INTERNATIONAL DEVICES & DIAGNOSTICS MONITOR

Vol. 1, No. 21
May 25, 2015

IN THIS ISSUE

21st Century Cures Passes House Panel 51-0, Moves on to House Floor

The House Energy & Commerce Committee voted resoundingly to approve the 21st Century Cures Act, sending the measure — which includes a provision to ease U.S. device trials by allowing a single central review board to monitor multiple trial sites — to the House floor for consideration.

Currently, device trials must be cleared by a local institutional review board at each research site, a requirement AdvaMed calls unnecessary and redundant. JC Scott, head of government affairs at the trade group, says the FDA is aware of the problem but lacks the power to change the policy.

In another change, the FDA overhaul package would simplify informed consent rules around device trials that pose no more

(See **21 Century**, *Page 2)*

Expert: Allow for Modifications In UDI Product Labeling Designs

As China and the European Union prepare to issue their own unique device identifier regulations by the end of the year, devicemakers should develop a design flexible enough to allow for use outside the U.S. with modest revisions, the FDA's former chief UDI architect says.

Jay Crowley, vice president and UDI practice lead at USDM Life Sciences, explains that the Chinese and EU regulations will differ slightly in details such as registration numbers, so a label that can be easily modified will be beneficial. Crowley spoke at an FDAnews webinar.

Crowley reminds devicemakers that their products already have stock keeping unit, or SKU, codes, so this is a good place to start when focusing on UDI labels. He suggests having each SKU line up with a single UDI, with the UDIs changing when SKUs do and vice versa.

SKUs can help in assembling a list of products subject to UDI, Crowley says. Frequently, companies discover that they don't have good internal data on how products are packaged or labeled, or occasionally

(See **UDI**, *Page 4)*

21st Century, *from Page 1*

than minimal risk to the patient, as long as they include appropriate safeguards.

In addition to clinical trial reforms, H.R. 6 would allow devicemakers developing so-called breakthrough technologies to ask the FDA for a priority review designation before submitting an application.

The bill also clarifies and expands the definition of "valid scientific evidence" in the context of device applications, ensuring that manufacturers can submit peer-reviewed journal studies, results from overseas trials and registry data.

Further, the bill would expand the humanitarian device exemption program to cover devices treating conditions affecting up to 8,000 people in the U.S., double the current definition.

Rules around medical device software would also be updated, limiting the FDA's authority to regulate products that don't pose a risk to patient health. Finally, the law would allow devicemakers to use third-party inspectors more broadly (*IDDM*, May 15).

The legislation includes an amendment from Reps. Anna Eshoo (D-Calif.) and Leonard Lance (R-N.J.) that would exempt FDA user fees from sequestration – a provision Eschoo said would ensure that private dollars are not locked up.

Scott praised the user fee amendment, but expressed reservations about a provision in the bill's offset package that would apply Medicare payments for durable medical equipment to Medicaid patients as of 2020.

Industry has had concerns over low rates set through Medicare competitive bidding and there hasn't been a good analysis done of possible patient access issues, he says.

Committee chairman Fred Upton (R-Mich.) hinted that more amendments might be added before the bill hits the House floor for approval. Scott declined to speculate on the chances of equivalent legislation in the Senate, where the issues are being researched.

View the bill at www.fdanews.com/05-20-15-21CCbill.pdf. — Lena Freund and Elizabeth Orr

Morcellation Makers Face Lawsuits; Aetna Drops Insurance Coverage

Manufacturers of power morcellators are facing mounting woes as patients file product liability lawsuits across the U.S. and at least one major insurance company narrows its coverage of treatments with the device.

The latest court actions came in Pennsylvania, where two women filed near-identical lawsuits against Olympus America on Thursday, claiming they were injured by the firm's PlasmaSORD bipolar morcellator. Olympus should have known of the risks before the 2009 and 2010 surgeries to treat uterine fibroids, the plaintiffs say.

The Olympus cases are only two of a growing number of lawsuits against manufacturers since the FDA warned that using morcellators to remove uterine tissue could spread cancer. Karl Storz Endoscopy-America was sued in a California court on May 13, while a New Orleans woman filed suit in Louisiana federal court against Ethicon Endo-Surgery and its parent Johnson & Johnson on April 22.

