CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-278

ADMINISTRATIVE DOCUMENTS

Smela Jr, Michael

From: Smela Jr, Michael
Sent: Monday, May 14, 2001 3:42 PM
): Dillahunt, Michelle
c: Brown, Shirley S
Subject: 75278

I am closing Mylan's Paclitaxel for chemistry. Please add to AP matrix. Following are pending:

Micro review of 9/29/00 amendment
EER pending
Response to EA deficiencies promised this week.

Mike

300 mg/50 mL

Vial: 50 cc ——— clear glass vial, USP Type I, manufactured by ——— (DMF ———

Closure: 20 mm ——— faced ——— gray stopper manufactured by ——— (DMF ——— The stopper is secured with a 20 mm red flip-off seal by ——— (DMF ——— .

Expiry date - 24 months.

LABELING: Satisfactory. Summary dated May 25, 2001.

STERILIZATION VALIDATION (IF APPLICABLE):

The submission is recommended for approval on the basis of sterility assurance per the microbiology May 31, 2001 review.

SIZE OF BIO BATCH - (FIRM'S SOURCE OF NDS O.K.?): (Yes. DMF ———

Batch 08110397, ———
Batch 10510400, ———

SIZE OF STABILITY BATCHES - (IF DIFFERENT FROM BIO BATCH, WERE THEY MANUFACTURED VIA SAME PROCESS):

Same Process

PROPOSED PRODUCTION BATCH - MANUFACTURING PROCESS THE SAME AS BIO/STABILITY?

Same Process

100 mg/16.7 ml - Batch size ———
300 mg/50 ml - Batch size ———
30 mg/5 ml - Batch size ———

Environmental Assessment: Acceptable per review of Nancy Sager on 6/15/01. FONSI recommended.

Review Chemist: Shirley S. Brown 7/10/01
Team Leader: Michael Smela
Date: July 3, 2001

V:\FIRMSAM\MYLAN\LTRS&REV\75278app.sum 7/10/01
F/T by: DJ 7/5/01

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-278

CORRESPONDENCE

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

January 25, 2002

MINOR AMENDMENT
(REQUEST FOR FINAL ANDA APPROVAL)

ORIG AMENDMENT

Office of Generic Drugs, CDER, FDA
Gary J. Buehler, Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RE: PACLITAXEL INJECTION, 6MG/ML
(30MG/5ML, 100MG/16.7ML AND 300MG/50ML)
ANDA 75-278

Dear Mr. Buehler:

Reference is made to the Abbreviated New Drug Application identified above and to the Agency's letter dated January 25, 2002 which rescinded approval of this application and granted this application tentative approval status.

The purpose of this amendment is to request final approval of this application. Since the date of tentative approval of our ANDA, no changes have been made to the labeling of the drug product, the method of manufacture for the drug product, or to any other conditions under which the application was tentatively approved. In addition, all patent and exclusivities for the reference listed drug as identified in the publication *Approved Drug Products with Therapeutic Equivalence Evaluations* have been addressed in either the patent certification submitted in the original ANDA filed on December 19, 1997 or in subsequent patent amendments to this application.

This amendment is being submitted in duplicate. Should you have any questions regarding this correspondence or require additional information, please contact the undersigned by telephone at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/dn

Enclosures

ANDA 75-278

JUL 23 2001

Mylan Pharmaceuticals, Inc.
Attention: Frank R. Sisto
781 Chestnut Ridge Road
P.O. Box 4310
Morgantown, WV 26504-4310

This is in reference to your abbreviated new drug application dated December 19, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Paclitaxel Injection, 6 mg/mL, (packaged in 30 mg/5 mL, 100 mg/16.7 mL, and 300 mg/50 mL multiple-dose vials).

By separate letter dated today, you are receiving approval for the abbreviated new drug application (ANDA) identified above. This letter provides background on the ANDA and addresses regulatory issues related to U.S. Patent Number 6,096,331.

ANDA 75-278 seeks approval of a generic version of paclitaxel, the brand name of which is Taxol, a drug manufactured by Bristol Myers Squibb (BMS). ANDA 75-278 was received by FDA on December 22, 1997. On July 21, 1997, BMS listed patent 5,641,803 (patent '803) with FDA, and on October 9, 1997, BMS listed patent 5,670,537 (patent '537) with the agency, asserting that these patents cover Taxol. Mylan filed Paragraph IV certifications to patents '803 and '537, claiming the patents were invalid, unenforceable, or not infringed. (See 21 U.S.C. § 355(j)(2)(A)(vii)(IV); 21 C.F.R. § 314.94(a)(12)(i)(A)(4)). Mylan notified BMS of these certifications on February 17, 1998. Bristol Myers Squibb filed a lawsuit against Mylan on April 2, 1998 in United States District Court in Newark, New Jersey alleging infringement of United States Patents No. '803 and '537. Because Mylan was sued by BMS within 45 days of giving BMS notice of its Paragraph IV certifications, approval of Mylan's ANDA was stayed for 30 months, pursuant to 21 U.S.C. § 355(j)(5)(B)(iii). The 30 month stay of approval of Mylan's ANDA expired on August 17, 2000.

On August 29, 1997, BMS listed U.S. Patent 5,496,804 with FDA. This patent was assigned a use code of U-204. On January 21, 1998, Mylan submitted a method of use statement pursuant to

section 505(j)(2)(a)(vii) of the Act to the '804 patent, and submitted revised labeling.

On August 1, 2000, the Patent and Trademark Office issued a new patent to American Bioscience Inc. (ABI), U.S. Patent Number 6,096,331 (the '331 patent). ABI claimed that this patent covered BMS's Taxol product. On August 11, 2000, ABI obtained a temporary restraining order (TRO) from a district court in California directing BMS to list the patent with FDA in *Approved Drug Products with Therapeutic Equivalence Evaluations* (the Orange Book). That order stated that, should ABI fail to prevail in the underlying litigation, BMS would be required to take all steps necessary to delist the patent. On August 11, 2000, BMS listed the patent in the Orange Book pursuant to the court order. This was an extremely unusual condition for patent listing and the first time it was requested that a patent be listed pursuant to a court order.

On September 7, 2000, the district court in California dissolved the TRO, dismissed ABI's complaint, and ordered BMS to delist the '331 patent from the Orange Book to restore the status quo. The court stayed its order until September 13, 2000.

On September 11, 2000, BMS submitted another listing for the patent. This listing made no mention of the original court-ordered August 11, 2000, listing.

In its September 7, 2000 Order, the California district court recommended that FDA "toll the period in which BMS may timely cause such listing." OGD did not follow this recommendation for four reasons: (1) FDA was not a party to the California litigation in which the order was issued, and therefore, FDA's views were not presented to the court nor did the court have jurisdiction over the agency; (2) the 30-day time period is a statutory limit for timely submission, and it is not clear that the agency has the authority to extend that period; rather FDA believes that the 30 day period represents a Congressional determination that 30 days is sufficient; (3) even if the agency did have the authority to toll the deadline, it would set an undesirable precedent that future holders of pioneer applications could use to try to obtain extensions of the 30 day period, thereby blocking the approval of generic applications; and (4) the agency saw no reason why BMS could not have voluntarily listed the '331 patent within 30 days of its issuance if BMS thought the listing was appropriate under the Federal Food, Drug, and Cosmetic Act.

On September 14, 2000, BMS submitted a letter to FDA to comply with the court order to delist the patent. The letter states "BMS hereby withdraws the Original Listing to the extent that listing was compelled by the TRO." Because the court order directing BMS to submit the patent to FDA was dissolved, and BMS withdrew the original submission made pursuant to the TRO, FDA considered BMS's first submission of the patent on August 11, 2000, to be without effect.

The September 11, 2000 submission of the '331 patent by BMS was given effect. However, patents must be listed with FDA within 30 days of their issuance. See 21 U.S.C. § 355(c)(2). An FDA regulation, the "late-listing regulation," directly applies to patents submitted to FDA more than 30 days after they are issued. 21 C.F.R. § 314.94(a)(12)(vi). That regulation provides that pending ANDAs that contain appropriate patent certifications before the late patent is submitted need not be amended to contain certifications to patents that are listed beyond the 30-day interval set out in the statute. Here, because BMS withdrew the August 11 listing, the only listing remaining for the '331 patent was the September 11 listing, which was submitted more than 30 days after the patent's August 1, 2000, issuance.

At the time the '331 patent was late filed, ANDA 75-278 contained no certification to the '331 patent, as submitted to FDA by BMS on August 11, 2000, pursuant to the California court's TRO. However, the absence of any certification to the '331 patent does not affect the application of the late-listing regulation to the Mylan ANDA. First, there is no requirement in the regulations or the statute that an ANDA applicant submit a certification to a newly listed patent within a certain time period. An applicant must submit a certification to a timely patent for the pending ANDA to be eligible for approval, but there is no specific deadline for such a submission. Second, because the August 11, 2000, submission of the '331 patent was nullified by the withdrawal of the submission pursuant to the California court's September 7, 2000 order, no certification to that patent would be required. Therefore, because ANDA 75-278 was pending before the agency on September 11, 2000, and had appropriate patent certifications at that time, Mylan was not required to certify to patent '331 under the late-listing regulation, 21 C.F.R. § 314.94(a)(12)(vi).

On September 15, 2000, Mylan submitted a statement indicating that no patent certification to the '331 patent is required since the patent was not submitted to FDA by the holder of the

approved application for the listed drug within 30 days of issuance.

On December 14, 2000, BMS submitted an additional patent for listing in the Orange Book. U.S. Patent Number 6,150,398 ('398) is a use patent identified by the patent use code U-380 in the Orange Book. U-380 is for "combinations of Taxol (paclitaxel)and cisplatin which are suitable for the treatment of ovarian and non-small cell lung carcinomas."

On April 21, 2001, the 180-day exclusivity period granted to ANDA 75-184, Baker Norton, paclitaxel injection, expired.

On May 11, 2001, Mylan submitted a method of use statement pursuant to the section 505(j)(2)(a)(vii) of Act to the '398 patent and submitted revised labeling.

