INTERNATIONAL DEVICES & DIAGNOSTICS MONITOR

Vol. 1, No. 19
May 11, 2014

IN THIS ISSUE

ISO 13485 Revision Could Force More Data Collection

A little-noted provision in revisions to ISO 13485 could force manufacturers to collect a mind-boggling amount of additional data, an FDA official warns.

As drafted, the revised version would require manufacturers to keep records documenting the supply chain for every device component from manufacturer to end user, a change FDA Associate Director of International Affairs Kim Trautman says would be overly burdensome and expensive. U.S. regulations generally stop at the initial purchaser, she told conference-goers at MedCon 2015 in Cincinnati on Wednesday.

Scott Sardeson, international regulatory manager at 3M Healthcare, says the revision is meant to more closely align the U.S. with Global Harmonization Task Force recommendations on risk-based quality management. New sections include standards tied to approval and

(See **ISO 13845***, Page 2)*

Combination Products Office Focusing On Consistency, GMP Guidance

The FDA's Office of Combination Products is reviewing its processes and systems and stepping up staff training in an effort to improve the consistency of product reviews, an OCP official says.

Specific concerns the office is attempting to address include design control issues for legacy products, cross-labeling where a drug and device are meant to be used together but may be made by separate manufacturers, and staff training before inspections that would focus on combination GMPs.

"If the review pathways ask different questions about similar products, that's a problem," says John Barlow Weiner, assistant director for policy in OCP, told a Wednesday session of MedCon 2015 in Cincinnati. "We want consistency."

As part of this effort, OCP is working to finalize guidance on combination product GMPs, Weiner says. The comment period closed in late April, and a preliminary review shows feedback is largely positive.

(See **OCP***, Page 4)*

Medtronic Deal Drives Strong Q1 for Medical Device Sector

Medtronic's $42.7 billion acquisition of Covidien led the medical device sector and helped drive a record-setting $166.3 billion in life science deals closed during the first quarter of 2015, a new report from Pricewaterhouse-Coopers shows.

Overall, the device sector brought in seven deals totaling $56.1 billion, more than 10 times as much as the $4.9 billion total for 10 deals in the fourth quarter of 2014.

The sector is expected to remain strong throughout the year as eight potential deals valued at $5.6 billion were announced during the first three months of the year.

One diagnostics deal, Takeda Pharmaceuticals' acquisition of Envoy Therapeutics, accounted for $140 million. This overshadowed the one of deal during the fourth quarter of 2014 — a $16 million transaction.

PwC lists four trends that are expected to continue throughout 2015 — divestures, consolidation, globalization and asset swaps. Consolidation played prominently in the medical device sector in the first quarter and is expected to continue this year as companies strive to maintain their bargaining power by expanding product offerings and adopting new business models, PwC says.

The sector was the second most lucrative behind pharmaceuticals, which closed 18 deals totaling $97.4 billion during the first quarter. In the biotechnology sector, six deals worth $6.4 billion closed, up from four valued at $3.3 billion in the previous quarter.

Contract research organizations also added to the strong quarter, based largely on Laboratory Corporation of America's acquisition of Covance for $6.2 billion.

View the report, *Pharmaceuticals and Life Sciences Deals Insights Quarterly*, at www.fdanews.com/05-06-15-pharmalifesciences.pdf. — John Bechtel

ISO 13845, *from Page 1*

monitoring of suppliers, as well as an expanded section on human resource factors that could affect device safety. The draft also adds a checklist on auditing techniques and discusses a unique device identifier requirement, though it doesn't call it UDI.

The draft would also add to postmarket feedback requirements by mandating that manufacturers actively gather data — for example, searching social media for complaints, Sardeson says. And a new section on complaint handling has been added and sections on corrective and preventive action clarified.

