 total jumps by a million cases every 12 days, passing 5 million infections on Thursday. The global total is now at 5,543,439 cases, and 347,836 people have died from their infections, according to the Johns Hopkins online dashboard. U.S. numbers total 1,669,040 confirmed cases and 98,426 deaths.

The Policy & Position Review Subcommittee of the MAB release updated guidance and COVID-19 screening recommendations on May 14, 2020, which are summarized below. All the latest regulatory updates related to COVID-19 are available on the EBAA COVID-19 page. We've recently redesigned the page into two categories: Regulatory Updates, and Business Operation Resources, making it easy for you to find the information you need most.

DONOR ELIGIBILITY CRITERIA

PCR Test Status[1]	COVID-19 Signs[2]	COVID-19 Symptoms[3]	Plausible Alternative Etiology of Signs or Symptoms	Close Contact[4]	Eligibility
Positive (in last 28 days)	Yes or No	Yes or No	Yes or No	Yes or No	**Not Eligible**
Negative (post-mortem or recent pre-mortem)	Yes	Yes or No	Yes	Yes or No	**Medical Director Review**
			No	Yes or No	**Not Eligible**
	No	Yes	Yes	Yes or No	**Medical Director Review**
			No	Yes or No	**Not Eligible**
		No	N/A	Yes	**Medical Director Review**
				No	**Eligible**
Not done	Yes	Yes or No	Yes or No	Yes or No	**Not Eligible**
	No	Yes	Yes	Yes	**Not Eligible**
				No	**Medical Director Review**
			No	Yes or No	**Not Eligible**
		No	N/A	No	**Eligible**

Comprehensive Database of Peer-reviewed COVID Articles

This COVID-19 database is a continuously updated and curated literature resource for tracking all English-language articles on COVID-19 that have been published in peer-reviewed journals since January 2020. Curated by former *AJIC* editor Elaine Larson and sponsored by Ovid, this website is updated throughout the week and is enhanced with recommendations and categorized research topics, with 35 filters such as case reports and retractions.

Coronavirus Does Not Spread Easily from Contaminated Surfaces

The CDC changed the wording on its website "How COVID-19 Spreads" to emphasize that the coronavirus primarily spreads from person to person and is not easily spread through contact with contaminated surfaces. The agency explains that touching contaminated objects or surfaces does not appear to be a significant mode of transmission. The same is true for exposure to infected animals. Nonetheless, the CDC still recommends routinely cleaning and disinfecting frequently touched surfaces.

Conjunctivitis Can Be the Only Presenting Sign and Symptom of COVID-19

Five cases of acute conjunctivitis turned out to be the sole presenting sign and symptom of COVID-19 in a case report from Bologna, Italy. These patients tested positive on RT-PCR of nasopharyngeal swabs and never developed fever, malaise, or respiratory symptoms throughout the course of their illness.

The authors emphasize the importance of eye protection, with goggles or face shields, regardless of patients' clinical presentation.

Potential for COVID-19 Transmission from the Human Eye

A new study published on the preprint server *bioRxiv* in May 2020 reports the presence of angiotensin-converting enzyme 2 (ACE2) receptors in the eye at high concentrations. These molecules are the entry points for the SARS-CoV-2 virus that is causing the ongoing COVID-19 pandemic. The virus attaches to the receptor through the spike or S protein, which is then cleaved by the host cell transmembrane protease serine 2 (TMPRSS2) leading to virus entry and cell infection.

Researchers analyzed gene expression patterns across tissues and cell types in the human eye. They found that 6% of corneal cells have high ACE2 gene expression, mostly epithelial cells. Conjunctival cells co-expressed both ACE2 and TMPRSS2, suggesting that they could serve as the entry points for the virus.

This highlights the importance of safety practices including face masks and eye protection in preventing the spread of COVID-19 disease.

Factors Associated with Prolonged Viral Shedding

Patients with COVID-19 outside of Wuhan, China, shed the virus for a median of 17 days, according to a retrospective cohort study published in the *International Journal of Infectious Diseases.*

Researchers studied the clinical factors, lab results, treatments, and outcomes of 147 adult COVID-19 patients in a single hospital in Changsha, China. Median time from symptom onset to admission was 6 days; 127 (86%) had moderate illness, while 20 (14%) had severe illness. Length of viral shedding ranged from 6 to 47 days. No patients required advanced respiratory support or died.

Identified risk factors for prolonged viral shedding included fever at hospital admission, longer time from symptom onset to admission, and lengthier hospital stays.

Multisystem Inflammatory Syndrome in Children Associated with COVID-19

The Centers for Disease Control and Prevention (CDC) released a Health Advisory regarding several cases of a recently reported multisystem inflammatory syndrome in children (MIS-C) associated with coronavirus disease 2019 (COVID-19) and a case definition for this syndrome.