OGD has resolved all the issues related to the Mylan ANDA that have arisen since the Agency issued a tentative approval dated September 19, 2000. The '331 patent is not a barrier to approval of the Mylan ANDA under the late listing regulation, 21 C.F.R. § 314.94(a)(12)(vi), since the '331 patent was not listed in a timely manner. Mylan has properly addressed all remaining patent and exclusivity issues.

Sincerely yours,

/S/

Gary Buehler 7/23/01
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

Cc:
ANDA 75-278
Division File
Field Copy
HFD-610/R.West
Endorsements:
Drafted:Cparise/7/13/01
Revised:L.Dickinson 7/20/01
V:\FIRMSAM\MYLAN\LTRS&REV\75278.803.DOC

LETTER OUT

/S/
7/23/2001

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

June 14, 2001

Office of Generic Drugs, CDER, FDA
Gary J. Buehler, Acting Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

NEW CORRESP
NC

CMC AMENDMENT
(Environmental Assessment Information Enclosed)

RE: PACLITAXEL INJECTION, 6MG/ML
(30MG/5ML, 100MG/16.7ML AND 300MG/50ML)
ANDA 75-278
RESPONSE TO AGENCY CORRESPONDENCE DATED JUNE 14, 2001

Dear Mr. Buehler:

Reference is made to the June 12, 2001 amendment to the Abbreviated New Drug Application identified above which provided a revised, complete Environmental Assessment (EA) in response to the Agency's June 8, 2001 request. Reference is also made to an additional comment from the Agency regarding the revised EA which was forwarded to Mylan by facsimile on June 14, 2001 (refer to Attachment 1).

In response to the Agency's June 14 comment, Mylan would like to further amend the EA as noted below. For ease of review, the Agency's comment is repeated below, followed by Mylan's response.

FDA COMMENT: The correction on page 8 is incomplete. The discussion should be revised to state "... and Yunnan, where confiscated and harvested bark from Taxus yunnanensis CAN BE obtained in a ..."

MYLAN RESPONSE: Mylan acknowledges the Agency's comment and has corrected the statement as requested. Enclosed in Attachment 2 is a replacement for page 8 (ANDA page 16) of the EA submitted on June 12, 2001, which provides for the requested revision.

In addition to the requested revision we are also making a typographical correction to page 14 (ANDA page 23) of the EA, paragraph 3, first sentence. This sentence has been changed from "All *Taxus yunnanensis* extract that [redacted] has purchased from [redacted] was produced from bark that had been confiscated from the [redacted] to read " [redacted] has purchased *Taxus yunnanensis* extract from [redacted] that was produced from confiscated bark obtained from the [redacted] A replacement page 14 (ANDA page 23) which incorporates the above noted change is also enclosed in Attachment 2.

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
JUN 15 2001
OGD

G:\PROJECT\ANDA\PACLITAXEL\AGENCY-LETTER-DATED-061401.doc

Department—Fax Numbers					
Accounting	(304) 285-6403	Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Administration	(304) 599-7284	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Business Development	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Human Resources	(304) 598-5406	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
		Medical Unit	(304) 598-5445		

Pursuant to 21 CFR 314.96(b), we certify that a true copy of this amendment, as submitted to the Office of Generic Drugs, is also being forwarded to the FDA's Baltimore and Kansas City District Offices.

This amendment is submitted in duplicate to ANDA #75-278. In addition, a copy of this amendment has been sent directly to Ms. Nancy Sager by facsimile, at her request. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/dn

Enclosures

cc: Ms. Nancy Sager (via facsimile)

APPEARS THIS WAY
ON ORIGINAL

MYLAN PHARMACEUTICALS INC.

TABLE OF CONTENTS

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

June 12, 2001

ORIG AMENDMENT

N/FA

Office of Generic Drugs, CDER, FDA
Gary J. Buehler, Acting Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

CMC AMENDMENT
(Environmental Assessment Enclosed)

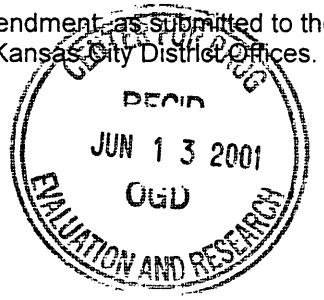
RE: PACLITAXEL INJECTION, 6MG/ML
(30MG/5ML, 100MG/16.7ML AND 300MG/50ML)
ANDA 75-278
RESPONSE TO AGENCY CORRESPONDENCE DATED JUNE 8, 2001

Dear Mr. Buehler:

Reference is made to the Environmental Assessment (EA) submitted in our December 29, 2000 amendment to the ANDA identified above and to the amendments to this EA which were submitted on May 14, May 22 and May 23, 2001. Reference is also made to the June 8, 2001 correspondence from the Agency which provided additional comments pertaining to the EA.

In response to the comments provided in the Agency's June 8, 2001 correspondence, Mylan would like to further amend this application as follows. Attachment 1 contains a listing of each comment provided in the Agency's June 8, 2001 correspondence along with a response to each comment as provided by our environmental assessment consultants, [redacted] Enclosed in Attachment 2 is a complete, revised EA which incorporates the information requested in the June 8, 2001 correspondence, along with all previous changes. This document supercedes all versions and amendments previously submitted. For ease of review, an additional copy of the revised EA, which highlights the changes made as a result of the comments in the June 8, 2001 correspondence, is provided in Attachment 3. New or revised information is highlighted in red print. For reviewer convenience, a copy of the June 8, 2001 correspondence is enclosed in Attachment 4.

Pursuant to 21 CFR 314.96(b), we certify that a true copy of this amendment, as submitted to the Office of Generic Drugs, is also being forwarded to the FDA's Baltimore and Kansas City District Offices.



G:\PROJECT\ANDA\PACLITAXEL\AGENCY-LETTER-DATED-060801.doc

Department—Fax Numbers		Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Accounting	(304) 285-6403	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Administration	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Business Development	(304) 599-7284	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
Human Resources	(304) 598-5406	Medical Unit	(304) 598-5445		

This amendment is submitted in duplicate to ANDA #75-278. In addition, a desk copy of this amendment has been sent directly to Ms. Nancy Sager, at her request. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/dn

Enclosures

APPEARS THIS WAY
ON ORIGINAL

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

ORIG AMENDMENT

May 30, 2001

Office of Generic Drugs, CDER, FDA
Gary J. Buehler, Acting Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ANDA AMENDMENT
RESPONSE TO MICROBIOLOGY DEFICIENCIES

RE: PACLITAXEL INJECTION, 6MG/ML
(30MG/5ML, 100MG/16.7ML AND 300MG/50ML)
ANDA 75-278
RESPONSE TO AGENCY CORRESPONDENCE DATED MAY 24, 2001

Dear Mr. Buehler:

Reference is made to the Abbreviated New Drug Application identified above and to the May 24, 2001 correspondence from the Agency containing comments resulting from the Microbiology Review of our September 29, 2000 amendment for the 100mg and 300mg vial sizes.

The Agency's May 24, 2001 correspondence contained only one comment, which requested the submission of Anti-microbial Preservative Effectiveness (APE) test data for the paclitaxel finished product. In response to the Agency's request Mylan would like to amend this application with the following information. For ease of review a copy of the May 24 correspondence is provided in Attachment 1.

FDA COMMENT 1: Please provide an Anti-microbial Preservative Effectiveness Test for multiple-dose use of the subject drug product.

MYLAN RESPONSE: Mylan acknowledges the Agency's comment and has discussed it with Dr. Andrea High, Microbiology Team Leader within OGD. Mylan indicated to Dr. High that APE testing on the 6 mg/mL formulation of paclitaxel injection was conducted and submitted to this application in an amendment to our original ANDA submission pertaining to the 30mg vial size. The results of APE testing were submitted to this application on March 24, 2000 in response to a February 2, 2000 telephone request from representatives from your Office. For ease of review a copy of the pertinent information from this amendment is provided in Attachment 2.

Department—Fax Numbers		Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Accounting	(304) 285-6403	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Administration	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Business Development	(304) 599-7284	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
Human Resources	(304) 598-5406	Medical Unit	(304) 598-5445		

As confirmed with Dr. High on May 29, 2001, APE testing is formulation/ concentration dependent and not dependent upon package/fill size. Since all three package/fill sizes of paclitaxel injection (30mg/5mL, 100mg/16.7mL and 300mg/50mL) are filled using an identical 6mg/mL formulation of paclitaxel, the APE testing conducted on the 5mL vial fulfills the APE testing requirements for all package/fill sizes of this product.

Pursuant to 21 CFR 314.96(b), we certify that a true copy of this amendment, as submitted to the Office of Generic Drugs, is also being forwarded to the FDA's Baltimore and Kansas City District Offices.

This amendment is submitted in duplicate to ANDA #75-278. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/dn

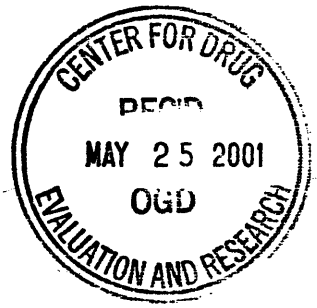
Enclosures

cc: Pat Beers-Block (via facsimile)
Dr. Andrea High (via facsimile)

APPEARS THIS WAY
ON ORIGINAL

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

May 23, 2001



ORIG AMENDMENT
N/FA

Office of Generic Drugs, CDER, FDA
Gary J. Buehler, Acting Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

CMC AMENDMENT
(Environmental Assessment Enclosed)

RE: PACLITAXEL INJECTION, 6MG/ML
(30MG/5ML, 100MG/16.7ML AND 300MG/50ML)
ANDA 75-278
RESPONSE TO AGENCY CORRESPONDENCE DATED MAY 23, 2001

Dear Mr. Buehler:

Reference is made to the December 29, 2000 amendment to the Abbreviated New Drug Application identified above, which is currently under review, and to the May 23, 2001 correspondence from the Agency which provided comments pertaining to the review of the amended environmental assessment (EA) submitted on May 22, 2001 in response to the comments contained in the Agency's correspondence, dated May 18, 2001.