Trautman believes the draft needs further revision before it is finalized. For one thing, it calls for investigators to categorize nonconformances down to a fourth or fifth decimal level (e.g., standard 3.4.8.5), while international standards call for a three-level nonconformance categorization. The latter should be maintained to ease the burden on regulators and limit the risk of coding error, she says.

In addition, the current draft has pushed several suggestions and best practices into subsections called notes.

Trautman fears some inspectors may incorporate the notes into audits and dock devicemakers who don't follow them, violating the key goal of consistency. "If there's something we want devicemakers to do, it should be required," Trautman says. "If it's not, we should leave it out of the standard."

The International Standards Organization is expected to discuss the draft in Denver, Colo., in June, and Sardeson anticipates at least two more meetings will follow before it is finalized. While comments are officially closed, manufacturers can contact the FDA or ISO with their thoughts.

The goal is for the revised standard to be approved by the first quarter of 2016 and take effect by 2019. — Elizabeth Orr

FDA Discusses Use of Adult Data To Support Pediatric Device Use

Devicemakers looking to market their products for use in children based on adult clinical trials should limit their use of that data to situations in which the course of the disease or condition and the device's effects are "sufficiently similar" in both populations, the U.S. FDA says.

Partial data extrapolation, combined through a statistical model with pediatric data sources to demonstrate a reasonable assurance of effectiveness, is preferred over full extrapolation of data from adult studies, the agency says in draft guidance published Wednesday.

The guidance addresses the use of adult clinical trial data to increase the availability of devices for pediatric patients. It also discusses how devices should be labeled to support their safe and effective use in patients 21 and younger.

The FDA lists three main factors for partial extrapolation of data: the similarity of the existing adult response data and/or population characteristics to the intended pediatric population; the quality of the adult data; and whether the data can be used fairly and responsibly to determine the safety and effectiveness of the device.

Dealing With Uncertainty

The FDA cautions devicemakers that using extrapolated data adds a degree of uncertainty to safety and effectiveness assessments. The extent of that uncertainty depends on the differences between adult and pediatric patients and the quality of the data. Manufacturers should consult the FDA's benefit-risk guidance to understand how the agency weighs extrapolated data during the course of premarket reviews, the guidance says.

The guidance is intended to address the pitfalls sponsors often face with pediatric trials. Among these are small and scattered populations leading to small trial sizes, challenges in enrollment and consent procedures and variations in physiology, anatomy and human factors in pediatric patients.

Comments are due Aug. 4 to docket no. 2015-10482. Read the draft guidance, *Leveraging Existing Clinical Data for Extrapolation to Pediatric Uses of Medical Devices*, at www.fdanews.com/05-11-15-pediatric-device.pdf. — John Bechtel

CDRH Withdraws 30 Draft Guidance Documents

The U.S. FDA plans to withdraw 30 draft guidance documents affecting medical devices issued between 1988 and 2011, because they are obsolete or no longer considered necessary.

Most of the drafts, part of a larger list of 47 drafts being withdrawn agencywide, were never finalized because of higher agency priorities and lack of resources, a Wednesday *Federal Register* notice says.

The majority of products addressed by the drafts are covered under current standards or will be addressed by future guidance and other FDA regulatory actions. Manufacturers of products covered in drafts that will not be replaced should check the 510(k) database to see what data the FDA has reviewed for similar products or request a presubmission meeting, the agency says.

A number of the withdrawn draft guidances from CDRH cover Class II special controls for devices. Others include:

- *"Help-Seeking" and Other Disease Awareness Communications by or on Behalf of Drug and Device Firms* (2004);
- *Assessing the Safety and Effectiveness of Home-Use In Vitro Diagnostic Devices: Draft Points to Consider Regarding Labeling and Premarket Submissions* (1988);
- *A Primer on Medical Device Interactions with Magnetic Resonance Imaging Systems* (1997); and
- *Heart Valves: Investigational Device Exemption and Premarket Approval Applications* (2010).

