The Focal Point: Advocacy & Legislative Update

April 28, 2020

COVID-19 Update

The global case total climbed to 3,094,829 in 185 nations by Tuesday night, with fatalities reaching 215,461, according to the Johns Hopkins online dashboard. The US total is at 1,004,908 with 57,812 deaths.

Preliminary results from serologic surveys suggest that coronavirus infections greatly outnumber confirmed COVID-19 cases by a factor of 10 or more. Higher infection rates mean that there is a much lower infection fatality rate than the 6 percent case fatality rate seen globally and, in the U.S.

COVID-19 Symptoms

The CDC added six new potential COVID-19 symptoms which typically appear 2-14 days after exposure. Originally listing only fever, cough and shortness of breath as coronavirus symptoms, the agency has now added chills, repeated shaking with chills, muscle pain, headache, sore throat and new loss of taste or smell.

Prolonged SARS-CoV-2 RNA Detection from Ocular Sections

A single case report published in the *Annals of Internal Medicine*, has demonstrated presence of infectious SARS-CoV-2 virus and viral RNA in the conjunctiva of a patient with a history of conjunctivitis up to 27 days. The first patient in Italy to be diagnosed with COVID-19 also had conjunctivitis in addition to fever and respiratory and gastrointestinal signs. RT-PCR on conjunctival swabs showed SARS-CoV-2 RNA from day 3 of hospitalization until day 21 (1 day after the conjunctivitis resolved), and again at day 27, at which point nasal swabs were negative. Infectious virus was isolated by cell culture from a sample taken on day 3.

Povidone-Iodine and COVID-19

A recent review about the persistence of coronaviruses on inanimate surfaces, as well as their inactivation with biocidal agents revealed that povidone iodine (0.23 - 7.5%) readily inactivated coronavirus infectivity by approximately 4 log10 or more, with exposure times of 15 seconds.

Current EBAA Medical Standard **E1.100 Recovery** procedures requiring double exposure of povidone-iodine to ocular tissue would result in rapid viricidal activity against coronaviruses and reduce the likelihood that COVID-19 may be transmitted through corneal transplantation.

The ocular surface is not an inanimate surface and it is not known if infectious virus particles inside ocular surface cells are eliminated by povidone iodine preparations. Nonetheless, the European Centre for Disease Prevention and Control (ECDC) considers this a disinfection or microbial inactivation step that is validated for enveloped viruses.

Latest Guidance and Publications on COVID-19:

The CDC has developed a new web page to provide summaries of hospitalization data due to COVID-19 in the U.S. See the COVID-NET page.

Information for Healthcare Professionals

Clinical Care Guidance for Healthcare Professionals about COVID-19

Guidance for U.S. Healthcare Facilities about COVID-19

COVID-19 Infection Prevention and Control in Healthcare Settings: Questions and Answers

Hospitalization Rates and Characteristics of Patients Hospitalized with Laboratory-Confirmed Coronavirus Disease 2019 — COVID-NET, 14 States, March 1–30, 2020

Characteristics of Health Care Personnel with COVID-19 — United States, February 12–April 9, 2020. MMWR Morb Mortal Wkly Rep 2020; 69:477–481. DOI: http://dx.doi.org/10.15585/mmwr.mm6915e6

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Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. *JAMA.* Published online April 22, 2020. doi:10.1001/jama.2020.6775https://jamanetwork.com/journals/jama/fullarticle/2765184

Chow EJ, Schwartz NG, Tobolowsky FA, et al. Symptom Screening at Illness Onset of Health Care Personnel With SARS-CoV-2 Infection in King County, Washington. *JAMA.* Published online April 17, 2020. doi:10.1001/jama.2020.6637 https://jamanetwork.com/journals/jama/fullarticle/2764953

Chen L, Liu M, Zhang Z, et al. Ocular manifestations of a hospitalised patient with confirmed 2019 novel coronavirus disease. *British Journal of Ophthalmology* Published Online First: 07 April 2020. doi: 10.1136/bjophthalmol-2020-316304 https://bjo.bmj.com/content/early/2020/04/07/bjophthalmol-2020-316304

EDQM Webinar: Tissue Donation from Deceased Donors During the COVID-19 Pandemic

The European Directorate for the Quality of Medicines and HealthCare (EDQM), Council of Europe held a webinar on April 28th, 2020 to discuss how the COVID-19 pandemic is affecting national programs for tissue donation from deceased donors and daily practices in tissue establishments.

