INTERNATIONAL DEVICES & DIAGNOSTICS MONITOR

Vol. 1, No. 49
Dec. 14, 2015

IN THIS ISSUE

Consumer Group Urges FDA to Investigate INRatio Testing Device, Califf's Role in Trial

Advocacy group Public Citizen is calling on the FDA to investigate the use of Alere's INRatio blood testing device during a clinical trial supporting approval of Bayer's blood thinner Xarelto, claiming that false readings by the device could have skewed trial results in favor of the drug.

From 2006 to 2010, the Rocket AF trial compared Xarelto (rivaroxaban) with warfarin for prevention of stroke and systemic embolism in patients with atrial fibrillation.

In a letter sent to the FDA last week, Public Citizen says its analysis of the FDA's Manufacturer and User Facility Device Experience database shows 9,469 malfunction reports and 1,445 injury reports from 2002 through November of this year with INRatio devices.

(See **INRatio**, *Page 4)*

India Considers Separating Device Regulations From Drugs

India's government is mulling a decision that would regulate medical devices separately from pharmaceuticals, in a move that could pave the way for greater investment and research and development in the country, an industry group says.

The Heath Ministry will soon solicit public input via the Central Drugs Standard Control Organization's website on proposed changes to the Drugs & Cosmetics Rules through the law ministry, says Rajiv Nath, forum coordinator of the Association of Indian Medical Device Industry.

The announcement follows a meeting held Dec. 5 between senior officials with the Health Ministry, the Indian government, CDSCO and industry stakeholders, including AIMED. The Health Ministry has prepared a draft proposal and circulated it to industry associations to provide feedback by Dec. 14, according to meeting minutes released by CDSCO.

(See **AIMED**, *Page 2)*

AIMED, *from Page 1*

Vince Suneja, CEO of TwoFour Insight Group, says this development could be significant if it actually happens.

"There is already a pending amendment to the Drugs & Cosmetics Act, which would give this separation a statutory basis versus what is being proposed here under the Drugs & Cosmetics Rules," he tells *IDDM*. The legal authority is greater with the statute versus the rules.

But the amendment to the Drugs & Cosmetic Act of 1940, which has been tabled in the Parliament, is "half-hearted," Nath says, adding devices need separate rules, and either a separate regulatory authority or a revamped CDSCO as an Indian Healthcare Products Regulatory Authority.

AIMED welcomed the Indian government's initial but firm steps to address this issue.

"Indian medical devices have for long been incorrectly and incompletely regulated," says Nath. The lack of an internationally equivalent regulatory framework has been confusing to overseas and Indian investors who were scared to invest with pharmaceutical type GMP demands being imposed by regulators in an arbitrary and prescriptive manner by unsure inspectors on an engineering industry, he adds.

Currently, India is dependent on imports for 70 percent of its devices, and the size of the market is estimated to be more than $10 billion in terms of retail level sales (*IDDM*, Nov. 13).

AIMED has been seeking changes in the Drug Rules covering regulatory quality management framework and infrastructure requirements on the lines of the Bureau of Indian Standards and International ISO 13485 standard for regulatory purposes, says Nath.

AIMED hopes India will adopt a risk proportionate regulatory framework, giving lower compliance requirements for low-risk devices like wheelchairs and moderate-risk devices like needles, and higher requirements for high-risk devices, such as orthopedic implants and cardiac stents, Nath says.

He also wants to see the unbundling of regulations and regulatory controls, so that regulators would delegate the task of compliance audits of manufacturers to third-party assessment and certification bodies.

"In India, there has been no onus on manufacturers to demonstrate compliance," says Anil Jauhri, CEO of the National Accreditation Board for Certification Bodies. "There is a need to provide this layer whereby manufacturers voluntarily use accredited third party conformity assessment bodies to verify and certify their compliance level to regulations."

Earlier this year, the Indian government announced the creation of a dedicated authority to oversee the regulation and production of medical devices (*IDDM*, July 10). — Jonathon Shacat

India Proposes Template for Reporting Medical Device Adverse Events

The Indian Pharmacopoeia Commission has released a proposed template for manufacturers or medical personnel to report adverse events involving medical devices.

