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House Panel Advances FDA Reauthorization With Device Amendments

The House Energy and Commerce Committee voted 54-0 on June 7 to advance the FDA's five-year user fee reauthorization package to the floor of the House — with several new amendments on devices.

The next generations of MDUFA is expected to bring in $183 million in fiscal 2018, up from the $126 million expected this fiscal year. Overall, the agency's user fees account for more than one quarter of the FDA's annual budget.

The panel approved by voice vote several device-related amendments, including:

- An amendment from Rep. Jan Schakowsky (D-Ill.) that would require the FDA to create a voluntary pilot program to develop post-market safety data on medical devices;
- An amendment from Rep. Mimi Walters (R-Calif.) that would allow the FDA to create a risk-based classification system for current device accessories without the added scrutiny of treating a simple device accessory like a device modification;

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FDA Will Issue Tougher Validation Requirements for Reusable Devices

Following a spate of superbug outbreaks and deaths from contaminated duodenoscopes and similar devices, the FDA will soon have tougher validation requirements for certain new devices.

According to a notification in the June 9 Federal Register, the agency will introduce new requirements for validating instructions for use and for validation of cleaning, disinfection and sterilization in premarket notification submissions for 11 types of devices, including laparoscopic tools and a variety of endoscopes.

The Centers for Disease Control and Prevention linked cases of multi-drug resistant bacteria to duodenoscopes in 2013 and found the infections were happening even though users followed the

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- An amendment by Rep. Scott Peters (D-Calif.) that would create a clear regulatory pathway for new diagnostic imaging devices intended for use with contrast agents; and
- A bipartisan amendment from Peters and Rep. Ryan Costello (R-Pa.) requiring the FDA to better define the agency's oversight and regulation of reconditioned medical devices and submit a report, within 180 days, detailing how the agency intends to ensure the quality, safety and continued effectiveness of devices serviced—meaning refurbishing, reconditioning, rebuilding, remarketing, remanufacturing or repairing—by someone other than the OEM.

The Senate's version of the user fee bill is also currently awaiting a floor vote. After both chambers pass their respective bills, they will reconcile any differences before final passage. The must-pass bill is expected to land on President Trump's desk sometime in July. The FDA's current user fee agreements expire at the end of September. — Gayle S. Putrich

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manufacturer's cleaning and disinfection or sterilization instructions.

Arthroscopes, laparoscopic instruments, and electrosurgical instruments, and their respective accessories with specific design features "may pose a challenge to adequate reprocessing," the FDA said. Any 510(k) notification for such devices with specified design features must include the additional validation details. Sleeves, crevices, stopcocks and fittings with very close tolerances are all risky design features listed by the agency as potentially problematic in reprocessing and sterilization.

The agency believes the devices included in the new list have the greatest risk of infection transmission and inadequate performance if not adequately reprocessed, though it may reevaluate or revise the list in the future.

It is in the medical device industry's best interest to make sure instructions for use, reprocessing and sterilization are "validated and as absolutely clear as possible," said Len Czuba, a Chicago-based medical device product development consultant. But even with those assurances, every time there is a problem, it will still reflect negatively on the device OEM, he said. Evolving device design to avoid common problems or to incorporate snap-off parts that can be replaced easily will go even farther to solve contamination problems, Czuba said.

See the Federal Register notice here: www.fdanews.com/06-09-17-MDInstructions.pdf. — Gayle S. Putrich

FDA Grants UDI Labeling Extension to Lower-Risk Devices

Responding to requests from numerous stakeholders, the FDA extended its unique device identification compliance dates for certain Class I devices and unclassified devices, such as manual surgical tools and mechanical wheelchairs from September 24, 2018 to September 24, 2020.

More than 4,000 device labelers have already made over 1.4 million UDI submissions, according to CDRH's Office of Surveillance and Biometrics.

Class III devices were already required to comply.

The FDA plans to issue new guidance on enforcement of device-labeling policies. The agency will also seek more feedback from stakeholders and industry leaders on the challenges they face and how to make the best use of existing data on higher-risk devices. — Zack Budryk

FDA Broadens Rules on Humanitarian Device Exemptions to Reflect Cures Act

The FDA updated its regulations on humanitarian device exemptions (HDEs) to reflect the 21st Century Cures Act.

Devices covered under the HDE program are intended for small patient populations, but the Cures Act doubled the threshold, broadening its use in populations involving "fewer than 4,000" to "not more than 8,000." The changes took effect June 7.