After opening remarks and an introduction from the chairs, representatives from different countries shared experiences from their tissue establishments, including:

- Isabelle Martinache – Agence de la Biomédecine, France
- Ralf Reinhard Tönjes, Paul Ehrlich Institute, and Martin Börgel, Deutsche Geselischaft fűr Gewebetransplantation, Germany
- Jorge Gayoso, Organización Nacional de Trasplantes, and Anna Vilarrondona, Banc de Sang Teixits, Spain
- Kyle Bennett, National Health Services Blood and Transplant, United Kingdom
- Massimo Cardello and Eliana Porta, Centro Nazionale Trapianti, Italy

Following the Q&A session, Dragoslav Domanovic from the European Centre for Disease Prevention and Control (ECDC) discussed the *Risk of transmission through tissues from diseased donors and testing practices.*

A common theme throughout was the deferral of donors with respiratory symptoms at the time of death, confirmed COVID-19 infection, or their close contacts. Italy and France have implemented RT-PCR testing for SARS-CoV-2 from NP swabs taken 24 hours after death, but Spain reported that PCR testing is very limited, and not readily available.

Germany reported that PCR testing is not mandatory, and that antibody and tissue testing is not available or useful/valid at this time. They advised against testing asymptomatic donors to save testing capabilities and stressed donor symptom screening. Similarly, the UK excludes any donor with respiratory symptoms at the time of death unless COVID-19 was excluded after testing at the hospital.

Both Germany and the UK mentioned that povidone iodine inactivates a variety of both enveloped and non-enveloped viruses, including influenza A, MERS-CoV and SARS-CoV and that tissue processed using pathogen reduction steps do not need to be excluded, because in such tissues the risk of disease transmission is negligible and acceptable.

Postponement of non-emergency surgeries has hit ocular recoveries particularly hard and the UK is currently working on a recovery plan.

The ECDC recommendation for testing is that tissues should not be collected from deceased donors who are without symptoms or diagnosis of COVID-19, and who lived in, or visited areas of sustained community transmission of the virus unless:

- There is disinfection, sterilization, or microbial inactivation step of procured tissues that is validated for enveloped viruses,

or

- Donors tested negative for the presence of SARS-CoV-2 in upper or lower respiratory tract specimens collected within 72 hours before procurement.

FDA Letter to HCP on Use of COVID-19 Serological Tests

The FDA issued information on the use of serological (antibody) tests to help identify people who may have been exposed to the SARS-CoV-2 virus or have recovered from the COVID-19 infection. However, these tests should not be used as the sole basis to diagnose COVID-19.

This information includes:

- Important Information on the Use of Serological (Antibody) Tests for COVID-19 - Letter to Health Care Providers;
- FDA Fact Sheet - Serological Testing for Antibodies to SARS-CoV-2 Infection; and
- New Serology/Antibody Test FAQs in the FAQs on Diagnostic Testing for SARS-CoV-2.

Nonbinding Feedback After Certain FDA Inspections of Device Establishments

The FDA finalized guidance formalizing a process for medical device makers to request nonbinding feedback on their proposed actions to address issues raised during inspections. This guidance identifies a standardized method for communicating and submitting requests for nonbinding feedback and describes how FDA evaluates and responds to such requests.

Requests for nonbinding feedback should come from either the individual at the company that received the Form FDA 483 during the inspection or from someone who can demonstrate that they are the owner, operator or agent in charge of the establishment. Requests should be made within 15 business days to be considered timely and that companies submitting a response to a 483 and request for feedback at the same time should include both in the same submission as two separate documents.