The form contains sections for patient information, details about the device, the incident date and location and the seriousness of the event. Details on the incident should include a description of the device's deficiency or malfunction, and a clarification of the hazards and the associated risks to patients or users, IPC says.

IPC issued a draft version of the form as part of the Materiovigilance Programme of India, which was launched earlier this year by India's health ministry to collect and monitor adverse events for devices. The system was designed by the Central Drugs Standard Control Organization and the Sree Chitra Tirunal Institute of Medical Sciences and Technology (*IDDM*, June 5).

Comments on the draft form are due to pvpi.ipcindia@gmail.com by Jan. 3. Access the proposed template here: www.fdanews.com/12-15-IPC-Form.pdf. — Jonathon Shacat

Ineffective Cybersecurity Poses Risks for Medical Device Safety

The FDA is exploring with stakeholders ways to ward off cybersecurity threats, as wireless, network-connected medical devices are increasingly used and health information is frequently exchanged electronically.

The agency will hold a public workshop on Jan. 20-21 to discuss a voluntary, risk-based framework to mitigate cybersecurity risks for devices. The *Framework for Improving Critical Infrastructure Cybersecurity*, developed by the National Institute of Standards and Technology, has been used within the healthcare and public health sector to reduce cybersecurity risks.

During the workshop, the FDA will also seek input on how to adapt the Common Vulnerability Scoring System assessment tool for medical devices. Manufacturers can manage the impact of vulnerability by using the CVSS, but incorporating the tool into assessments for medical devices has proven to be a challenge because it does not directly incorporate patient risk, says the FDA.

If device cybersecurity vulnerabilities are exploited, products could malfunction, healthcare services could be disrupted and patient information could be compromised, the FDA says.

The FDA's announcement of the upcoming workshop follows a recent report by Forrester Research predicting that as early as next year hackers will target medical devices for cyber extortion, such as GPS-enabled asthma inhalers to wearable tech-tattoos that monitor vital functions. But, one expert says better candidates would be large machines like MRIs or CAT scanners — systems that directly interact with the health electronic record (*IDDM*, Dec. 4).

Like all computer systems, medical imaging devices are subject to risks that may harm software, hardware or data security. As imaging systems become increasingly connected to networks, security risks move beyond the system itself to intrusions across digital networks, says the Medical Imaging & Technology Alliance.

In a recently released white paper, MITA says medical imaging manufacturers should prioritize cybersecurity best practices on incident risk mitigation. Manufacturers should consider options for robust, yet rapid authentication, including passwords allowing long strings, access options for smart cards and biometric identification.

More information on the FDA's workshop *Moving Forward: Collaborative Approaches to Medical Device Cybersecurity* is here: www.fdanews.com/12-15-FDA-Cybersecurity.pdf. MITA's white paper *Cybersecurity for Medical Imaging* can be accessed here: www.medicalimaging.org/2015/11/05/nema-publishes-nemamita-csp-1-2015-cyber-security-for-medical-imaging/. — Jonathon Shacat

eVent Medical Recalls Inspiration Ventilators

eVent Medical has implemented a Class 1 recall of its Inspiration ventilators, citing a faulty switch on the power board that may fail, causing the device to shut down without sounding an alarm.

The ventilator systems provide constant breathing support to infants and adults. eVent received one report of the ventilator shutting down without sounding an alarm, but there were no injuries or deaths, the FDA says.

The nationwide recall, which involves 251 units, affects all LS, 5i and 7i models manufactured prior to Jan. 21, 2015, with distribution dates of Feb. 14, 2013, to Dec. 31, 2014.

The firm sent an urgent field safety notice to all customers on Oct. 13 advising them to immediately discontinue use of the ventilators until corrective actions could be taken, according to a recall notice issued Dec. 7 by the FDA.

