

A surgeon's perspective regarding the regulatory, compliance, and legal issues involved with physician-modified devices

Benjamin W. Starnes, MD, *Seattle, Wash*

Physician-modified endovascular devices are becoming commonplace in a modern climate where innovation outpaces regulated technological advancement. Off-label use of medical devices occurs on a daily basis throughout many institutions across the United States and when performed by physicians, is both legal and unregulated. The purpose of this invited commentary is to review the regulatory, compliance, and legal issues regarding the practice of medical device modification. (*J Vasc Surg* 2013;57:829-31.)

Immediate stent graft modification with fenestrations was initially described in 2006 by Krasi Ivancev and colleagues in a series of three patients.¹ In April of 2007, we began treating patients with asymptomatic, symptomatic, or ruptured juxtarenal aortic aneurysms by modifying a Food and Drug Administration (FDA)-approved medical device (Zenith Flex; Cook, Inc, Bloomington, Ind) with the creation of fenestrations to maintain branch vessel patency (Fig). These procedures were performed on patients who were deemed not to be suitable candidates for open surgical repair and had no other treatment options.² The purpose of this invited commentary is to review the regulatory, compliance, and legal issues regarding the practice of medical device modification. Off-label use of medical devices occurs on a daily basis throughout many institutions across the United States and when performed by physicians, is both legal and unregulated. This is according to the “practice of medicine doctrine,” which was explicitly articulated in the Food and Drug Administration Modernization Act of 1997.³

“Nothing in this chapter shall be construed to limit or interfere with the authority of a health care practitioner to prescribe or administer any legally marketed device to a patient for any condition or disease within a legitimate health care practitioner-patient relationship.”³

What actually composes a “legitimate health care practitioner-patient relationship” is poorly defined in the

current literature. Just because off-label use by a physician is legal and unregulated does not necessarily mean that it is safe, smart, well-justified, or legal with respect to billing practices. The defense of an “unsafe” off-label use would actually be an ex post facto liability matter, not a regulatory matter. The author will address the separate but equally important topic of product liability later in this article. According to the FDA, device modifications are a regulated activity,³ although within the FDA’s regulatory discretion, it has not actively pursued in-house device modifications. A critically important feature of regulatory discretion is that it can change without notice, and/or be exercised sporadically. If everything goes well, the FDA will not become interested, but if something bad happens, the FDA will become interested and have the unlimited authority to act. They could very well find the practitioner out of compliance even though they had no previous interest in the provider’s activities. The Food and Drug Administration Modernization Act of 1997 further states that its provisions do nothing to limit the existing FDA regulatory powers.³

In general, the FDA has the authority over a device and any person or facility where anyone is engaged in the manufacture, preparation, propagation, compounding, assembly, or processing of a device intended for human use (21 CFR 807.20). Title 21 CFR 807.81 makes it crystal clear that anyone introducing a medical device into commercial distribution must meet the existing pre-market requirements. However, physicians who produce or alter a device for use within their own practice are exempted from the pre-market notification requirement (21 CFR 807.65(d)), but they are not exempted from the premarket approval requirements for a class III medical device.

Even though physicians may modify a device and have a good outcome, the Center for Medicaid and Medicare Services (CMS), a sister governmental organization to the FDA without any reciprocal influence, may choose not to reimburse the practitioner or the institution for the procedure, citing that the device modifications are “investigational.” Furthermore, it is considered fraudulent to bill the CMS for services that are investigational without

From the Division of Vascular Surgery, Department of Surgery, University of Washington.

Author conflict of interest: Dr Starnes has intellectual property with Cook, Inc (Bloomington, Ind). He has received no financial remuneration to date.

Reprint requests: Dr Benjamin W. Starnes, Division of Vascular Surgery, Department of Surgery, University of Washington, Box 359796, 325 Ninth Ave, Seattle, WA 98104 (e-mail: starnes@uw.edu).

The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

0741-5214/\$36.00

Copyright © 2013 by the Society for Vascular Surgery.

