The Focal Point: Advocacy & Legislative Update

June 23, 2020

COVID-19 Update

The World Health Organization (WHO) reported the largest single-day increase in global coronavirus cases on Sunday, with the total rising by 183,020 in a 24-hour period, edging past 9 million cases worldwide. The Americas, especially U.S and Brazil, are the source of the biggest increase.The WHO Director-General warned that the pandemic is entering a dangerous phase, with people tired of staying home and countries eager to reopen economies, but with COVID-19 activity still spreading fast and much of the world's population still susceptible.

The global total rose to 9,121,337 cases, and 472,683 people have died from their infections, according to the Johns Hopkins online dashboard. The United States reported 2,312,302 confirmed cases and 120,402 deaths.

CDC's weekly surveillance summary of U.S. COVID-19 activity can be found here.

Cases in the United States are up 15 percent over the past two weeks, as 29 states and territories logged an increase in their 7-day average of new reported cases. The White House is preparing for a second wave in the Fall, while a top epidemiologist, Michael Osterholm, MD warns of a new U.S. trajectory: not waves, but a "forest fire of cases."

The CDC reported in its forecast, which is a combination of data from 21 national models,that there will likely be between 129,000 and 145,000 total reported COVID-19 deaths by July 11th. Fatalities are expected to increase in over the next four weeks in Alaska, Arizona, Arkansas, Florida, Hawaii, North Carolina, Oregon, South Carolina, and Utah. For other states, the number of new deaths is expected to be similar or decrease slightly compared to the previous four weeks.

Comorbidities Increase COVID-19 Deaths by Factor of 12

Patients with underlying health conditions are six times more likely to be hospitalized and 12 times more likely to die from COVID-19, according to the CDC's Morbidity and Mortality Weekly Report released June 15.

The CDC examined data on more than 1.7 million COVID-19 cases and 103,700 related deaths reported by state and local health departments between Jan. 22 and May 30. Hospitalizations were six times higher for people with underlying health conditions, the most common being cardiovascular disease (32%), diabetes (30%), and chronic lung disease (18%).

Study Finds 1 in 5 People Worldwide at Risk of Severe Covid-19

Roughly 1.7 billion people, 22 percent of the world population, have at least one underlying health conditions that could increase their risk of severe COVID-19 if infected, according to an analysis published in *The Lancet Global Health.*

The new modeling study uses data from 188 countries. The authors estimated that 349 million people (4% of the global population) are at high risk of severe COVID-19 and would require hospital admission if infected (ranging from <1% of those younger than 20 years to approximately 20% of those aged 70 years or older). They estimated 6% of males to be at high risk compared with 3% of females. The share of the population with at least one underlying health condition is highest in countries with ageing populations, African countries with high HIV/AIDS prevalence, and small island nations with high diabetes prevalence.

As lockdown restrictions are eased, governments could use the estimates to understand who should be prioritized for enhanced physical distancing measures and vaccination, if available.

Antibodies in COVID-19 Patients May Fade Quickly

A new study published in *Nature Medicine* showed that antibodies faded quickly in both asymptomatic and symptomatic COVID-19 patients during convalescence, raising questions about whether the illness leads to any lasting immunity to the virus afterward.

The study compared 37 asymptomatic and 37 symptomatic patients, who had been infected with SARS-CoV-2, as determined by repeated tests for viral RNA. More than 90% of both groups showed steep declines in levels of SARS-COV-2–specific immunoglobulin G (IgG) antibodies within 2 to 3 months after onset of infection. Furthermore, 40% of the asymptomatic group tested negative for IgG antibodies 8 weeks after they were released from isolation. The researchers also found declines in specific neutralizing antibodies and noted that IgG levels were significantly higher in the symptomatic patients than the asymptomatic ones in both the acute and convalescent phases of infection.

In other findings, asymptomatic patients shed the virus significantly longer than those with symptoms—a median of 19 days versus 14 days. But they cautioned that detectable viral RNA does not necessarily mean that the viral particles shed were infectious. The virus load upon initial detection was indistinguishable between the two infected groups, so the amount of virus detected in nasal swabs is not an indication of subsequent disease progression.

One unexpected finding is that CAT-scans of the lung showed that two-thirds of those with no clinical signs of COVID-19 had ground-glass opacity abnormalities in at least one lung, and one-third showed ground-glass opacities in both lungs.

CDC Releases Consolidated COVID-19 Testing Recommendations

The CDC has released consolidated recommendations for COVID-19 testing, including interim testing guidelines healthcare personnel, as well as testing strategy options for high-density critical infrastructure workplaces after a COVID-19 case is identified.

The **Overview of Testing for SARS-CoV-2**, compile and update previous testing guidance and are subject to change as additional information becomes available.

