

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-759

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

PATENT INFORMATION

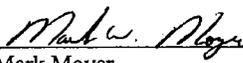
Central Document Room
Center for Drug Evaluation and Research
Food and Drug Administration
Park Building, Room 2-14
12420 Parklawn Drive
Rockville, Maryland 20857

Re: Patent Information for ELOXATIN™ (oxaliplatin)
New Drug Application 21-759

Under the provisions of 21 U.S.C. 355(b)(1) and 21 CFR 314.53, submitted herewith is the information on each patent that claims the drug, drug product, or a method of using said drug product that is the subject of the above-identified new drug application and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use or sale of the drug product.

The patent information is submitted on FDA form 3542A, in duplicate and concurrently with submission of the subject application.

Date: 3/9/04



Mark Moyer
Vice President, Drug Regulatory Affairs

Sanofi-Synthelabo Research

A division of Sanofi-Synthelabo Inc.

9 Great Valley Parkway, Malvern, PA 19355 - Tel.: (610) 889-8600

EXCLUSIVITY SUMMARY FOR NDA # 21-759 SUPPL # _____

Trade Name Eloxatin Injection Generic Name oxaliplatin

Applicant Name Sanofi-Synthelabo, Inc. HFD # 150

Approval Date If Known January 31, 2005 (PDUFA goal date) _____

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following question about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?
YES / / NO / /

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

505(b)(1)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES / / NO / /

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES / / NO / /

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

e) Has pediatric exclusivity been granted for this Active Moiety?

YES /___/ NO /_X_/

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES /___/ NO /_X_/

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /_X_/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# 21-492 Eloxatin (oxaliplatin) for Injection

NDA# _____

NDA# _____

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# _____

NDA# _____

NDA# _____

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.) IF "YES" GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete

remainder of summary for that investigation.

YES /___/ NO /_X_/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /___/ NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /___/ NO /___/

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /___/ NO /___/

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ NO /___/

If yes, explain:

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1 !

IND # _____ YES /___/ ! NO /___/ Explain: _____

Investigation #2

IND # _____ YES /___/ ! NO /___/ Explain: _____

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1

YES /___/ Explain _____ ! NO /___/ Explain _____

Investigation #2

YES /___/ Explain _____ ! NO /___/ Explain _____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /___/

If yes, explain: _____

Signature Date
Christy Cottrell, Consumer Safety Officer

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/s/

Christy Cottrell
2/16/05 10:33:26 AM

Richard Pazdur
2/17/05 07:27:03 AM

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA #: 21-759 Supplement Type (e.g. SE5): _____ Supplement Number: _____

Stamp Date: March 31, 2004 Action Date: January 31, 2005 (PDUFA goal date)

HFD-150 _____ Trade and generic names/dosage form: Eloxatin (oxaliplatin) Injection

Applicant: Sanofi-Synthelabo, Inc. Therapeutic Class: 5 S

Indication(s) previously approved: Eloxatin, used in combination with 5-FU/LV, is indicated for the treatment of advanced carcinoma of the colon or rectum.

Each **approved** indication must have pediatric studies: **Completed, Deferred, and/or Waived.**

Number of indications for this application(s): 0 - This NDA is for a new formulation only - Indications are unchanged

Indication #1: _____

Is there a full waiver for this indication (check one)?

Yes: Please proceed to Section A.

No: Please check all that apply: Partial Waiver Deferred Completed

NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Other: _____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for partial waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed

Other: _____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Christy Cottrell
Consumer Safety Officer

cc: NDA 21-759
HFD-960/ Grace Carmouze

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE DIVISION OF PEDIATRIC DRUG DEVELOPMENT, HFD-960, 301-594-7337.

(revised 12-22-03)

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/s/

Christy Cottrell
6/9/04 03:41:23 PM

Module 1.3.2 DEBARMENT CERTIFICATION

Sanofi-Synthelabo hereby certifies that they did not and will not use in any capacity the services of any person debarred under subsection (a) or (b) [section 306(a) or (b)] of the FD&C Act in connection with this application.



