CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20449/S11

CORRESPONDENCE

RHÔNE-POULENC

Rhône-Poulenc Rorer Pharmaceuticals Inc.

DUPLICATE

500 Arcola Road
PO Box 1200
Collegeville, PA 19426-0107
Tel 610-454-8000

December 8, 1999

Richard Pazdur, M.D., Director
Division of Oncology Drug Products (HFD-150)
Food and Drug Administration, CDER
Woodmont Office Complex 2, Document Room
1451 Rockville Pike
Rockville, MD 20852

SUPPL NEW CORRESP
(SNC to SE1-011)

NDA 20-449/SE011
Taxotere® (docetaxel) for
Injection Concentrate

GENERAL CORRESPONDENCE:
Response to Request for Information

Dear Dr. Pazdur:

Reference is made to Taxotere® (docetaxel) for Injection Concentrate and the above-captioned supplement, which is scheduled to be discussed at the Oncologic Drugs Advisory Committee meeting on Monday, December 13, 1999. We also refer to the end-of-review meeting held on December 3, 1999, wherein I provided Project Manager Ann Staten with a draft version of our proposed presentation slides regarding the aforementioned meeting.

In accordance with my discussion with Ms. Staten and Dr. Griebel, I am pleased to provide you, in duplicate, with paper copies of our proposed final version of the slides. They are still marked "draft" in the event that a change needs to be made based on our rehearsals this weekend. We have also enclosed a diskette containing the information electronically in Microsoft PowerPoint Version 4.0c.

Please call me at (610) 454-3037 should you have any questions or comments regarding this submission.

Sincerely,

Anne-Margaret Martin
Director, Oncology Liaison
Worldwide Regulatory Affairs

AMM:aes
cc: Reg. file

RHÔNE-POULENC

Rhône-Poulenc Rorer Pharmaceuticals Inc.

DUPLICATE

500 Arcola Road
PO Box 1200
Collegeville, PA 19426-0107
Tel 610-454-8000

December 6, 1999

Richard Pazdur, M.D., Director
Division of Oncology Drug Products (HFD-150)
Food and Drug Administration, CDER
Woodmont Office Complex 2, Document Room
1451 Rockville Pike
Rockville, MD 20852

SUPPL NEW CORRESP
(SNC to SE1-011)

NDA 20-449/SE011
Taxotere® (docetaxel) for
Injection Concentrate

GENERAL CORRESPONDENCE:
Response to Request for Information

Dear Dr. Pazdur:

Reference is made to the above-captioned supplemental New Drug Application and to our meeting on December 3, 1999.

In accordance with the request made by your team during our meeting, please find enclosed a copy of the literature that was under discussion. On behalf of RPR's Taxotere® NSCLC team, I would like to extend my thanks to you and your team for meeting with us on Friday. We found the meeting to be most helpful, and we will provide a copy of our proposed final ODAC slides shortly.

Please call me at (610) 454-3037 should you have any questions or comments regarding this submission.

Sincerely,

Anne-Margaret Martin

Anne-Margaret Martin
Director, Oncology Liaison
Worldwide Regulatory Affairs

AMM:tcb

cc: Reg. file

DUPLICATE

RHÔNE-POULENC DUPLICATE

Rhône-Poulenc Rorer Pharmaceuticals Inc.

500 Arcola Road
PO Box 1200
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December 1, 1999

Richard Pazdur, M.D., Director
Division of Oncology Drug Products (HFD-150)
Food and Drug Administration, CDER
Woodmont Office Complex 2, Document Room
1451 Rockville Pike
Rockville, MD 20852

NDA 20-449/SE011
Taxotere® (docetaxel) for
Injection Concentrate

NDA SUPP AMEND
SE1-011
(BM)

GENERAL CORRESPONDENCE:
Response to Request for Information

Dear Dr. Pazdur:

Reference is made to the above-captioned supplemental New Drug Application and to a telefax dated November 24, 1999 from Project Manager Ann Staten, which contains comments from one of your medical reviewers.

Attached please find 10 copies of our response to the aforementioned telefax as well as a diskette containing the information electronically in Microsoft WORD, Version 6.0c. Please be advised that our response was also conveyed to FDA today via telefax to Ms. Ann Staten.

We are looking forward to our meeting on Friday, December 3, 1999 from 1:00 - 2:00 p.m. in Conference Room "B", and I have attached our attendee list.

Please call me at (610) 454-3037 should you have any questions or comments regarding this submission.

Sincerely,

Anne-Margaret Martin

Anne-Margaret Martin
Director, Oncology Liaison
Worldwide Regulatory Affairs

AMM:aes
cc: Reg. file

DUPLICATE

DUPLICATE

RHÔNE-POULENC

Rhône-Poulenc Rorer Pharmaceuticals Inc.