Under the program, makers of humanitarian use devices (HUDs) may apply for an exemption from the requirement that they prove the device's effectiveness if they can prove it will not put patients at risk of illness or injury.

The agency also updated regulations for oversight of HUDs to eliminate the requirement that the institutional review board overseeing the devices be local.

Read the final rule here: www.fdanews.com/06-09-17-HumanitarianUseDevices.pdf.
— Zack Budryk

French Safety Agency Sees No Need To Update Bayer Essure Labels

In contrast to the FDA, France's National Agency for the Safety of Medicines and Health Products is not recommending label changes for Bayer's Essure sterilization device.

Late last year, FDA required Bayer to use a boxed warning and a patient decision checklist (*IDDM*, Nov. 18, 2016).

An expert committee heard testimony from patient and physician groups in an April 19 public meeting, and considered new preclinical data from Bayer and an epidemiological study carried out by the ANSM.

The committee concluded that available data from the scientific literature, as well as the surveillance and the results of an epidemiological study did not negate the favorable risk-benefit assessment of the implant.

One group, the Resist Association, which represented women who testified, had requested the suspension of the device.

In-House IVDs Require Conformity Assessments in Australia

Austrailian regulatory authorities July 1 will begin charging fees to makers of in-house IVDs.

The Therapeutic Goods Administration classifies in-house IVDs as pathology tests developed within a laboratory to carry out testing on human samples, where the results are intended to assist in clinical diagnosis or to be used in making clinical management decisions.

The agency will charge fees for IVDs beginning July 1 and will require:

- IVDs to comply with essential quality, safety and performance principles;
- A risk-based classification scheme with different levels of regulation for each class of device;

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- A choice of conformity assessment procedures based on the risk classification, so manufacturers can demonstrate initial and on-going compliance with the essential principles;
- Compliance with recognized standards to demonstrate that the essential principles and conformity assessment procedures have been met; and
- Provisions for post market activities, including monitoring and adverse event reporting.

In-house tests developed for research purposes only — where there is no reporting of patient results — are not required to comply.

IVD makers first need to determine how the devices are classified, because there are different conformity assessments for Class IV and for Class I-III IVDs.

Class I-III IVDs will not have to be included in the Australian Register of Therapeutic Goods (ARTG), but labs must comply with conformity assessment procedures.

Higher risk Class III in-house IVDs will be subject to greater scrutiny than lower risk Class 1 in-house IVDs. Class IV in-house IVDs will not be included on the register, but they also will need to comply with conformity assessment procedures.

Makers of Class IV IVDs can either obtain TGA conformity assessment certificates prior to applying for the ARTG listing, or they can use their existing NATA accreditation to ISO 15189 to apply for the listing.

The ARTG listing application will be subject to a mandatory audit, and the TGA will assess the analytical and clinical evidence for the Class IV in-house IVD. Labs may also be required to provide evidence that they have procedures in place to adequately monitor ongoing performance of the device and to report adverse events or problems associated with its use.

Read the TGA notice here: www.fdanews.com/06-06-17-TGAIVDs.pdf.

Highlights of China's Proposal To Exempt IVD Reagents

Grace Fu Palma, founder and CEO of Boston-based China Med Device, LLC, a firm specializing in commercialization and funding for medtech companies entering China, considers CFDA's proposal for exempting certain IVD reagents from clinical trials.

On May 24, CFDA issued a draft document on clinical evaluation basic requirements for clinical exempt IVD reagents, adding a second batch of clinical exempt class II IVD reagents — 130 reagents — to the agency's directory.

Key provisions in the draft include the clinical evaluation comparison method, sample selection and sample size, and the content of the clinical evaluation report.

The exempt IVD reagents will need a clinical performance evaluation based on the assessment of the intended use, interference factors, a comprehensive literature review and other non-clinical-trial elements to get products approved by CFDA.

The document includes the following key provisions:

Clinical Evaluation Comparison Method

- Choose approved products that have a good reputation in current clinical application as the predicate reagent. The information for the predicate reagent should include methodology, clinical indications, main performance indicators, traceability of the predicate device, recommended positive parameters, or reference interval etc.

- Choose the reference methodology for the comparative study test, and select the reference laboratory for research. The reference methodology and reference laboratory should have the certification recognized by the China National Accreditation Service for Conformity Assessment.

- Depending on the intended use of the product, applicants also can use patients' clinical diagnosis, disease progression, efficacy observations and other objective indicators for clinical performance studies.

Sample Selection and Sample Size

- Select clinical samples that cover the intended use and interference factors.