CDC recommends healthcare providers report any patient who meets the case definition to local, state, and territorial health departments to enhance knowledge of risk factors, pathogenesis, clinical course, and treatment of this syndrome.

Case Definition for Multisystem Inflammatory Syndrome in Children (MIS-C)

- An individual aged <21 years presenting with fever[i], laboratory evidence of inflammation[ii], and evidence of clinically severe illness requiring hospitalization, with multisystem (>2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological); **AND**
- No alternative plausible diagnoses; **AND**
- Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to the onset of symptoms

[i]Fever >38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours
[ii]Including, but not limited to, one or more of the following: an elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, d-dimer, ferritin, lactic acid dehydrogenase (LDH), or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes and low albumin.

FDA Releases Annual Summary of HCT/P Deviations for FY19

FDA released the annual summary report providing an overview of the Biological Product and HCT/P Deviation Reports received during the fiscal year encompassing October 1, 2018, through September 30, 2019.

Manufacturers of nonreproductive Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/P) regulated by FDA solely under section 361 of the Public Health Service Act and 21 CFR Part 1271 [21 CFR 1271.350(b)] are required to submit HCT/P deviation reports to CBER, if the deviation or unexpected event involving a distributed product is related to a

Core Current Good Tissue Practice requirement [21 CFR 1271.150(b)] and to the prevention of communicable disease transmission or HCT/P contamination.

Of the 115 reports submitted by tissue 361 HCT/P manufacturers in FY19, 27% of the reports involved recovery, 26% involved receipt, pre-distribution, shipment and distribution and 19% of the reports involved donor eligibility. The increase in the number of reports involving recovery was due to eye tissue recovered using an eyewash that was recalled due to potential contamination.

FDA Posts HCT/P Inspection Information for FY 2019

The FDA published their compliance summary for HCT/P inspections performed in fiscal years 2015 through 2019. Of the 563 inspections completed in FY 2019, 440 inspections were classified as NAI – no action indicated; 111 were VAI – voluntary action indicated; and 12 were classified as OAI – official action indicated. The average hours per inspection increased from 37.8 in FY18 to 41.3 in FY19.

IDSA Issues Guidance on COVID-19 Testing

The Infectious Diseases Society of America (IDSA) issued guidelines on the diagnostics for COVID-19, making 15 recommendations for SARS-CoV-2 nucleic acid testing based on systematic reviews of the diagnostic literature.

The IDSA panel weighed available diagnostic evidence and recommends SAR-CoV-2 nucleic acid testing for all symptomatic individuals suspected of having COVID-19. In addition, testing is recommended for asymptomatic individuals with known or suspected contact with a COVID-19 case. Testing asymptomatic individuals without known exposure is suggested when the results will impact isolation/quarantine/personal protective equipment (PPE) usage decisions, dictate eligibility for surgery, or inform administration of immunosuppressive therapy. Ultimately, prioritization of testing will depend on institutional-specific resources and the needs of different patient populations.

FDA Names Companies Removed from List of COVID-19 Antibody Tests

After tightening its oversight of antibody tests for COVID-19, the FDA posted a listing of commercial manufacturers that have either failed to submit an emergency use authorization (EUA) request or voluntarily withdrew notification for their antibody tests distributed under the agency's former policy.

Currently, the list includes 28 tests made by more than 20 mostly US- or China-based companies that have been removed from the agency's notification list. Eleven of the 28 test notifications have been withdrawn voluntarily by their manufacturers. FDA expects that tests added to the removal list will no longer be marketed or distributed and that the list will continue to be updated going forward.

CDC Releases COVID-19 Reopening Guidelines

The CDC has published a 60-page guidance document on how to reopen the United States from coronavirus pandemic stay-at-home orders on the agency's website. The guidance follows a three-step or phased approach to reopening schools, child-care facilities, restaurants, and mass transit. The first "gating" criteria—or when to move to the next step—for each sector is a decrease in newly identified cases, followed by a decrease in emergency department or outpatient visits for COVID-19 or influenza-like illnesses. The final gating criteria is a robust testing program, with 14 days of 20% or less of tests turning out positive for the novel coronavirus.

The guidance instructs entities to follow familiar social distancing and hygiene practices, while also tailoring recommendations to the specific entities. Eye banks should refer to the *Interim Guidance for Employees with Workers at High Risk* found on page 49 of the guidance.

The guidelines do not address religious services or faith communities, although a recent MMWR article showed a high COVID-19 attack rate among 92 attendees at an Arkansas church events during March 6–11. CDC released a separate Interim Guidance for Communities of Faith on May 22.