500 Arcola Road
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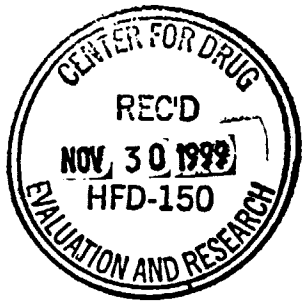
Collegeville, PA 19426-0107
Tel 610-454-8000

November 29, 1999



Richard Pazdur, M.D., Director
Division of Oncology Drug Products (HFD-150)
Food and Drug Administration, CDER
Woodmont Office Complex 2, Document Room
1451 Rockville Pike
Rockville, MD 20852

NDA SUPP AMEND
SE1-011
(BB)

NDA 20-449/SE011
Taxotere® (docetaxel) for
Injection Concentrate

GENERAL CORRESPONDENCE:
Response to Request for Information

Dear Dr. Pazdur:

Reference is made to the above-captioned supplemental New Drug Applications and to a telefax dated November 3, 1999 from Project Manager Ann Staten, which contains a request from your Clinical Pharmacology and Biopharmaceutics reviewer for information regarding the potential for drug-drug interactions between Taxotere® and other drugs commonly prescribed to patients with both previously untreated and previously treated NSCLC.

Attached in duplicate is our response to the aforementioned telefax. Please be advised that our response was also conveyed to FDA today via telefax to Ms. Ann Staten.

Please call me at (610) 454-3037 should you have any questions or comments regarding this submission.

Sincerely,

Anne-Margaret Martin

Anne-Margaret Martin
Director, Oncology Liaison
Worldwide Regulatory Affairs

AMM:aes
cc: Reg. file

DUPLICATE

RHÔNE-POULENC

DUPLICATI

Rhône-Poulenc Rorer Pharmaceuticals Inc.

500 Arcola Road
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Tel 610-454-8000

NDA SUPP AMEND
(N 82)

November 22, 1999

Richard Pazdur, M.D., Director
Division of Oncology Drug Products (HFD-150)
Food and Drug Administration, CDER
Woodmont Office Complex 2, Document Room
1451 Rockville Pike
Rockville, MD 20852

NDA 20-449/SE011
Taxotere® (docetaxel) for
Injection Concentrate

GENERAL CORRESPONDENCE:
Response to Request for Information

Dear Dr. Pazdur:

Reference is made to the above-captioned supplemental New Drug Application and to a telefax dated November 8, 1999 from Project Manager Ann Staten which contains questions/comments from your medical and statistical reviewers.

Attached in duplicate is our response to the aforementioned telefax. Please be advised that our response was also conveyed to FDA today via telefax to Ms. Ann Staten.

Please call me at (610) 454-3037 should you have any questions or comments regarding this submission.

Sincerely,

Anne-Margaret Martin

Anne-Margaret Martin
Director, Oncology Liaison
Worldwide Regulatory Affairs

AMM:aes
cc: Reg. file

RHÔNE-POULENC

Rhône-Poulenc Rorer Pharmaceuticals Inc.

500 Arcola Road
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Tel 610-454-8000

DUPLICATE

November 18, 1999

Richard Pazdur, M.D., Director
Division of Oncology Drug Products (HFD-150)
Food and Drug Administration, CDER
Woodmont Office Complex 2, Document Room
1451 Rockville Pike
Rockville, MD 20852

SUPPL NEW CORRESP
(SNC to S-011)

NDA 20-449/SE011
Taxotere® (docetaxel) for
Injection Concentrate

GENERAL CORRESPONDENCE:
Response to Request for Information

Dear Dr. Pazdur:

Reference is made to the above-captioned supplemental New Drug Application and to a telefax dated November 10, 1999 from Project Manager Ann Staten which contains the reviewing statistician's request for information.

Attached in duplicate is our response to the aforementioned telefax. Please be advised that our response was also conveyed to FDA today via telefax to Ms. Ann Staten.

Please call me at (610) 454-3037 should you have any questions or comments regarding this submission.

Sincerely,

Anne-Margaret Martin
Director, Oncology Liaison
Worldwide Regulatory Affairs

AMM:aes

cc: Reg. file

RHÔNE-POULENC

Rhône-Poulenc Rorer Pharmaceuticals Inc.

500 Arcola Road
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DUPLICATE

NDA SUPP AMEND

November 18, 1999

Richard Pazdur, M.D., Director
Division of Oncology Drug Products (HFD-150)
Food and Drug Administration, CDER
Woodmont Office Complex 2, Document Room
1451 Rockville Pike
Rockville, MD 20852

NDA 20-449/SE011
Taxotere® (docetaxel) for
Injection Concentrate

GENERAL CORRESPONDENCE:
Response to Request for Information

Dear Dr. Pazdur:

Reference is made to the above-captioned supplemental New Drug Application, our Safety Update Report submitted on November 5, 1999 and to a telephone conversation with Project Manager Ann Staten on November 17, 1999 wherein she requested survival update data for TAX317 and TAX320 in electronic format.

In accordance with the aforementioned request, this submission contains in duplicate, the SAS dataset of updated survival data on CD ROM. Also enclosed is documentation for the codes.

Please call me at (610) 454-3037 should you have any questions or comments regarding this submission.

Sincerely,

Anne-Margaret Martin

Anne-Margaret Martin
Director, Oncology Liaison
Worldwide Regulatory Affairs

cc: Reg. file
AMM:aes

DUPLICATE

RHÔNE-POULENC

Rhône-Poulenc Rorer Pharmaceuticals Inc.