The agency is accepting comments at docket no. FDA-2015-N-1419. View the *Federal Register* notice at www.fdanews.com/05-11-15-withdrawal.pdf. — Elizabeth Orr

OCP, *from Page 1*
But companies are requesting clarification on certain terms in the guidance, such as the difference between a manufacturer and a sponsor.

Devicemakers also want more information on the role of suppliers in the manufacturing process — for example, whether GMPs would be imposed on makers of components for use in a combination product if they don't make the finished goods, Weiner says.

Weiner singled out the use of reserve samples to explain how companies might work together, through a trade group, to draft a proposal for an entire device class, with the aim of ensuring guidance is properly addressed.

In 2014, OCP issued 17 product designations after the manufacturer and FDA couldn't reach agreement on how to review a product. Of those, five were drug-device combinations, one was a drug-biologic and two were innovative drug-device-biologic combinations. The remaining nine products were not considered combination products, OCP Director Thinh Nguyen says. The number of designations has been trending down in recent years, from a high of 44 in 2010, he said.

Still, the number of combination products is trending up, Nguyen says. In fiscal year 2014, 310 combination products were submitted to the FDA. Forty-four of those were reviewed by the FDA's drugs center, 154 by its biologics center and 112 by CDRH. The largest product classes were drug-coated devices, prefilled syringes and drug pumps.

In addition, OCP was involved in 1,013 intra-FDA consultations on combo products, 650 requests for advice on premarket review and 110 requests to address postmarket issues, Nguyen says. — Elizabeth Orr

Patent Outlook Improving, Experts Say at MDMA

Patent troll cases filed against devicemakers have dropped dramatically in the wake of recent legal challenges, an attorney says.

Stephen Jensen, a partner with Knobbe, Martens, Olson and Bear, says patent law case filings have dropped from about 700 per month at their peak in 2012 to roughly 300 a month now, mostly due to recent U.S. Supreme Court rulings and legal changes. For example, a legal requirement that patent trolls file each case individually stops them from issuing claims against several dozen patent-holders at the same time, Jensen told attendees at the Medical Device Manufacturers Association annual meeting in Washington, D.C.

Further, of 119 cases where patent holders have asked to be reimbursed court costs, they were successful 58 times. Previously, "that would have been zero," Jensen says.

Recent U.S. Patent and Trademark Office trends, such as an increase in *inter partes* review cases, 68 percent of which go to trial, also favor innovators, Jensen says. More than a third of patents reviewed through this process are found to be unenforceable, yet legal fees can exceed $100,000.

Currently, the Federal Circuit is reviewing a case, *Lexmark International v. Impression Products*, which questions whether use restrictions on product packaging are enough to prevent other manufacturers from making generic accessories for the products. The court has asked for *amicus* briefs on the question, Jensen says.

Since the Supreme Court's *Alice Corp. v. CLS Bank* decision in 2014 made it harder to patent steps in a process, 76 of 99 cases on similar issues that went to trial resulted in the patent being struck down, Jensen adds. Another important case for devicemakers, *Nautilus Inc. v. Biosig Instruments Inc.*, says patents have to be specific to apply. Previously, patents could be held valid as long as they were not "insolubly ambiguous," Jensen says.

According to Angela Sykes, director of USPTO's technology center, the agency issued 14,000 medical device patents in 2014, more than double the historic average. The agency established a new Office of Patent Training to bring examiners on up to speed on current patent issues, including patent subject matter eligibility. — Elizabeth Orr

Experts: Data from Women Key to Successful Trials

Devicemakers that want to ensure enough women participate in their clinical trials should set a clear and prespecified goal and stick to it, experts say.

The issue of lower female enrollment in clinical trials has been a concern at the FDA for decades, says Rita Redberg, director of women's cardiovascular services at the University of California-San Francisco, and Sanket Dhruva, a fellow in cardiology at UC-Davis Medical Center. So far, the agency has stopped short of mandating a specific percentage of female patients in trials, but that may change if FDA officials don't think sponsors are making every effort to recruit more women.