Mark Moyer
Vice President
Drug Regulatory Affairs
Oncology Projects
Sanofi-Synthelabo

FAX

FOOD AND DRUG ADMINISTRATION
DIVISION OF ONCOLOGY DRUG PRODUCTS
Center for Drug Evaluation and Research, HFD-150
5600 Fishers Lane, Rockville, MD 20857



To: Mark Moyer

From: Christy Cottrell

Fax: (610) 889-6993

Fax: (301) 594-0499

Phone: (610) 889-6417

Phone: (301) 594-5761

Pages, including cover sheet: 1

Date: 12-16-04

Re: NDA 21-759 for Eloxatin [REDACTED] (oxaliplatin) Injection

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination or other action based on the content of the communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us at the above address by mail. Thank you.

Mark,

Please refer to your pending NDA 21-759 for Eloxatin [REDACTED] (oxaliplatin) Injection. Included in this fax is the final recommendation from DMETS regarding your proposed tradename, Eloxatin [REDACTED]

1. DMETS does not recommend the use of the modifier [REDACTED] or any modifier, for this formulation of Eloxatin. DMETS recommends revising the proposed proprietary name from Eloxatin [REDACTED] to Eloxatin Injection.
2. DMETS does not have any container label and/or labeling comments at this time.

If you have any questions, feel free to call me at (301) 594-5761.

Thanks,

Christy Cottrell

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/s/

Christy Cottrell
12/16/04 11:27:29 AM
CSO

8 Page(s) Withheld

Trade Secret / Confidential

Draft Labeling

Deliberative Process

3 Page(s) Withheld

Trade Secret / Confidential

Draft Labeling

Deliberative Process

Withheld Track Number: Administrative-2



FILING COMMUNICATION

NDA 21-759

Sanofi-Synthelabo, Inc.
9 Great Valley Parkway
P.O. Box 3026
Malvern, PA 19355

Attention: Mark Moyer
Vice President, Drug Regulatory Affairs

Dear Mr. Moyer:

Please refer to your March 31, 2004, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Eloxatin (oxaliplatin) Injection.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application has been filed under section 505(b) of the Act on May 30, 2004, in accordance with 21 CFR 314.101(a).

At this time, we have not identified any potential filing review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review.

If you have any questions, call Christy Cottrell, Consumer Safety Officer, at (301) 594-5761.

Sincerely,

{See appended electronic signature page}

Richard Pazdur, M.D.
Director
Division of Oncology Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

Richard Pazdur
6/10/04 11:35:25 AM

NDA 21-759

Page 2

U.S. Postal Service:

Center for Drug Evaluation and Research
Division of Oncology Drug Products
Attention: Division Document Room
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Oncology Drug Products, HFD-150
Attention: Document Room
1451 Rockville Pike
Rockville, Maryland 20854

If you have any questions, call Christy Cottrell, Consumer Safety Officer, at (301) 594-5761.

Sincerely,

{See appended electronic signature page}

Dotti Pease
Chief, Project Management Staff
Division of Oncology Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

Christy Cottrell
6/10/04 09:53:20 AM
Signing for Dotti Pease

MEMORANDUM OF TELECON

DATE: November 7, 2002
APPLICATION NUMBER: NDA 21-492
DRUG: Eloxatin (oxaliplatin) for Injection

BETWEEN:

John Purpura, Director, CMC Drug Regulatory Affairs

REPRESENTING: Sanofi-Synthelabo, Inc.

AND

Dr. John Simmons, Director, DNDC1
Dr. Hasmukh Patel, Deputy Director, DNDC1
Dr. Rik Lostritto, Chemistry Team Leader
Dr. Hari Sarker, Chemistry Reviewer
Christy Cottrell, Consumer Safety Officer

REPRESENTING: Division of Oncology Drug Products, FDA

SUBJECT: Supplement vs. new NDA for oxaliplatin injectable

BACKGROUND:

On October 23, 2002, the sponsor sent a fax to Dr. Rik Lostritto proposing a filing strategy for the submission of oxaliplatin injection (versus the oxaliplatin *for* injection that is currently approved). The October 23, 2002, submission is included as Attachment A.