500 Arcola Road
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November 5, 1999

Richard Pazdur, M.D., Director
Division of Oncology Drug Products (HFD-150)
Food and Drug Administration, CDER
Woodmont Office Complex 2, Document Room
1451 Rockville Pike
Rockville, MD 20852

NDA SUPP AMEND
SE1-011
(SU)

NDA 20-449/SE011
Taxotere® (docetaxel) for
Injection Concentrate

GENERAL CORRESPONDENCE:
Safety Update Report

Dear Dr. Pazdur:

Reference is made to Taxotere® NDA 20-449 and to supplement SE011 which was submitted under Fast Track on December 23, 1998 and June 23, 1999. We also refer to our pre-sNDA meeting held on December 22, 1998, wherein is was agreed that Rhône-Poulenc Rorer would submit the Safety Update Report (SUR) four months after submission of the TAX317 final study report, and that the SUR would comprise an updated analysis of survival data from studies TAX317 and TAX320.

In accordance with 21 CFR §314.50(5)(vi)(b) and pursuant to the aforementioned meeting, we are pleased to provide you with the Safety Update Report.

Please contact me at (610) 454-3037 should you have any questions or comments regarding this submission.

Sincerely,

Anne-Margaret Martin

Anne-Margaret Martin
Director, Oncology Liaison
Worldwide Regulatory Affairs

cc: Reg. file
AMM:aes

DUPLICATE

DUPLICATE

RHÔNE-POULENC

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500 Arcola Road
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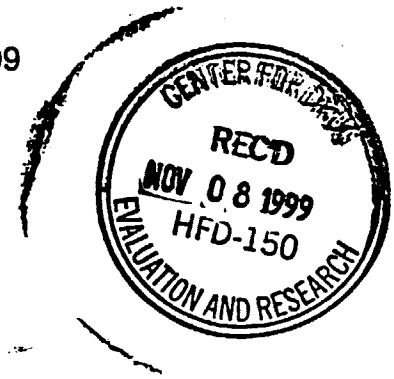
Collegeville, PA 19426-0107
Tel 610-454-8000

November 5, 1999



Richard Pazdur, M.D., Director
Division of Oncology Drug Products (HFD-150)
Food and Drug Administration, CDER
Woodmont Office Complex 2, Document Room
1451 Rockville Pike
Rockville, MD 20852

NDA SUPP AMEND
SE1-011
(BZ)

NDA 20-449/SE011
Taxotere® (docetaxel) for
Injection Concentrate

GENERAL CORRESPONDENCE:
Response to Request for Information

Dear Dr. Pazdur:

Reference is made to our approved New Drug Application for Taxotere® (docetaxel) for Injection Concentrate and to the Fast Track efficacy supplement SE011 submitted in part on December 23, 1998 and concluding on June 23, 1999. We also refer to two telefaxes dated October 21, 1999 from Project Manager Ann Staten which contain a total of 11 questions from the Medical and Statistical reviewers.

Attached is our response to questions 1 through 9, provided in triplicate per Project Manager Ann Staten's request. We will submit our response to questions 10 and 11 shortly.

Please call me at (610) 454-3037 should you have any questions or comments regarding this submission.

Sincerely,

Anne-Margaret Martin

Anne-Margaret Martin
Director, Oncology Liaison
Worldwide Regulatory Affairs

AMM:aes
cc: Reg. file

DUPLICATE

ORIGINAL

RHÔNE-POULENC

Rhône-Poulenc Rorer Pharmaceuticals Inc.

500 Arcola Road
PO Box 1200
Collegeville, PA 19426-0107
Tel 610-454-8000

October 26, 1999

Richard Pazdur, M.D., Director
Division of Oncology Drug Products (HFD-150)
Food and Drug Administration, CDER
Woodmont Office Complex 2, Document Room
1451 Rockville Pike
Rockville, MD 20852

NDA SUPP AMEND
SE1-011
(BL)

NDA 20-449/SE011
Taxotere® (docetaxel) for
Injection Concentrate

RESPONSE TO FDA REQUEST
FOR INFORMATION

Dear Dr. Pazdur:

Reference is made to the above-captioned NDA and to Efficacy Supplement SE011 submitted on June 23, 1999 and June 30, 1999, respectively. We also refer to a telefax received from Project Manager Ann Staten on August 9, 1999 regarding our proposed package insert.

In response to the August 9 telefax, this submission contains in duplicate, the draft package insert, along with a diskette containing the information electronically in Microsoft WORD, Version 6.0c.

Please call me at (610) 454-3037 should you have any questions or comments regarding this submission.

Sincerely,

Anne-Margaret Martin
Director, Oncology Liaison
Worldwide Regulatory Affairs

cc: Reg. file
AMM:aes

ORIGINAL

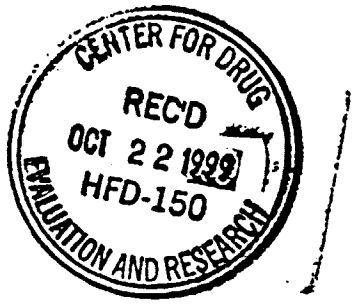
ORIGINAL

RHÔNE-POULENC

Rhône-Poulenc Rorer Pharmaceuticals Inc.