OSHA Revises Guidance for Recording COVID-19 Cases

On May 19, 2020, the Occupational Safety and Health Administration (OSHA) issued new enforcement guidance regarding an employer's obligation to record cases of COVID-19 on the OSHA injury and illness logs. The new guidance takes effect Tuesday, May 26, 2020, and will supersede OSHA's previous guidance that was issued on April 10, 2020.

Under the new recordkeeping procedure, employers are responsible for conducting a reasonable analysis of COVID-19 cases and recording cases of COVID-19, *if*:

1. The case is a confirmed case of COVID-19, as defined by the Centers for Disease Control and Prevention (CDC);
2. The case is "work-related"—*i.e*., an event or exposure in connection with the employee's work either caused or contributed to the COVID-19 case; and
3. The case involves one or more of the general recording criteria, including, among other things, death; days away from work; or restricted work or transfer to another job.

OSHA specifically recognizes the difficulty of determining whether a COVID-19 illness is work-related, especially when an employee has experienced potential exposure both in and out of the workplace. OSHA provides some examples for when COVID-19 illnesses are likely work related, including:

- Several cases develop among workers who work closely together *and there is no alternative explanation*.
- It is contracted shortly after a *lengthy, close exposure* to a particular customer or coworker who has a confirmed case of COVID-19 *and there is no alternative explanation*.
- The employee's job duties include *frequent, close exposure to the general public* in a locality with ongoing community transmission *and there is no alternative explanation*.

If, after making a reasonable inquiry under the factors outlined above, an employer cannot determine whether it is *more likely than not* that the COVID-19 case is work-related, then the employer does not need to record the illness.

The guidance reiterates that the recording of a COVID-19 case does not necessarily mean that an employer has violated an OSHA standard. Companies that employ fewer than ten workers, and employers in certain low-hazard industries need only report work-related COVID-19 illnesses that result in a fatality or an employee's in-patient hospitalization, an amputation, or the loss of an eye.

OSHA Issues New Interim Enforcement Response Plan for COVID-19

OSHA recently issued an updated interim enforcement response plan for dealing with workplace investigations during the COVID-19 pandemic. It provides instructions and guidance to Area Offices and compliance safety and health officers (CSHOs) for handling COVID-19-related complaints, referrals, and severe illness reports. This guidance is intended to be "time-limited to the current public health crisis," will be effective on May 26, 2020 and will remain in effect until further notice.

For high-risk areas, OSHA will prioritize inspections for fatalities and imminent danger exposures. If an onsite inspection is not allowable due to insufficient resources, the investigation will be initiated remotely.

OSHA also notes that several of its standards may apply to its inspections of workplaces triggered by COVID-19, including:

- Section 5(a)(1), General Duty Clause of the Occupational Safety and Health (OSH) Act of 1970
- 29 CFR Part 1904, Recording and Reporting Occupational Injuries and Illness
- 29 CFR § 1910.132, General Requirements – Personal Protective Equipment
- 29 CFR § 1910.133, Eye and Face Protection
- 29 CFR § 1910.134, Respiratory Protection
- 29 CFR § 1910.141, Sanitation
- 29 CFR § 1910.145, Specification for Accident Prevention Signs and Tags
- 29 CFR § 1910.1020, Access to Employee Exposure and Medical Records
- 29 CFR § 1910.1030, Bloodborne Pathogens

Cal/OSHA Releases Interim General Guidelines on Protecting Workers from COVID-19

Cal/OSHA requires employers covered by the Aerosol Transmissible Diseases (ATD) Standard (California Code of Regulations, title 8, section 5199) to protect employees from airborne infectious diseases such as COVID-19 and pathogens transmitted by aerosols.

Cal/OSHA released interim guidelines for protecting workers from COVID-19 on May 14, 2020. This interim guidance does not impose new legal obligations but provides employers and workers with information for preventing exposure to SARS-CoV-2. Employers and employees should review their own health and safety procedures as well as the recommendations and standards detailed in the guidance to ensure workers are protected.

FDA Updates COVID-19 Clinical Trials Guidance

FDA released an updated guidance on conducting clinical trials amid the coronavirus disease (COVID-19) pandemic, by updating to address how and when sponsors and application holders should report serious adverse events (SAE).

The updated question-and-answer appendix to its March 2020 guidance addresses the use of alternate laboratories or imaging centers, holding trial participant visits via videoconference and conducting required postmarketing studies. The guidance also includes updated information on managing protocol deviations, amendments to ongoing trials and consulting with the FDA regarding administering investigational product infusions at home.

FDA Authorizes First Standalone At-Home Sample Collection Kit

FDA issued an emergency use authorization (EUA) to Everlywell, Inc. for the Everlywell COVID-19 Test Home Collection Kit, the first standalone at-home sample collection kit that can be sent to specified laboratories for COVID-19 diagnostic testing.