Redberg, who spoke with Dhruva during a recent FDAnews webinar on gender distribution in clinical trials, advises companies to set a goal for the number of women in each trial, track whether the goal is being met and keep the enrollment period open, as necessary. She also recommends that sponsors place recruitment ads where women are likely to read or see them and suggests hiring female investigators, if possible.

Avoid Age Cut-Offs

Not having age cut-offs could help increase the number of women in studies, too, says Dhruva. Women of childbearing age are left out of trials over fears of pregnancy complications, but the FDA no longer prevents their enrollment as a matter of policy, he notes. Avoiding an upper age cutoff also would help since women tend to live longer, meaning more older women in treatment populations.

In 2010, the Institute of Medicine recommended that all FDA evaluations present efficacy and safety data separately for men and women. That advice should be mandatory and the FDA should post the sex-specific device trial data online, Dhruva and Redberg say.

Despite efforts to enroll more women in trials dating back to the 1990s, the numbers remain skewed. In her review of 123 studies of high-risk cardiovascular devices approved between 2000 and 2007, only 89 reported sex ratios, Redberg says. The average study population was 33 percent female. And only 41 percent of the studies included FDA-mandated analysis addressing gender bias.

In another analysis, only 24.6 percent of patients in trials used for Medicare coverage decisions were female, even though women comprise 58.2 percent of Medicare beneficiaries, Redberg says.

(See **Trials***, Page 8)*

UDI Database Goes Public With High-Risk Device Info

The U.S. FDA has taken a giant step toward encouraging the use of unique device identifiers, with the launch of a public website making UDI data available to the public.

AccessGUDID debuted May 4 and allows users to search for and download any information labelers have submitted about medical devices. For example, an MRI technician might use the database to learn whether a patient's implanted device is safe for use while undergoing a scan.

Specific information available through AccessGUDID includes the device identifier, device characteristics, such as safety information, whether the device is in commercial distribution, alternative identifiers and the manufacturer's contact information.

The UDI program requires devicemakers to include an identifying code on the product's label to make it easier to track postmarket data and to submit the data to the Global Unique Device Identification Database, or GUDID. The UDI final rule was issued in 2013, and the program took effect for high-risk devices last September. More device data will be added to the database as UDIs become mandatory for them.

View the database at http://accessgudid.nlm.nih.gov/. — Elizabeth Orr

Robust Simplicity.

EtQ features the most comprehensive Compliance Solution that is completely configurable to your business needs

- Automated processes such as Corrective Action, Audits, Risk Management, Complaint Handling, Document Control, and more
- Flexible to adapt to unique business processes, without programming
- Scalable solution that integrates with other business systems
- Make any application mobile and access your data from anywhere, anytime

EtQ
info@etq.com
800.354.4476
http://www.etq.com/fda

Thermedx Warned by FDA Over Unreported Upgrades

The FDA issued a warning letter to Thermedx, a Solon, Ohio-based manufacturer of gynecological and urological fluid management systems, for failing to notify the agency of device upgrades and other GMP violations.

According to the April 8 letter, Thermedx made 21 software upgrades to its System P4000 between April 2010 and October 2013, in response to reported hazards such as incorrect calculation of fluid deficit on the device canister. Although all of the upgrades were assigned a "10," Thermedx's highest hazard severity level, the firm didn't submit written notification of the actions within the required timeframe.

The investigator also notes that between April 2011 and April 2014, Thermedx released at least six software upgrades to eliminate or reduce the likelihood of fluid measurement deficiencies, but didn't properly notify the FDA.

Further, the company's device history records didn't indicate that the product met requirements and was manufactured in accordance with the master record. A review of 17 DHRs for the fluid management system showed that six didn't conform to required pressure specifications and eight devices weren't tested.

Thermedx's validation plan also came in for a hit because it didn't ensure that process results could be verified by subsequent inspection. The company deviated five times from fixed values for its ultrasonic welding process, which is used to manufacture cartridges, and some complaints could be attributed to the welding process, the warning letter says.