FDA Authorizes First COVID-19 Test for At-Home Collection

FDA granted an emergency use authorization (EUA) to LabCorp allowing it to test self-collected nasal swab samples from patients for coronavirus disease (COVID-19) using LabCorp's Pixel by LabCorp COVID-19 Test home collection kit.

The kits include a Q-tip-style cotton swab that people can use to collect samples in their nose; the swabs would then be mailed in an insulated package to a LabCorp facility for testing. The company says it plans to have the Pixel kits available in in most states within the next few weeks and according to their website they cost $119 a test. However, the test can only be administered with a doctor's order and after passing a questionnaire.

FDA Issues Updated Table of COVID-19 Diagnostic EUAs

FDA updated the table of emergency use authorizations (EUAs) for in vitro diagnostics for detection and/or diagnosis of the novel coronavirus. The updated table now includes a column for the technology (molecular or serology) and the assigned complexity (high, moderate, waived) for each test. There are also links to authorization documents including the healthcare provider (HCP) and patient fact sheets and either the manufacture instructions/package insert or the EUA Summary.

AATB Names New President and CEO

The American Association of Tissue Banks (AATB) recently announced Marc Pearce, MBA as the organization's new President and Chief Executive Officer. Pearce will begin his new role on June 1. Since 2011, Pearce has served as the Vice President, Business Systems for Creative Testing Solutions (CTS). He also worked at AABB for more than a decade and was AABB's Chief Marketing Officer upon his departure.

NIH Study Seeks to Quantify Undetected COVID-19 Cases

Investigators at the National Institutes of Health (NIH) announced the launch of a new study to help determine how many adults in the U.S. without a confirmed history of infection with SARS-CoV-2have antibodies to the virus.

In this serosurvey, investigators will collect and analyze blood samples from as many as 10,000 volunteers to help illuminate the extent to which the novel coronavirus has spread in the U.S. and provide insights into which communities and populations are most affected.

Healthy adults from anywhere in the U.S. can participate. Individuals with a confirmed history of COVID-19 or current symptoms consistent with COVID-19 are not eligible to participate. Individuals interested in joining this study may contact clinicalstudiesunit@nih.gov.

What Impact Has COVID-19 Had on Outpatient Visits?

A new analysis shows that COVID-19 has had a devastating impact on outpatient care across the United States. The number of visits to ambulatory practices declined nearly 60 percent in mid-March and has remained low through mid-April.

Ophthalmology saw the largest percent change in ambulatory practice visits from the beginning of March to the week of April 5, with a 79 percent drop.

CMS Issues Recommendations on Reopening Facilities to Provide Non-Emergent, Non-COVID-19 Health Care

The Centers for Medicare and Medicaid Services (CMS) issued recommendations to begin a phased approach to reopening non-emergent health care services in areas with low or stable incidence COVID-19. Elective surgeries can resume, as clinically appropriate, on an outpatient basis at facilities that adhere to CDC guidelines once a state or region meets certain "gating criteria" outlined in the Opening Up America Again guidelines.

Facilities would be able to begin Phase One opening if the state or region has met these criteria:

- Symptoms: Downward trajectory of influenza-like illnesses (ILI) ***and*** COVID-like syndromic cases reported within a 14-day period.
- Cases: Downward trajectory of documented cases within a 14-day period ***or*** downward trajectory of positive tests as a percent of total tests within a 14-day period (flat or increasing volume of tests).
- Hospitals: Treat all patients without crisis care ***and*** robust testing program in place for at-risk healthcare workers, including emerging antibody testing.

Please note that these are *guidelines* and that the federal government will defer to the states with respect to implementation of its reopening policies.

Medical Associations Issue Roadmap for Resuming Elective Surgery

The American College of Surgeons, American Society of Anesthesiologists, Association of periOperative Registered Nurses, and American Hospital Association have issued a Joint Statement entitled *Roadmap for Resuming Elective Surgery after COVID-19 Pandemic*.