In response to the comments provided in the May 23, 2001 correspondence, Mylan would like to further amend this application as described herein. Attachment 1 contains a listing of each comment provided in the Agency's May 23, 2001 correspondence along with a response to each comment as provided by our environmental assessment consultants, ——————————Enclosed in Attachment 2 is an amended EA which incorporates the information requested in the May 23, 2001 correspondence. This document amends the EA submitted in the May 22, 2001 amendment. For ease of review, an additional copy of the amended EA, which illustrates the changes made, is provided in Attachment 3. New information is highlighted in red print. For ease of review, a copy of the Agency's May 23, 2001 correspondence is enclosed in Attachment 4.

Pursuant to 21 CFR 314.96(b), we certify that a true copy of this amendment, as submitted to the Office of Generic Drugs, is also being forwarded to the FDA's Baltimore and Kansas City District Offices.

Department—Fax Numbers		Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Accounting	(304) 285-6403	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Administration	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Business Development	(304) 599-7284	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
Human Resources	(304) 598-5406	Medical Unit	(304) 598-5445		

This amendment is submitted in duplicate to ANDA #75-278. In addition, a desk copy of this amendment has been sent directly to Ms. Nancy Sager, at her request. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/dn

Enclosures

APPEARS THIS WAY
ON ORIGINAL

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

May 22, 2001

Office of Generic Drugs, CDER, FDA
Gary J. Buehler, Acting Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ORIG AMENDMENT
N/FA
CMC AMENDMENT
(Environmental Assessment Enclosed)

RE: PACLITAXEL INJECTION, 6MG/ML
(30MG/5ML, 100MG/16.7ML AND 300MG/50ML)
ANDA 75-278
RESPONSE TO AGENCY CORRESPONDENCE DATED MAY 18, 2001

Dear Mr. Buehler:

Reference is made to the December 29, 2000 amendment to the Abbreviated New Drug Application identified above, which is currently under review, and to the May 18, 2001 correspondence from the Agency which provided comments pertaining to the review of the revised environmental assessment (EA) submitted on May 14, 2001 in response to the comments contained in the Agency's correspondence, dated April 17, 2001.

In response to the comments provided in the May 18, 2001 correspondence, Mylan would like to further amend this application as described herein. Attachment 1 contains a listing of each comment provided in the Agency's May 18, 2001 correspondence along with a response to each comment as provided by our environmental assessment consultants, _____. Enclosed in Attachment 2 is an amended EA which incorporates the information requested in the May 18, 2001 correspondence. This document amends the EA submitted in the May 14, 2001 amendment. For ease of review, an additional copy of the amended EA, which illustrates the changes made, is provided in Attachment 3. New information is highlighted in red print. For ease of review, a copy of the Agency's May 18, 2001 correspondence is enclosed in Attachment 4.

Pursuant to 21 CFR 314.96(b), we certify that a true copy of this amendment, as submitted to the Office of Generic Drugs, is also being forwarded to the FDA's Baltimore and Kansas City District Offices.

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
MAY 24 2001
OGD

G:\PROJECT\ANDA\PACLITAXEL\AGENCY-LETTER-DATED-051801.doc

Department—Fax Numbers					
Accounting	(304) 285-6403	Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Administration	(304) 599-7284	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Business Development	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Human Resources	(304) 598-5406	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
		Medical Unit	(304) 598-5445		

This amendment is submitted in duplicate to ANDA #75-278. In addition, a desk copy of this amendment has been sent directly to Ms. Nancy Sager, at her request. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/dn

Enclosures

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

May 11, 2001

ORIG AMENDMENT
N/AF

NEW CORRESP
NC

5/17/01

Office of Generic Drugs, CDER, FDA
Gary Buehler, Acting Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

LABELING AMENDMENT
PATENT/EXCLUSIVITY AMENDMENT

RE: **ANDA 75-278; PACLITAXEL INJECTION, 6MG/ML**
(30MG/5ML, 100MG/16.7ML and 300MG/50ML)
Response to Agency Correspondence Dated October 11, 2000

Dear Mr. Buehler:

Reference is made to the above-referenced application that is currently under review. Reference is also made to the Agency's correspondence dated October 11, 2000 that provided Baker Norton's patient leaflet for paclitaxel injection. The Agency requested, in a telephone conversation, that Mylan amend the labeling to provide for a patient leaflet. At this time Mylan is amending the referenced application with revised labeling that addresses the Agency's request for a patient leaflet. In addition, Mylan is amending the referenced application with an updated patent certification and exclusivity statement that addresses a newly filed patent.

Mylan filed its original patent certification and exclusivity information on January 21, 1998. On November 9, 1999, and on September 15, 2000, Mylan amended the application to provide information regarding additional exclusivity filings. Subsequent to these filings, the holder of the referenced drug listed an additional patent as noted on the Agency's webpage listing entitled "Patent Term Extension and New Patents – May 7, 2001, Docket Number *95S-0017". Accordingly, an amended patent certification and exclusivity statement is provided in Attachment 1 that certifies that the referenced product is now covered by a new method of use patent which expires May 08, 2011. The amended certification further notes that the patent is for a method of use that Mylan's labeling does not claim. At this time, Mylan is not seeking approval for the use covered by the listed patent.

As previously noted, Mylan is also amending the referenced application with labeling revised to add a patient leaflet pursuant to the Agency's correspondence dated October 11, 2000. For the reviewer's reference, a copy of the Agency's correspondence is provided in Attachment 2. In addition to adding the patient leaflet, Mylan has made format and editorial revisions throughout all of the product labeling to reflect that the product will be marketed by UDL Laboratories, Inc., a wholly owned subsidiary of Mylan.

Department—Fax Numbers		Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Accounting	(304) 285-6403	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Administration	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Business Development	(304) 599-7284	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
Human Resources	(304) 598-5406	Medical Unit	(304) 598-5445		

All of the revisions made to the outsert, vial labels and cartons are annotated in side-by-side comparisons of the revised, final printed labeling to the previously submitted labeling. Mylan's final printed patient leaflet was annotated against the Baker Norton patient leaflet provided by the Agency. The annotations for each piece of labeling are provided in Attachment 3. Enclosed in Attachment 4 are twelve (12) copies of final printed labeling for the vial labels, cartons and outsert with the attached patient leaflet as follows:

VIAL LABELS

30 mg/5 mL	RUD961WW
100 mg/16.7 mL	RUD962AJ
300 mg/50 mL	RUD963DD

CARTONS

30 mg/5 mL	UD961-34-01C:R1
100 mg/16.7 mL	UD962-13-01C:R1
300 mg/50 mL	UD963-09-01C:R1

OUTSERT
UDPLTL:R3 Revised May 2001

PATIENT LEAFLET
PL:UDPLTL:R3 Revised May 2001

Should you have any questions regarding this amendment, please contact the undersigned by telephone at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

EMS/enclosures

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

September 15, 2000

Office of Generic Drugs, CDER, FDA
Gary J. Buehler, Acting Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

REQUEST FOR TENTATIVE APPROVAL
(PATENT/EXCLUSIVITY INFORMATION ENCLOSED)

NEW CORRESP
NC

RE: PACLITAXEL INJECTION, 30MG/5ML (6MG/ML)
ANDA #75-278

Dear Mr. Buehler:

This correspondence to the above referenced ANDA for Paclitaxel Injection is being submitted to request that tentative approval for this application be granted. This request is based on Mylan's contention that:

1) with regard to U.S. Patent No. 6,096,331, dated August 1, 2000, an amendment to Mylan's previously submitted patent certification for Paclitaxel Injection is not required pursuant to 21 CFR 314.94(a)(12)(vi) since this patent was not submitted to FDA by the holder of the approved application for the listed drug within 30 days of issuance, and

2) there are no other outstanding regulatory or review issues which would preclude the tentative approval of this application.

Enclosed, however, is an update to the patent and exclusivity information which was previously submitted to this application on January 21, 1998 and November 9, 1999. This update addresses exclusivity filings by the holder of the reference listed drug which were filed subsequent to our January 21, 1998 and November 9, 1999 submissions.

This correspondence is submitted in duplicate. Should you have any questions or require additional information, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

CENTER FOR DRUG
RECD
SEP 18 2000
OGD
EVALUATION AND RESEARCH

FRS/dn

Enclosures

cc: Mr. Peter Rickman (via facsimile)

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

July 25, 2000

ORIG AMENDMENT
N/AM

Office of Generic Drugs, CDER, FDA
Gary J. Buehler, Acting Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

TELEPHONE AMENDMENT
(CMC INFORMATION ENCLOSED)

RE: PACLITAXEL INJECTION, 30MG/5ML (6MG/ML)
ANDA #75-278
RESPONSE TO AGENCY TELEPHONE CALL OF JULY 24, 2000

Dear Mr. Buehler:

Reference is made to the Abbreviated New Drug Application identified above, which is currently under review, and to a July 24, 2000 telephone call from Dr. Allan Rudman and Ms. Michelle Dillahunt of your Office pertaining to the review of this application. As requested by the Agency, Mylan is amending the application as follows:

E

7

2. With this letter, Mylan commits to revise the product name in all documentation to reflect the strength of the drug product in accordance with the product labeling [i.e., Paclitaxel Injection, 30mg/5mL (6mg/mL)] and provide the revised documents in the first post-approval ANDA Annual Report.

3. Mylan has revised the finished product specifications to include a requirement for Foreign Matter, pursuant to USP <1>. The revised finished product specifications for Paclitaxel Injection, 30mg/5mL are provided in Attachment A.

Pursuant to 21 CFR 314.96(b), we certify that a true copy of this amendment, as submitted to the Office of Generic Drugs, is also being forwarded to the FDA's Baltimore and Kansas City District Offices.