The letter also chides the firm for its evaluation and control of suppliers. For example, the investigator found no evidence of review or acceptance of validated processes used by critical suppliers to manufacture components for the system. The devicemaker's purchasing control procedures also didn't describe methods and frequency of monitoring suppliers.

A Thermedx spokesman says the firm is taking actions to remedy the FDA's findings. Read the letter at www.fdanews.com/04-27-15-Thermedx.pdf. — Charlotte Astor

Better Health Systems Warned For Failing to Submit Applications

GMP violations including failure to submit a premarket approval application for its denture liner and failure to register the device in 2015 prompted an FDA warning letter to Better Health Systems.

According to the April 7 letter, the company doesn't have an approved PMA for its Bio-Soft Oraliner and didn't notify FDA of its intent to introduce the device into commercial distribution.

During a December 10 to 12, 2014, inspection of BHS' Monument, Colo., facility, FDA Denver district office investigators also found failures in process controls. For example, the company wasn't able to provide instructions or procedures to determine and control the packaging and labeling of the device, the letter says.

The firm also was rapped for lacking procedures for maintaining lot history records to demonstrate that the device is manufactured in accordance with the master record, and for not implementing procedures for accepting or rejecting incoming products and documenting acceptance or rejection.

The FDA requires devicemakers to demonstrate that their products meet specified requirements, but BHS — which also develops specifications for Oraliner — had no documentation of inspections, tests or other verification of component shipments, the warning letter says.

BHS President Richard Betts tells *IDDM* the company is working to correct the violations cited in the letter and has received a time extension from the FDA. Read the letter at www.fdanews.com/04-27-15-Oraliner.pdf — Charlotte Astor

Canada Proposes Changes To List of Device Standards

Health Canada is proposing 52 changes to its list of recognized standards for medical devices, including the addition of 26 new standards and updates to nine others.

Seventeen standards are slated for removal because they are outdated or no longer relevant, the agency says.

Most of the new standards focus on cleanroom and controlled environment procedures, and aseptic processing of products. The updated standards cover topics such as cardiac pacemakers, infusion pumps, laser products, spinal implants and orthopedic implants.

Slated for removal are standards on electromagnetic compatibility test protocols for active implantable devices and requirements for medical electric equipment.

Comments are due July 6. Access the list of proposed changes at www.fdanews.com/05-11-15-HC-standards.pdf. — Jonathon Shacat

Groups Agree to Promote India-Made Medical Devices

In a new initiative that could be a game changer for local industry, Indian devicemakers and a group representing doctors have agreed to collaborate on promoting the use of homegrown medical devices.

The Indian Medical Association says it will encourage physicians to use India-made devices that it approves based on stringent internationally accepted quality parameters.

The Association of Indian Medical Device Industry reached the agreement in a memorandum of understanding signed late last month with the Indian Medical Association. The initiative, known as Cure in India, will help reduce the country's huge import dependency in the sector while encouraging exports, says Rajiv Nath, AIMED's forum coordinator.

Nath says the MOU will also help to address current inequities where insurers and purchasing organizations restrict market access to homegrown Indian brands by insisting on U.S. FDA-approved products. Most Indian brands wouldn't have FDA approval as the U.S. is not their primary market, he says. — Jonathon Shacat

Trials, *from Page 5*

This lack of data on women can adversely affect treatment choices, the doctors say. A meta-analysis of study data on ICDs found that women receiving the devices saw no benefit in terms of mortality and faced a 70 percent higher risk of adverse events. Further, a post-market study of Thoratec's Heartmate II heart failure device found women were three times more likely than men to experience a stroke, infection and bleeding. The product's marketing had emphasized that it could be used in smaller patients, including women. — Elizabeth Orr

Applied Medical Warned After Patient Death Reports

Inadequate complaint and CAPA procedures following reports of serious incidents including patient deaths led to a warning letter for a California surgical equipment manufacturer.

