

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-102

ENVIRONMENTAL ASSESSMENT

b(4)

1.12.14 Environmental Analysis

Fleming claims a categorical exclusion from an environmental assessment in accordance with the criteria set forth in 21 CFR 25.31(a) through (c) and 25.15 based on the following information:

- The requested action is not expected to increase the use of the active moiety since it will be used in lieu of other marketed therapies containing Cyanocobalamin.
- The anticipated amount of Cyanocobalamin drug substance used in the projected peak (fifth) year of marketing for manufacture of commercial drug product will be about corresponding to an Expected Introduction Concentration (EIC) into the aquatic environment as follows:

$$\text{EIC} = \frac{10^9 \mu\text{g/kg}}{(1.214 \times 10^{11} \text{ L/day})(365 \text{ days/yr})}$$

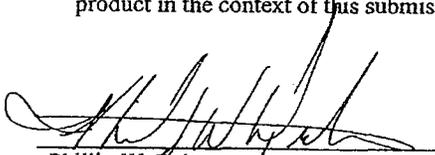
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This level is more than four orders of magnitude below the threshold level of 1 ppb established in 21 CFR §25.31(b).

- The drug substance occurs naturally in the environment and, as previously stated, the requested action does not significantly alter the concentration or distribution of the substance, its metabolites, or degradation products in the environment.
- Fleming is not aware of any extraordinary circumstances that exist with the use of this drug product in the context of this submission.


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Aug. 30 '06
Date