Advisory statement on clinical use of modified aortic endografts from the Society for Vascular Surgery®

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Recent enthusiasm to extend the application of aortic endografts has led to the development of new techniques that require modification of approved endografts to accommodate anatomic variations. For the purposes of this report, a modified aortic endograft is defined as a physical modification of an existing approved device (including the implant or deployment system) in such a way that its potential risks and benefits cannot be extrapolated from the United States Food and Drug Administration (FDA)-approved studies upon which the approval of the original unmodified commercial device was based. Examples of such modification include surgeon-constructed fenestrations and side branches.

All aortic endografts are defined by federal law as significant-risk devices, and regulations for their use are enforced by the FDA. Accordingly, clinical studies using modified aortic endografts must comply with these regulations to ensure patient safety and accurate reporting of clinical outcomes.

Currently, there are two mechanisms to conduct FDA-approved clinical studies of significant risk devices: manufacturer-sponsored or investigator-sponsored Investigational Device Exemptions (IDEs). To get FDA approval to market an endovascular graft, manufacturers must submit a Premarket Approval (PMA) application that provides a reasonable assurance of safety and effectiveness using valid scientific evidence. PMA approval usually includes requirements for training programs and postmarket follow-up programs to provide surveillance after introduction. Investigator-sponsored IDEs enable investigational device evaluation using the same criteria for scientific justification and study conduct but are generally not intended to support a device marketing application or to address training.

As outlined in the Federal Food, Drug, and Cosmetic Act and interpreted in the Federal Register and the Code of Federal Regulations that codifies the rules published in the Federal Register, the medical device law and regulations apply equally to manufacturers and investigators conducting studies. These laws and regulations must be considered when new devices or modification of devices are studied.

If significant-risk devices or modifications of significant-risk devices are used in clinical studies, Institutional Review Board (IRB) and IDE approval are required. For modified aortic endografts, IRB approval alone is not adequate because the FDA has determined that all aortic endovascular graft studies are significant-risk studies.

This requirement has implications on the investigator and institutional responsibilities, the patient consent, conduct of the study, collection of data, reimbursement for procedures, and reporting to the IRB and the FDA. Scientific presentations and publications must clearly delineate the nature of the study, method of approval, and mechanism to assess outcomes of interventions. To date, the Center for Medicare & Medicaid Services has identified endografts as nonexperimental/investigational devices and is more likely to reimburse for studies that are conducted in an approved IDE protocol.

HOW DO THESE REGULATORY REQUIREMENTS TRANSLATE TO FREQUENTLY ASKED CLINICAL QUESTIONS?

Question: In an emergency, can an off-label modified endograft be used without additional requirements?

Yes, a physician has the discretion to recommend any treatment if it is judged to be in the patient’s best interest. Compassionate-use approvals can also be used for planned novel treatment of conditions not amenable to conventional treatment. Compassionate use requires IRB approval and, in addition, may require FDA and manufacturer approval. Serial planned use of modified endografts is not compassionate use. If serial use is planned, IRB and IDE approvals are required. Local IRBs have different rules, and some require that elective one-time compassionate use be approved by an IRB chair using the expedited route, but if that chair is uncomfortable with making the decision, it can be sent for full IRB review. Clinical studies of modified aortic endografts must have IRB and IDE approval.

Refer to:
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm051345.htm
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionsIDE/ucm051345.htm#emergencyuse

Question: How does one consent a patient for modification of a commercial endograft?
Modified aortic endografts should only be used within a study that has been approved by an IRB and the FDA to determine the safety and effectiveness of these devices. The IRB and the FDA both review the draft informed consent forms to ensure that the study patients are appropriately informed of their rights, safety, and welfare.

**Question:** Can an IRB grant approval to perform modification of an aortic endograft without requiring FDA approval?

The IRB can only grant approval and not require FDA approval if it believes a study is not a significant-risk study. As mentioned, because all aortic endovascular graft studies using modifications of approved devices are significant-risk studies, IRB and FDA approval are both required before elective modification and use of a device.

**Question:** How can I train for a new unapproved modification of an aortic endograft procedure?

Until the safety and effectiveness of each type of endograft device modification is confirmed, training is not recommended. Training in the context of an approved fellowship in an institution that has an approved IDE is acceptable.

**Question:** Can presentations at meetings and publication of papers describing novel modified aortic endograft treatments be made if patients were treated outside of an approved IDE?

Presentations of one-time emergency use or compassionate use are acceptable. If a report of a clinical series is prepared, the IRB and IDE approval status should be clearly described.

**Question:** How do I apply for an IDE if I want to prospectively treat patients with complex anatomy using modified commercially available aortic endografts devices?

Contact your IRB and ask how to prepare a submission to evaluate the risk of your proposed study and how to prepare an IDE.

Further information is available at:
http://www.fda.gov/MedicalDevices/DeviceRegulation andGuidance/HowtoMarketYourDevice/Investigational DeviceExemptionIDE/ucm046706.htm

For specific information regarding these questions, refer to
http://www.fda.gov/MedicalDevices/DeviceRegulation andGuidance/HowtoMarketYourDevice/InvestigationalDevice ExemptionIDE/default.htm

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