500 Arcola Road
PO Box 1200
Collegeville, PA 19426-0107
Tel 610-454-8000

October 21, 1999



Richard Pazdur, M.D., Director
Division of Oncology Drug Products (HFD-150)
Food and Drug Administration, CDER
Woodmont Office Complex 2, Document Room
1451 Rockville Pike
Rockville, MD 20852

NDA SUPP AMEND
SE1-011
(BL)

NDA 20-449/SE011
Taxotere® (docetaxel) for
Injection Concentrate

DRAFT: Packaging Components

Dear Dr. Pazdur:

Reference is made to the above-captioned NDA and to Efficacy Supplement SE011 submitted on June 23, 1999 and June 30, 1999, respectively. We also refer to a telephone conversation between Project Manager Ann Staten, from your reviewing division, and myself on October 20, 1999, wherein it was agreed that mock-ups of our proposed revised packaging would be submitted under separate cover from the draft package insert.

This submission contains in duplicate, mock-up presentations of the packaging components for Taxotere.

Please call me at (610) 454-3037 should you have any questions or comments regarding this submission.

Sincerely,

Anne-Margaret Martin
Director, Oncology Liaison
Worldwide Regulatory Affairs

cc: Reg. file
AMM:aes

ORIGINAL

RHÔNE-POULENC

Rhône-Poulenc Rorer Pharmaceuticals Inc.

500 Arcola Road
PO Box 1200
Collegeville, PA 19426-0107
Tel 610-454-8000

DUPLICATE
NDA SUPP AMEND
(SE-011 BS)

September 22, 1999

Robert Justice, M.D., Deputy Director
Division of Oncology Drug Products (HFD-150)
Food and Drug Administration, CDER
Woodmont Office Complex 2, Document Room
1451 Rockville Pike
Rockville, MD 20852

NDA 20-449/SE011
Taxotere® (docetaxel) for
Injection Concentrate

GENERAL CORRESPONDENCE:
Response to Request for Information

Dear Dr. Justice:

Reference is made to our approved New Drug Application for Taxotere® (docetaxel) for Injection Concentrate and to the fast track efficacy supplement SE011 submitted in part on December 23, 1998 and concluding on June 23, 1999. We also refer to a telefax dated September 14, 1999 from Project Manager Ann Staten which contains the statistician's information request.

Attached is our response to the aforementioned telefax.

Please call me at (610) 454-3037 should you have any questions or comments regarding this submission.

Sincerely,

Anne Schwanger for

Anne-Margaret Martin
Director, Oncology Liaison
Worldwide Regulatory Affairs

AMM:aes

cc: Reg. file

The question from the FDA (9/14/1999):

For TAX 320 and 317, the statistical analysis plan states that a factor analysis will be performed on the LCSS "to examine if the factor structure agrees with the validated one in a larger population." Please provide the report that validates the factor analysis in the larger patient population, or if it has been included in the application, please direct us to its location in the volumes.

RPR reply:
Although the reference factor structure from a larger population has been expected, neither the authors of LCSS nor any user group of LCSS published such results yet. Somewhat related works to the issue of the factor structure that we are thus far aware of were reported by the LCSS authors group, Hollen, Gralla, Kris and Cox in "Quality of life during clinical trials: conceptual model for the Lung Cancer Symptom Scale (LCSS), Support Care Cancer (1994) 2:213-222.

In lack of such information of the factor structure today, we examined the structure in a combined population of TAX 317 and 320: A total of 432 patients, 286 from TAX 320 and 146 from TAX 317, has the LCSS assessed at baseline. Pooling the baseline observations only in the factor analysis, two orthogonal factors of the LCSS have been identified: The first factor consists of fatigue, appetite, pain, daily activities, LC symptoms and QoL today and the second is loaded with shortness of breath, cough and blood in sputum. The factor loading coefficients are shown in Table 1 below.

This structure is exactly the same with the one separately found in each study of TAX 317 and 320. The very consistent results in each study were already reported in the application, Statistical Appendix Table 4.07A4.

Table 1. : Factor Structure of the LCSS based on the pooled Tax 317 and 320

LCSS Patient Scales	Orthogonal Factors	
	I	II
Fatigue	0.69	0.43
Appetite	0.65	0.03
Pain	0.76	-0.02
Daily activities	0.72	0.38
LC symptoms	0.79	0.25
QoL today	0.78	0.15
Shortness of breath	0.38	0.73
Coughing	0.17	0.83
Blood in sputum	-0.02	0.50

Note: Underlined scores indicate to which factor the item is loaded.

DUPLICATE
SUPPL NEW CORRESP

(SNC to S-011)

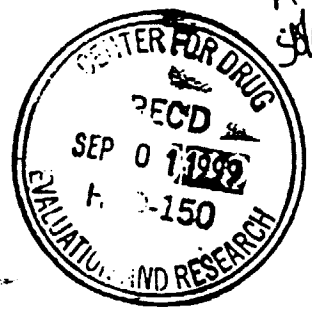
RHÔNE-POULENC

Rhône-Poulenc Rorer Pharmaceuticals Inc.