- The sample size for the Class II product should not be fewer than 100. Clinical cases should fully reflect a product's clinical safety and efficacy.

- The type of samples to be used for the evaluation should be consistent with the type used in the registration application. The comparable sample types are serum and plasma. One of the sample types can be selected for clinical evaluation. If there is no comparable sample type such as serum and urine, they should be evaluated separately.

Basic Content of the Clinical Evaluation Report

- The clinical evaluation report should include: the reagent's generic name, test start date, test completion date, test site, signature of the principal investigator and the seal of the unit, the signature of the person in charge of the statistic and the seal of the unit, the name of the applicant (seal), the applicant's contact and contact information, and the report date.

- The test sample information should include: testing reagents, compared reagents, other reagents used in conjunction with calibration, quality control, dilution,

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test equipment, etc. Including: the specific reagent name, manufacturer, specifications, batch number, expiration date, equipment should include Name, manufacturer, model and so on.

- The evaluation proposal should include: background information of the product, purpose of the evaluation, evaluation method, sample size, sample type, crowd selection, disease selection, interference samples, statistical methods, data processing.

- The evaluation results report should include: 1) A description of the implementation of the evaluation proposal, such as the specific sample selection, and the basic testing process; 2) Statistical analysis of the testing data according to the test results, population distribution, disease distribution, interference samples, etc.; 3) For the samples that have unmatched test results in the comparative study, they should be rechecked to analyze the results of the tests. If they do not need to be rechecked, applicants should give a detailed explanation detail; 4) Test conclusions.

- The evaluation data sheet should include at least the following: The sample number, age, sex, tested reagents' test results, comparative reagent test results, recheck test results (if any), clinical diagnostic information (including interference sample information) etc. The applicant should also provide relevant clinical documents of the tested product and the evaluation documents should reside in the institution itself.

Areas that need special attention:

- The evaluation sample should be traceable.

- The original documents of evaluation samples should include but not be limited to: patient sample source, unique and traceable number, age, gender, department, very clear clinical diagnostic information, treatment tracking information (if any) etc.

- Registration changes relating to clinical evaluation should be implemented according to this requirement.

- If the applicant cannot do a clinical evaluation based on the above requirements, they can choose a clinical trial for clinical evaluation.

In summary, although the listed IVDs would be exempt from clinical trials, CFDA will require sponsors to assemble a significant amount of data and supporting information to get products approved.

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New Zealand Updates Plan To Boost Surgical Mesh Safety

New Zealand's government released an updated action plan to boost the safety of surgical mesh, prompted by adverse events linked to the device in recent years.

Currently, Medsafe, the New Zealand medicines and medical devices safety authority, simply monitors the safety of devices based on adverse event reports. Now, however, the government plans to introduce pre-market assessment of medical devices, as part of comprehensive regulatory framework to regulate all therapeutic products including medical devices.

Other changes the New Zealand government is supporting include a review best practices around informed consent for mesh procedures, and better reporting of adverse events.

Read the updated plan here: www.fdanews.com/06-06-17-NZmesh.pdf.

483 Roundup: FDA Cites Firms Over Complaint Handling, Other Deficiencies

The FDA cited device manufacturer US Vascular for a wide range of deficiencies, including inadequate procedures for handling complaints.

Following an April inspection of the firm's Beaverton, Ore., facility, the FDA issued a Form 483 with 14 observations.

Inspectors found at least six complaints the firm failed to evaluate to see if they required further investigation or reporting to the FDA as an MDR.

The agency also faulted the device manufacturer on its design history file for its diagnostic devices, which failed to include documentation of design verification or validation.

The FDA also cited the facility's controls for nonconforming products. The company failed to segregate the products, and to document investigations, risk assessments and further actions before retesting.

Inspectors further noted that the firm had not established a required audit schedule or conducted an internal audit as of April 11, 2017. The facility also lacked adequate corrective and preventive action procedures.

Kronner Prototypes: The FDA cited Kronner Prototypes for its complaint handling, reporting procedures and quality issues, following an April inspection of the devicemaker's Roseburg, Ore., facility.

The agency issued a Form 483 noting the firm had three different, often contradictory, complaint handling procedures. Several complaints failed to include an evaluation of whether they should be reported to the FDA — and the company had no written MDR procedures.

The company also failed to document verification or validation of corrective actions taken in response to two complaints, and it did not properly implement procedures for measuring instrument calibration, the agency said. Other deficiencies included incomplete checklists for finished device acceptance.

The firm had also failed to document any quality audits since the previous FDA inspection in April 2014.