This document describes five categories of people for SARS-CoV-2 testing with viral tests (i.e., nucleic acid or antigen tests):

- Testing individuals with signs or symptoms consistent with COVID-19
- Testing asymptomatic individuals with recent known or suspected exposure to SARS-CoV-2 to control transmission
- Testing asymptomatic individuals without known or suspected exposure to SARS-CoV-2 for early identification in special settings
- Testing to determine resolution of infection (i.e., test-based strategy for Discontinuation of Transmission-based Precautions, HCP Return to Work, and Discontinuation of Home Isolation)
- Public health surveillance for SARS-CoV-2

No Measurable Risk for SARS-CoV-2 Transmission Through Blood Components in Asymptomatic Donors

There is no measurable risk for transmission of SARS-CoV-2 through blood components donated by asymptomatic SARS-CoV-2-infected individuals, according to findings published recently in *Transfusion*. Investigators reported on 18 German patients with RT-PCR confirmed SARS-CoV-2 infection. Of these, 15 patients developed symptoms of different severity. Investigators performed SARS-CoV-2 testing targeting the E and RNA-dependent RNA polymerase gene.

Three of the 18 patients fulfilled the requirements for blood donation in Germany. Oral swabs or sputum from the lower respiratory tract from all 18 patients tested RT-PCR positive, but investigators detected SARS-CoV-2 genomes in 1 of 77 blood samples. This sample was one of eight serum/plasma samples taken from a patient with acute respiratory distress syndrome.

Investigators noted that RNAemia is not equivalent to infectiousness and that there have been no documented hematogenous transmissions for SARS-CoV-2. Furthermore, symptomatic donors would not be eligible for blood donation in Germany. Therefore, the risk for transfusion transmission of SARS-CoV-2 is considered negligible.

Mutation Could Make Coronavirus More Infectious

Researchers at the Scripps Research Institute in Florida have discovered that a specific mutation called D614G increases the number of spike proteins on the novel coronavirus, boosting its ability to infect cells.

Hyeryun Choe and colleagues ran a series of experiments in lab dishes that show a mutation called D614G increased the number of "spikes" on the coronavirus - which allow the virus to bind to and infect cells and makes those spikes more stable.

"The number—or density—of functional spikes on the virus is 4 or 5 times greater due to this mutation," said Choe. That in turn allowed the virus to become more infectious. The researchers will post their findings on a preprint server called BioRxiv.

Other research has showed that the new coronavirus SARS-CoV-2 is mutating and evolving as it adapts to its human hosts. The D614G mutation in particular has been flagged as an urgent concern because it appeared to be emerging as a dominant strain spreading in Europe, the U.S., and Latin America.

FDA Issues GMP Guidance for COVID-19-Infected Employees

A new guidance from FDA clarifies how manufacturers of drugs and biological products should address COVID-19 infection in their employees.

Employees who are ill or infected with SARS-CoV-2, must be excluded from drug manufacturing areas and not permitted to return until they have met home isolation criteria established by the CDC. This guidance holds true for individuals who have a positive test for COVID-19, even if they do not have symptoms, and for individuals with COVID-19 symptoms, regardless of testing status. Evaluation of the employee's status should be made "in consultation with healthcare providers," according to the guidance, which is immediately effective for the duration of the public health emergency of the COVID-19 pandemic.

Employees should report any exposures or potential exposures to their supervisors, who should follow the CDC guidance. Manufacturers should consider implementing CDC-recommended social distancing measures that minimize the risk of transmission of COVID-19.

The guidance points to current good manufacturing practices (CGMPs) that already address infected or potentially infected employees who are engaged in drug manufacturing. 21 CFR 211.28(d) mandates that an individual with apparent illness that may adversely affect drug product safety or quality be excluded from the production area and process until the individual can be medically evaluated, or the condition has been deemed corrected. Under this regulation, personnel are required to report any health conditions that could adversely affect drug safety or quality to their supervisors. For biological products, 21 CFR 600.10(c)(1) similarly requires that individuals who could adversely affect the safety or purity of a product be restricted from rooms where manufacturing is in progress.

The guidance also recommends that employees continue to practice good sanitation and health practices, and that ongoing risk management consider known characteristics of SARS-CoV-2. Cleanroom processes such as air filtration and movement should be reviewed, and manufacturers should consider the potential for cross-contamination. Biological product manufacturers need to conduct their risk assessments with an eye to such factors as the potential that a production cell line could itself replicate SARS-CoV-2 and whether current virus testing would detect the novel coronavirus, among others.

Manufacturers can take specific steps to minimize the risk of workplace transmission of COVID-19, including more frequent cleaning and sanitizing of non-production areas and high-touch areas within production areas; expanding use of gloves, masks, and gowns; and further restricting any unnecessary employee access to manufacturing areas.