The Statement sets forth principles and considerations to guide physicians and facilities in their resumption of care in operating rooms and all procedural areas, including:

- Timing for Reopening of Elective Surgery
- COVID-19 Testing within a Facility
- Personal Protective Equipment
- Case Prioritization and Scheduling
- Post-COVID-19 Issues for the Five Phases of Surgical Care
- Collection and Management of Data
- COVID-related Safety and Risk Mitigation Surrounding Second Wave

The roadmap emphasizes that the reopening of facilities should be guided by state and local directives.

FDA Updates Q&A Appendix in Guidance on Conducting Clinical Trials of Medical Products During the COVID-19 Pandemic

FDA added content to the question-and-answer appendix in its March 2020 guidance entitled Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency.

The updated guidance includes new content on conducting remote clinician-reported outcome or performance outcome assessments; remote site monitoring; electronic common technical document requirements; investigational product administration by a local health care provider who is not a sub-investigator; and information for sponsors on contacting FDA regarding certain changes to ongoing trials. There is also updated information about obtaining informed consent from a patient who is unable to travel to the clinical trial site due to COVID-19 illness or travel restrictions in situations where electronic informed consent is not an option.

The FDA is aware that protocol modifications may be required, and that there may be unavoidable protocol deviations due to COVID-19. Although the impact of COVID-19 on trials will vary depending on factors such as the nature of disease under study, the trial design, and in what region(s) the study is being conducted, FDA's guidance outlines general considerations to assist sponsors in assuring the safety of trial participants, maintaining compliance with good clinical practice, and minimizing risks to trial integrity. The appendix further explains those considerations by responding to related questions the agency has received.

FDA Updates Letter to Sponsors, Applicants and Regulated Entities on COVID-19

FDA's Center for Biologics Evaluation and Research (CBER) has updated their letter issued on March 27th pertaining to CBER operations during the COVID-19 public health emergency. CBER has taken steps to address day-to-day operations in CBER and industry, while ensuring that government and private sector efforts to respond to this national emergency receive the highest priority.

FDA Sends Untitled Letter to Kimera Labs Regarding Unapproved Exosome Products

FDA sent an untitled letter to Florida-based Kimera Labs, Inc. regarding the company's unapproved exosome products. The company markets exosome products to treat numerous diseases or conditions, including Parkinson's disease, multiple sclerosis, brain injuries, diabetes, stroke and spinal cord injuries. Kimera Labs also supplies products to other companies, one of which has marketed products to prevent or treat COVID-19.

FDA believes that the company's exosome products would be regulated as both a drug and biological product. In order to lawfully market these products, a valid biologics license application or investigational new drug application must be in effect, as specified by FDA regulations. The agency requested a written response from the company within 30 days of receipt of the letter.

FDA Sends Untitled Letter to Regenerative Solutions of New Jersey

FDA sent an untitled letter to Regenerative Solutions of New Jersey regarding the company's marketing of unapproved exosome products from Kimera Labs, Inc. The company markets these exosome products to mitigate, prevent, treat, or cure Coronavirus Disease 2019 (COVID-19). The firm also markets these exosome products to treat numerous diseases or conditions, including COPD, spinal cord injury, Parkinson's disease, Alzheimer's disease, lupus, and multiple sclerosis.

These exome products would be marketed as both drugs and biological products, requiring a valid biologics license or investigational new drug application (IND). FDA requested a written response within 30 days.

President Signs Paycheck Protection Program and Health Care Enhancement Act

The latest COVID-19 funding bill, officially known as H.R. 266 "Paycheck Protection Program and Health Care Enhancement Act," was signed by President Trump on Friday, April 24, 2020, after being passed by the House and Senate earlier in the week.

The bill provides $484 billion in additional funding to replenish and supplement key programs under the CARES Act, including the Paycheck Protection Program (PPP), small business disaster loans and grants, and includes new hospital and health care funding as well as additional money for testing.

- The new $484 billion bill serves as interim funding legislation as Congress begins discussions on Phase 4 of its COVID-19 stimulus and relief programs.
- The lion's share of the money, $370 billion, goes to small businesses.
- Sets aside $60 billion for small banks to address concerns that too much of original PPP funds went to large companies.
- About $75 billion goes to hospitals and $25 billion to testing.