<http://dx.doi.org/10.1016/j.jvs.2012.11.043>

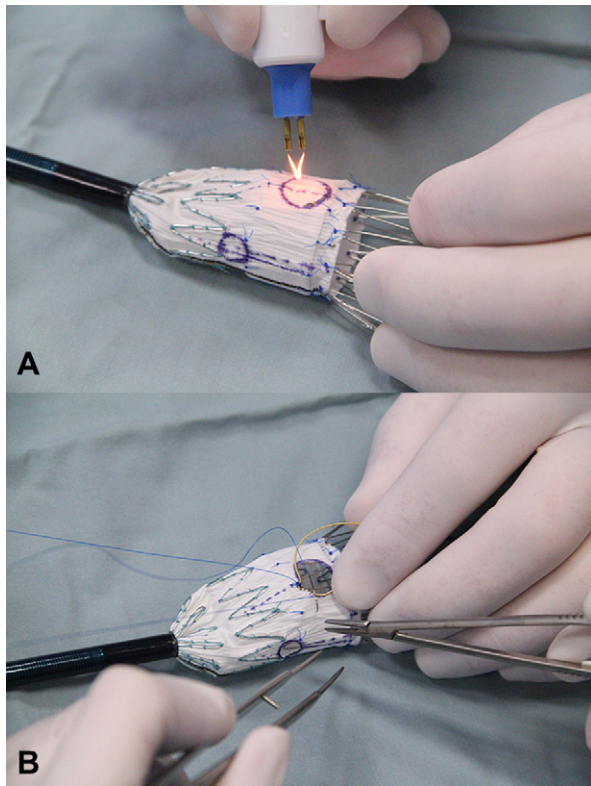


Fig. Physician modification of a currently available Food and Drug Administration-approved stent graft. **A**, Creation of a fenestration for the superior mesenteric artery with an ophthalmic bovie. **B**, Suturing of a radio-opaque marker around the same fenestration to aid in fixation and visibility. This device was modified under an investigator-sponsored investigational device exemption.

formal prior approval from CMS. This is exactly what happened at the University of Washington in 2009 (CMS chose not to reimburse our institution for the procedures), after carrying out dozens of physician-modified endovascular graft (PMEG) procedures beginning in April 2007. The only recourse to continue to treat patients with PMEG was to pursue a formal investigational device exemption (IDE) with oversight from the FDA.

The issue of product liability is germane to this topic. Many people have had medical devices used to better their health only to suffer injuries related to the use of that same device. Sometimes, these injuries serve as the basis for a product liability claim on behalf of the treated patient. All defective product liability claims come in three varieties. Product liability claims resulting from defective medical devices are based on one or more of the following three entities:

1. Defectively manufactured medical devices. These are devices that were manufactured improperly or somehow damaged during the manufacturing process. This may have happened because of an error in the manufacturing process, a problem with

shipping of the device, or an error that occurs in the hospital setting during device implantation or use (failure of quality control).

2. Medical devices with a defective design. These are devices that were properly manufactured but have an inherently and unreasonably dangerous design that results in injury. Sometimes, the device will have been on the market for a long period of time but then fails in some way and causes serious injury.
3. Defectively marketed medical devices. "Marketing" of a medical device refers to any recommendation, warning, lack of warning, or instruction concerning the use of that device by a potential defendant. This claim category involves anything from a failure to provide adequate or accurate warnings regarding the danger posed by the medical device to a failure to provide adequate instructions regarding its safe and appropriate use.⁴

Every person or entity involved in the "chain of distribution" of a medical device (the path the medical device took from the manufacturer to the consumer), is potentially liable for the claim. This includes the manufacturer, the medical sales representative who counsels and makes recommendations to the treating physician, the doctor, and the hospital.⁵ The use of a new FDA-approved device in the hands of an inexperienced operator can also lead to potential liability. With PMEG, since the device had been modified after the manufacturing process and used outside the instructions for use, the manufacturer essentially became exempt from any product liability claim. It is therefore extremely prudent on the part of the physician, in this case practicing PMEG, to initiate an IDE for the proper study of the safety and effectiveness of the technique.

An investigator-initiated IDE requires extensive regulatory and compliance knowledge on the part of the principal investigator. As an IDE holder, the physician is not simply a site investigator but also the sponsor of the clinical study. Sponsor responsibilities are considerably different than site-investigator responsibilities. When our team finally decided to move forward with the application process for an IDE, we had no concept of the amount of work that would eventually be required to win approval and sustain the entire process. The cost of running an IDE is considerable and includes a research coordinator's salary and monitoring service fees. Staffing requirements, secure database management, clinical events committees, data safety monitoring boards, reporting of adverse events and deviations from the predescribed study plan, and annual progress reports add up to a mountain of work for even the most motivated of individuals. A list of steps for obtaining an IDE at our institution is listed in the Table. Furthermore, we quickly realized after receiving approval to conduct the IDE that our team was subject to inspection by the FDA at any time. Interestingly, the author used to believe that the FDA was a prohibitive entity, but after working closely with this organization for over 2 years, we now believe the FDA to be incredibly facilitative. The FDA