Any potential or actual coronavirus contamination should trigger thorough cleaning, disinfecting, sanitization, and – if necessary – sterilization of all affected areas and equipment before manufacturing begins again. All evaluations of production controls, including COVID-19-focused risk assessments, should be approved by a drug or API manufacturer's quality unit and documented within the quality management system.

To maintain the drug supply, drugmakers of medically necessary human drugs should have contingency production plans in place should they see a spike in COVID-19 cases and high absenteeism. The contingency plan could include provisions for remote work, where feasible. Any anticipated disruption in the drug supply must be reported to FDA immediately; the guidance provides contact links for each FDA regulatory branch.

FDA Authorizes Next Generation COVID-19 Diagnostic Test

The FDA issued an emergency use authorization (EUA) to Illumina, Inc. for their COVIDSeq Test, the first COVID-19 diagnostic test utilizing next generation sequence technology.

This test is for the qualitative detection of SARS-CoV-2 RNA from nasopharyngeal or oropharyngeal swabs as well as aspirates and bronchoalveolar lavage specimens collected by a healthcare provider. Only laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) to perform high complexity tests may employ the new COVIDSeq Test.

Next generation sequencing is a type of diagnostic technology that can determine, among other things, the genetic sequence of a virus. Comparing sequencing results over time can help scientists understand if and how viruses mutate. Read the FDA statement.

Health Providers Warned Against Using Certain COVID-19 Serology/Antibody Tests

The FDA issued a Letter to Clinical Laboratory Staff and Health Care Providers recommending that they stop using COVID-19 antibody tests that are listed on the FDA's "removed" test list. The "removed" test list includes:

- tests where significant clinical performance problems were identified that cannot be or have not been addressed by the commercial manufacturer in a timely manner,
- tests for which an Emergency Use Authorization request has not been submitted by a commercial manufacturer of a serology test within a reasonable period of time as outlined in the FDA's guidance, and
- tests voluntarily withdrawn by the respective commercial manufacturers.

To date, the FDA has authorized 144 tests under EUAs; these include 122 molecular tests, 21 antibody tests, and 1 antigen test.

FDA Issues Warnings to Fraudulent COVID-19 Test Manufacturers

The FDA has issued warning letters to three companies for marketing adulterated and misbranded COVID-19 antibody tests. Violations outlined in the warning letters include:

- offering test kits for sale in the United States directly to consumers for at-home use without marketing approval, clearance, or authorization from the FDA;
- misbranding products with labeling that falsely claims products are "FDA approved"; and

- labeling that bears the FDA logo, which is only for the official use by the FDA and not for use on private sector materials.

The FDA reminds the public that, at the present time, there are no diagnostic or antibody COVID-19 test kits that are authorized, cleared or approved to be used completely at home. Read the FDA statement.

FDA Issues a Warning Letter to EUCYT Laboratories

The FDA issued a warning letter to EUCYT Laboratories, LLC, for marketing an unapproved exosome product for the treatment or prevention of COVID-19. None of their products have an approved biologics license application (BLA), nor an Investigational New Drug application in effect for any of them.

In the warning letter, FDA quoted EUCYT Laboratories' website, which claimed that "COVIXO drives cellular functionality including augmenting the type 1 interferon pathway ... that is important for anti-SARS-CoV-2 activity" and "[t]he unique mechanism of action for COVIXO enables each patient to generate their own adaptive immune response against SARS-CoV-2, including memory T cells and antibodies, which will further protect each patient from subsequent exposures and infections."

FDA inspection of the company's Las Vegas facility also uncovered significant deviations from current good manufacturing practice (cGMP) and current good tissue practice (cGTP). These deviations include deficient donor eligibility practices, unvalidated manufacturing processes, deficient environmental monitoring and inadequate aseptic practices. 152 sterility failures were identified between April 2018 and November 2019, and EUCYT destroyed the batches containing pathogenic organisms without thoroughly investigating the contamination.

FDA requested the company respond in writing within 15 working days of receipt of the letter, outlining the specific steps it has taken or plans to take to correct the noted violations and prevent their recurrence.

FDA Names New Director for Office of Infectious Diseases

The FDA has appointed John Farley as director of the Office of Infectious Diseases (OID), which is part of the Center for Drug Evaluation and Research's Office of New Drugs. Farley, who led the OID's COVID-19 pandemic response, has been serving as the office's acting director since August 2019.

FDA Offers Statistical Guidance for Trials Impacted by COVID-19

The FDA issued immediately effective guidance offering statistical advice to clinical trial sponsors with the aim of maintaining trial integrity and mitigating the effects of COVID-19 on clinical trials.

Public health measures to control the virus may impact the ability to collect data, for example, if trial participants are not able to visit clinical sites for endpoint assessments. To help ensure that the trial will provide interpretable findings with correct statistical quantification of

uncertainty, this guidance addresses statistical considerations for proposed changes to a trial due to the COVID-19 pandemic that may impact the analysis and interpretation of the primary or key secondary endpoints in the trial.

