CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

20-449/S-018

Chemistry Review(s)

CHEMIST'S REVIEW

1. ORGANIZATION	2. NDA NUMBER
HFD-150 DODP	20-449

3. NAME AND ADDRESS OF APPLICANT (City and State)

Aventis Pharmaceuticals
Route 202-206
P.O. Box 6800
Bridgewater, NJ 08807-2800
Attention: Steve Caffe
Vice President, Head GRAMS-North America
Telephone: (908)-231-5863

4. AP NUMBER

5. SUPPLEMENT (S)
NUMBER(S) DATES(S)

6. NAME OF DRUG	7. NONPROPRIETARY NAME	SE1-018	1-Feb-02
Taxotere	docetaxel		

8. SUPPLEMENT PROVIDES FOR:

a claim of categorical exclusion for an Environmental Assessment to support the use of Taxotere plus cis-platin for the first-line treatment of patients with unresectable locally advanced or metastatic non-small cell lung cancer (NSCLC)

9. AMENDMENTS DATES

10. PHARMACOLOGICAL CATEGORY	11. HOW DISPENSED	12. RELATED IND/NDA/DMF
antineoplastic	RX X OTC ___	
13. DOSAGE FORM(S)	**14. POTENCY**	
Injection Concentrate	20 mg and 80 mg	

15. CHEMICAL NAME AND STRUCTURE

16. RECORDS AND REPORTS
CURRENT YES___NO___
REVIEWED YES___NO___

17. COMMENTS

See page 2

cc:
NDA 20-449
HFD-150/Div. File
HFD-150/RWood
HFD-150/YAHsieh
HFD-150/AStaten
R/D Init. by:

18. CONCLUSIONS AND RECOMMENDATIONS

It is recommended that the request for a claim of categorical exclusion for an Environmental Assessment should be approved.

19. REVIEWER

NAME	SIGNATURE	DATE COMPLETED
Yung-Ao Hsieh, Ph.D.	/S/	30-May-02

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HFD-150/AStaten

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/s/

Yung-Ao Hsieh
6/6/02 02:36:42 PM
CHEMIST

Rebecca Wood
6/6/02 02:40:59 PM
CHEMIST

Aventis Pharmaceuticals Inc. requests Categorical Exclusion from the environmental assessment requirements under 21 CFR Part 25.31(b).

Aventis Pharmaceuticals Inc. is submitting a supplementary new drug application to the approved NDA for Taxotere® for Injection Concentrate. The purpose of this supplement is to apply for a new indication for the treatment of patients with locally advanced or metastatic non-small cell lung cancer, in combination with cisplatin, in patients who have not previously received chemotherapy for this condition.

In the five coming years, the highest yearly quantity of docetaxel to be marketed in the United States for all Taxotere® (docetaxel), including the subject of this application and all currently approved applications, is — Kg of docetaxel drug substance. From this quantity the Expected Introduction Concentration (EIC) value for the docetaxel drug substance is calculated to be ——— as follows:

EIC-Aquatic (ppb) = A x B x C x D where

A = kg/year produced for direct use (— kg/year)

B = ——— liters per day entering publicly owned treatment works (POTWS)

C = year/ 365 days

D = — µg/kg (conversion factor)

As this value represents a level far below 1 ppb for the EIC, the categorical exclusion is requested for this supplement. There are no extraordinary circumstances that would prohibit the claim for a categorical exclusion for this supplement.

The following information is provided in support of this claim related to docetaxel that is prepared by synthetic modification of naturally derived 10-deacetyl baccatin III (10-DAB). 10-DAB is obtained by extraction from needles of the yew (genus Taxus). The yew needles are harvested as clippings from ornamental (non-wild) specimens and from cultivated yews. The geographic areas for collection of yew clippings are described in Section 9 of the original EA filed as part of NDA #20-449. Taxus is an internationally protected plant, the controlled harvest of yew clippings does not threaten or endanger these plants.

The information provided above forms the basis for a claim for categorical exclusion under 21 CFR Part 25.31(b).