This amendment is submitted in duplicate to ANDA #75-278. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/dn
Enclosures

Department—Fax Numbers					
Accounting	(304) 285-6403	Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Administration	(304) 599-7284	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Business Development	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Human Resources	(304) 598-5406	Medical Unit	(304) 598-5445	Sales & Marketing	(304) 598-3232

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

June 20, 2000

Office of Generic Drugs, CDER, FDA
Gary J. Buehler, Acting Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

NEW CORRESP

CMC AMENDMENT
(Environmental Assessment Information Enclosed)

RE: PACLITAXEL INJECTION, 30MG/5ML (6MG/ML)
ANDA #75-278
RESPONSE TO AGENCY TELEPHONE CALL OF JUNE 20, 2000

Dear Mr. Buehler:

Reference is made to the Abbreviated New Drug Application identified above, which is currently under review, and to a June 20, 2000 telephone call from Ms. Nancy Sager pertaining to the review of the environmental assessment (EA) submitted in support of this application. As per Ms. Sager's request, the format of Mylan's previously submitted June 19th response has been revised and is provided in this amendment.

Pursuant to 21 CFR 314.96(b), we certify that a true copy of this amendment, as submitted to the Office of Generic Drugs, is also being forwarded to the FDA's Baltimore and Kansas City District Offices.

This amendment is submitted in duplicate to ANDA #75-278. In addition, a desk copy has been sent to Ms. Nancy Sager under separate cover. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Marilyn A. Freddy for

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/dn

Enclosures

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
JUN 21 2000
OGD

Department—Fax Numbers
Accounting (304) 285-6403
Administration (304) 599-7284
Business Development (304) 599-7284
Human Resources (304) 598-5406
Information Systems (304) 285-6404
Label Control (800) 848-0463
Legal Services (304) 598-5408
Maintenance & Engineering (304) 598-5411
Medical Unit (304) 598-5445
Purchasing (304) 598-5401
Quality Control (304) 598-5407
Research & Development (304) 285-6409
Sales & Marketing (304) 598-3232

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

June 19, 2000

NEW CORRESP
Nc

Office of Generic Drugs, CDER, FDA
Gary J. Buehler, Acting Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

CMC AMENDMENT
(Environmental Assessment Information Enclosed)

RE: PACLITAXEL INJECTION, 30MG/5ML (6MG/ML)
ANDA #75-278
RESPONSE TO AGENCY CORRESPONDENCE DATED JUNE 15, 2000

Dear Mr. Buehler:

Reference is made to the Abbreviated New Drug Application identified above, which is currently under review, and to the June 15, 2000 letter from the Agency which provided comments pertaining to the review of the environmental assessment (EA) submitted in support of this application. For ease of review, a copy of the Agency's June 15, 2000 letter is enclosed in Attachment 1.

FDA COMMENT 1: The EA should be clarified as to whether the "National Accord for the Protection of Species at Risk" referenced in Appendix 21 is the same as Bill (C-33) referenced in Appendix 2. If not, additional information about this "National Accord" which BC has signed should be provided.

MYLAN RESPONSE: "The National Accord for the Protection of Species at Risk" referenced in Appendix 21 is **not** the same as "Bill (C-33)" referenced in Appendix 2. The National Accord was agreed by the provincial and federal ministers, including those of ———, in October of 1996; Bill (C-33) is still under consideration by the parliament of ——. The policies and regulations of ——— are developed in accord with The National Accord. Please see the pages from the Environment ——— website provided in Attachment 2 for additional information.

FDA COMMENT 2: The statement confirming (section II.A.5) "Past yew bark harvesting within ——— was performed in accordance with then-current regulations relating to the protection of endangered, threatened and vulnerable species should be clarified to state "... with then-current Forest Practices Code and policies, otherwise revised as appropriate).

MYLAN RESPONSE: As requested, the text has been revised accordingly. A replacement page 36 encompassing the revision is provided in Attachment 3.

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
JUN 20 2000
OGD

Department—Fax Numbers
Accounting (304) 285-6403
Administration (304) 599-7284
Business Development (304) 599-7284
Human Resources (304) 598-5406
Information Systems (304) 285-6404
Label Control (800) 848-0463
Legal Services (304) 598-5408
Maintenance & Engineering (304) 598-5411
Medical Unit (304) 598-5445
Purchasing (304) 598-5401
Quality Control (304) 599-[illegible]
Research & Development (304) 28[illegible]
Sales & Marketing (304) 59[illegible]

Pursuant to 21 CFR 314.96(b), we certify that a true copy of this amendment, as submitted to the Office of Generic Drugs, is also being forwarded to the FDA's Baltimore and Kansas City District Offices.

This amendment is submitted in duplicate to ANDA #75-278. In addition, a desk copy has been sent to Ms. Nancy Sager under separate cover. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/dn

Enclosures

APPEARS THIS WAY
ON ORIGINAL

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

JUN 2 2000

Office of Generic Drugs, CDER, FDA
Gary J. Buehler, Acting Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

NEW CORRESP

NC

CMC AMENDMENT
(Environmental Assessment Information Enclosed)

RE: PACLITAXEL INJECTION, 30MG/5ML (6MG/ML)
ANDA #75-278
RESPONSE TO AGENCY CORRESPONDENCE DATED MAY 28, 2000

Dear Mr. Buehler:

Reference is made to the Abbreviated New Drug Application identified above, which is currently under review, and to the May 28, 2000 letter from the Agency which provided comments pertaining to the review of the environmental assessment (EA) submitted in support of this application.

In response to the comments provided in the May 28, 2000 deficiency letter, please find enclosed revised pages 1 through 44 (ANDA pages 13 through 56) which incorporate the requested information (see Attachment 2). For ease of review, a copy of the Agency's May 28, 2000 letter is enclosed in Attachment 1.

Pursuant to 21 CFR 314.96(b), we certify that a true copy of this amendment, as submitted to the Office of Generic Drugs, is also being forwarded to the FDA's Baltimore and Kansas City District Offices.

This amendment is submitted in duplicate to ANDA #75-278. In addition, a desk copy illustrating the changes has been sent to Ms. Nancy Sager under separate cover. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/dn

Enclosures

CENTER FOR DRUG
RECD
JUN 05 2000
CGD
EVALUATION AND RESEARCH

Department—Fax Numbers
Accounting (304) 285-6403
Administration (304) 599-7284
Business Development (304) 599-7284
Human Resources (304) 598-5406
Information Systems (304) 285-6404
Label Control (800) 848-0463
Legal Services (304) 598-5408
Maintenance & Engineering (304) 598-5411
Medical Unit (304) 598-5445
Purchasing (304) 598-5401
Quality Control (304) 598-5407
Research & Development (304) 285-6409
Sales & Marketing (304) 598-3232

6-2-00

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

MAY 12 2000

Office of Generic Drugs, CDER, FDA
Gary J. Buehler, Acting Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ORIG AMENDMENT
N/AM

CMC AMENDMENT
(Environmental Assessment Enclosed)

RE: PACLITAXEL INJECTION, 30MG/5ML (6MG/ML)
ANDA #75-278
RESPONSE TO AGENCY CORRESPONDENCE DATED APRIL 11, 2000

Dear Mr. Buehler:

Reference is made to the Abbreviated New Drug Application identified above, which is currently under review, and to the April 11, 2000 letter from the Agency which provided comments pertaining to the review of the environmental assessment (EA) submitted in support of this application.

In response to the comments provided in the April 11, 2000 deficiency letter, please find enclosed a revised EA which incorporates the requested information (see Attachment 3). This document supercedes the EA submitted in the original application, as well as the EA amendment dated August 18, 1999. For ease of review, a copy of the Agency's April 11, 2000 letter and a summary of the responses are enclosed in Attachments 1 and 2, respectively.

Pursuant to 21 CFR 314.96(b), we certify that a true copy of this amendment, as submitted to the Office of Generic Drugs, is also being forwarded to the FDA's Baltimore and Kansas City District Offices

This amendment is submitted in duplicate to ANDA #75-278. In addition, a desk copy illustrating the changes made is enclosed for Ms. Nancy Sager. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/dn

Enclosures

CENTER FOR DRUG
REC'D
MAY 15 2000
OGD
EVALUATION AND RESEARCH

G:\PROJECT\ANDA\PACLITAXEL\AGENCY-LETTER-DATED-041100.WPD

Department—Fax Numbers
Accounting (304) 285-6403
Administration (304) 599-7284
Business Development (304) 599-7284
Human Resources (304) 598-5406
Information Systems (304) 285-6404
Label Control (800) 848-0463
Legal Services (304) 598-5408
Maintenance & Engineering (304) 598-5411
Medical Unit (304) 598-5445
Purchasing (304) 598-5401
Quality Control (304) 598-5407
Research & Development (304) 285-6409
Sales & Marketing (304) 598-3232

5-17-00

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

MAY 5 2000

ORIG AMENDMENT

Office of Generic Drugs, CDER, FDA
Gary J. Buehler, Acting Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

MINOR AMENDMENT
(CMC INFORMATION ENCLOSED)

RE: PACLITAXEL INJECTION, 30MG/5ML (6MG/ML)
ANDA #75-278
RESPONSE TO AGENCY CORRESPONDENCE DATED MARCH 28, 2000

Dear Mr. Buehler:

Reference is made to the Abbreviated New Drug Application identified above, which is currently under review, and to comments from the Agency pertaining to this application dated March 28, 2000. In response to the Agency's March 28 comments, Mylan wishes to amend this application as follows.

A. CHEMISTRY COMMENTS

FDA COMMENT 1. The drug product release specification for Description and the stability specification for Appearance should be revised to include "free of visible foreign material" to comply with USP 24 <1> Foreign Matter.

MYLAN RESPONSE: Mylan has responded to this comment in previous correspondence. Please refer to Mylan's telephone amendment dated March 24, 2000 for the response to Comment 1.

FDA COMMENT 2. As the drug product will be marketed as a multiple dose vial, USP 24 <51> Antimicrobial Effectiveness Testing data for the drug product should be provided.

MYLAN RESPONSE: Mylan has responded to this comment in previous correspondence. Please refer to Mylan's telephone amendment dated March 24, 2000 for the response to Comment 2.