500 Arcola Road
PO Box 1200
Collegeville, PA 19426-0107
Tel 610-454-8000

August 31, 1999

See M.O.'s 9-14-99 note on SAC dated 8/31/99 As stated 9-15-99 No mtg but will convey issues as they arise



Robert Justice, M.D., Deputy Director
Division of Oncology Drug Products (HFD-150)
Food and Drug Administration, CDER
Woodmont Office Complex 2, Document Room 3067
1451 Rockville Pike
Rockville, MD 20852

NDA 20-449/SE011
Taxotere® (docetaxel) for
Injection Concentrate

REQUEST FOR 90-DAY CONFERENCE

Dear Dr. Justice:

Reference is made to our approved New Drug Application for Taxotere® (docetaxel) for Injection Concentrate and to the fast track efficacy supplement SE011 submitted in part on December 23, 1998 and concluding on June 23, 1999. We understand that this sNDA is considered filable and is currently under priority review.

In accordance with 21 CFR §314.102(c), we respectfully request that a 90-day conference be scheduled so that we may discuss the general progress and status of the subject application. We would like to suggest a meeting date during the week of September 27, 1999.

Thank you for entertaining our request. We enthusiastically await your reply.

Sincerely,

Anne-Margaret Martin

Anne-Margaret Martin
Director, Oncology Liaison
Worldwide Regulatory Affairs

cc: Reg. file
AMM:aes

RHÔNE-POULENC

Rhône-Poulenc Rorer Pharmaceuticals Inc.

500 Arcola Road
PO Box 1200
Collegeville, PA 19426-0107
Tel 610-454-8000

DUPLICATE

NDA SUPP AMEND
(SE1-011 BC)

August 2, 1999

Robert Justice, M.D., Ph.D., Deputy Director
Division of Oncology Drug Products (HFD-150)
Food and Drug Administration, CDER
Woodmont Office Complex 2, Doc. Rm. 3067
1451 Rockville Pike
Rockville, MD 20852

NDA #20-449/S011
Taxotere® (docetaxel)
for Injection Concentrate
(Second-line NSCLC)

Response to FDA Request
for Information

Dear Dr. Justice:

Reference is made to our approved NDA #20-449 for Taxotere® (docetaxel) for Injection Concentrate, and to our rolling submission which began on December 23, 1998 and concluded on June 23, 1999. We also refer to a telefax from Project Manager, Ms. Ann Staten on July 30, requesting that we provide the FDA with our formal request for categorical exclusion from the environmental assessment requirements cited in 21 CFR §25.31b.

In accordance with the aforementioned request, we are pleased to provide, in duplicate, our request for categorical exclusion from the environmental assessment requirements.

If you have any questions concerning this submission, please contact me at (610) 454-3037.

Sincerely,

Anne-Margaret Martin

Anne-Margaret Martin
Director
Worldwide Regulatory Affairs

AMM/aes
Enc.
cc: Regulatory file

Title: Drug Product - Environmental Assessment Categorical Exclusion

NDA #20-449/S-011

Rhône-Poulenc Rorer requests Categorical Exclusion from the environmental assessment requirements under 21 CFR Part 25.31(b).

Rhône-Poulenc Rorer is submitting a supplementary new drug application to the approved NDA for Taxotere® for Injection Concentrate. Docetaxel (RP 56976A) is the active pharmaceutical ingredient in Taxotere® for Injection Concentrate. This application requests approval for the use of Taxotere® for Injection Concentrate for the treatment of patients with locally advanced or metastatic non-small cell lung cancer after failure of prior chemotherapy.

A fifth year market projection, for the United States, for all Taxotere® (docetaxel), the subject of this application, and all current and expected approved applications, gives a total of 115 Kg of docetaxel drug substance. From this quantity the Expected Introduction Concentration (EIC) value for the docetaxel drug substance is calculated to be 0.28×10^{-2} ppb or 2.8 ppt. 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 which is prepared by

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

RHÔNE-POULENC

Rhône-Poulenc Rorer Pharmaceuticals Inc.

500 Arcola Road
PO Box 1200
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Tel 610-454-8000

June 28, 1999

Robert Justice, M.D., Deputy Director
Division of Oncology Drug Products (HFD-150)
Food and Drug Administration, CDER
Woodmont Office Complex 2, Doc. Rm. 3067
1451 Rockville Pike
Rockville, MD 20852

DUPLICATE

~~SUPPL NEW CORRESP~~
(~~SNC to~~
SE1-011)
BZ

NDA #20-449
Taxotere® (docetaxel)
for Injection Concentrate

FAST TRACK SUPPLEMENTAL
NEW DRUG APPLICATION

Completion of December 23, 1998
and June 23, 1999 Rolling Submission

Electronic Datasets

Dear Dr. Justice:

Reference is made to our approved NDA #20-449 for Taxotere® (docetaxel) for Injection Concentrate and to our Fast Track supplemental New Drug Application submitted on December 23, 1998 and June 23, 1999 for Taxotere® in Second-line Non-small Cell Lung Cancer (NSCLC). We also refer to the FDA's fax dated February 12, 1999 and to our responsive submission dated March 1, 1999, which included one CD containing the database documentation and SAS codes for the December 23, 1998 submission.