Pulsar Vascular: The FDA faulted device manufacturer Pulsar Vascular for its process validation and design control procedures.

The agency issued a Form 483 following a February/March inspection of the company's Los Gatos, Calif., facility. According to the FDA, Pulsar's master process validation plan inaccurately stated several in-house processes required validation and revalidation. The agency requested validation and revalidation records for all processes inaccurately documented as requiring both processes, but was told none.

Inspectors also observed deficiencies in the design history file for Pulsar's PulseRider aneurysm neck reconstruction device. The file did not clearly define planned design phases and formal design reviews, and the reviews failed to include a reviewer without direct responsibility for the design stage in question.

Tena Group: The FDA slammed hearing aid manufacturer Tena Group for its quality systems and audit procedures.

The agency issued a Form 483 following a June 2016 inspection of Tena's Windham, Maine, facility. According to inspectors, the firm created a quality manual and quality policy in 2011 but failed to apply it throughout the organization.

In addition, the facility had an internal audit procedure, but could not provide evidence that any quality system audits had been conducted. Inspectors also found no documentation of nonconforming products, and no evidence that the facility conducted internal audits or recorded service repairs that would require a corrective and preventive action plan. The facility also lacked written procedures for medical device reports and complaint reviews.

The companies did not respond to requests for comment.

Read the Form 483s here: www.fdanews.com/06-09-17-FourForm483s.pdf. — Zack Budryk

APPROVALS

FDA Clears Roche Diagnostic For Non-Small Cell Lung Cancer

Roche received FDA clearance for the Ventana ALK (D5F3) CDx assay as a companion diagnostic to identify ALK-positive non-small cell lung cancer patients eligible for treatment with the Novartis drug Zykadia.

The assay detects the anaplastic lymphoma kinase protein in formalin-fixed, paraffin-embedded non-small cell lung cancer tissue stained with a BenchMark XT or BenchMark Ultra automated staining instrument. It is indicated as an aid in identifying patients eligible for treatment with Xalkori or Zykadia.

Cardiac Troponin Test Receives CE Mark

Singulex has received the CE Mark for its Singulex Sgx Clarity cTnl assay for the biomarker troponin.

The assay is indicated for use in conjunction with clinical evaluation for ruling out cardiac ischemia in patients suspected of having coronary artery disease. The company will submit data for FDA clearance of the assay in 2018.

Medovex Wins CE Mark For DenerveX System

Medovex Corp. has received a CE Mark for the DenerveX system.

The system consists of a single-use medical device kit and the DenerveX Pro-40 power generator. The device's slowly rotating burr removes targeted facet joint synovial membrane and joint surface while heat ablation destroys tissue and removes residual nervous and synovial membrane overlying the joint. The system is not yet FDA cleared.

Claret Medical Gains FDA Clearance For Its Sentinel Cerebral Protection System

Claret Medical has received de novo clearance from the FDA for the Sentinel cerebral protection system.

The device removes debris dislodged during transcatheter aortic valve replacement before it reaches the brain. In a clinical trial, use of Sentinel reduced strokes by 63 percent in the first 72 hours after TAVR and maintained a substantial difference at 90 days.

FDA Approves Expanded Indication For Sapien 3 Heart Valve

Edwards Lifesciences' Sapien 3 THV artificial heart valve received FDA clearance for an expanded indication to include treatment for patients with symptomatic heart disease due to failure of a previously placed bioprosthetic aortic or mitral valve.

Valve-in-valve procedures offer an alternative to repeat surgery, since the replacement valve is inserted inside the failing surgical bioprosthetic valve through a blood vessel or a small cut in the chest.

Boston Scientific Wins CE Mark For Deep Brain Stimulation System

The European Commission has awarded Boston Scientific a CE Mark for the Vercise primary cell deep brain stimulation system.

The system provides precise neural targeting for patients suffering from Parkinson's disease, primary and secondary dystonia and essential tremor. It is not available for use or sale in the United States.

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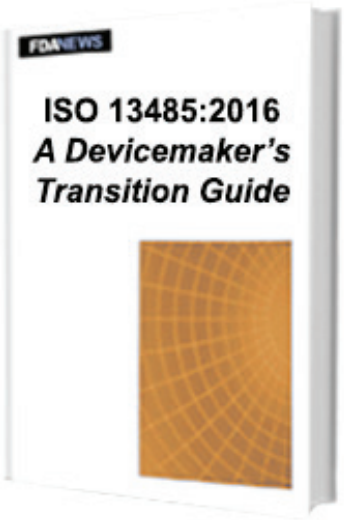

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