Sponsors should discuss any proposed protocol changes and changes to their statistical analysis plan with the relevant FDA review division.

Electronic Submission of Postmarket Safety Reports

FDA updated its webpage to provide human drug and biological product manufacturers, distributors, packers, and other parties subject to mandatory reporting requirements with the instructions on how to electronically submit postmarket Individual Case Safety Reports (ICSRs) to the FDA.

ICSR content and format requirements for drug and non-vaccine biologics postmarket reporting are based upon the International Council on Harmonisation (ICH) E2B(R2) specifications.

Visit the FDA Adverse Event Reporting System (FAERS) Electronic Submissions website for step-by-step instructions for submitting drug and non-vaccine biologics ICSRs to the FDA: https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm115894.htm

---

FDA Publishes FRNs for April 2020 CJD, HIV and Malaria Guidance Documents

The FDA published*Federal Register*notices on Tuesday for the Creutzfeldt-Jakob Disease (CJD), HIV and malaria guidance documents which were posted to FDA's website on April 2, 2020 for immediate implementation to address the urgent need for blood during the COVID-19 pandemic.

The CJD guidance finalizes the draft guidance of the same title dated January 2020. FDA is revising or removing their prior recommendations to screen blood donors for: (1) Geographic risk of possible exposure to bovine spongiform encephalopathy, including time spent on U.S. military bases in Europe; (2) receipt of a blood transfusion in certain vCJD risk countries; (3) risk factors for iatrogenic CJD (i.e., a history of taking human cadaveric pituitary-derived growth hormone); (4) having blood relatives with CJD; and (5) a history of injecting bovine insulin.

The final HIV guidance supersedes the guidance of the same title dated December 2015. It revised the donor deferral recommendations to three months for individuals with increased risk for transmitting human immunodeficiency virus (HIV) infection.

Although issued without prior public comment, FDA is soliciting comments, will review all comments received and revise the documents as appropriate. Each guidance document and FRN specifies the docket number to which comments can be submitted.

EBAA Submits Comments to the FTC Regarding Funeral Rule

EBAA submitted comments to the Federal Trade Commission (FTC) on the Funeral Industry Practices Rule on behalf of the membership. We applaud their efforts to ensure that consumers have access to sufficient information to make informed decisions about the final disposition of their loved ones, particularly during a time of emotional strain.

We proposed an addition to the list of services required on the General Price List (GPL), to include the cost, if any, for the use of facilities and staff to permit eye/cornea donation. A funeral home's policy of not disclosing fees that it requires to facilitate an altruistic cornea donation should certainly qualify as a deceptive practice.

If no fee is charged, as is the case in the overwhelming majority of cases, the GPL could include a statement such as "XXX Funeral Home supports eye and cornea donation and will not charge a fee for the use of our facilities to recover donated eye tissue."

The comments are found here.

SBA Releases Updated PPP Guidance and a New PPP Loan Application Form

On June 11, 2020, the Small Business Administration (SBA) released interim final rule #17 adopting changes to Paycheck Protection Program (PPP) loan terms as a result of the new law, the Paycheck Protection Program Flexibility Act of 2020 enacted last week. In addition, the SBA released a new PPP loan application form that incorporates those changes.

As a reminder, the new law extends the forgiveness period for PPP loans from eight to 24 weeks, reduces payroll spending requirements from 75% of loan funds to 60% of loan funds, and extends the June 30th deadline for rehiring workers to the end of this year. Businesses now also have up to five years, instead of two years, to repay any money owed on a loan.

AAO Statement on Rubber Bullets for Crowd Dispersion

The American Academy of Ophthalmology (AAO) released a statement condemning the use of rubber bullets as a means of crowd dispersion. While classified as non-lethal, they are not non-blinding.

The AAO calls on domestic law enforcement officials to immediately end the use of rubber bullets to control or disperse crowds of protesters. The Academy asks physicians, public health officials and the public to condemn this practice.

Americans have the right to speak and congregate publicly and should be able to exercise that right without the fear of blindness. Using your voice shouldn't mean losing your vision

---

Tick-Borne Diseases Working Group Announces Virtual Meeting

The Tick-Borne Diseases Working Group (TBDWG) will review the draft 2020 report to the secretary of HHS and Congress at its next virtual meeting, held on July 8, 2020. The report will address ongoing tick-borne disease research, including research related to causes, prevention, treatment, surveillance, diagnosis, diagnostics, and interventions for individuals

with tick-borne diseases; advances made pursuant to such research; federal activities related to tick-borne diseases; and gaps in tick-borne disease research.

The public will have an opportunity to present views to the Working Group during the meeting's public comment session. Interested individuals should submit a request to make verbal comments or submit their views in writing prior to June 24. Pre-registration is encouraged for participants. The meeting agenda is available online.