Table. Steps for obtaining an IDE at the University of Washington

1. Review FDA website for the appropriate submission format to use <http://www.fda.gov/MedicalDevices/default.htm>.
2. Write protocol, obtain references, and justification for why this study is being proposed.
3. Request trusted colleagues to review the protocol for accuracy and readability.
4. After protocol is written, write CRFs.
5. Submit protocol to IRB and at the same time, request an in-person meeting to present directly to them. With nonsponsored studies, the IRB may have many questions and it is easier to answer them in person rather than have delay of approval by a back-and-forth dialogue. This may not be possible with all IRBs, but it does help pave the way to approval.
6. Obtain "conditional approval" from the IRB meaning that the study cannot begin until FDA approval is obtained and the FDA-amended protocol is resubmitted to the IRB.
7. Submit an IRB conditional approval letter and pre-IDE application to the FDA. Follow the guidelines on the [FDA.gov](http://www.fda.gov) website.
8. Once comments and suggestions are received back from the FDA, submit full IDE application to the FDA. One must follow new IDE submission requirements or one will have a delay in getting approval.
9. The budget can be done at any time. If one needs buy-in from the host institution, start this process after the protocol and case report forms are written (the coordinator/budget personnel will have a better idea of the time involved if they have these two sets of documents). In truth, one really needs the institutional buy-in before even starting the protocol-writing process.
10. Once FDA approval is received, submit this approval letter to the IRB for their final approval. One may get approval to start the study, but there may be requested changes or corrections to make to the protocol.
11. Once final IRB approval is received, submit this document back to the FDA. The initial FDA approval letter will state that the investigator can begin the study after the FDA has received the final approval from the host institution IRB, and they (the FDA) have acknowledged receipt of this approval.
12. Submit to CMS part A and B. Currently, part A can be submitted electronically, but part B needs to be sent in paper form. Part B will not be approved until part A approval is received. (We recommend simultaneously submitting part A electronically and part B in paper form. Once part A approval is received, the part A approval letter can be sent to part B personnel.)

CRF, Case report form; *FDA*, Food and Drug Administration; *IDE*, investigational device exemption; *IRB*, institutional review board. Investigators should check the FDA website, their individual IRB requirements, and their regional Medicare submission requirements.

sincerely promotes the message that they want to help physicians successfully treat their patients. Our institution has recently received FDA approval of a second IDE to perform device modification in patients presenting with thoracoabdominal aneurysms.

In conclusion, the practice of device modification is legal and unregulated in most instances. However, the FDA has wide and unlimited authority to intervene when patient safety or effectiveness of the device becomes a concern. The CMS, depending on the regional carrier, may choose to fully compensate or pay absolutely nothing for these cases based on an assessment of "investigational use." Any practitioner who chooses to modify an existing FDA-approved medical device outside of an IDE should weigh heavily the ramifications of a product liability claim and/or a criminal or civil liability claim, as the manufacturer becomes exempt once the device has been modified. It is the author's opinion that physicians performing device

modification of the nature described herein are obliged to obtain an IDE.

REFERENCES

1. Uflacker R, Robison JD, Schonholz C, Ivancev K. Clinical experience with a customized fenestrated endograft for juxtarenal abdominal aortic aneurysm repair. *J Vasc Interv Radiol* 2006;17:1935-42.
2. Starnes BW. Physician-modified endovascular grafts for the treatment of elective, symptomatic, or ruptured juxtarenal aortic aneurysms. *J Vasc Surg* 2012;56:601-7.
3. "Food and Drug Administration Modernization Act of 1997." The National Academies. Available at: http://www7.nationalacademies.org/ocga/laws/PL105_115.asp. Accessed August 18, 2012.
4. Gee T. Impact of Modifying FDA Regulated Devices, October 25, 2009. Available at: <http://medicalconnectivity.com/2009/10/25/impact-of-modifying-fda-regulated-devices>.
5. Brown OW. Legal implications of pushing the endovascular envelope. *J Vasc Surg* 2012;56:273-4.

Submitted Sep 2, 2012; accepted Nov 8, 2012.