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FDA Issues Final Guidance on Medical Device Safety and Performance-Based Pathway

The Food and Drug Administration (FDA) issued a final guidance entitled "Safety and Performance Based Pathway," which finalizes the April 2018 draft guidance entitled "Expansion of the Abbreviated 510(k) Program: Demonstrating Substantial Equivalence through Performance Criteria." The intent of the guidance is to describe an optional pathway – the Safety and Performance Based Pathway – for certain, well understood device types, where a submitter would demonstrate that a new device meets FDA-identified performance criteria to demonstrate that the device is as safe and effective as a legally marketed device.

The Safety and Performance Based Pathway is appropriate when FDA has determined that:

(1) the new device has indications for use and technological characteristics that do not raise different questions of safety and effectiveness than the identified predicate,
(2) the performance criteria align with the performance of one or more legally marketed devices of the same type as the new device, and
(3) the new device meets all the performance criteria.

If any of the above factors are not met, the submitter has the option to submit a Traditional, Special or Abbreviated 510(k).

The final guidance includes a new high-level table outlining the types of information that may be required to support a finding of substantial equivalence under the Safety and Performance Based Pathway, which varies depending on the type of performance criteria and test methodology referenced in the submission.

The FDA plans to issue future guidance to apply this Safety and Performance Based Pathway to certain types of devices with corresponding FDA-identified performance criteria. The agency also set up a new webpage on the Safety and Performance Based Pathway in conjunction with issuing the final guidance.

FDA Finalizes Accelerated Approval Labeling Guidance

The FDA finalized guidance on labeling drugs and biologics approved under the accelerated approval pathway.

The FDA's accelerated approval program allows the agency to approve products to treat serious or life-threatening conditions based on surrogate or intermediate clinical endpoints "that are reasonably likely to predict clinical benefit." When granting accelerated approval, FDA will require a sponsor to complete post marketing clinical trials to confirm the product's benefits.

The guidance finalizes a draft version released for comment in 2014 and focuses on the Indications and Usage section of labeling for products granted accelerated approval based on a surrogate endpoint or a clinical endpoint other than survival or irreversible morbidity.

The guidance also provides labeling recommendations for products granted accelerated approval that have subsequently had their clinical benefit confirmed, as well as labeling considerations for products that have had an indication with accelerated approval withdrawn while other indications for the same product remain approved.

FDA Drafts Guidance on Marketing Status Notifications

The FDA unveiled a new draft guidance to help sponsors of new drug applications (NDAs) and abbreviated new drug applications (ANDAs) understand what information they're now required to share with FDA on the marketing status of their brand and generic drugs.

The guidance identifies the required content for marketing status notifications, the recommended format for submitting these notifications to FDA and the required timelines for submission.

FDA Drafts Two New Guidances on Assessing the Effectiveness of REMS

The FDA released two new draft guidance documents aiming to ensure that Risk Evaluation and Mitigation Strategies (REMS) put in place for certain drugs and biologics are working properly.

The guidances provide industry with a framework to develop a REMS Assessment Plan to better develop a REMS program and improve the quality of the information used to assess the effectiveness of it, and to provide postmarket evidence that the REMS is meeting its risk mitigation goals.

A REMS is a drug safety program that FDA can require for certain medications with serious safety concerns to help ensure the benefits of the medication outweigh its risks.
Most REMS require communication between a doctor and patient about specific safety risks and monitoring to reduce the frequency and/or severity of any side effects.

The REMS Assessment draft guidance describes how to develop a REMS Assessment Plan by considering how the REMS program goals, objectives and REMS design may impact the types of metrics and data sources that could be used to assess whether the program is meeting its risk mitigation goals. The draft also discusses how to assess the impact of REMS on patient access to a drug and its burden to the health care delivery system.

The other draft guidance on REMS survey methodologies, provides recommendations on conducting REMS assessment surveys to evaluate patient or health care provider knowledge of REMS-related information, such as the serious risks and safe use of a medication. The draft guidance discusses general principles and recommendations related to conducting such assessment knowledge surveys, including study design, survey data collection and processing and data analysis.

Rates of Deceased Donor Organs with HCV, HBV, HIV Increasing in the US

A recent report from the CDC analyzed deceased donor data for the period 2010–2017 reported to the Organ Procurement and Transplantation Network for increased risk donors (IRDs) and standard risk donors (SRDs). During this period, the proportion of IRDs increased approximately 200%, from 8.9% to 26.3%; the percentage with drug intoxication reported as the mechanism of death also increased approximately 200%, from 4.3% to 13.4%; and the proportion of these donors with reported injection drug use (IDU) increased approximately 500%, from 1.3% to 8.0%.

Compared with SRDs, IRDs were significantly more likely to be anti-HBc–positive (7.0% versus 4.3%, p<0.001), HBV DNA–positive (0.4% versus 0.1%, p<0.001), anti-HCV–positive (19.1% versus 2.3%, p<0.001), and HCV RNA–positive (14.9% versus 1.2%, p<0.001).

The researchers observed no substantial changes in HBsAg or anti-HBc positivity among IRDs during the study period. However, anti-HCV positivity increased (15.9% vs. 21.6%). From 2014 to 2017, HCV RNA positivity also increased (8.6% to 15.7%). 5.3% of all HCV RNA–positive IRDs were anti-HCV negative (i.e., acute infection before antibody response).

The authors conclude that an increasing number of organ donors have a history of drug intoxication as the mechanism of death, mirroring the U.S. opioid crisis. These organ donors have high prevalence of HCV infection, but low prevalence of HIV and HBV infections. Identification of risk factors for viral bloodborne pathogen infection among organ donors and nucleic acid testing is critical to mitigate transmission risk.

Researchers Estimate More Than 7 Million WNV Cases in US Since 1999

More than seven million people may have been infected with West Nile virus (WNV) since its introduction in the United States in 1999, according to research published recently in the CDC's *Emerging Infectious Diseases Journal*.

Researchers collected data from CDC's ArboNET national surveillance system for state-specific and national WNV seroestimates. They then estimated the number of WNV cases for persons ≥16 years of age and cases for persons <16.

The seven million estimated infections is more than double the 2010 estimate of 3 million infections, but investigators believe the true number of infections may be higher due to underdiagnosis. Nearly 98% of the US population remains vulnerable to WNV infection. The authors note that these findings highlight the need for improved disease surveillance and reporting and provide additional support for the economic benefit of insecticide and vaccine interventions.

4D Corneal Tissue Engineering

Tissue engineers at Newcastle University can create cell structures of "4D tissues" which can change shape over time into a desired form. They hope to produce cornea-shaped, curved stromal tissue equivalents via the controlled, cell-driven curving of collagen-based hydrogels.

In a paper in *Advanced Functional Materials*, they showed the structural and mechanical properties of self-curved gels acquired through a 4D engineering method are more similar to those of the native tissue, "with undifferentiated corneal limbal epithelial stem cells located in the softer limbus and the differentiated epithelium spanning the stiffer centre of the anterior cornea."