In a brief teleconference with Mr. Purpura, Dr. Lostritto explained the Division's initial feeling that the injectable should be submitted as a new NDA. Mr. Purpura stated that Sanofi was concerned about the review timeline differences between a supplement (4 months) versus a new NDA (10 months). There was additional concern that more resources were needed to put together a new NDA as opposed to a supplement. Given these differences of opinion, Dr. Lostritto and Mr. Purpura agreed that a teleconference would be beneficial.

On November 1, 2002, Mr. Purpura submitted a request for teleconference along with a two-page backgrounder providing Sanofi's justification for submitting the injectable as a supplement instead of a new NDA. The November 1, 2002, submission is included as Attachment B.

DISCUSSION:

A teleconference was held on November 7, 2002. During the teleconference, the Division reiterated that the injectable should be submitted as a new NDA. While the Division agreed with the sponsor's points 1-3, point 4 was arguable. Sanofi cited Platinol and Platinol-AQ as examples of two configurations that were submitted under the same NDA. However, the Division explained that Platinol-AQ was approved in 1984 and was pre-PDUFA. The Division stated that it has since received another injectable submitted after the implementation of PDUFA that was submitted as a separate NDA, therefore providing a more recent and relevant precedent. Additionally, the Division noted that separate NDAs make the application cleaner should the sponsor decide to stop marketing one of the configurations.

While the Division could not commit to a shorter review time than the 10 months that is standard for new NDAs since a microbiology review and inspections would both be needed, the team felt that a shorter review period would likely be feasible.

The sponsor agreed to submit the injectable as a new NDA. There were no action items or unresolved issues.

Christy Cottrell
Consumer Safety Officer

Concurrence:

Rik Lostritto, Ph.D.
Chemistry Team Leader

MEMO OF FILING MEETING

DATE: May 24, 2004 (cancelled)

BACKGROUND:

Eloxatin (oxaliplatin) for Injection was approved August 9, 2002 for use in combination with infusional 5-FU/LV for the treatment of patients with metastatic carcinoma of the colon or rectum whose disease has recurred or progressed during or within 6 months of completion of first line therapy with the combination of bolus 5-FU/LV and irinotecan.

On January 9, 2004, S-002 was approved and expanded the indication to use in combination with infusional 5-Fluorouracil (5-FU) and Leucovorin (LV) for the treatment of patients previously untreated for advanced colorectal cancer.

On November 7, 2002, the Division had a teleconference with the sponsor about whether a new aqueous solution formulation needed to be submitted as a supplement to the existing NDA 21-492 or as a new NDA. It was determined that the new formulation should be submitted as a new NDA. Therefore, this NDA provides for a new aqueous solution formulation of Eloxatin.

ATTENDEES: Haripada Sarker, Ph.D., Chemistry Reviewer (by phone)
Margaret Brower, Ph.D., Pharm/Tox Reviewer (by email)
Christy Cottrell, Consumer Safety Officer

ASSIGNED REVIEWERS:

<u>Discipline</u>	<u>Reviewer</u>
Medical:	N/A
Secondary Medical:	N/A
Statistical:	N/A
Pharmacology:	Margaret Brower
Statistical Pharmacology:	N/A
Chemistry:	Haripada Sarker
Environmental Assessment (if needed):	N/A
Biopharmaceutical:	Angela Men (if needed)
Microbiology, sterility:	Not yet assigned
Microbiology, clinical (for antimicrobial products only):	N/A
DSI:	N/A
Regulatory Project Management:	Christy Cottrell
Other Consults:	N/A

Per reviewers, are all parts in English or English translation? YES
If no, explain:

CLINICAL N/A X FILE _____ REFUSE TO FILE _____

- Clinical site inspection needed: NO

- Advisory Committee Meeting needed? NO
- If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance? N/A

CLINICAL MICROBIOLOGY N/A FILE REFUSE TO FILE

STATISTICS N/A FILE REFUSE TO FILE

BIOPHARMACEUTICS FILE REFUSE TO FILE

- Biopharm. inspection needed: NO

PHARMACOLOGY N/A FILE REFUSE TO FILE

- GLP inspection needed: NO

CHEMISTRY FILE REFUSE TO FILE

- Establishment(s) ready for inspection? NO
- Microbiology YES

ELECTRONIC SUBMISSION:

Any comments: None

REGULATORY CONCLUSIONS/DEFICIENCIES:

The application is unsuitable for filing. Explain why:

The application, on its face, appears to be well organized and indexed. The application appears to be suitable for filing.