The April 10 letter followed a Form 483 resulting from a Nov. 3 through Dec. 16, 2014, inspection of Applied Medical Resource's Santa Margarita, Calif., facility.

According to the investigator from the FDA's Los Angeles district office, the company failed to adequately evaluate and investigate complaints involving possible failure of a device. Applied Medical didn't fully document test methods used in its investigations and didn't provide raw test results or perform trending on multiple, repeat complaint types.

Applied Medical received 94 complaints in 2014 related to buttons on a suction/irrigation device getting stuck in the "on" position. The company also received reports that its Kii Trocar cannula installer malfunctioned. In another customer report involving the company's Kii Shielded Blade System, the knife didn't return to the trocar and a patient's artery was cut, resulting in death a few days later, the warning letter says. In yet another report, a patient died after an artery was cut during introduction of the trocar.

Gary Johnson, group president of Applied Medical's surgical group, tells *IDDM* that the deaths were not caused by failure of device performance. The products used in those cases were returned to Applied Medical and found to meet all applicable specifications and performed as intended.

The two incidents are consistent with the inherent risks of laparoscopic surgery, and user error or abnormal patient anatomy may have contributed, Johnson adds.

The warning letter faults Applied Medical for failing to implement CAPA procedures in response to complaints. Specifically, the company didn't analyze quality data so that appropriate corrective actions could be identified.

The FDA chides the devicemaker's design validation procedures, citing a missing "Use by Date" report for the Kii Shielded Blade Access System and missing temperature data for the samples being tested. The investigator asked for the data during the inspection, but it wasn't provided, the warning letter says.

The company provided temperature logs and said it opened a corrective action request regarding data logging, but the FDA called the response inadequate because it didn't include the report and lacked acceptance criteria.

Johnson says the company is cooperating with FDA.

Read the warning letter at www.fdanews.com/04-28-15-AppliedMed.pdf . — Charlotte Astor

China Proposes Policy Requiring Clinical Trial Records Filings

The China Food and Drug Administration is proposing to require medical devicemakers to file clinical trial record forms, as the agency strengthens its oversight of devices.

Under the plan, companies would need to submit detailed information about the device's classification and the testing facility, as well as copies of the sponsor's business license, the ethics committee's opinion and the researcher's contact information.

The record would need to be filed with the provincial CFDA where the company registered before the trial kicks off. A number would be assigned to the record as soon as it's submitted. Filings would be accepted within 10 business days after the provincial CFDA notifies its municipal counterpart where the trial site is located.

More information on the proposal is available, in Chinese, at www.fdanews.com/05-15-CFDA-TrialRecord.pdf. — Jonathon Shacat

BRIEFS

Boston Sci Resolves 2,970 Claims

Boston Scientific has settled part of a series of lawsuits alleging the devicemaker's transvaginal mesh product for urinary incontinence is defective and causes complications, the Marlborough, Mass., company said. Boston Scientific plans to pay an estimated $119 million to resolve 2,970 cases, a fraction of the more than 25,000 mesh claims it is contending with in U.S. federal and state courts. The agreement is tied to a $35 million verdict in a Dallas County, Texas, district court case that is subject to appeal. The devicemaker denied allegations the product was to blame for plaintiffs' complications.

Medtronic Evaluates Stent Graft System

Medtronic has initiated a clinical study to evaluate the efficacy of the Endurant Evo abdominal aortic aneurysm treatment stent graft system, the Ireland-based devicemaker announced recently. The multicenter clinical trial will enroll 140 infrarenal abdominal or aortoiliac aneurysm patients at up to 30 sites in the U.S. and Europe. The study's primary safety endpoint is the proportion of patients experiencing a major adverse event within 30 days of implantation.

