The Focal Point: Advocacy & Legislative Update
September 24, 2019

A Notification from Bausch + Lomb for the Eye Bank Association of America

EBAA received the following notification from Bausch + Lomb:

Bausch + Lomb recently received several complaints regarding vials of Optisol that appear to be a darker in color than typically observed. Since then, several other Eye Banks have reported similar experiences and we have identified the lot number of the product to be the same - 1843-017.

As a result, we immediately commenced a thorough investigation into this observation, including reviewing the release documentation, conducting color comparisons of multiple lots and testing the pH of samples from the lot of solution in question. A known property of Optisol is that it takes on a deeper red hue as the pH value increases within the specification range. Based on our investigation, we have determined that all the product tested is within our strict release specifications, including the pH specification. Eye Banks should accordingly be confident in the continued use of Optisol solution from lot number 1843-017.

The safety and quality of our products is of the utmost importance to us, and we take customer feedback very seriously. Any customer who has a question, comment or concern regarding Optisol or any Bausch + Lomb products should contact our customer service team at 1-800-338-2020.

Draft Guidance Released on Interacting with FDA on Complex Innovative Trial Designs

The Food and Drug Administration (FDA) released a draft guidance for industry entitled "Interacting with the FDA on Complex Innovative Clinical Trial Designs for Drugs and Biological Products." This document provides recommendations to sponsors and applicants on interacting with the FDA on complex innovative clinical trial design (CID) proposals for drugs or biological products. In accordance with the 21st Century Cures Act mandate, this guidance discusses the use of novel trial designs in the development and regulatory review of drugs and biological products, how sponsors may obtain feedback on technical issues related to modeling and simulation, and the types of quantitative and qualitative information that should be submitted for review.

The primary focus of this guidance is on FDA and sponsor interactions for CID proposals for trials intended to provide substantial evidence of effectiveness. In most cases, interactions related to CID proposals will occur in the context of investigational new drug applications (INDs) or Pre-IND meetings. Novel clinical trial designs call for clear communication between sponsors and FDA on aspects of the design, and how the trial data will be analyzed and presented. The guidance also provides examples of clinical trial designs that FDA would

consider to be CID and describes the type of information FDA recommends submitting with the proposals to facilitate a productive discussion between sponsors and FDA. Additionally, the guidance addresses the role of simulations in clinical trial design and planning.

FDA Introduces New Safer Technologies Program

FDA released draft guidance to introduce a new, voluntary program for certain medical devices and device-led combination products that are expected to improve the safety of currently available treatments or diagnostics but are used for morbidities and mortalities less serious than those eligible for the Breakthrough Devices Program.

FDA believes that this ''Safer Technologies Program'' or ''STeP'' will help patients have more timely access to these medical devices and device-led combination products by expediting their development, assessment, and review, while preserving the statutory standards for premarket approval, De Novo marketing authorization, and 510(k) clearance.

Similar to the Breakthrough Devices Program, STeP is comprised of two phases where interested sponsors formally request inclusion in STeP through a Q-submission and where FDA takes action to expedite the development of the device and the prioritized review of subsequent regulatory submissions.

Devices that would be eligible for STeP would not be eligible for the breakthrough devices program but "should be reasonably expected to significantly improve the benefit-risk profile of a treatment or diagnostic through substantial safety innovations that provide for one or more of the following:

a) a reduction in the occurrence of a known serious adverse event
b) a reduction in the occurrence of a known device failure mode,
c) a reduction in the occurrence of a known use-related hazard or use error, or
d) an improvement in the safety of another device or intervention."

CDRH Releases Four Final Guidances on 510(k) Submissions

FDA's Center for Devices and Radiological Health (CDRH) released four final guidance documents on the Special 510(k) program, the abbreviated 510(k) program, how to format traditional and abbreviated 510(k)s and CDRH's refuse to accept policy for 510(k)s.

The Special 510(k) Program offers an optional pathway for manufacturers to make modifications to its own legally marketed devices. This guidance clarifies the types of technological changes appropriate for review as Special 510(k)s. Specifically, they are including certain design and labeling changes, including changes to the indications for use, by focusing on whether the method(s) to evaluate the change(s) are well-established, and whether the results can be sufficiently reviewed in a summary or risk analysis format.

FDA will host a webinar on October 31, 2019 at 1:00 pm for device manufacturers and industry to discuss and answer questions about the Special 510(k) Program Final Guidance.

The Abbreviated 510(k) Program provides recommendations on an optional approach that may be used to demonstrate substantial equivalence in premarket notifications (510(k)s). The

Abbreviated 510(k) program is centered on the use of an efficient submission preparation and review process that relies on guidance documents, special controls and/or voluntary consensus standards. The alternative approach described in this guidance document is intended to facilitate 510(k) submission preparation by manufacturers and review by FDA.

The Format for Traditional and Abbreviated 510(k)s final guidance explains how to format an original submission for a traditional or abbreviated 510(k) submission.

The Refuse to Accept Policy for 510(k)s final guidance explains the procedures and criteria that CDRH intends to use in assessing if a 510(k) submission can be accepted for review.

The Abbreviated 510(k) Program

Format for Traditional and Abbreviated 510(k)s

Refuse to Accept Policy for 510(k)s

FDA Finalizes Three Guidances on De Novo Classification Requests

FDA finalized three guidance documents related to de novo classification requests for medical devices. Devices using the de novo classification process are those for which there is no predicate device to rely on, and devices granted a de novo request can serve as a predicate device for a later 510(k) submission.

