

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-203

ENVIRONMENTAL ASSESSMENT

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

Date: October 31, 2008

From: Ravindra K. Kasliwal, Ph.D.
CMC Reviewer
Branch V, DPAMS, ONDQA

Through: Sarah Pope, Ph.D.
Acting Branch Chief
Branch V, DPAMS, ONDQA

Sponsor: Cephalon, Inc.
41 Moores Rd.
Frazer, PA 19355

Drug: TREANDA® (bendamustine hydrochloride) for injection

Subject: CMC review of environmental assessment of NDA 22-303 [original submission 28-Dec-2007]

Remarks: The chemistry, manufacturing and controls (CMC) section of this NDA has been referenced to the Treanda NDA 22-249 submitted by Cephalon on 19-Sep-2007 and approved on 20-Mar-2008. The claim for categorical exclusion is provided in NDA 22-303.

Cephalon, Inc. has requested a Categorical Exclusion for submission of an Environmental Assessment as per 21 CFR Part 25.31(b), since the use of the active moiety, bendamustine hydrochloride, is expected to be below 1 ppb. To the best of the Company's knowledge, no extraordinary circumstances exist in regard to the action.

The Expected Introduction Concentration (EIC) has been calculated per the formula contained in the FDA Guidance "Environmental Assessment of Human Drugs and Biologics Applications." The calculation was made using the highest quantity of active moiety expected to be used directly in any of the next five years; this value is about 12 kg in 2010 (for both indications, under NDA 22-303 and NDA 22-249)

$$\begin{aligned} \text{EIC} &= (12 \text{ kg/yr}) \times (1/1.214 \times 10^{11} \text{ L/day}) \times (1 \text{ year}/365 \text{ days}) \times (10^9 \text{ } \mu\text{g}/\text{kg}) \\ &= 2.71 \times 10^{-4} \text{ } \mu\text{g}/\text{L} = 2.71 \times 10^{-4} \text{ ppb} \end{aligned}$$

Comments: Since this value is below the threshold value of 1 $\mu\text{g}/\text{L}$ (1 ppb), the claim for Categorical Exclusion for submission of an Environmental Assessment is adequately justified and is acceptable.

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/s/

Ravi Kasliwal
10/31/2008 10:53:43 AM
CHEMIST

Sarah Pope
10/31/2008 11:52:30 AM
CHEMIST