Stryker Settles Howmedica Lawsuit

Stryker has settled a $3 million class-action lawsuit filed in 2013 that alleged its Howmedica subsidiary didn't reimburse for business expenses and didn't have a reimbursement policy, which is illegal under California law. Stryker failed to have the case dismissed in 2014 in the U.S. District Court for the Northern District of California. The settlement is to be paid to 134 plaintiffs as part of the class action pending court approval.

Device Treats Postpartum Hemorrhaging

Cambridge Design Partnership is seeking funding for its uterine balloon tamponade, designed to help medical professionals treat life-threatening postpartum hemorrhage in developing countries, the UK devicemaker said. Current UBTs cost as much as $200 and have to be inserted by trained clinicians, which limit their use in the developing world.

Companies OK Catheter Distribution Pact

Vascular Pathways has signed a three-year contract to distribute its AccuCath line of catheters with Novation. The intravascular catheters feature a coiled tip Nitinol guidewire, blood control valve and needlestick safety options. The product's design is intended to increase first-time success, reduce complication rates, extend dwell times, increase patient satisfaction and lower overall provider costs, the devicemaker says.

Stentys Wins CE Mark for Coronary Stent

French devicemaker Stentys plans to launch its Xposition S self-apposing coronary stent later this month, following receipt of a CE mark, which came ahead of schedule, the company says. Using Cappella Peel Away technology, the delivery system works by having a small balloon split open the sheath containing the stent and releasing it at the exact intended location.

FDANEWS

Customer Service
(888) 838-5578 • +1 (703) 538-7600
customerservice@fdanews.com

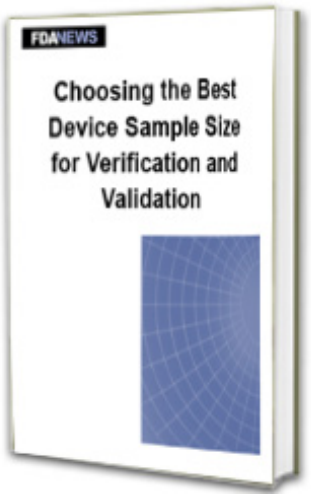
Editor: Elizabeth Orr
(703) 538-7652
eorr@fdanews.com

Ad Sales: Jim Desborough
(703) 538-7647
jdesborough@fdanews.com

300 N. Washington St., Suite 200 • Falls Church, VA 22046-3431 • Phone: (888) 838-5578 • +1 (703) 538-7600 • Fax: +1 (703) 538-7676
www.fdanews.com

Reporters: Lena Freund, Kellen Owings, Jonathon Shacat; Jason Scott; Jessica Grinspan

President: Cynthia Carter; **Editor-in-Chief:** Meg Bryant; **Managing Editor:** John Bechtel



Choosing the Best Device Sample Size for Verification and Validation

If you're like many manufacturers, you understand the essence of the *21 CFR 820.30* requirement: you must run enough test samples of a product so its test results can be successfully applied to full-scale production runs. And, like many manufacturers, you've probably had trouble for years determining exactly how many units of a product you should test to satisfy the FDA.

Choosing the Best Device Sample Size for Verification and Validation will help you select the right statistical methods to make this determination. With it, you'll learn how to get the right sample size to ensure that user requirements are met in the product design. This management report will also help you understand how to:

- Examine the discrete or continuous statistical data you collect.
- Look at variability, including variation from unit to unit or from batch to batch, as well as variation in their measurement systems.
- Design verification and validation tests, particularly regarding choice of sample size.
- Fully understand the requirements for statistical techniques, including how different techniques can affect the design control process.
- And much, much more.

Finally, you can gain a clearer understanding of how to put together a statistical methods program for design verification and validation that will satisfy FDA auditors.

Order your copy today!