FDA COMMENT 3. Our laboratory has the following comments regarding the Methods Validation for the drug product:

FDA COMMENT 3a: [redacted]

MAY 08 2000
OGD
EVALUATION AND RESEARCH

Department—Fax Numbers		Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Accounting	(304) 285-6403	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Administration	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Business Development	(304) 599-7284	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
Human Resources	(304) 598-5406	Medical Unit	(304) 598-5445		

MYLAN RESPONSE: Mylan has been informed by Ms. Michelle Dillahunt of the Office of Generic Drugs, in an April 25, 2000 telephone conversation, that this observation has been resolved to the Agency's satisfaction and further information from Mylan is no longer necessary.

FDA COMMENT 3b: The Paclitaxel house standard used for the assays is apparently the same lot as the drug substance analyzed so that an independently derived standard was not used.

MYLAN RESPONSE: Mylan acknowledges that the same lot of Paclitaxel was submitted as drug substance and Paclitaxel House Standard. At the time of the methods validation request (August 20, 1999) each of Mylan's Paclitaxel drug substance lots were beyond the established expiration period. Therefore, Mylan provided a sample of Paclitaxel House Standard lot QC-7L076 for use as both drug substance and House Standard. This lot was originally released according to Mylan's drug substance specifications as lot #7L076. Subsequently, this lot was also released as House Standard lot #QC-7L076 according to Mylan's House Standard specifications which includes the following additional testing: elemental analysis [redacted]
Mylan has established these additional House Standard specifications in order to more completely evaluate the identity, strength, quality and purity of material used as an analytical reference standard.

FDA COMMENT 3c: Absorptivity values for the related compounds are not provided. Results are based on the assumption that related compounds have the same absorptivity as Paclitaxel.

MYLAN RESPONSE: As requested by the Agency, Mylan has determined the absorptivity values of the known impurities and Paclitaxel as follows:

Related Compound	Absorptivity ($L \cdot g^{-1} \cdot mm^{-1}$)
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
Paclitaxel	[redacted]

As described in the November 1997 ICH Guidance "Q3B Impurities in New Drug Products," because the absorptivity values are close, the assumption that the related compounds have the same absorptivity as Paclitaxel is valid.

B. ADDITIONAL DEFICIENCIES

In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

FDA COMMENT 1. Microbiologist review for the January 13, 2000 sterility assurance amendment is pending.

MYLAN RESPONSE: Mylan acknowledges the microbiological review for the January 13, 2000 sterility assurance amendment is pending.

FDA COMMENT 2. Review of the Environmental Assessment amendment of August 18, 1999 is pending.

MYLAN RESPONSE: Currently, the review of the August 18, 1999 Environmental Assessment amendment has been completed and Mylan received comments from the Agency in a letter dated April 11, 2000. The response to the April 11, 2000 comments will be forwarded to the Agency in a separate amendment to this application.

FDA COMMENT 3: The test failure in Item 3.a. above is considered a significant issue. Please contact the Philadelphia District Laboratory, if needed, to resolve this problem.

MYLAN RESPONSE: As previously stated, based on a conversation with Ms. Michelle Dillahunt of your Office, no further action is required for Comment 3.a.

A copy of the Agency correspondence dated March 28, 2000 is included in Attachment A, for the convenience of the reviewer.

Pursuant to 21 CFR 314.96(b), we certify that a true copy of this amendment, as submitted to the Office of Generic Drugs, has been forwarded to the FDA's Baltimore and Kansas City District Offices.

This amendment is submitted in duplicate. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/dn

Enclosures

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

December 29, 2000

Office of Generic Drugs, CDER, FDA
Gary J. Buehler, Acting Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

CMC AMENDMENT

RE: PACLITAXEL INJECTION, 6MG/ML
(30MG/5ML, 100MG/16.7ML and 300MG/50ML)
ANDA #75-278
(Amendment to provide for use of additional yew tree species in manufacture of paclitaxel drug substance.)

Dear Mr. Buehler:

Mylan wishes to amend the above referenced, tentatively approved Abbreviated New Drug Application to include use of the *Taxus yunnanensis* species of the yew tree in the manufacture of the paclitaxel drug substance. This is in addition to the *Taxus brevifolia* species currently provided for in the tentatively approved application.

[redacted] is the [redacted] of the paclitaxel drug substance used by Mylan in the production of paclitaxel injection. Although paclitaxel derived only from *T. brevifolia* was listed for use in the original ANDA submission, [redacted] DMF #[redacted] provides for the manufacture of paclitaxel derived from both *T. brevifolia* and *T. yunnanensis*. This DMF was updated to include the applicable information on *T. yunnanensis* prior to the submission of Mylan's original ANDA for paclitaxel on December 19, 1997. It has therefore been previously reviewed by the Agency in conjunction with Mylan's original ANDA submission, which was tentatively approved on September 19, 2000.

Exhibit batches of paclitaxel injection containing paclitaxel drug substance derived from both of the noted yew tree species have been manufactured by Mylan and submitted in either the original ANDA or the September 29, 2000 amendment. The exhibit lot submitted in the original application (Lot 081I0397) was manufactured with paclitaxel drug substance Lot 96M0051, derived from *T. brevifolia*. The exhibit lot submitted in the September 29, 2000 amendment (Lot 105I0400) was manufactured using material from 4 different paclitaxel drug substance lots derived from *T. brevifolia* or *T. yunnanensis* (Lots 96M0051, 97K0149 and 97M0167 were derived from *T. brevifolia* and Lot 97F0100 was derived from *T. yunnanensis*).

Department—Fax Numbers		Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Accounting	(304) 285-6403	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Administration	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Business Development	(304) 599-7284	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
Human Resources	(304) 598-5406	Medical Unit	(304) 598-5445		

All lots of paclitaxel drug substance, whether derived from *T. brevifolia* or *T. yunnanensis*, must meet the same set of specifications as listed in the ANDA. These specifications have not changed from those submitted in the original ANDA. In addition, there are no differences in either the release or stability specifications for the drug product based on the source of the drug substance. Therefore, the origin of the drug substance, whether it is *T. brevifolia* or *T. yunnanensis*, has no deleterious effect on the finished drug substance or finished drug product.

The purpose of this amendment is to clarify that, in accordance with ——— , DMF ——, the paclitaxel drug substance to be utilized by Mylan in the manufacture of paclitaxel injection may be derived from either *T. brevifolia* or *T. yunnanensis*. No other changes are proposed. The paclitaxel drug substance and drug product release and stability specifications, along with the drug product manufacturing process, remains as previously submitted in this application.

Included in this current amendment is a copy of the Letter of Authorization for DMF ——— submitted in our September 29, 2000 amendment, and an Environmental Assessment pertaining to the harvesting and use of *T. yunnanensis* from China. For the convenience of the reviewer we are also providing a copy of the paclitaxel drug substance specifications which were previously submitted to this application (page 373 of the original ANDA submission and page 571 of the September 29, 2000 amendment), and the Certificates of Analysis for all lots of drug substance previously used in the manufacture of the ANDA exhibit lots of paclitaxel injection. Please refer to the original ANDA submission and our amendments of January 18, 1999 and January 13, March 24, July 25 and September 29, 2000 for supportive data pertaining to the manufacture, testing, and stability of the exhibit lots of paclitaxel injection. As our September 29, 2000 amendment has not yet been reviewed we would like to propose that this current amendment be reviewed in conjunction with our amendment of September 29, 2000.

This amendment is being submitted in duplicate to the above referenced application. As required by 21CFR 314.96(b), we certify that true copies of this amendment, as submitted to the Office of Generic Drugs, have been forwarded to the FDA's Baltimore and Kansas City District Offices.

All correspondence regarding this amendment should be directed to the attention of the undersigned at Mylan Pharmaceuticals Inc., P.O. Box 4310, 781 Chestnut Ridge Road, Morgantown, WV 26504-4310. Telephone and facsimile inquiries may also be directed to the undersigned at telephone number (304) 599-2595, ext. 6600 and/or facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/tlr

Enclosures

cc: Ms. Nancy Sager

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

SEP 29 2000

See Tcon 13! 10/20/00

ORIG AMENDMENT
N/AC

Office of Generic Drugs, CDER, FDA
Gary J. Buehler, Acting Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

GRATUITOUS AMENDMENT
(CMC and Biowaiver Information Enclosed)

RE: PACLITAXEL INJECTION, 30MG/5ML (6MG/ML)
ANDA 75-278
(Amendment to Provide for Additional Package Sizes of 100mg/16.7mL (6mg/mL) and 300mg/50mL (6mg/mL))

Dear Mr. Buehler:

Mylan wishes to amend the above referenced, tentatively approved application to provide for the manufacture and marketing of two additional package sizes of paclitaxel injection [100mg/16.7mL (6mg/mL) and 300mg/50mL (6mg/mL)]. This amendment consists of a total of 9 volumes:

Archival Copy - 3 volumes.
Review Copy - 4 volumes.
Technical Section For Chemistry -3 volumes.
Technical Section For Pharmacokinetics - 1 volume.
Analytical Methods - 2 extra copies; 1 volume each.

The manufacture, packaging and labeling of Paclitaxel Injection, 100mg/16.7mL (6mg/mL) and 300mg/50mL (6mg/mL) will be performed by Pharmaceutical Service, University of Iowa, College of Pharmacy, 20 Pharmacy Building, Iowa City, IA 52242-1112, following procedures similar to the 30mg/5mL (6mg/mL) package size as currently provided for in ANDA 75-278, which was tentatively approved on September 19, 2000. All three package sizes of paclitaxel injection are filled from a common solution containing 6mg of paclitaxel per mL.

As an aid to the reviewer, this amendment has been assembled according to the traditional ANDA format. This amendment is being submitted in duplicate to the above referenced application. As required by 21 CFR 314.96(b), we certify that true copies of the technical sections of this application, as submitted to the Office of Generic Drugs, has been forwarded to the FDA's Baltimore and Kansas City District Offices.