"To mitigate the risk of ventilator failure, the firm attached the instructions for removing the potentially faulty component from the power board," the FDA says.

eVent did not respond to a request for comment by press time. Read the FDA's recall notice here: www.fdanews.com/12-15-eVent-RecallNotice.pdf. — Jonathon Shacat

INRatio, *from Page 1*

However, last week, the Rocket AF Clinical Trial Executive Committee released its secondary analysis of the Phase 3 trial, claiming the findings are consistent with the results from the original trial and do not alter the conclusions that rivaroxaban is a reasonable alternative to warfarin for preventing stroke and systemic embolism with less intracranial hemorrhage and fatal bleeding.

Califf's Role

Public Citizen also raises questions on FDA Commissioner nominee Robert Califf's role in choosing the measuring device to interpret the study. At the time, Califf was co-chairman of the industry steering committee advising Johnson & Johnson on the study.

"Hundreds of reports of injuries or malfunctions with the INRatio device occurred before this trial started," says Sidney Wolfe, co-founder and senior adviser of Public Citizen's Health Research Group.

"The device was known to give faulty readings and injure patients. Why did Dr. Califf and the steering committee that he co-chaired agree to use it in the trial?" Wolfe adds.

FDA spokeswoman Katie Conover did not respond to a request for comment on Public Citizen's call to investigate Califf's role in choosing the device for the study.

However, she tells *IDDM* that Califf is recused from the matter, and that the agency is reviewing relevant trial data.

Manesh Patel, a member of the Rocket AF Executive Committee, told *IDDM* that the device was chosen for several technical reasons, and because it had FDA and CE Mark approval in the U.S., Europe and other potential countries.

He maintains that during the planning and execution of the trial, the executive committee was not aware of any issues with the device.

Read Public Citizen's letter here: www.fdanews.com/12-15-PC-Letter.pdf.
— Jonathon Shacat

Boston Scientific Recalls Chariot Guiding Sheath

Boston Scientific has voluntarily recalled its Chariot guiding sheath, due to a risk of shaft separation.

Roughly 8,000 units were recalled from the field when the recall began on Nov. 19, the company announced last week. The FDA classified the action as a Class 1 recall.

The device helps introduce interventional devices during peripheral vascular procedures.

The company said it has received 14 complaints for shaft separation, four of which involved separation of the distal shaft. The events occurred during device preparation or use. The most severe outcome of this failure is embolism of device fragments, which could lead to obstruction of blood flow or additional intervention to remove a device fragment. Obstruction of blood flow can result in injuries such as stroke, kidney damage or damage to the intestines or limbs.

"An investigation is currently being conducted by Boston Scientific to determine the cause," Boston Scientific spokesman Tom Keppeler tells *IDDM*.

No permanent injuries or patient deaths have been reported, according to the company.
— Jonathon Shacat

New Ethics Codes Adopted In Europe, Asia-Pacific Region

Ethics codes have been getting more attention this year in Europe and the Asia-Pacific region, with industry groups adopting new business practices standards in the medical device sector.

The European Diagnostics Manufacturers Association and the European Medical Technology Industry adopted a common code on Dec. 2.

The new MedTech Europe Code, which will become binding for EDMA and Eucomed corporate members by Jan. 1, 2017, sets minimum standards by which industry members operate across Europe.

The code regulates all aspects of the industry's relationships with healthcare professionals and healthcare organizations, such as company-organized events, arrangements with consultants and research and financial support to medical education. The code also introduces a common independent enforcement mechanism.

For example, member companies may provide products as samples at no charge for healthcare professionals to evaluate, as long as they don't improperly reward, induce or encourage them to purchase, recommend or prescribe the products.

The two codes were aligned because both EDMA and Eucomed codes, established in 2007 and 2008, respectively, had their own specificities, which created inconsistencies in the rules applied to the industry.

In the Asia-Pacific Economic Cooperation region, the number of industry associations with codes of ethics in the medical device sector has expanded from nine in 2012 to 20 in 2015, according to AdvaMed.

Today, the number of APEC economies with a local medical device industry code is at 17, with first-ever industry association codes launched in China, Indonesia, Malaysia, Philippines, Singapore and Chinese Taipei

"Together, the 20 medical device industry associations across APEC economies represent over 11,000 companies, nearly 8,000 of which are small- and medium-sized," says Christopher White, senior vice president and general counsel of AdvaMed.

