

The Gore TAG Approval

What took so long?!

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For many years, the FDA has received patient, clinician, and even congressional inquiries as to why we had not yet approved an endovascular graft for treatment of thoracic aortic aneurysms. The potential for significant improvement in patient care for those with thoracic aortic aneurysms was clear to all. So what took so long? Some candid answers follow.

We cannot approve a PMA before one is submitted.

Although the potential benefits of endovascular repair of thoracic aortic aneurysms was clear, valid scientific evidence (ie, data) had to be collected to demonstrate that a specific endovascular graft was reasonably safe and effective for this indication. This required both non-clinical and clinical evaluations. As with endovascular grafts for treatment of abdominal aortic aneurysms (AAAs), 1-year clinical data on a statistically justified number of nonrandomized patients were needed.

Many may argue that these data have been available for quite some time. Regardless, if a PMA was not submitted based on these data, we could not approve the device.

Once the Gore TAG PMA was submitted, we had to conduct a scientific review.

PMA's have a 180-day review cycle. This cycle starts with a filing review during which all of the members of the review team

look over the submission to determine whether adequate information has been provided to allow for a substantive review. The sponsor should be notified as to whether its PMA is filed within 45 days of the receipt of the PMA. We then complete our review; identify any questions or concerns, communicate them to the sponsor, and attempt to resolve the issues with the sponsor. This entire process should be completed well in advance of the FDA advisory panel meeting to optimize the panel discussions.

For the Gore TAG (W. L. Gore & Associates, Flagstaff, AZ) PMA, the panel meeting was held January 13, 2005, only 3 months after receipt of the file. Examples of interactions for the Gore PMA included our request for a propensity score analysis to take a closer look at whether there were any differences in the patient populations

enrolled in the various arms of the study and clarification regarding the corrosion properties of the metallic components of the implant. These and other concerns raised during our review of the PMA were presented at the panel meeting as part of our briefing on our review findings.

After the panel meeting, we had to complete the close-out process.

The panel recommended approval with conditions in

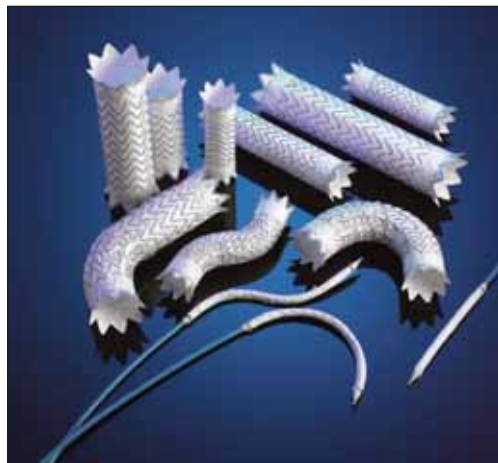


Figure 1. The Gore TAG Thoracic Endoprosthesis.

January, but the approval was not granted until March 23, 2005. The time between the panel meeting and final approval was primarily spent finalizing the labeling and the summary of safety and effectiveness data, as well as establishing the conditions of approval.

This was a first-of-a-kind approval, with only the AAA endovascular grafts providing partial precedent. Although some warnings and precautions are generic to all endovascular grafts used to treat aneurysms, specific concerns related to thoracic repair had to be incorporated in the product labeling. Similarly, although some of the conditions of approval were comparable to the AAA devices, others had to be specifically crafted for this PMA.

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The comparable conditions included the need to follow IDE subjects (approximately 400 patients) through 5 years of follow-up and provide clinical updates to device users on an annual basis. A new requirement was a postapproval study requiring enrollment of an additional 150 patients with descending thoracic aortic aneurysms at 35 geographically separate sites. This study will provide an assessment of the training program by comparing the results for these patients to those enrolled under the IDE.

The postmarket patients are also to be followed through 5 years postimplant. In addition, the sponsor has been requested to increase the size of the surgical control group through a comprehensive literature review. The combination of IDE and postmarket patients will provide adequate numbers to determine whether the reduction in aneurysm-related mortality associated with the Gore TAG device observed in the IDE is maintained post-approval.

The new requirements for the Gore TAG device as compared to the AAA devices resulted from the transfer of the Conditions of Approval (CoA) Study program from the Office of Device Evaluation (ODE) to the Office of Statistics and Biometrics (OSB). For first-of-a-kind products such as the Gore TAG device, epidemiologists at OSB will be working with the sponsors to incorporate statistical methods into the CoA studies to improve the scientific rigor of these studies. Additional information regarding this transfer of responsibilities is to follow in a separate article.

This PMA sets the standard for future PMAs for endovascular grafts intended to treat descending thoracic aneurysms.

The Gore TAG device was approved less than 180 days after the PMA was received. It is difficult to envision approval of future endovascular grafts for the treatment of descending thoracic aortic aneurysms to be completed in less time. Often files are put on hold while issues are being addressed, something that did not happen with the Gore PMA. Even if the file is not put on hold, there are almost always clinical and/or nonclinical questions that require a significant amount of time for the sponsor to address.

New applicants will benefit, however, by using the W. L. Gore & Associates experience in writing their PMAs and device labeling. Future sponsors should proactively incorporate information to address issues raised at the Gore TAG panel in their PMAs. In addition, they should use the Gore TAG labeling as a template when writing their labels, as many of the warnings and precautions are relatively generic and may also apply to their device.

Sponsors of future PMAs may or may not need to go before the advisory panel. If no new issues are identified in their submission; that is, if the concerns are consistent with those already discussed by the panel, panel review would be unnecessary.

Indications other than treatment of descending thoracic aneurysms may be approved in the future.

Now that W. L. Gore & Associates has an approved PMA for an endovascular graft for use in the thoracic aorta, they could possibly submit a PMA supplement to change their labeling to include treatment of other etiologies, such as aortic dissections and transections. Such a supplement could be panel tracked, meaning that panel input may be obtained in the review of the file. Clearly, these indications would need to be discussed by a full panel if a new device were to come in under PMA without a prior approval for treatment of descending thoracic aortic aneurysms.

Additional information on FDA Advisory Panels can be found in the November/December 2002 issue of *Endovascular Today*. Information on the PMA process can be found in the April 2004 issue of *Endovascular Today*. Each of these articles can be accessed electronically at <http://www.evtoday.com/Pages/FDA.html> ■

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