All correspondence regarding this application should be directed to the attention of the undersigned at Mylan Pharmaceuticals Inc., P.O. Box 4310, 781 Chestnut Ridge Road, Morgantown WV, 26504-4310. Telephone and facsimile inquiries may also be directed to the undersigned at telephone number (304) 599-2595, extension 6600 and/or facsimile number (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/dn

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
OCT - 3 2000
OGD

10-2-00

Department—Fax Numbers		Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Accounting	(304) 285-6403	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Administration	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Business Development	(304) 599-7284	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
Human Resources	(304) 598-5406	Medical Unit	(304) 598-5445		

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

JAN 13 2000

Office of Generic Drugs, CDER, FDA
Douglas L. Sporn, Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

[illegible] AMENDMENT
AS

STERILITY ASSURANCE AMENDMENT

RE: PACLITAXEL INJECTION, 30MG/5ML (6MG/ML)
ANDA #75-278
RESPONSE TO AGENCY CORRESPONDENCE DATED JUNE 25, 1999

Dear Mr. Sporn:

Reference is made to the Abbreviated New Drug Application identified above, which is currently under review, and to the microbiology comments from the Agency pertaining to this application which were provided to Mylan in a facsimile dated June 25, 1999. In response to the Agency's June 25 comments, Mylan wishes to amend this application as follows.

A. REGARDING MICROBIOLOGY ISSUES

FDA COMMENT 1.

MYLAN RESPONSE:

Department—Fax Numbers		Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Accounting	(304) 285-6403	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Administration	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Business Development	(304) 599-7284	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
Human Resources	(304) 598-5406	Medical Unit	(304) 598-5445		

Redacted 10

pages of trade secret and/or confidential commercial information

This amendment is submitted in duplicate. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/dn

Enclosures

APPEARS THIS WAY
ON ORIGINAL

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

revised exclusivity statement OK
fsl 11/16/99
fsl

NEW CORRESP
NC

November 9, 1999

Office of Generic Drugs, CDER, FDA
Douglas L. Sporn, Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

PATENT AMENDMENT

RE: PACLITAXEL INJECTION 30mg/5mL (6mg/mL)
ANDA NO. 75-278

Dear Mr. Sporn:

Reference is made to the Abbreviated New Drug Application identified above, which is currently under review, and to the patent and exclusivity information associated with this application.

This amendment to the referenced application is being submitted to address exclusivity information which was listed in the "Orange Book" subsequent to submission of our original application. Should you have any questions regarding this amendment, please contact the undersigned by telephone at (304) 599-2595, ext. 6600 or by facsimile at (304) 285-6407.

This amendment is submitted in duplicate.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/tlr

Enclosures

NOV 10 1999
CDD
DRUG EVALUATION AND RESEARCH

Department—Fax Numbers
Accounting (304) 285-6403
Administration (304) 599-7284
Business Development (304) 599-7284
Human Resources (304) 598-5406
Information Systems (304) 285-6404
Label Control (800) 848-0463
Legal Services (304) 598-5408
Maintenance & Engineering (304) 598-5411
Medical Unit (304) 598-5445
Purchasing (304) 598-5401
Quality Control (304) 598-5407
Research & Development (304) 285-6
Sales & Marketing (304) 598-3

fsl 11-9-99

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

AUG 18 1999

Office of Generic Drugs, CDER, FDA
Douglas L. Sporn, Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

NEW CORRESP
NC

CMC AMENDMENT
(Environmental Assessment Enclosed)

RE: PACLITAXEL INJECTION, 30MG/5ML (6MG/ML)
ANDA #75-278
RESPONSE TO AGENCY CORRESPONDENCE DATED NOVEMBER 24, 1998

Dear Mr. Sporn:

Reference is made to the Abbreviated New Drug Application identified above, which is currently under review, and to the November 24, 1998 letter from the Agency which provided comments pertaining to the review of the environmental assessment (EA) submitted in support of this application.

In response to the comments provided in the November 24, 1998 deficiency letter, please find enclosed a revised EA which incorporates the requested information (see Attachment 1). This document supercedes the EA submitted in the original application. For ease of review, an additional copy of the revised EA, which illustrates the changes made, is provided in Attachment 2. Information removed from the original EA is designated by a line drawn through the deleted text while new information is typed in red. For ease of review, a copy of the Agency's November 24, 1998 letter is enclosed in Attachment 3.

Pursuant to 21 CFR 314.96(b), we certify that a true copy of this amendment, as submitted to the Office of Generic Drugs, is also being forwarded to the FDA's Baltimore and Kansas City District Offices.

This amendment is submitted in duplicate to ANDA #75-278. In addition, a desk copy is enclosed for Ms. Nancy Sager, at her request. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/tlr

enclosures

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
AUG 19 1999
OGD

G:\PROJECT\ANDA\PACLITAXEL\AGENCY-LETTER-DATED-112498.WPD

Department—Fax Numbers		Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Accounting	(304) 285-6403	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Administration	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Business Development	(304) 599-7284	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
Human Resources	(304) 598-5406	Medical Unit	(304) 598-5445		

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

May 18, 1999

NEW CORRESP
/S/
5/21/99

Office of Generic Drugs, CDER, FDA
Douglas L. Sporn, Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RE: PACLITAXEL INJECTION, 30MG/5ML (6MG/ML)
ANDA #75-278

Dear Mr. Sporn:

Reference is made to the Abbreviated New Drug Application identified above, which is currently under review, and to the Agency's comments pertaining to the Environmental Assessment submitted in support of this application, which were forwarded to Mylan by facsimile on November 24, 1998.

This letter provides authorization to the Food and Drug Administration to interact directly with [redacted] with regard to issues relating to the Environmental Assessment (EA) for Mylan's ANDA 75-278. [redacted] was also listed on page 1313 of the original ANDA submission as the contact person for any questions regarding the EA for this application.

Should you have any questions regarding this authorization please contact the undersigned by telephone at (304) 599-2595, ext. 6600 or by facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/tlr

cc: [redacted] (via facsimile)

Ms. Nancy Sager (via facsimile)
Office of Pharmaceutical Science, FDA

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
MAY 19 1999
OGD

5/20/99

G:\PROJECT\ANDA\PACLITAXEL\LETTER-TO-AGENCY-051898.WPD

Department—Fax Numbers		Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Accounting	(304) 285-6403	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Administration	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Business Development	(304) 599-7284	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
Human Resources	(304) 598-5406	Medical Unit	(304) 598-5445		

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

April 23, 1999

NDA ORIG AMENDMENT
N/AM

Office of Generic Drugs, CDER, FDA
Douglas L. Sporn, Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

CMC AMENDMENT
(STERILITY ASSURANCE INFORMATION INCLUDED)

Re: PACLITAXEL INJECTION, 30MG/5ML (6MG/ML)
ANDA #75-278

Dear Mr. Sporn:

Reference is made to the Abbreviated New Drug Application identified above, which is currently under review. Mylan wishes to amend the application with the following additional sterility assurance information:

[redacted]

[redacted]

3. Summary of Validation Studies

The components and equipment are sterilized using previously validated processes as established by The University of Iowa Division of Pharmaceutical Service. Summaries of the validation studies for the [redacted] are provided in Attachment 3. Updated information regarding requalification studies is addressed in the following comment.

RECEIVED
APR 28 1999
GENERIC DRUGS

Department—Fax Numbers					
Accounting	(304) 285-6403	Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Administration	(304) 599-7284	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Business Development	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Human Resources	(304) 598-5406	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
		Medical Unit	(304) 598-5445		

Pursuant to 21 CFR 314.96(b), we certify that a true copy of this amendment, as submitted to the Office of Generic Drugs has been forwarded to the FDA's Baltimore District Office and the FDA's Kansas City District Office.

This amendment is submitted in duplicate. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599,2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

MAF/tlr

enclosures

APPEARS THIS WAY
ON ORIGINAL

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

JAN 18 1999

Office of Generic Drugs, CDER, FDA
Douglas L. Sporn, Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

NDA ORIG AMENDMENT
N/AC

MAJOR AMENDMENT
(CMC AND LABELING INFORMATION ENCLOSED)

RE: PACLITAXEL INJECTION, 6MG/ML, 5ML VIAL
ANDA #75-278
RESPONSE TO AGENCY CORRESPONDENCE DATED JULY 27, 1998

Dear Mr. Sporn:

Reference is made to the Abbreviated New Drug Application identified above, which is currently under review, and to the comments from the Agency which were provided to Mylan in a facsimile dated July 27, 1998. In response to the Agency's July 27, 1998 comments Mylan wishes to amend this application as follows.

A. REGARDING CHEMISTRY ISSUES

FDA COMMENT 1. Your cover letter dated December 19, 1997 states that "All operations in the manufacture, packaging and labeling of the drug product are performed by Mylan Pharmaceuticals, Inc. ..." Per pages 506, 507, 509, and 521 of the ANDA, the University of Iowa's Pharmaceutical Service is the contract organization responsible for manufacturing, processing, packaging and labeling the finished dosage form. Please clarify these statements.

MYLAN RESPONSE: Mylan's submitted cover letter dated December 19, 1997 inadvertently states that "All operations and in the manufacture, packaging and labeling of the drug are performed by Mylan Pharmaceuticals, Inc...." Mylan acknowledges that The University of Iowa, Pharmaceutical Service is responsible for the manufacturing, packaging and labeling of the finished dosage form.

FDA COMMENT 2. The [redacted] should be included in the Components and Composition Statement.

MYLAN RESPONSE: As requested, Mylan has added [redacted] to the Qualitative Composition [redacted] The revised Qualitative Composition Statement can be found in Attachment A.

RECEIVED

G:\PROJECT\ANDA\PACLITAXEL\CMC-LABELING-AGENCY-LETTER-DATED-7-27-98.WPD

JAN 19 1999

GENERIC DRUGS

Department—Fax Numbers					
Accounting	(304) 285-6403	Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Administration	(304) 599-7284	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Business Development	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Human Resources	(304) 598-5406	Maintenance & Engineering	(304) 598-5445	Sales & Marketing	(304) 598-3232
		Medical Unit	(304) 598-5445		

Redacted 4

pages of trade secret and/or confidential commercial information

FDA COMMENT 2. The Office of Compliance will evaluate cGMP compliance status of facilities involved in the manufacture/testing of the subject drug product. A satisfactory evaluation is required for approval.