All of the cases seek damages related to the spread of cancer caused by the procedure. In the California case, a woman died and her daughters have filed wrongful death charges.

Insurers also are stepping back on morcellation. Aetna, the nation's third-largest insurance company, announced earlier this month that it will no longer cover the routine use of power morcellators.

The FDA required a black box warning on the devices in December 2014 after an advisory panel concluded they might not be safe. J&J recalled its Morcelex version last summer.
— Elizabeth Orr

MDUFA IV Negotiations to Get Underway With July Meeting

Negotiations on the fourth iteration of the Medical Device User Fee Act will swing into full gear July 13, with an FDA public meeting to assess the current MDUFA and ways to improve it.

Much is at stake as MUDFA IV will set fees for much of CDRH's regulatory review activities and performance goals for the center for fiscal years 2018 through 2022. The last reauthorization process in 2011-2012 generated two public meetings, 14 stakeholder discussions and about three dozen industry conclaves.

One issue expected to come up is whether laboratory-developed tests will be included in user fee requirements, as the FDA moves ahead with plans to regulate them (*IDDM*, Feb. 6). In 2012, disagreement on whether labs should pay user fees delayed the agency's final MDUFA III proposal by several months. In the end, the FDA didn't subject labs to the fees, but CDRH Director Jeffrey Shuren has hinted that may not be the case in the upcoming reauthorization.

However, the FDA has never imposed fees on an industry that didn't agree to pay them. If labs are going to pay user fees, they'll need to feel they're getting something out of the process, an industry source says.

AdvaMed and other industry insiders contacted by *IDDM* say it's too early for MDUFA IV "wish lists." During the 2012 negotiations, industry pressures led to the first concrete CDRH performance goals in the user fee agreement.

CDRH review times have significantly improved since MDUFA III as the agency moved to meet those goals. According to FDA data, the total average time to PMA decision dropped from 419 days for in 2010 to 321 days in 2013, while the 510(k) decision time shrank from 154 days to 126 days.

In 2014, the FDA collected $43.5 million in device application fees and $81.6 million in registration fees. – Elizabeth Orr

MicroAire Warned Over MDR, Validation Issues

A Virginia maker of implants used in plastic surgery was slapped with a warning letter after an FDA inspection found flaws with the company's validation and MDR reporting practices.

According to the letter, Charlottesville-based MicroAire Surgical Instruments failed to properly explain why it grouped its Ultratine and Endotine device lines together in validating a sterilization process.

The company provided the FDA with additional materials on the decision after investigators detailed the problem in a Form 483, but the response was inadequate because it didn't include a thorough retrospective review of MicroAire's rationale or documentation of independent sterilization validations for the devices.

MicroAire also hadn't validated software used in production. The company's response on this point was adequate and will be verified during a follow-up inspection, the warning letter says.

The FDA also dinged MicroAire for its adverse event reporting procedures. The company's MDR policy didn't define certain key terms such as "MDR reportable event" and failed to explain how to obtain an MDR reporting form.

The policy also gave no timeline for submitting supplemental reports and didn't ensure that reports would be filed in a timely manner.

The Dec. 29, 2014, warning letter, which was posted online recently, followed an Aug. 11 to 22, 2014, inspection by the FDA's Baltimore district office.

The company did not respond to a request for comment by press time.

View the warning letter at www.fdanews.com/05-25-15-microaire.pdf.
— Elizabeth Orr

UDI, *from Page 1*

even whether the device was FDA-approved or reached the market through some other means.

Besides SKUs, devicemakers may need to refer to UDI guidance to confirm whether a specific device is considered an accessory subject to the tracking rule, Crowley says. He encourages companies to write SOPs defining how they determine if a product is an accessory, a standalone device or something else.

When it comes to registering the UDI and listing it in the Global UDI Database, companies should name one party to serve as labeler, Crowley says. This is particularly useful if the device is manufactured and labeled by several different companies or in several different locations, or if contract manufacturers are involved, he adds.

Devicemakers should also use the "own name" rule of thumb, Crowley says. If a device is distributed under your brand name, you're probably the labeler even if you don't physically get the product to market.