Read the new MedTech Europe Code here: www.fdanews.com/12-15-EU-EthicsCode.pdf.
— Jonathon Shacat

Australia's TGA Updates Guideline On In Vitro Diagnostic Classification

Australia's Therapeutic Goods Administration has revised its guideline on how manufacturers should classify in vitro diagnostics based on risk.

IVDs will be placed in one of four risk-based categories, ranging from Class 1 for the lowest risk to Class 4 for the highest risk. If an IVD is

(See **TGA**, *Page 6)*

Saudi FDA Sets Criteria for Medical Device Advertising

The Saudi FDA is clarifying expectations for devicemakers when it comes to advertising.

Content must not be misleading in terms of a product's performance. All advertising and marketing material must be approved by the SFDA before it can be used. Any modification, including translation, will require a new approval, the agency says in guidance released last week.

Importantly, the language used in advertisements depends on the intended audience. Ads should be in English for professionals and in Arabic for lay persons.

In addition, ads must include the device's name, manufacturer's contact information, document control reference number and advertising license number.

Ads can be submitted in one of two ways, either by a manufacturer as part of the marketing authorization procedure, or as a separate approval if the material is prepared by a licensed distributor or registered healthcare facility on its behalf.

Read the guidance here: www.fdanews.com/12-15-SFDA-Ads.pdf. — Jonathon Shacat

TGA, *from Page 5*

designed to be used in combination with other IVDs, non-IVD medical devices or accessories to medical devices, then each device must be classified separately.

The guidance, which was released Dec. 7 and replaces a November 2011 version, contains updated information to reflect an amendment to the Therapeutic Goods (Medical Devices) Regulations 2002 that removed a clause in the IVD classification rules that referred to IVDs intended to detect transmissible agents included in the Australian National Notifiable Disease Surveillance System list (*IDDM*, Nov. 20).

In the section on examples provided for Class 2 IVDs, a list has been provided of transmissible agents that are of public health importance but pose a moderate personal risk because they generally cause self-limiting diseases. IVDs to detect these agents were previously deemed to be Class 3 IVDs but are now classified as Class 2 IVDs, TGA spokesman Neil Branch tells *IDDM*.

The new guidance reiterates that if IVDs are supplied as part of a system or procedure pack, the highest class of any component in the pack applies to the pack overall. Similarly, if IVDs are included in a pack with non-IVD devices, the highest class of product in that group applies.

The guidance also contains a detailed explanation of how to apply the classification rules, including examples for detection of transmissible agents posing a high public health risk, and detection of red blood cell antigens and antibodies and non-red cell typing.

Read the guidance here: www.fdanews.com/12-15-TGA-IVDs.pdf. — Jonathon Shacat

FDA Reopens Comment Period On Strategies for NGS Tests

The FDA is reopening the comment period for feedback on challenges and opportunities of regulating next-generation sequencing-based clinical tests, responding to requests from stakeholders who need additional time to submit input.

The comment period closed on Nov. 25, but it has been extended until Dec. 24, the FDA announced last week.

The FDA held two workshops on the topic on Nov. 12 and 13.

The first workshop focused on analytical performance evaluation standards that developers can use to ensure accuracy and reliability of tests results. The second explored how stakeholders can develop curated databases that correlate genetic changes with different conditions and diseases (*IDDM*, Sept. 11).

Read the Federal Register notices here: www.fdanews.com/12-15-FDA-NGS.pdf and www.fdanews.com/12-15-FDA-HGV.pdf. — Jonathon Shacat

FDA Clarifies Standards for eCopy Medical Device Submissions

The FDA has issued new guidance clarifying the processing and technical standards for electronic copies for medical device submissions, based on the agency's experience so far with the program.

The guidance, released last week, replaces an Oct. 10, 2013, version. The new version focuses on ways to help improve the efficiency of the review process.

In the new guidance, the FDA recommends that bookmarks and hyperlinks within a single PDF file be used to assist reviewers in navigating through the content of a submission. Also, the agency prefers creating a PDF file from the source document to create automatic searchable text.