The prescription-only kit may be used by individuals at home who have been screened using an online questionnaire that is reviewed by a health care provider. Components of the Everlywell COVID-19 Test Home Collection Kit include nasal swabs and a saline-filled vial for transport. Currently, just two laboratories are authorized to collect and test the specimens, which they receive from patients via overnight express shipment. Everlywell has an independent physician network to communicate results to patients; an online portal for results is also available.

FDA Warns of Potential Accuracy Issues with Abbott ID NOW COVID-19 Test

The FDA issued a warning that the Abbott ID NOW point-of-care test to diagnose COVID-19 could yield false negative results. The test, which was authorized for emergency use in March, is said to be capable of delivering a positive result in five minutes and a negative result in 13 minutes.

Several scientific studies have identified accuracy issues with Abbott ID NOW and FDA is investigating whether it could be due to the types of swabs used or the type of viral transport media. The FDA has received 15 adverse event reports about the Abbott ID NOW device that suggest some users are receiving inaccurate negative results.

CDC to Launch Nationwide COVID-19 Antibody Study

The CDC plans to collect data from as many as 325,000 people from 25 metropolitan areas in order to track the spread of the novel coronavirus into 2021 and beyond, according to CDC spokeswoman Kristen Nordlund. The study, expected to start by June or July, will test samples from blood donors for the presence of antibodies to the virus.

The CDC study, expected to launch in June or July, will test samples from blood donors in 25 metropolitan areas for antibodies created when the immune system fights the coronavirus, said Dr. Michael Busch, director of the nonprofit Vitalant Research Institute.

A preliminary version of the study - funded by the National Heart, Lung and Blood Institute and the National Institute of Allergy and Infectious Diseases - is testing the first 36,000 samples. The CDC-funded portion, will expand the scope and time frame, taking samples over 18 months to see how antibodies evolve over time.

FDA Announces ICH E6 Web Conference

FDA is announcing a free public web conference for discussion of the International Council for Harmonisation's (ICH's) good clinical practice guidelines, ICH E6. This conference entitled ''Stakeholder Engagement on ICH E6: Guideline for Good Clinical Practice,'' is being convened and supported by a cooperative agreement between the Clinical Trials Transformation Initiative (CTTI) and FDA.

The purpose of the web conference is to obtain input on stakeholder experiences with the current ICH E6 guidelines for good clinical practice (GCP) and suggested changes to improve the guideline's applicability to the changing clinical trial landscape.

The public web conference will be held on Thursday and Friday, June 4 and 5, 2020, from 10 a.m. to 1 p.m. Eastern Time.

FDA Releases New Guidances to Advance Investigational COVID-19 Therapies

FDA released two guidance documents to accelerate the development of prevention and treatment options for COVID-19. The first guidance, "COVID-19 Public Health Emergency: General Considerations for Pre-IND Meeting Requests for COVID-19 Related Drugs and Biological Products," outlines a more efficient process for researchers to receive feedback from FDA on their supporting data with the goal of starting clinical trials as soon as possible. The guidance also provides clarity on the types of data and information that sponsors should provide to address clinical, nonclinical and quality considerations before submitting an application to initiate studies.

The second guidance, "COVID-19: Developing Drugs and Biological Products for Treatment or Prevention," provides FDA's current recommendations regarding phase 2 or phase 3 clinical trials intended to establish safety and effectiveness for COVID-19 treatments. This guidance focuses on the population, trial design, efficacy endpoints, safety considerations, and statistical considerations for such clinical trials.

FDA Issues Several Untitled Letters for Unapproved Cellular Therapies

FDA recently issued untitled letters to two companies regarding their marketing of unapproved products that appear to be human cells, tissues, or cellular or tissue-based products (HCT/Ps).

FDA issued an untitled letter to New Jersey-based Valeo MD regarding the company's marketing of an unapproved stem cell therapy derived from adipose tissue. According to the April 28 letter, the company markets the therapy, administered intravenously, to treat various serious and life-threatening diseases or conditions.

FDA sent a second untitled letter to Sparrow Health and Performance, LLC, of Hoover, AL, on May 11. Sparrow Health and Performance offers cellular products derived from adipose tissue as a "stem cell therapy" to treat numerous diseases and conditions, including COVID-19. The company also lists exosomes as one of its provided services.

FDA believes that these products appear to be an HCT/P that should be regulated as both a drug and biological product. In order to lawfully market these products, a valid biologics license application or IND application must be in effect, as specified by FDA regulations. The agency also noted that the product's higher-risk administration method, if contaminated, could cause a range of adverse events. FDA directed the company to its comprehensive regenerative medicine policy framework for HCT/Ps and requested a written response within 30 days of receipt of the letter.

April 28, 2020 Untitled Letter - ValeoMD
May 11, 2020 Untitled Letter - Sparrow Health & Performance, LLC