This submission includes three copies of one CD (one for the Medical Reveiwer, one for the statistician, and one for the archives) containing the database, documentation and SAS codes for the sNDA submission of Taxotere® on June 23, 1999. All data provided are PC SAS datasets based upon version 6.12. SAS transport files are also included.

Also enclosed in duplicate is a loose-leaf binder which provides in hardcopy the contents of the CD. This includes output of the SAS PROC CONTENTS and data listings of five observations in each data file.

Rhone-Poulenc Rorer Pharmacecuticals Inc. considers the information in this submission to be confidential and proprietary, and we request that no portions thereof be disclosed to third parties, under FOIA or otherwise, without first obtaining written permission from us.

Should you have any questions or require any additional information, please contact me at telephone number (610) 454-3037, or via fax number (610) 454-5779.

Sincerely,

Anne-Margaret Martin

Anne-Margaret Martin
Associate Director
Worldwide Regulatory Affairs

AMM/aes

cc: Ms. Ann Staten, Project Manager, HFD-150 (Via Fax)

RHÔNE-POULENC

Rhône-Poulenc Rorer Pharmaceuticals Inc.

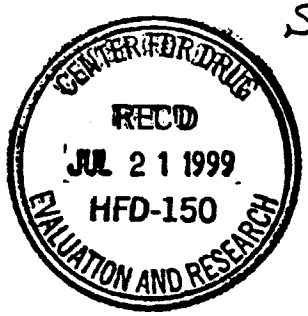
500 Arcola Road
PO Box 1200
Collegeville, PA 19426-0107
Tel 610-454-8000

ORIGINAL

SUPPL NEW CORRESP

SNC

July 20, 1999



Ms. Ann Staten, Project Manager
Division of Oncology Drug Products (HFD-150)
Food and Drug Administration, CDER
Woodmont Office Complex 2
1451 Rockville Pike
Rockville, MD 20852

RA1 Acted 7/23/99

NDA #20-449
Taxotere® (docetaxel)
for Injection Concentrate

Response to FDA Request
Electronic Datasets

Dear Ms. Staten:

Reference is made to our approved NDA #20-449 for Taxotere® (docetaxel) for Injection Concentrate and to our supplemental New Drug Application submitted on December 23, 1998 for Taxotere® in Second-line Non-small Cell Lung Cancer (NSCLC). We also refer to our submission dated March 1, 1999, which provided a CD of the database documentation and SAS codes for the December 23, 1998 submission. Further reference is made to your fax dated July 20, 1999 requesting an additional copy of the aforementioned CD.

In accordance with your request, enclosed please find an additional copy of the subject CD. (CD-ROM TO A. STATEN as DeskCopy)

Should you require any additional information, please contact me at telephone number (610) 454-3037, or via fax number (610) 454-5779.

Sincerely,

Anne-Margaret Martin
Associate Director
Worldwide Regulatory Affairs

AMM/aes
Enc.
cc: Regulatory file

RHÔNE-POULENC

Rhône-Poulenc Rorer Pharmaceuticals Inc.

500 Arcola Road
PO Box 1200
Collegeville, PA 19426-0107
Tel 610-454-8000

ORIGINAL

SUPPL NEW CORRESP

(SN) BZ

March 1, 1999

Robert Justice, M.D., Deputy Director
Division of Oncology Drug Products (HFD-150)
Food and Drug Administration, CDER, ODE I
Woodmont Office Complex 2
Document Room 3067
1451 Rockville Pike
Rockville, MD 20852

NDA #20-449
Taxotere® (docetaxel)
for Injection Concentrate

Response to FDA Request
for Information

Dear Dr. Justice:

Reference is made to our approved NDA #20-449 for Taxotere® (docetaxel) for Injection Concentrate, to our supplemental New Drug Application submitted on December 23, 1998 for Taxotere in second-line Non-Small Cell Lung Cancer (NSCLC), and to FDA's February 12, 1999 fax detailing the electronic information the reviewers will want to see for the aforementioned sNDA.

Pursuant to FDA's February 12, 1999 fax, we are pleased to include one CD containing the database, documentation and SAS codes for the sNDA submission of Taxotere on December 23, 1999. This CD contains the following three directories:

1. FDADATA, which contains the SAS 6.12 data sets, documentation of formats and coding description of variables, and the listings of PROC CONTENTS and five observations for each study.

2. FDAPGM, which contains the SAS codes divided into MARCO and PROGRAM subdirectories for each study.

3. FDATRAN, which contains the transport files for each study.

In addition, duplicate copies of the following three loose-leaf binders are included for FDA's convenience:

1. Volume I contains a paper copy of the documentation of formats and coding variables by study.

2. Volume II contains a paper copy of the listing of SAS codes.

3. Volume III contains a paper copy of the listing of PROC CONTENTS and the five observations for each data set.

Rhône-Poulenc Rorer Pharmaceuticals Inc. considers the information in this submission to be confidential and proprietary, and we request that no portions thereof be disclosed to third parties, under FOIA or otherwise, without first obtaining written permission from us.

