

Review of Original BLA - RECOTHROM

MEMORANDUM

Food and Drug Administration
Center for Biologics Evaluation and Research
Office of Compliance and Biologics Quality
Division of Manufacturing and Product Quality

Date: 13 December 2007

To: STN 125248/0 Thrombin (Recombinant)
ZymoGenetics, Inc. (License No. 1758)

From: Nancy Waites, Reviewer, MRB1/DMPQ/OCBQ/HFM-675

Through: Caroline Renshaw, Branch Chief /MRB1/DMPQ/OCBQ/HFM-675

Subject: Review of original BLA submitted electronically by ZymoGenetics, received 18 December 2006, for Thrombin (recombinant).

Recommendation: I recommend approval of this submission if all other review offices do not have any issues with the submission.

Review Narrative and Comments

Description:

Recombinant human Thrombin (rhThrombin) drug product is a sterile, lyophilized white to off-white solid and/or powder that contains no preservative and it is reconstituted with 0.9% sodium chloride injection, USP. Upon reconstitution, rhThrombin drug product is a clear colorless solution. It is intended for topical administration to bleeding surfaces. In various types of surgeries, solutions of rhThrombin are used in combination with an absorbable gelatin sponge, USP, for hemostasis. Solutions of rhThrombin must not be injected.

Manufacturers:

Manufacturer	Address	Responsibility
ZymoGenetics, Inc.	1201 Eastlake Ave East, Seattle, WA 98102	BLA applicant: Process development Process validation Methods development and validation Shipping validation Stability studies (rhPrethrombin-1 and BDS) Impurity clearance studies and analytical Support ----- -----

Recall SOP -----

If the Product is being returned due to a product complaint, -----
----- ZGI, will obtain the following information from the end customer
returning the Product:

- Number of units to be returned
- Physician name
- Fax number
- Identify source of product (i.e. name of hospital)

----- ZGI authorization, will fax instructions for returning
the Product to the end customer, which will include, at a minimum, instructions to return the
Product to the ZGI designated location.

Recalls will be directed by ZGI. -----

----- ZGI in contacting consignees and in retrieval of recalled Product and/or kits.

Additionally, --- will provide the following support in the event of a recall:

- Storage and control of on-hand inventory of recalled Product.
- Receipt, storage, and control of returned recalled Product.
- Documentation of recalled Product used, destroyed, or returned to the distributor through
established document systems at -----.
- Shipment of samples of recalled Product to ZGI or a designated testing site for analysis, if
applicable.

----- maintains an on-site Quality Assurance/Regulatory
Affairs department. This department has ----- employees who manage quality assurance,
regulatory compliance and training needs. The function of this department includes
quarantine, receipt, and release of product as well as day-to-day quality assurance. Training
includes industry overviews as well as functional skills.