By the end of 2015, Class III devices, Class II implants and devices that are life-supporting or life-sustaining will have to carry UDIs. Identifiers for the remainder of Class II devices are due next year, followed by Class I devices in 2018. — Elizabeth Orr

Medtronic Venous Veins Kit Recalled Just Weeks After PMA Was Approved

A novel way to seal varicose veins is being recalled less than three months after the PMA was approved.

The FDA approved the marketing of Medtronic's VenaSeal closure system on Feb. 20. However, on May 12 the agency announced the Class II recall of 1,661 units of the device distributed worldwide. According to the announcement, the devices are being recalled because of a possible sterility breach in the outer packaging material. None had made it to U.S. shelves; instead, the kits had been sold in Australia, Canada, Europe, Hong Kong and the UAE.

Medtronic contacted purchasers of the kits by email on April 28. According to the company, the recall is not being triggered by a regulatory agency or field complaint. Instead, it discovered the possibility of a sterility breach during standard internal package testing. Medtronic is asking owners of unused kits to return them as part of the recall.

The VenaSeal system is used in patients with superficial but symptomatic varicose veins of the legs. It is made up of an adhesive and delivery system components including a catheter, guidewire, dispenser gun, dispenser tips and syringes. It was the first varicose vein closure system to use an adhesive. Previous treatment methods used drugs, lasers, radio waves or surgery. The PMA was filed by Covidien, which has since merged with Medtronic.

View the recall announcement at www.fdanews.com/05-25-15-venaseal.pdf.
— Elizabeth Orr

Report Outlines 'Building Code' For Medical Device Software

Developers of medical device software should use secure coding standards that address known memory access vulnerabilities to protect their products from hacking, a new report says.

The right choice of programming language can help prevent memory errors that make it easy for hackers to break into a system. The Institute of Electrical and Electronics Engineers, which released the report, recommends using restricted subsets of language, such as C or Ada, that have been crafted to avoid ambiguities.

IEEE also recommends using automated tools such as thread safety analysis and memory safety error mitigation to secure software systems.

For each code element, companies need to consider four subtexts: a description of the element, the vulnerabilities addressed, developer resources that are required and evaluator resources required.

To prevent tampering after software is installed, IEEE suggests using digital signatures and building in a "whitelist" so the program will run only approved applications.

The report also recommends:

- Using the least operating system privilege to limit access to the code;
- Employing hardware or software solutions to protect against malicious observation or modification of the code;
- Providing a tamper-resistant audit trail for security-related events such as software installation; and
- Including design elements that can help to ensure safe functioning of software during an attack, or restoration in the wake of one.

(See **Code***, Page 6)*

FDA Asked to Not Enforce UDI Deadline on Existing Ortho Devices

Orthopedic companies should be allowed to continue distributing devices that don't bear unique device identifiers even after the FDA's compliance deadline, Globus Medical says in a recent citizen's petition to the agency.

The final rule gives devicemakers three years to use or relabel preexisting stock after UDIs are required for new devices. For Class III devices, that deadline falls in 2018; for Class II devices, it's a year later. After that, the agency may take enforcement action against companies whose products don't carry UDIs.

That's unrealistic for orthopedic implants because of their distribution model, Globus Senior Group Manager Kelly Quick writes in the petition. Because patients have such varying implant needs, devicemakers commonly provide many choices for each surgery. Implants that aren't used are put back into storage, she says, adding that implants are paid for only when they are used.

The upshot of this model is that many implants could remain in commercial distribution, unsold, for years past the UDI compliance date. The process of recalling devices already shipped to healthcare facilities to apply UDI markings would be expensive, technically difficult and offer few benefits in terms of product traceability, Quick says. The FDA offered a similar pass to drugmakers when introducing universal product codes in 2004, she notes.

The issue isn't a new one, says former FDA officer and UDI architect Jay Crowley, now vice president and UDI practice lead at USDM Life Sciences. When the FDA considered the question of consignment stocks during development of the UDI final rule, it concluded that two years to UDI implementation plus three years to comply was ample time to use up or relabel supplies.

"For FDA to consider this petition, it will need to consider more broadly the issues of consignment and existing inventory," he tells *IDDM*. "It is not clear to me if they really want to do that."