FOUR EASY WAYS TO ORDER

1. **PHONE:** Toll free (888) 838-5578 or +1 (703) 538-7600
2. **WEB:** www.fdanews.com/46876
3. **FAX:** +1 (703) 538-7676
4. **MAIL:** FDAnews 300 N. Washington St., Suite 200 Falls Church, VA 22046-3431

☑Yes! Please send me ____ copy(ies) of ***Choosing the Best Device Sample Size for Verification and Validation*** at the price of $397 each for the format I've selected: ❑ Print ❑PDF

Name _____

Title _____

Company _____

Address _____

City_____ State _____ Zip code _____

Country _____

Telephone _____

Fax _____

Email _____

METHOD OF PAYMENT

❑ Check enclosed (payable to FDAnews)

❑ Bill me/my company. Our P.O.# _____

❑ Charge my credit card:
❑ Visa ❑ MasterCard ❑ American Express

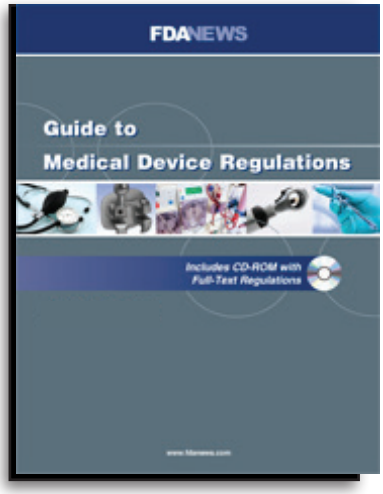
Credit card no. _____

Expiration date _____

Signature _____
(Signature required on credit card and bill-me orders)

Add $10 shipping and handling per book for printed books shipped to the U.S. and Canada, or $35 per book for books shipped elsewhere. Virginia customers add 6% sales tax.

14FLYR-N



Guide to FDA Medical Device Regulations: *2015 Edition*

Whether you need to help your company convince the FDA to accept a predicate device in a simple 510(k) filing or you're responsible for implementing UDI across a family of high-risk implantable devices, there's one thing all regulatory professionals need. The most up-to-date, latest FDA regulations available.

That's why the **Guide to FDA Medical Device Regulations** is an FDAnews best-seller.

The 2015 **Guide** includes full texts of every device-related regulation and guidance — included on a fully searchable CD — plus executive summaries and analyses that will help your company avoid regulatory missteps, get to market faster and improve profitability. For newcomers and veterans alike, this is a must-have quick-reference encyclopedia.

Discover the changes and best practices regarding:

- Determining substantial equivalence of predicate devices
- Home use devices
- Cybersecurity requirements
- UDI
- De Novo classifications
- Expedited access for devices addressing unmet medical needs
- New Policy on General Wellness Devices
- Labelling
- And much more

Stay up-to-date on key medical device regulation changes with the 2015 edition of **FDAnews' Guide to FDA Medical Device Regulations** — the most authoritative and comprehensive guide ever assembled.

FOUR EASY WAYS TO ORDER

1. **PHONE:** Toll free (888) 838-5578 or +1 (703) 538-7600
2. **WEB:** www.fdanews.com/49166
3. **FAX:** +1 (703) 538-7676
4. **MAIL:** FDAnews
   300 N. Washington St., Suite 200
   Falls Church, VA 22046-3431

☑**Yes!** Please send me ____ copy(ies) of ***Guide to FDA Medical Device Regulations*** at the price of $397 each for the format I've selected: ❑ Print ❑PDF

Name _____

Title _____

Company _____

Address _____

City_____ State _____ Zip code _____

Country _____

Telephone _____

Fax _____

Email _____

METHOD OF PAYMENT

❑ Check enclosed (payable to FDAnews)

❑ Bill me/my company. Our P.O.# _____

❑ Charge my credit card:
❑ Visa ❑ MasterCard ❑ American Express

Credit card no. _____

Expiration date _____

Signature _____
(Signature required on credit card and bill-me orders)

Add $10 shipping and handling per book for printed books shipped to the U.S. and Canada, or $35 per book for books shipped elsewhere. Virginia customers add 6% sales tax.

15FLYR-N