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RESEARCH**

*APPLICATION NUMBER:*  
**125293**

**ENVIRONMENTAL ASSESSMENT**

## Sista, Ramani V

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**From:** Chi, Bo  
**Sent:** Tuesday, August 10, 2010 4:09 PM  
**To:** Sista, Ramani V; Turner-Rinehardt, Sharon  
**Subject:** FW: Final TB-EER response for BLA STN 125293  
**Attachments:** Final TB-EER response 125293.doc

FYI

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**From:** Pohlhaus, Timothy  
**Sent:** Monday, August 09, 2010 12:47 PM  
**To:** Chi, Bo  
**Cc:** CDER-TB-EER; Pohlhaus, Timothy  
**Subject:** Final TB-EER response for BLA STN 125293

The New and Generic Drug Manufacturing Team in the Division of Manufacturing and Product Quality has completed its review and evaluation of the final TB-EER for Savient's STN 125293. Please see the attached form for individual site compliance statuses. There are no pending or ongoing compliance actions that prevent approval of this BLA.

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209 Pages has been withheld in full immediately following this page as B4 (CCI/TS)

MODULE 1

1.12.14 Environmental Analysis or Categorical Exclusion

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**1.12.14. ENVIRONMENTAL ASSESSMENT OR CATEGORICAL EXCLUSION**

**1.12.14.1 Biological Identification**

Puricase® is a colorless, clear, sterile solution containing 8 mg/mL uricase protein conjugated to methoxypolyethylene glycol (mPEG) in phosphate buffered saline.

**1.12.14.2 Categorical Exclusion Justification**

The greatest annual production of uricase (active moiety of the Drug Substance) in the finished product is expected to be (b) (4) for the five year marketing period (2009-2013) following anticipated approval of submission in 2009.

The expected introduction concentration (EIC) of an active moiety into the aquatic environment should be calculated as follows:

$$\text{EIC-Aquatic (ppb)} = A \times B \times C \times D$$

Where

A = kg/year produced for direct use (as active moiety)

B = 1/liters per day entering POTWs\*

C = year/365 days

D =  $10^9$  µg/kg (conversion factor)

\*  $1.214 \times 10^{11}$  liters per day entering publicly owned treatment works (POTWs),  
or

$$\text{EIC} = \frac{(b) (4)}{(b) (4)} \times (1/1.214 \times 10^{11} \text{ liters per day}) \times (\text{year}/365 \text{ days}) \times 10^9 \mu\text{g}/\text{kg} =$$

Based on this calculation Biologics License Application for Puricase® meets the criteria for categorical exclusion under 21 CFR Section 25.31(b). Section 25.31(b) provides for a categorical exclusion regarding an action on this BLA, if the action increases the use of the active moiety, but the estimated concentration of the substance at the point of entry into the aquatic environment will be below 1 part per billion.

*Approved  
for submission  
just M. Fernandez  
6/30/09*