One of the guidances deals with the criteria the agency intends to use in assessing whether a De Novo request meets a minimum threshold of acceptability and should be accepted for substantive review. This document includes both an Acceptance Checklist (Appendix A. Acceptance Checklist for De Novo Classification Requests) as well as a Recommended Content Checklist (Appendix B. Recommended Content Checklist for De Novo Classification Requests). FDA also reiterated that industry and FDA will have 60 days to operationalize the policies within this guidance.

FDA also finalized guidance on user fees related to de novo requests, which began under the *Medical Device User Fee Amendments of 2017* (MDUFA IV). The guidance explains (1) the types of De Novo requests subject to user fees; (2) exceptions to user fees; and (3) the actions that may result in refunds of user fees that have been paid.
The third final guidance deals with the different actions FDA may take on de novo requests, the effect each action has on goals under MDUFA IV for de novo requests received in FY 2018-2022 and the different industry actions that may be taken on de novo requests.

FDA and Industry Actions on De Novo Classification Requests: Effect on FDA Review Clock and Goals

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Ireland to End Permanent vCJD Deferral Policy

The Irish Blood Transfusion Service (IBTS) will end its permanent deferral of donors who lived in the United Kingdom for one year or more between Jan. 1, 1980, and Dec. 31, 1996, due to risk of variant Creutzfeldt-Jakob disease (vCJD). The decision follows an April 29 meeting of

the IBTS Medical Advisory Committee to consider the evidence for reversal, which found that the risk of transmitting vCJD by blood transfusion is remote.
IBTS estimates the deferral resulted in the loss of approximately 10,000 donors since its implementation in 2004. Donors previously affected by the deferral will be eligible to donate beginning Oct. 7, 2019.

Permanent deferrals on donations will remain in place for certain individuals, including those with a family history of CJD, who had received human growth hormone or donated eggs or embryos since January 1st, 1980.

Legislation Introduced in the House to Modernize Payments for ASCs Under Medicare

Reps. John Larson (D-CT) and Devin Nunes (R-CA) introduced the bipartisan Ambulatory Surgical Center Quality and Access Act of 2019 (H.R. 4350) "to amend title XVIII of the Social Security Act to modernize payments for ambulatory surgical centers under the Medicare program, and for other purposes."

H.R. 4350 would enact the following reforms:

- Slow the widening disparity in Medicare payments between ASCs and hospital outpatient departments (HOPDs) by making permanent the hospital market basket as the inflationary update factor.
- Create transparency of quality reporting and Medicare beneficiary information by requiring CMS to post the results online in a "side-by-side comparison" in the event that a measure is applicable to both the ASC and HOPD settings.
- Add an ASC representative to the advisory panel on hospital outpatient payment.
- Disclose criteria used to determine ASC procedure list and add transparency to the CMS review process by requiring the agency to disclose which of the criteria trigger the exclusion and prohibit CMS from excluding procedures reported with unlisted codes from the ASC setting.

AAMI Releases TIR102;2019

A new Technical Information Report (TIR) from the Association for the Advancement of Medical Instrumentation compares regulatory requirements found in the US FDA's Quality System Regulation (QSR) to those in quality systems standard ISO 13485:2016 from the International Organization for Standardization.

AAMI TIR102:2019, is aimed at US device manufacturers and includes a bi-directional mapping tool to assist in identifying the regulatory requirements in the Quality System Regulation to be addressed through an ISO 13485-compliant quality management system.

IRS Issues New Rules to Reduce Donor Disclosure

The Treasury Department issued proposed rules to once again reduce donor disclosure rules for certain tax-exempt groups weeks after a federal judge vacated similar guidance because there had not been a notice and comment period.

Under the proposed rules, trade associations and other 501(c) tax-exempt organizations would no longer be required to report the names and addresses of major donors on their Form 990 returns to the IRS. Organizations would still be required to collect donor information and provide it upon request to the IRS. Charities and other 501(c)(3) groups and Section 527 political groups would still be required to disclose donors as usual.

Candida auris Tied to Vision Loss in Case Report

Infection with *Candida auris* likely led to panophthalmitis and vision loss in an immunocompromised patient, according to a case report published online in the *Annals of Internal Medicine*.

A 30-year-old man with history of HIV and syphilis, presented to the emergency department with acute vision loss of the right eye, despite lacking history of trauma, surgery, or corneal ulceration. A CT scan suggested panophthalmitis with orbital cellulitis.

He underwent enucleation and orbital washout with vancomycin and ceftazidime. Vitreous cultures grew out *Pseudomonas aeruginosa* and "yeast-like cells" later identified to be *C. auris*.

The patient continued to improve with intravenous micafungin therapy, as well as an appropriate prophylaxis regimen for his HIV infection and oral antibiotics. The patient was subsequently lost to follow-up.

KRS Global Biotechnology, Inc., Issues Voluntary Nationwide Recall of All Sterile Drug Products

KRS Global Biotechnology is voluntarily recalling all lots of unexpired drugs intended to be sterile due to lack of assurance of sterility. The company is notifying its customers by mail, telephone, or email and is arranging for credit of all recalled products. Eye banks and practices that have these products that are being recalled should stop using them and return them to KRS Global Biotechnology, Inc.

If you have questions regarding this recall, you may contact KRS Global Biotechnology at 888-398-9950 Monday through Friday, from 9:00 a.m. to 5:00 p.m. ET, or recall@krsbio.com.

Adverse reactions or quality problems experienced with the use of these products may be reported to the FDA's MedWatch Adverse Event Reporting program online.