In addition, the previous version of the guidance contained a sentence stating that "The size of the submission is irrelevant." However, that sentence was removed in the new guidance. Instead, it says, "Although there is no maximum total submission size restriction, it is recommended that the total package submission not exceed 1 GB to avoid possible load time failures that may delay the submission process."

The FDA originally released guidance on eCopies in December 2012. The Food and Drug Administration Safety and Innovation Act requires companies to submit an eCopy, in the form of a CD, DVD or flash drive, along with a paper submission.

eCopies are still required for a variety of submission types, including premarket notification submissions, premarket approval applications, product development protocols, investigational device exemptions, humanitarian device exemptions and emergency use authorizations, according to the new guidance.

Read the guidance on *eCopy Program for Medical Device Submissions* here: www.fdanews.com/12-15-FDA-eCopy.pdf. — Jonathon Shacat

Vericel Submits HDE Supplement to Revise Label Indications for Epicel

Vericel has submitted a humanitarian device exemption supplement to the FDA to revise the labeled indications of Epicel to specifically include use in pediatric patients.

Epicel (cultured epidermal autografts) is a permanent skin replacement for treatment of patients with burns comprising at least 30 percent of the body. It has been used in the U.S. and internationally to treat severely burned patients since 1988, and was approved in 2007 as a humanitarian use device.

HUDs are intended to treat or diagnose diseases or conditions that affect fewer than 4,000 individuals in the U.S. per year. A HUD is eligible to be sold for profit after receiving HDE approval if the device meets certain eligibility criteria, including treating a disease or condition that occurs in pediatric patients. — Jonathon Shacat

BRIEFS

FDA Clears Spinal Cord Stimulation System

Wireless medical devicemaker Stimwave Technologies has scored FDA clearance for its Stimwave Freedom-8A Spinal Cord Stimulation System for treatment of chronic back and leg pain. The wireless, micro-technology neuromodulation system features eight-electrodes placed near surrounding nerves, to which the miniature device delivers small pulses of energy. The system previously received FDA clearance for its four-electrode device last year. Stimwave has also begun marketing the device, and a nationwide launch is expected in January 2016.

Medtronic Gets Approval for Neurostimulator

The FDA has given the green light to Irish devicemaker Medtronic for systems within its Activa portfolio of deep brain stimulation neurostimulators for full-body MRI scans. Previously, patients with Medtronic DBS could receive head scans at a low radiofrequency power limit, and the DBS system had to be turned off prior to the MRI scan. The approved full body MRI and higher power limits enable improved image quality, faster scan times and larger scan coverage for better diagnostic capabilities. According to the devicemaker, its MR Conditional DBS systems are the only approved for full-body MRI scans.

FDA Grants 510(k) Clearance to Qfix

The FDA has awarded radiotherapy devicemaker Qfix 510(k) clearance for its Encompass SRS Immobilization System for stereotactic radiosurgery. The device is cleared for sub-millimeter immobilization to treat multiple lesions with a single isocenter. The system uses a posterior thermoplastic and anterior open view mask compatible with optical tracking systems. It also features an optional IntegraBite, which can reduce motion to enable maximum exposure to the tumor while minimizing radiation delivery to surrounding healthy tissue. The device is currently used for intracranial radiotherapy treatments.

Allurion Technologies Wins CE Mark

Wellesley, Mass.-based Allurion Technologies has won CE mark for its Elipse Gastric Balloon for obesity. The swallowable balloon – made of thin, flexible polymer film – fills the stomach and assists patients in feeling full and eating less. It remains in the stomach for four months, before automatically emptying and being naturally excreted. The device will initially be available in weight loss centers in France, Italy and the UK, and eventually the Middle East, according to the company. The product is not approved in the U.S.

FDA Clears RevMedX's Wound Dressing

The FDA has given its blessing to RevMedX's XSTAT 30 wound dressing to treat adults and adolescents in the general population. The expandable, multi-sponge dressing – used to control life-threatening bleeding from wounds in areas that a tourniquet cannot be placed, such as the groin or armpit – was previously only cleared for military use. It is indicated for patients at high risk for immediate, life-threatening and severe hemorrhagic shock and non-compressible junctional wounds when care at emergency rooms is not available within a few minutes.

