The Focal Point: Advocacy & Legislative Update
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CBER Finalizes Guidance on Use of Standards in Regulatory Submissions

The US Food and Drug Administration's (FDA) Center for Biologics Evaluation and Research (CBER) finalized guidance on the use of standards in product development and the use of such standards in CBER's review process. CBER encourages sponsors of regulatory submissions and manufacturers to use appropriate voluntary consensus standards.

While this guidance "does not endorse the activities of specific Standards Development Organizations (SDOs) or recommend specific standards for use in regulatory submissions", it does explain how the wider use of voluntary consensus standards "can facilitate product development and reduce the amount of documentation needed in a regulatory submission", resulting in more efficient submission evaluation and improving time to market.

CBER may, in some cases, take accreditation standards into consideration when assessing compliance to regulatory requirements. Examples cited include the blood donor history questionnaire developed by AABB, International Council for Commonality in Blood Banking Automation (identification and labeling of blood and tissues), and American Association of Tissue Banks (tissue banking).

This guidance finalizes the draft guidance of the same title dated December 2017. The guidance expands on what was written in the draft, with more information on reference materials/physical standards, compendial standards and data standards.

FDA Drafts Guidance on Inspections of Medical Device Establishments

FDA has issued a draft guidance to implement uniform processes and standards for FDA inspections of domestic and foreign medical device establishments.

FDA has updated processes and standards for uniformity within and across inspections other than for-cause and to establish a standard timeframe for such inspections of device establishments. The draft guidance also describes standardized methods of communication during the inspection process and identifies practices for investigators and device establishments to facilitate the continuity of inspections of such establishments.

FDA will pre-announce a domestic inspection generally within five calendar days. For foreign inspections, this may be longer due to requirements of particular country clearances. The notification should include information about the type and nature of the inspection, such as whether the inspection is scheduled as abbreviated, comprehensive, or pre-approval.

The agency's inspections can range from three to six consecutive business days, though factors such as the nature of FDA-observed deficiencies can impact inspection duration and extensions may be needed under certain situations.

Comments on the draft guidance should be submitted by May 28, 2019, to ensure that FDA considers your comment before it begins work on the final guidance.

BPAC Considers ZIKV Testing and MSM Deferral Policies

The FDA's Blood Products Advisory Committee (BPAC) met March 20 - 21, 2019, to consider new information on blood safety related to the risks posed by Zika virus (ZIKV) and to revisit the deferral policy for men who have sex with men (MSM).

The first day focused on the decline of the ZIKV epidemic in the United States and worldwide, and whether universal testing of blood donations for ZIKV continues to be an appropriate strategy. The Committee voted to continue universal testing for ZIKV using mini-pool (MP) or individual (ID) nucleic acid testing (NAT), as recommended in the July 2018 Final Guidance. There was no policy change at this time, with BPAC agreeing that more data was needed to make a change.

On the second day, the Committee discussed possible changes to the current deferral approach for MSM donors, including a move from a 1-year to a 3-month deferral for monogamous MSM. FDA asked the Committee to examine the current scientific data on HIV and MSM and to identify additional information that could support alternatives to the current MSM donor deferral policy that would maintain the safety of the blood supply.

BPAC agreed that FDA should pursue data to support a shorter deferral period while ensuring the current level of safety, and improved assessment of risk for all individuals.

Adhesive Gel Could Repair Corneal Injuries Without Surgery

Researchers from the Massachusetts Eye and Ear Infirmary have developed an adhesive biomaterial for corneal repair and regeneration that could circumvent the need for corneal transplant surgeries.

The new technology, named GelCORE (gel for corneal regeneration), is made of chemically modified gelatin and photoinitiators, which are activated by a short-time exposure to blue light. Initially, the gel is a clear, viscous material designed to be applied with a dropper or syringe. When exposed to light, the material hardens and seals the cuts or ulcers on the cornea. Over time, the tissue showed signs of regeneration, according to a preclinical study published online in *Science Advances*.

The authors hope to begin clinical trials to test the technology in human patients in approximately one year.

UNH Researchers Create Hydrogel for Serious Eye Disease

Researchers at the University of New Hampshire have created a hydrogel that could one day be made into a contact lens to more effectively treat corneal melting, a condition that is a significant cause of blindness.

The incurable eye disease can be initiated by a number of causes, such as autoimmune diseases (like rheumatoid arthritis, Lupus, or Stevens-Johnson syndrome), chemical burns, and some surgical procedures (like LASIK and cataract procedures). The patient's cornea melts due to the uncontrolled production of certain zinc-dependent enzymes called matrix metalloproteinases (MMPs) by the patient’s immune cells in the cornea.

To help prevent the disease, the researchers developed a new hydrogel that deactivates those enzymes by removing the zinc ions. The goal is to make the hydrogel into a contact lens that would allow more localized treatment of the eye and avoid side effects in the rest of the body.

Injection Drug Use Associated with Candidemia

Candidemia, a bloodstream infection caused by *Candida* species, is typically considered a health care–associated infection, but injection drug use (IDU) has emerged as an increasingly common condition associated with candidemia.

Among 203 candidemia cases in the Denver metropolitan area during May 2017–September 2018, 23 (11%) occurred in 22 patients who had a recent history of IDU. During the first 6 months of the surveillance program, they observed that approximately one in 10 cases of candidemia occurred in patients who had a documented history of IDU, and the majority of their *Candida*-positive blood cultures were collected on the day of hospital admission or shortly thereafter.

First-Ever Living Donor HIV-To-HIV Kidney Transplant

The world's first kidney transplant from a living HIV-positive donor to another HIV-positive person was successfully performed March 25, by doctors at a Johns Hopkins University Hospital. Both the donor and recipient are doing well.

Nina Martinez of Atlanta traveled to Baltimore to donate a kidney to an HIV-positive stranger, saying she "wanted to make a difference in somebody else's life" and counter the stigma that too often still surrounds HIV infection.

Access to HIV-positive organs became possible in 2013, with the passage of the federal HIV Organ Policy Equity Act (the HOPE Act). Since 2016, 116 such kidney and liver transplants have been performed in the U.S. as part of a research study, according to the United Network for Organ Sharing (UNOS). By not having to rely solely on organs from the deceased, doctors may now have a larger number of kidneys available for transplant which could free up space on the transplant waiting list for everyone.

Prediction Models Forecast Spread of Disease-Carrying Mosquitoes

New prediction models factoring in climate change, urbanization and human travel and migration offer insight into the recent spread of two key disease-spreading mosquitoes -- Aedes aegypti and Aedes albopictus. These species transmit dengue virus, yellow fever, chikungunya virus and Zika virus. The models forecast that by 2050, 49 percent of the world's population will live in places where these species are established if greenhouse gas emissions continue at current rates.

The models, published recently in *Nature Microbiology*, estimate that in the U.S., *A. aegypti* may spread as far north as Chicago, although the species may decline in the southern and central parts of the U.S., which are predicted to become more arid. In Europe, the models estimate that *A. aegypti* will be limited to Southern Italy and Turkey. The models estimate that *A. albopictus* will spread widely throughout Europe but will be limited to northern parts of the U.S. in North America.