No filing issues have been identified.

Filing issues to be communicated by Day 74. List (optional):

ACTION ITEMS:

- Document filing issues/no filing issues conveyed to applicant by Day 74.

Christy Cottrell
Consumer Safety Officer

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/s/

Christy Cottrell
6/9/04 03:36:25 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

PRESCRIPTION DRUG USER FEE COVER SHEET

Form Approved: OMB No. 0910-0297
Expiration Date: December 31, 2008

See Instructions on Reverse Side Before Completing This Form

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: <http://www.fda.gov/cder/pdufa/default.htm>

1 APPLICANT'S NAME AND ADDRESS Sanofi-Synthelab, Inc 9 Great Valley Parkway Malvern, PA 19355		4 BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER NDA No 21-759	
2 TELEPHONE NUMBER (Include Area Code) (610) 889-6417		5 DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW: <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION <input checked="" type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO: NDA 21-492 (APPLICATION NO. CONTAINING THE DATA)	
3 PRODUCT NAME Eloxatin (Oxaliplatin Injection)		6 USER FEE I.D. NUMBER 4726	

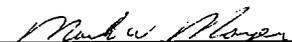
7 IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION

<input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/82 (Self Explanatory)	<input type="checkbox"/> A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE (See Item 7, reverse side before checking box.)
<input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 738(a)(1)(E) OF THE FEDERAL Food, Drug, and Cosmetic Act (See item 7, reverse side before checking box.)	<input type="checkbox"/> THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY (Self Explanatory)

8 HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION?
 YES NO
(See Item 8, reverse side if answered YES)

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services Food and Drug Administration CDER, HFM-99 1401 Rockville Pike Rockville, MD 20852-1448	and	Food and Drug Administration CDER, HFD-94 12420 Parklawn Drive, Room 3046 Rockville, MD 20852	An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number
--	-----	--	---

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE 	TITLE Mark W. Moyer Vice President, Drug Regulatory Affairs	DATE 3/31/2004
---	---	-------------------

If yes, is the drug considered to be the same drug according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]? N/A

Is the application affected by the Application Integrity Policy (AIP)? NO
 If yes, explain.

If yes, has OC/DMPQ been notified of the submission? N/A

• Does the submission contain an accurate comprehensive index? YES

• Was form 356h included with an authorized signature? YES
If foreign applicant, both the applicant and the U.S. agent must sign.

• Submission complete as required under 21 CFR 314.50? YES
 If no, explain:

• If an electronic NDA, does it follow the Guidance? YES
If an electronic NDA, all certifications must be in paper and require a signature.
 Which parts of the application were submitted in electronic format?
 Entire application

Additional comments:

• If in Common Technical Document format, does it follow the guidance? N/A

• Is it an electronic CTD? NO
If an electronic CTD, all certifications must be in paper and require a signature.
 Which parts of the application were submitted in electronic format?

Additional comments:

• Patent information submitted on form FDA 3542a? YES

• Exclusivity requested? NO
 Note: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.

• Correctly worded Debarment Certification included with authorized signature? YES
If foreign applicant, both the applicant and the U.S. Agent must sign the certification.

NOTE: Debarment Certification should use wording in FD&C Act section 306(k)(1) i.e., "[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application." Applicant may not use wording such as "To the best of my knowledge . . ."

• Financial Disclosure forms included with authorized signature? N/A
(Forms 3454 and 3455 must be used and must be signed by the APPLICANT.)

• Field Copy Certification (that it is a true copy of the CMC technical section)? YES

Refer to 21 CFR 314.101(d) for Filing Requirements

- PDUFA and Action Goal dates correct in COMIS? YES
 If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.
- Drug name/Applicant name correct in COMIS? If not, have the Document Room make the corrections. YES
- List referenced IND numbers: IND 41,817
- End-of-Phase 2 Meeting(s)? NO
 If yes, distribute minutes before filing meeting.
- Pre-NDA Meeting(s)? YES (11-7-02)
 If yes, distribute minutes before filing meeting.