FDANEWS

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

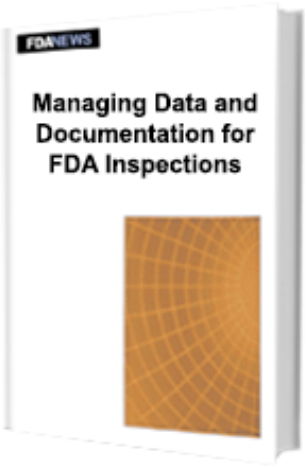
Editor: Jonathon Shacat
(703) 538-7663
jshacat@fdanews.com

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: Kellen Owings, Michael Cipriano, Victoria Pelham, Cameron Ayers
President: Cynthia Carter; **Editorial Director:** Tamra Sami; **Managing Editor:** Elizabeth Hollis

FDANEWS



Managing Data and Documentation for FDA Inspections

Do you understand the FDA's document access authority? Is your company's data and documentation organized and ready for your next FDA inspection?

If not, your next inspection could become a scavenger hunt.

Managing Data and Documentation for FDA Inspections will help you get control of your data by using industry best practices and SOPs.

You will also learn:

- Documentation the FDA is entitled to see;
- Documentation the FDA is not entitled to see;
- How to create unique naming conventions to handle masses of data;
- How to prioritize data that might be requested during an inspection;
- The "Top 10" questions to ask about your archival process;
- What to do when documents are not in the general archives;
- When does email count as documentation;
- If source data is electronic, how to provide access to the regulatory authority;
- If source data is paper that was scanned, what to do with the originals; and
- Tips for dealing with more than one "original."

Order your copy of **Managing Data and Documentation for FDA Inspections** TODAY!

FOUR EASY WAYS TO ORDER

1. **PHONE:** Toll free (888) 838-5578
   or +1 (703) 538-7600
2. **WEB:** www.fdanews.com/51287
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 **Managing Data and Documentation for FDA Inspections** at the price of $397 each for the format I've selected:
❑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

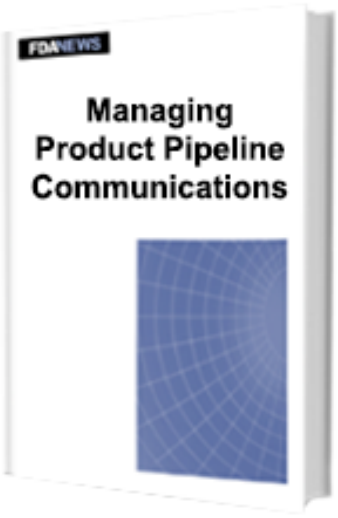
Credit card no. _____

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. or $35 per book for books shipped elsewhere. Virginia customers add 6% sales tax.

15FLYR-N



Managing Product Pipeline Communications

When your company has a product in development, whether drug, device or biotech, what you can — and can't — say about it is tightly regulated by the FDA.

At the same time, the SEC requires that information of material value to investors be properly disclosed to them.

Of course, this SEC requirement involves exactly the same products you have in your pipeline, the ones that the FDA wants you to be very careful about discussing.

This management report will tell you how to balance these seemingly contradictory demands and how to handle all the forms "communication" takes today — from tweets to talking points, from press releases to the slides investors see on a conference call. You will learn:

- The specific laws and regulations the FDA and SEC must enforce;
- 6 dos and 6 don'ts for speaking publicly about a product in development;
- 4 dos and 3 don'ts when talking with analysts and investors;
- Examples from case studies about communication that resulted in FDA enforcement actions, SEC penalties, and investor lawsuits;
- And much more.

With **Managing Product Pipeline Communications** you'll be able to confidently account for the various perspectives — regulators on both sides, investors and the general public — and ensure that the right people get the information they should from you every time.

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/51092
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 **Managing Product Pipeline Communications** at the price of $397 each for the format I've selected: ❑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. or $35 per book for books shipped elsewhere. Virginia customers add 6% sales tax.

15FLYR-N