Should you have any questions or require any additional information, please contact me at telephone number (610) 454-3037, or via fax number (610) 454-5779.

Sincerely,

Anne-Margaret Martin

Anne-Margaret Martin
Associate Director
Worldwide Regulatory Affairs

AMM/bwr

Enc.

cc: Regulatory file

RHÔNE-POULENC RORER

RHÔNE-POULENC RORER RESEARCH AND DEVELOPMENT
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P.O. BOX 1200
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MAX W. TALBOTT Ph.D.
VICE PRESIDENT
WORLDWIDE REGULATORY AFFAIRS
TEL. 610-454-5618
FAX: 610-454-2268

NDA NO. 20-449 REF NO. 011
NDA SUPPL FOR SE1
SNC

December 23, 1998

Robert Justice, M.D., Deputy Director
Division of Oncology Drug Products (HFD-150)
Center for Drug Evaluation and Research
Food and Drug Administration
Woodmont Office Complex 2
Document Room 3067
1451 Rockville Pike
Rockville, MD 20852

NDA #20-449
Taxotere® (docetaxel)
for Injection Concentrate

DUPLICATE

SUPPLEMENTAL NEW DRUG APPLICATION

New Indication
Request for Fast Track Designation and Application Review
Request for Priority Review

Dear Dr. Justice:

Reference is made to our approved NDA #20-449 for Taxotere® (docetaxel) for Injection Concentrate, which is currently indicated for the treatment of patients with locally advanced or metastatic breast cancer after failure of prior chemotherapy.

New Indication for an Unmet Medical Need:
In accordance with 21 CFR §314.50 and §314.71 and with reference to NDA #20-449, which was originally approved on May 14, 1996, Rhône-Poulenc Rorer Pharmaceuticals Inc. (RPR) hereby submits this Supplemental New Drug Application (sNDA) for Taxotere® (docetaxel) for Injection Concentrate, which demonstrates safety and efficacy of the product in the treatment of patients with locally advanced or metastatic non-small cell lung cancer, after failure of prior chemotherapy.

This new indication for Taxotere® is supported by the results of one large comparative randomized phase 3 trial, TAX320, entitled "A Multicenter, Randomized Phase III Study of Docetaxel (RPR 56976, Taxotere®) 100 mg/m^2 or 75 mg/m^2 Versus Vinorelbine/Ifosfamide in Patients with Non-small Cell Lung Cancer Previously Treated With Platinum-based Chemotherapy", along with four supportive single-agent Phase 2 trials at a dose of 100 mg/m^2, two additional studies, one at a dose of 60 mg/m^2 and another at 75 mg/m^2, as well as a planned interim analysis of one large, TAX317 entitled "A Multicenter, Randomized Phase III Study of Docetaxel (RP 56976, Taxotere®) Versus Best Supportive Care in Patients With Non-small Cell Lung Cancer Previously Treated With Platinum-based Chemotherapy".

Request for Fast Track Designation and Application Review:
As discussed at the pre-sNDA Meeting held on December 22, 1998, we believe that the safety and efficacy analyses contained in this application reflect an important option in the treatment of patients with locally advanced or metastatic non-small cell lung cancer after failure of prior chemotherapy.

As defined in 21 CFR §312.81 in its entirety, this patient group represents a serious and life-threatening disease setting in which no FDA-approved therapy exists. In fact, to the best of our knowledge, this Supplemental New Drug Application (sNDA) represents the first effort in the oncologic pharmaceutical community to bring forward into the Regulatory arena, a data package which contains a pivotal, randomized Phase 3 trial designed to address this patient population's heretofore unmet medical need.

Therefore, in accordance with the Food and Drug Administration Modernization Act (FDAMA) of 1997 (P.L. 105-115), we respectfully request that the FDA assign Fast Track Designation and Application Review of this application.

While today's submission represents the majority of the data which will constitute our complete filing in this matter, as jointly agreed upon at the December 22, 1998 pre-sNDA meeting, RPR will submit a Final Study Report (FSR) for study TAX317 upon its completion. It is understood that the regulatory review clock will begin upon notification from Rhône-Poulenc Rorer that the sNDA filing is complete, but, due to the nature of the fast track request, the FDA may commence review of this rolling application in accordance with FDAMA (*supra*). It is further understood that preparation of a new Integrated Summary of Efficacy (ISE) will not be required, and that an updated version of the Integrated Summary of Safety (ISS) will be provided via the Safety Update Report (SUR) in accordance with 21 CFR 314.50(d)(5)(vi)(b) four (4) months after the submission of the Final Study Report TAX317.

Previous Interactions with the FDA:
An end-of-Phase 2 meeting was held with the FDA on June 6, 1995 to discuss future development of Taxotere® in lung cancer, including the treatment of non-small cell lung cancer patients with locally advanced or metastatic disease (second line), a condition for which there was no FDA-approved therapy at that time. As mentioned previously, this indication continues to represent an unmet medical need.

On April 30, 1998 and again on December 22, 1998 pre-sNDA meetings were conducted to discuss the contents of this application. The background documents for these meetings were supplied on April 15, 1998 and October 7, 1998 respectively.