View the petition at www.fdanews.com/05-25-15-globus.pdf. — Elizabeth Orr

EU Parliament Adopts Draft Conflict Minerals Law

European lawmakers voted 402 to 118, with 171 abstentions, on Wednesday to require devicemakers that use tin, tantalum, tungsten or gold in their products to certify that the minerals aren't sourced from certain conflict zones.

The draft law would mandate compliance for all importers sourcing the minerals in the Democratic Republic of the Congo and other high-risk conflict-affected areas around the world.

Companies that purchase those minerals from importers for use in consumer products would need to file reports detailing the steps they take to address and identify risks related to conflict minerals. The rules could ultimately affect up to 880,000 companies, Parliament says. Small- and medium-sized devicemakers would be able to get financial support to meet the certification requirements under an EU competitiveness program. The conflict minerals program would be reviewed two years after it launches and every three years thereafter.

Parliament also voted 343 to 331, with nine abstentions, to leave the first reading version of the bill open and enter into talks with member states to reach agreement on a final version of the law. No date is set for final adoption.

The law is modeled on 2012 guidance from the Organization for Economic Co-operation and Development, and hews closely to a U.S. law that took effect last year requiring firms to publicly disclose use of conflict minerals from the DRC, Central African Republic, South Sudan, Zambia or Angola. — Elizabeth Orr

Code, *from Page 5*

Device cybersecurity made headlines recently when Hospira recalled two of its infusion pumps over concerns the software could be hacked (*IDDM*, May 14). The devicemaker stressed that no breaches in a care setting had been reported.

The IEEE report, *Building Code for Medical Device Software Security*, drew from a November workshop supported by IEEE's Cybersecurity Initiative. View the report at www.fdanews.com/05-25-15-code.pdf. — Elizabeth Orr

India's New Investment Policy Allows Foreign Ownership of Devicemakers

Foreign entities may now own up to 100 percent of an established Indian devicemaker without first getting government approval, under revisions to the country's consolidated foreign direct investment policy.

Previously, companies could invest up to 100 percent in new device ventures, called "greenfield" investments, but were restricted from investing more than 49 percent in existing, or "brownfield," ventures unless they had government consent.

The policy, issued May 12 by the Department of Industrial Policy and Promotion, incorporates sector-specific changes and updates issued over the past year. The Indian government carved out devices from pharmaceuticals in its FDI policy in December (*IDDM*, Jan. 2).

Read the FDI policy here: www.fdanews.com/5-15-DIPP-FDI.pdf. — Jonathon Shacat

India Takes Aim at Overpriced Orthopedics, Cardiac Stents

The Indian government is waging a two-pronged attack on pricey implants, with the National Pharmaceutical Pricing Authority investigating reports of excessively high prices on orthopedic implants while a regional regulator office asks NPPA to look at cardiac stent pricing.

Indian law limits price increases on most medical products to no more than 10 percent of the suggested retail price in any given year. To determine if orthopedics makers violated the policy, NPPA requested detailed information on each product made, imported or marketed—including production and distribution costs, the maximum retail price and the percentage by which the maximum retail price has increased each year since 2013.

Companies charging excessive prices will be required to reimburse the government for the overcharged amount, plus interest, going back to the date of the price increase.

Meanwhile, the Maharashtra FDA is asking NPPA to cap prices on cardiac stents after a probe found markups as high as 700 times the actual cost of the implant.

According to Commissioner Harshadeep Kamble, stent prices are inflated when they are imported into the country and local distributors then sell them to hospitals at a profit margin of up to 125 percent.

Kamble's charges were based on an investigation of six distributors and seven hospitals in and around Mumbai, Pune and Nasik.

View the notice on pricing of orthopedic implants at www.fdanews.com/05-25-15-pricing.pdf. — Elizabeth Orr

Lamp Manufacturers Must Submit 510(k)s in 90 Days

Manufacturers of tanning bed ultraviolet and sunlamps that were offered for sale prior to Sept. 2, 2014, must submit 510(k)s to the FDA by Aug. 26.

The agency issued a final reclassification order in June 2014 moving the products from Class 1 to Class II, subjecting them to 510(k) scrutiny. For products not on the market before Sept. 2, 2014, and for products offered for sale before that date that required a 510(k) for a significant modification, the effective date for the 510(k) requirement was Sept. 2.

