

DRAFT Issues for Discussion
Gastroenterology and Urology Devices Advisory Panel
Enteryx™ for GERD
January 17, 2003

Evaluation of Safety and Effectiveness

1. The device, once injected, is intended as a permanent implant. Please discuss whether the current data provides adequate assurance of safety. Within your discussion, please specifically address the 12-month histology findings (persistent inflammation and mineralization) from the animal data.
2. Tantalum was added as a component to the device to aid in visualization under x-ray and to assess indirectly the residual volume of implant at follow-up. Please comment on the degree to which the data in the PMA demonstrates that the amount of *tantalum* visualized on x-ray directly correlates with the amount of *polymer* remaining implanted.
3. Over 40% of evaluable subjects had a $\geq 25\%$ reduction in residual implant volume (as assessed by measurement of residual tantalum) at 6 and 12 months when compared to baseline at 1 month. Please discuss this finding and whether it poses any safety or effectiveness concerns. In addition, please comment on whether the conclusion that the “missing” material sloughed into, and was passed out of, the GI tract is reasonable and supported by the data.
4. Reduction in proton pump inhibitor (PPI) dose was used as the primary effectiveness endpoint for the clinical trial. The objective of the study, i.e., to show a $\geq 50\%$ reduction in PPI dose in at least half of the enrolled subjects, was met at 12 months. The objective secondary endpoints, however, did not appear to demonstrate the same degree of improvement. Please discuss the significance of the results from the intra-esophageal pH, esophagogastroduodenoscopy (EGD), and manometry procedures, and whether they support the use of Enteryx™ as a safe and effective treatment for GERD. Within your discussion, please comment on whether you believe that these results suggest patients may be at continued risk for developing complications of GERD including erosive esophagitis, strictures, and/or Barrett’s Esophagus despite symptom improvement while off their PPI medications.
5. Based on your deliberations to this point, please discuss whether the overall benefits, including improvement in symptom as well as objective measures, outweigh any risks associated with use of this device.

6. Nineteen of the 85 patients underwent re-injection within the first 3 months. Please discuss whether sufficient data has been presented to support re-treatment with Enteryx™. If you believe the data is adequate, please comment on whether you believe any of the following should be recommended:
 - a. maximum number of repeat procedures (if so, what number);
 - b. maximum number of repeat injections per procedure (if so, what number);
 - c. maximum implantable volume at each procedure and overall (if so, what volumes); and
 - d. timing of retreatment procedures relative to the initial treatment (if so, the length of time).

Labeling

7. The sponsor has proposed the following Indication for Use for Enteryx™:
“The Enteryx™ procedure kit is indicated for endoscopic injection into the lower esophageal sphincter (LES) for the treatment for gastroesophageal reflux disease (GERD).”

Please discuss whether this Indication for Use accurately reflects the data obtained during the clinical trial.

8. The proposed labeling lists portal hypertension as the only contraindication for use. Please discuss any other clinical conditions for which you believe the labeling of the device should include specific contraindications, warnings, or precautions. In your discussion, please include comments on the following:
 - a. patients with Barrett’s Esophagus;
 - b. patients with erosive esophagitis;
 - c. patients with esophageal ulcers;
 - d. patients with esophageal strictures; and
 - e. patients with GERD symptoms refractory to proton pump inhibitors.
9. Please discuss whether you believe the Physician and Patient Labeling brochures, as written, are adequate or whether certain ***major*** additions, deletions, or revisions should be made.

Post-Market Issues

10. Please comment on the sponsor’s proposed post-market evaluation of the device. Please specifically comment on and make recommendations concerning the
 - a. study design;
 - b. number of patients;
 - c. length of follow-up; and
 - d. endpoints to be evaluated.

Training

11. Please comment on the sponsor’s proposed physician training program and whether you believe it is adequate for proper use of the device.