The Present Submission:

Technical Aspects:
Organization of this application is in accordance with 21 CFR §314.50. Technical sections for Chemistry, Manufacturing and Controls, Preclinical, Pharmacokinetics and Microbiology are not relevant to this efficacy supplement, and are therefore, not included.

Pagination of this application reflects the technical section number which coincides with the Contents of Application section of form FDA 356h. The overall application pagination numbers are located on the bottom right corner of each page. Individual reports within the technical sections have maintained their original internal page numbers as well, and will relate to the individual report's table of contents.

For ease of review, the proposed revised package insert is provided herein in Microsoft Word for Windows™, Version 6.0 format on diskette as Attachment 1 to this letter.

Clinical Data:
As previously mentioned, this submission contains data from one adequate and well controlled pivotal Phase 3 study to support this proposed new indication for Taxotere®, as well as six Phase 2 second line chemotherapy non-small cell lung cancer studies, and an interim analysis of Phase 3 study TAX317, which has completed enrollment and will be finalized soon. To completely describe the safety profile of Taxotere® in the non-small cell lung cancer patient population, we have included Tabulated Study Reports (TSRs) which contain data from twelve first-line lung cancer studies.

Case Report Forms (CRFs) for all second line patients enrolled in the pivotal study, as well as supportive studies TAX270, TAX271, TAX297, TAX317, SI002A, CHI202 and TAX241, who died within 30 days of treatment or withdrew from study due to toxicity, are contained in technical section #12.

Other Information:
As required by §306(k)(1) of the Generic Drug Enforcement Act [21 U.S.C. §335a(k)(1)], we hereby certify that, in connection with this application, Rhône-Poulenc Rorer Pharmaceuticals Inc. did not and will not use in any capacity the services of any person debarred under subsections 306(a) or (b) of the act.

As cited under 21 CFR §314.108(b)(5), we have included a request for patent exclusivity with this sNDA.

Rhône-Poulenc Rorer Pharmaceuticals Inc. considers the information in this application to be confidential and proprietary, and we request that no portions thereof be disclosed to third parties, under FOIA or otherwise, without first obtaining written permission from us.

On behalf of Rhône-Poulenc Rorer, we would like to take this opportunity to thank the Agency for its consistent willingness to meet with us and provide ongoing comment and guidance regarding this filing.

Should you have any questions or require any additional information during what we hope will be a rolling review of this application, please contact Ms. Anne-Margaret Martin, Associate Director, Worldwide Regulatory Affairs, Liaison Oncology, at telephone number (610) 454-3037, or via fax number (610) 454-5779.

Sincerely,

Max W. Talbott

Max W. Talbott, Ph.D.
Vice President
Worldwide Regulatory Affairs

MWT/amm

DUPLICATE
N(60)24

RHÔNE-POULENC RORER

RHÔNE-POULENC RORER PHARMACEUTICALS INC.
500 ARCOLA ROAD
P.O. BOX 1200
COLLEGEVILLE, PA 19426-0107
TEL. 610-454-8000

July 7, 1995

Charles P. Hoiberg, Ph.D., Acting Director
Oncology Group (HFD-150)
Center for Drug Evaluation and Research
Food and Drug Administration
Woodmont Office Complex 2 Document Room
1451 Rockville Pike
Rockville, MD 20852

IND
Taxotere® (docetaxel)
Serial No. 367
GENERAL CORRESPONDENCE
End of Phase 2 Meeting

Dear Dr. Hoiberg:

Reference is made to the above-captioned Investigational New Drug Application and to the End of Phase 2 meeting held on June 6, 1995 between Rhône-Poulenc Rorer and members of your staff. This submission contains in triplicate a summary of the results of the End of Phase 2 meeting for both Breast Cancer and Non-Small Cell Lung Cancer. We have also included copies of the slides which were used in our presentation.

We are pleased to have had the opportunity to gain valuable feedback from members of your team as well as ODAC members who participated telephonically, and we look forward to continued positive interaction with the agency.

Sincerely,

Anne-Margaret Martin
Manager, Regulatory Affairs

AMM/aes
Enclosure

RHÔNE-POULENC RORER

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RONALD F. PANNER
SENIOR DIRECTOR
WORLDWIDE REGULATORY AFFAIRS

December 15, 1998

Food and Drug Administration
P. O. Box 360909
Pittsburgh, PA 15251-6909

User Fee Payment
User Fee ID #3629
Taxotere® (docetaxel) for
Injection Concentrate
NDA 20-449

Dear Sir:

Enclosed with this letter is check totaling which is payment for User Fees under the Prescription Drug User Fee Act of 1992 (PDUFA) as amended under the Food and Drug Administration Modernization Act of 1997 (FDAMA). This check is the full supplemental new drug application fee for NDA 20-449, Taxotere® (docetaxel) for Injection Concentrate. A copy of Form 3397 is also included.

If you have any questions concerning this user fee payment, please contact me at (610) 454-3026.

Very truly yours,

Ronald F. Panner
Senior Director
Worldwide Regulatory Affairs

RFP/ccr

Enclosures