The order didn't apply to UV lamps used to treat dermatological conditions or cancer. Those lamps were already classified as Class II devices.

To obtain clearance, devicemakers must demonstrate their tanning bed lamp meets performance standards such as wavelength, energy density and lamp life, has properly functioning safety features and is mechanically safe. Read the final order at www.fdanews.com/05-25-15-tanningbed.pdf. — Jonathon Shacat

BRIEFS

HeartWare Recalls Heart Kit

Framingham, Mass.-based HeartWare has initiated a Class I recall of its ventricular assist system pump driveline splice kit because they fail to work properly when exposed to excessive force. The company is asking consumers to contact them with questions and concerns. View the recall notice at www.fdanews.com/05-18-15-HeartWareRecall.pdf.

Ecuador Drafts Reg on Surgical Gloves

Ecuador has issued a draft technical regulation establishing performance and safety requirements for single-use surgical and examination/procedure gloves. The measure would apply to both domestically manufactured and imported gloves marketed in the country. Comments are due Aug. 2, and the regulation is slated for adoption Aug. 4, with a Feb. 4, 2016, effective date. Read the draft, in Spanish, at www.fdanews.com/5-15-Ecuador-Gloves.pdf.

Siemens Reaches $6M Settlement

Siemens' imaging division has agreed to pay $6 million to settle allegations that it overcharged the U.S. Department of Defense and Veterans Affairs Administration between 2002 and 2008. Prosecutors say the company didn't offer DOD the best price on certain purchases and hiked prices for the VA for imaging devices that were converted to newer models. Siemens denied the allegations, but agreed to settle to avoid protracted litigation, according to the settlement agreement.

Kips Bay May Shut Down

Kips Bay Medical could be forced to shut down after a clinical trial on its sole product, the eSVS mesh for use in coronary artery bypass grafting surgery, failed to prove effective. The company reorganized in January, going from 13 to eight employees. In March, the devicemaker was able to raise private equity under the condition that the mesh clinical trial reached a specified benchmark in preliminary results released earlier this month. Of an initial 10 patients implanted with the device, seven displayed lower efficacy than those in the control arm at six-month's follow-up. The FDA issued a nonapprovable letter in September 2011 for the eSVS mesh, requesting more information on the device before allowing a feasibility study. The agency approved the study in November 2012.

Medtronic Pacemaker Meets Safety Goals

The first 140 patients in a global trial of Medtronic's Micra transcatheter pacing system met clinical safety and performance measures, the company says. The patients suffered from a wide range of conditions, including chronic obstructive pulmonary disease and pulmonary hypertension. Mean electrical pacing measurements at one- and three-month follow-ups came in at expected ranges for all subjects. The multinational trial will eventually enroll up to 780 patients. The device — which is the size of a large vitamin, or less than one-tenth the size of most pacemakers — won CE mark approval last month.

FDANEWS

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

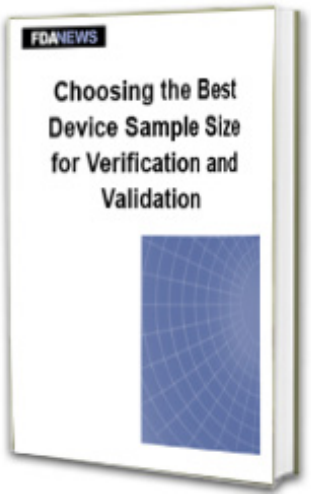
Editor: Elizabeth Orr
(703) 538-7652
eorr@fdanews.com

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

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

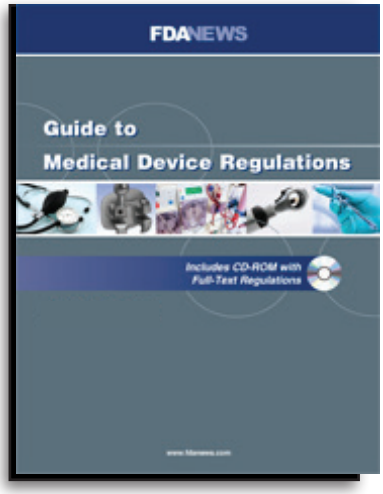
Credit card no. _____

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