MYLAN RESPONSE: Mylan acknowledges that the Office of Compliance will evaluate the cGMP compliance status of the facilities involved in the manufacture/testing of the drug product. In addition, Mylan is aware that a satisfactory evaluation is required prior to approval.

FDA COMMENT 3. The drug product is not listed in USP 23. Methods Validation will be requested following resolution of the release specifications and testing issues.

MYLAN RESPONSE: Mylan acknowledges that the drug product is not listed in the USP 23 and that a methods validation will be requested following resolution of the release specifications and testing issues.

FDA COMMENT 4. Review of your Environmental Assessment is pending.

MYLAN RESPONSE: Mylan acknowledges that the review of the Environmental Assessment has been completed. Comments from the Agency pertaining to this review were forwarded by facsimile and received by Mylan on November 24, 1998. Mylan's response to these comments will be addressed in a separate amendment to this application.

FDA COMMENT 5. Your response must also address the labeling deficiencies.

MYLAN RESPONSE: As noted below, this response addresses the labeling deficiencies as listed in the July 27, 1998 correspondence from OGD's Division of Labeling and Program Support.

C. REGARDING LABELING ISSUES FROM THE AGENCY'S JULY 27, 1998 CORRESPONDENCE

MYLAN RESPONSE: Attachment O contains twelve (12) copies of the following final printed vial label, carton, and insert for Paclitaxel Injection, 30mg/5mL (6mg/mL):

VIAL LABEL

Code RM1022WW - Multiple Dose Vial, 5mL

CARTON

Code M1022-34-01C:R1 - One Multiple Dose Vial, 5mL

INSERT

Code PLTL:R1, Revised October 1998

The enclosed labeling incorporates the revisions requested in the Agency's July 27, 1998 correspondence. A copy of this correspondence is provided in Attachment K for the convenience of the reviewer.

In order to facilitate the review of this labeling, Attachments L, M, and N contain side-by-side comparisons of the final printed vial label, carton, and insert (respectively) to those previously submitted. It is noted that prior to approval of this application, the Agency reserves the right to request further changes in the Mylan labeling based upon the changes in the approved labeling of the listed drug or upon further review of the application.

Pursuant to 21 CFR 314.96(b), we certify that a true copy of the technical sections of this amendment, as submitted to the Office of Generic Drugs, has been forwarded to the FDA's Baltimore District Office.

This amendment is submitted in duplicate. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/tlr

enclosures

APPEARS THIS WAY
ON ORIGINAL

NDA ORIG AMENDMENT
AB

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

AUG 26 1998

Office of Generic Drugs, CDER, FDA
Douglas L. Sporn, Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

BIOEQUIVALENCE AMENDMENT

RE: PACLITAXEL INJECTION, 6MG/ML
ANDA #75-278
RESPONSE TO AGENCY CORRESPONDENCE DATED JULY 27, 1998

Dear Mr. Sporn:

Reference is made to the ANDA identified above, which is currently under review, and to the comment from Office of Generic Drug's Division of Bioequivalence which was forwarded to Mylan in a correspondence dated July 27, 1998. In response to the July 27 correspondence, Mylan wishes to amend the application as follows:

A. REGARDING BIOEQUIVALENCE ISSUES:

FDA COMMENT 1. The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

MYLAN RESPONSE: Mylan acknowledges that the Division of Bioequivalence has completed its review and has no further questions at this time. It is acknowledged and understood that the bioequivalency comments expressed in the letter dated July 27, 1998 are preliminary and may be revised after review of the entire application.

For your reference, a copy of the Agency correspondence dated July 27, 1998 is enclosed. Responses to the chemistry, manufacturing and controls comments contained in the June 27 correspondence, along with requested revisions to the proposed product labeling, will be submitted in a separate amendment to this application.

This amendment is submitted in duplicate. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/tlr

enclosures

RECEIVED
AUG 27 1998
GENERIC DRUGS

Department—Fax Numbers
Accounting (304) 285-6403
Administration (304) 599-7284
Business Development (304) 599-7284
Human Resources (304) 598-5406
Information Systems (304) 285-6404
Label Control (800) 848-0463
Legal Services (304) 598-5408
Maintenance & Engineering (304) 598-5411
Medical Unit (304) 598-5445
Purchasing (304) 598-5401
Quality Control (304) 598-5407
Research & Development (304) 285-6409
Sales & Marketing (304) 598-3232

Bristol-Myers Squibb Company
Legal Division
P.O. Box 4000 Princeton, NJ 08543-4000
609 252-4956 Fax: 609 252-4526

NEW CORRESP
NC

Thomas R. Savitsky
Assistant Counsel
Patents

April 29, 1998

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Generic Drugs, HFD-600
7500 Standish Place, Room 150
Rockville, Maryland 20855

Re: Bristol-Myers Squibb Company v. Mylan Pharmaceuticals, Inc.

Gentlemen:

ANDA 75-278, filed by Mylan Pharmaceuticals, Inc. ("Mylan"), is directed to its paclitaxel injection generic version of Bristol-Myers Squibb's ("BMS") Taxol® and contains a certification under 21 U.S.C. §355(j)(2)(A)(vii)(IV) asserting that United States Patents Nos. 5,641,803 and 5,670,537 are invalid, unenforceable or will not be infringed. Notice of the certification was received by BMS by certified mail on February 17, 1998.

This letter is to advise the Food and Drug Administration ("FDA") that on April 2, 1998, BMS filed a lawsuit against Mylan in federal district court in Newark, New Jersey, alleging infringement of United States Patents Nos. 5,641,803 and 5,670,537. A copy of the complaint is enclosed (Civil Action No. 98-1488 (WHW), United States District Court, District of New Jersey).

BMS has filed its action within 45 days of receipt of notice of the certification, and pursuant to the Federal Food, Drug and Cosmetic Act ("FFDCA"), §505(j)(4)(B)(iii), the FDA cannot approve ANDA 75-278 until "the expiration of the thirty (30) month period beginning on the date of the receipt of the notice...or such shorter or longer period as the court may order..."

Should any questions concerning this matter arise, please feel free to contact me directly.

Very truly yours,

Thomas R. Savitsky

Thomas R. Savitsky

TRS:mk

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

NEW CORRESP.
NC

MAR 23 1998

Office of Generic Drugs, CDER, FDA
Douglas L. Sporn, Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

PATENT AMENDMENT

RE: PACLITAXEL INJECTION, 30MG/5ML (6MG/ML)
ANDA #75-278

Dear Mr. Sporn:

This amendment to the ANDA identified above provides documentation of receipt of the notice required by 21 CFR 314.95(a), as it pertains to the Paragraph IV patent certification submitted in our application. The attached letter from our Legal Department provides the necessary details pertaining to the enclosed documentation.

This amendment is submitted in duplicate. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Executive Director
Regulatory Affairs

FRS/tlm

enclosures

RECEIVED
MAR 24 1998
GENERIC DRUGS

R:\ANDA\PACLITAXEL\PATENT-AMENDMENT_032398.WPD

Department—Fax Numbers		Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Accounting	(304) 285-6403	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Administration	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Business Development	(304) 599-7284	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
Human Resources	(304) 598-5406	Medical Unit	(304) 598-5445		

ANDA 75-278

Mylan Pharmaceuticals Inc.
Attention: Frank R. Sisto
781 Chestnut Ridge Road
P.O. Box 4310
Morgantown, WV 26504-4310

FEB 5 1998

Dear Sir:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is also made to the telephone conversation dated January 14, 1998 and your correspondence dated January 21, 1998.

NAME OF DRUG: Paclitaxel Injection, 6 mg/mL, 5 mL vial

DATE OF APPLICATION: December 19, 1997

DATE (RECEIVED) ACCEPTABLE FOR FILING: December 22, 1997

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Sheila O'Keefe
Project Manager
(301) 827-5848

Sincerely yours,

/S/

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

505(j)(1)(A) OK
11/26/98
/S/

ORIG AMENDMENT
10/AA

January 21, 1998

Office of Generic Drugs, CDER, FDA
Douglas L. Sporn, Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

NEW CORRESPONDENCE

RE: PACLITAXEL INJECTION, 30MG/5ML
ANDA #75-278
RESPONSE TO JANUARY 15, 1998 TELEPHONE REQUEST

Dear Mr. Sporn:

Reference is made to the Abbreviated New Drug Application identified above, which is currently undergoing administrative regulatory review, and to a request from the Office of Generic Drugs for additional information, which was received at Mylan by telephone on January 15, 1998. In response to OGD's request we are providing the following information:

1) Revised patent certification for Paclitaxel Injection, 30mg/5mL (Attachment A). This certification addresses all 3 patents listed in the publication entitled "Approved Drug Products with Therapeutic Equivalence Evaluations" (17th Edition through Cumulative Supplement 9) and supercedes that submitted on December 19, 1997, in Section III of the original application.

2) Draft vial and carton labeling for Mylan's Paclitaxel Injection, 30mg/5mL, which has been annotated against the vial and carton labeling of the reference listed drug, Taxol®. Two copies of the annotated vial and carton labeling are provided in Attachment B (one copy each for Section IV and V of the application) and one copy of the innovator's vial and carton labeling for Taxol® is provided (Attachment C) for inclusion in Section V of the application.

Based on a telephone conversation with Mr. Jerry Phillips, it was not considered necessary to annotate our package insert labeling against the Taxol® package insert labeling. We annotated our package insert against the Labeling Guidance for Paclitaxel Injection, which was issued by the Office of Generic Drugs in September 1997. This labeling guidance is based on the approved labeling for Taxol® (NDA 20-262/S-022; Approved August 14, 1997; Revised July 25, 1997).

RECEIVED
JAN 29 1998
GENERIC DRUGS

Department—Fax Numbers		Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Accounting	(304) 285-6403	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Administration	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Business Development	(304) 599-7284	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
Human Resources	(304) 598-5406	Medical Unit	(304) 598-5445		

This submission is provided in duplicate. Should you have any questions regarding this submission please contact the undersigned by phone at (304) 599-2595, ext. 6600 or by facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Executive Director
Regulatory Affairs

FRS/tlm

enclosures

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

Office of Generic Drugs, CDER, FDA
Douglas L. Sporn, Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

JAN 21 [illegible]

RE: PACLITAXEL INJECTION 30mg/5mL (6mg/mL)
U.S. PATENT NOs. 5,641,803 and 5,670,537
PARAGRAPH IV CERTIFICATION

Dear Mr. Sporn:

Pursuant to Section 505(j)(2)(A)(vii) of the Federal Food, Drug and Cosmetic Act ("FFDCA"), Mylan certifies that in its opinion and to the best of its knowledge, U.S. Patent Nos. 5,641,803 and 5,670,537 are invalid, unenforceable or will not be infringed by the manufacture, use, sale, offer for sale, or importation of Paclitaxel Injection 30mg/5mL (6mg/mL), for which this application is submitted.

Mylan further certifies that according to the patent information published by the FDA in that document entitled "Approved Drug Products with Therapeutic Equivalence Evaluations" 17th Edition through the ninth Cumulative Supplement thereto, the referenced product has use patent coverage for the treatment of metastic carcinoma of ovary after first-line failure or subsequent chemotherapy, treatment of breast cancer after failure of combination chemotherapy for metastatic disease and [redacted] (U.S. Patent Nos. 5,641,803 and 5,670,537). In addition, U.S. Patent No. 5,496,804 is a patent which claims a method of use, that is not a use for which Mylan is currently seeking approval. (Said use covers the use of Taxol in combination with G-CSF for [redacted]. Therefore, pursuant to Section 355 (j)(2)(A)(viii) of the FFDCA, it is not necessary for Mylan to submit information with respect to the 5,496,804 patent.

Mylan further certifies that according to the exclusivity information published by the FDA in that document entitled "Approved Drug Products with Therapeutic Equivalence Evaluations" 17th Edition through the ninth Cumulative Supplement thereto, the referenced product is covered by the following exclusivity provisions: [redacted] which expires August 4, 2000, for which Mylan is not currently seeking approval; and Orphan Drug Exclusivity for the [redacted] which expires August 4, 2004, for which Mylan is not currently seeking approval. In addition, exclusivity provisions have expired for the following: NCE exclusivity which expired December 29,1997; Indication exclusivity for the treatment of metastatic carcinoma of the breast after failure of first-line or subsequent chemotherapy which expired April 13, 1997; and New Dosing Schedule exclusivity for ovarian cancer, for which the recommended regimen is 135mg/m^2 or 175mg/m^2 intravenously over three hours every three weeks, which expired June 22, 1997.

Mylan is currently seeking approval only for the indications related to the treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy, and after failure of first-line or subsequent chemotherapy for the treatment of metastatic carcinoma of the ovary.

In addition, pursuant to Section 505(j)(2)(B)(i) of the Federal Food, Drug and Cosmetic Act, Mylan will provide notice to each owner of the patents which are the subject of the certification, or their representatives, and also to the holder of the approved application for the listed drug claimed by said patents. Said notice will comply with the requirements set forth in 21 CFR 314.95(c) with respect to the content of the notice. Said notice will be provided as set forth in 21 CFR 314.95(b), when Mylan receives from FDA an acknowledgment letter stating that this ANDA is sufficiently complete to permit a substantive review. Further, Mylan commits to amend this application pursuant to 21 CFR 314.95(e) to provide certification that notifications sent to the patent owner and application holder have been received.

Mylan will market its Paclitaxel Injection 30mg/5mL (6mg/mL) upon approval of this application and resolution of the validity, enforcement, or infringement of patent numbers 5,641,803 and 5,670,537.

Sincerely,

Dawn J. Beto, Esq.
Corporate Counsel

DJB/dc

APPEARS THIS WAY
ON ORIGINAL

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

Office of Generic Drugs, CDER, FDA
Douglas L. Sporn, Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

DEC 19 1997

RE: PACLITAXEL INJECTION 30mg/5mL (6mg/mL)
U.S. PATENT NO. 5,641,803
PARAGRAPH IV CERTIFICATION

Dear Mr. Sporn:

Pursuant to Section 505(j)(2)(A)(vii) of the Federal Food, Drug and Cosmetic Act, Mylan certifies that in its opinion and to the best of its knowledge, U.S. Patent 5,641,803 is invalid, unenforceable or will not be infringed by the manufacture, use, sale, offer for sale, or importation of Paclitaxel Injection 30mg/5mL (6mg/mL), for which this application is submitted.

Mylan further certifies that according to the exclusivity information published by the FDA in that document entitled "Approved Drug Products with Therapeutic Equivalence Evaluations" 17th Edition through the eighth Cumulative Supplement thereto, the referenced product is covered by the following exclusivity provisions: NCE exclusivity which expires December 29 1997; Use exclusivity for the treatment of metastic carcinoma of ovary after first-line failure or subsequent chemotherapy, treatment of breast cancer after failure of combination chemotherapy for metastatic disease and [redacted] Indication [redacted], which expires August 4, 2000; and Orphan Drug Exclusivity for the [redacted] which expires August 4, 2003. Mylan is currently seeking approval only for the indications related to the treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy, and after failure of first-line or subsequent chemotherapy for the treatment of metastatic carcinoma of the ovary.

In addition, pursuant to Section 505(j)(2)(B)(i) of the Federal Food, Drug and Cosmetic Act, Mylan will provide notice to each owner of the patent which is the subject of the certification, or their representatives, and also to the holder of the approved application for the listed drug claimed by said patent. Said notice will comply with the requirements set forth in 21 CFR 314.95(c) with respect to the content of the notice. Said notice will be provided as set forth in 21 CFR 314.95(b), when Mylan receives from FDA an acknowledgment letter stating that this ANDA is sufficiently complete to permit a substantive review. Further, Mylan commits to amend this application pursuant to 21 CFR 314.95(e) to provide certification that notifications sent to the patent owner and application holder have been received.

Department—Fax Numbers
Accounting (304) 285-6403
Administration (304) 599-7284
Business Development (304) 599-7284
Human Resources (304) 598-5406
Information Systems (304) 285-6404
Label Control (800) 848-0463
Legal Services (304) 598-5408
Maintenance & Engineering (304) 598-5411
Medical Unit (304) 598-5445
Purchasing (304) 598-5401
Quality Control (304) 598-5407
Research & Development (304) 285-6409
Sales & Marketing (304) 598-3232

Mylan will market its Paclitaxel Injection 30mg/5mL (6mg/mL) upon approval of this application and resolution of the validity, enforcement, or infringement of patent number 5,641,803.

Sincerely,

Dawn J. Beto, Esq.
Corporate Counsel

DJB/dc

APPEARS THIS WAY
ON ORIGINAL

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

DEC 19 1997

Office of Generic Drugs, CDER, FDA
Douglas L. Sporn, Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RE: PACLITAXEL INJECTION 30MG/5ML (6MG/ML)

Dear Mr. Sporn:

Mylan certifies the following:

1) The conditions of use prescribed, recommended or suggested in the labeling proposed by Mylan for this product, Paclitaxel Injection, have been previously approved for the listed drug. This certification is based upon a comparison of Mylan's proposed labeling to that currently approved for the reference listed drug;

2) The active ingredient (Paclitaxel) contained in the proposed drug product is the same as that of the reference listed drug;

3) The route of administration, dosage form and strength of the proposed drug product are the same as those for the reference listed drug.

Please see attached Table of Comparison and Annotated Labeling illustrating the foregoing.

Sincerely,

Frank R. Sisto
Executive Director
Regulatory Affairs

FRS/tlm

enclosures

Department—Fax Numbers
Accounting (304) 285-6403
Administration (304) 599-7284
Business Development (304) 599-7284
Human Resources (304) 598-5406
Information Systems (304) 285-6404
Label Control (800) 848-0463
Legal Services (304) 598-5408
Maintenance & Engineering (304) 598-5411
Medical Unit (304) 598-5445
Purchasing (304) 598-5401
Quality Control (304) 598-5407
Research & Development (304) 285-6409
Sales & Marketing (304) 598-3232

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

DEC 19 1997

BIOEQUIVALENCE DATA ENCLOSED
(BIOWAIVER)

Office of Generic Drugs, CDER, FDA
Douglas L. Sporn Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RE: PACLITAXEL INJECTION 30MG/5ML (6MG/ML)

Dear Mr. Sporn:

Pursuant to section 505(j) of the Federal Food, Drug and Cosmetic Act and 21 CFR § 314.92 and 314.94, we submit the enclosed abbreviated new drug application for:

Proprietary Name: None
Established Name: Paclitaxel Injection
This application consists of a total of 9 volumes.
- Archival Copy - 3 volumes.
- Review Copy - 4 volumes.
  - Technical Section For Chemistry -3 volumes.
  - Technical Section For Pharmacokinetics - 1 volumes.
- Analytical Methods - 2 extra copies; 1 volume each.

This application provides for the manufacture of Paclitaxel Injection 30mg/5mL (6mg/5mL) All operations in the manufacture, packaging, and labeling of the drug product are performed by Mylan Pharmaceuticals Inc., 781 Chestnut Ridge Road, Morgantown, WV 26505-2730.

As required by 21 CFR 314.94(d)(5) we certify that a true copy of the technical sections of this application, as submitted to the Office of Generic Drugs, has been forwarded to the FDA's Baltimore District Office. The following Table of Contents and Reader's Guide detail the documentation submitted in support of this application.

All correspondence regarding this application should be directed to the attention of the undersigned at Mylan Pharmaceuticals Inc., P.O. Box 4310, 781 Chestnut Ridge Road, Morgantown WV, 26504-4310, or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Executive Director
Regulatory Affairs

FRS/tlm

RECEIVED
DEC 22 1997
GENERIC DRUGS

Department—Fax Numbers

Accounting	(304) 285-6403	Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Administration	(304) 599-7284	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Business Development	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Human Resources	(304) 598-5406	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
		Medical Unit	(304) 598-5445		