Project Management

- All labeling (PI, PPI, MedGuide, carton and immediate container labels) consulted to DDMAC? NOT YET
 (awaiting final generic name from sponsor)
- Trade name (plus PI and all labels and labeling) consulted to ODS/DMETS? NOT YET
 (awaiting final generic name from sponsor)
- MedGuide and/or PPI (plus PI) consulted to ODS/DSRCS? N/A
- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling, submitted? N/A

If Rx-to-OTC Switch application:

- OTC label comprehension studies, all OTC labeling, and current approved PI consulted to ODS/DSRCS? N/A
- Has DOTCDP been notified of the OTC switch application? N/A

Clinical

- If a controlled substance, has a consult been sent to the Controlled Substance Staff? N/A

Chemistry

- Did applicant request categorical exclusion for environmental assessment? YES
 If no, did applicant submit a complete environmental assessment?
 If EA submitted, consulted to Nancy Sager (HFD-357)?
- Establishment Evaluation Request (EER) submitted to DMPQ? NO

- If a parenteral product, consulted to Microbiology Team (HFD-805)? YES

If 505(b)(2) application, complete the following section:

- Name of listed drug(s) and NDA/ANDA #:
- Describe the change from the listed drug(s) provided for in this (b)(2) application (for example, "This application provides for a new indication, otitis media" or "This application provides for a change in dosage form, from capsules to solution").
- Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? (Normally, FDA will refuse-to-file such NDAs.) YES NO
- Is the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (See 314.54(b)(1)). If yes, the application should be refused for filing under 314.101(d)(9). YES NO
- Is the rate at which the product's active ingredient(s) is absorbed or otherwise made available to the site of action unintentionally less than that of the RLD? (See 314.54(b)(2)). If yes, the application should be refused for filing under 314.101(d)(9). YES NO
- Which of the following patent certifications does the application contain? Note that a patent certification must contain an authorized signature.

_____ 21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA.

_____ 21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired.

_____ 21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire.

_____ 21 CFR 314.50(i)(1)(i)(A)(4): The patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted.

IF FILED, and if the applicant made a "Paragraph IV" certification [21 CFR 314.50(i)(1)(i)(A)(4)], the applicant must submit a signed certification that the patent holder was notified the NDA was filed [21 CFR 314.52(b)]. Subsequently, the applicant must submit documentation that the patent holder(s) received the notification ([21 CFR 314.52(e)].

_____ 21 CFR 314.50(i)(1)(ii): No relevant patents.

_____ 21 CFR 314.50(i)(1)(iii): The patent on the listed drug is a method of use patent and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications

_____ 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above.)

_____ Written statement from patent owner that it consents to an immediate effective date upon approval of the application.

- Did the applicant:
 - Identify which parts of the application rely on information the applicant does not own or to which the applicant does not have a right of reference?
 YES NO
 - Submit a statement as to whether the listed drug(s) identified has received a period of marketing exclusivity?
 YES NO
 - Submit a bioavailability/bioequivalence (BA/BE) study comparing the proposed product to the listed drug?
 N/A YES NO
 - Certify that it is seeking approval only for a new indication and not for the indications approved for the listed drug if the listed drug has patent protection for the approved indications and the applicant is requesting only the new indication (21 CFR 314.54(a)(1)(iv).?
 N/A YES NO
- If the (b)(2) applicant is requesting exclusivity, did the applicant submit the following information required by 21 CFR 314.50(j)(4):
 - Certification that each of the investigations included meets the definition of "new clinical investigation" as set forth at 314.108(a).
 YES NO
 - A list of all published studies or publicly available reports that are relevant to the conditions for which the applicant is seeking approval.
 YES NO
 - EITHER
 The number of the applicant's IND under which the studies essential to approval were conducted.
 IND # _____ NO
 - OR
 A certification that it provided substantial support of the clinical investigation(s) essential to approval if it was not the sponsor of the IND under which those clinical studies were conducted?
 N/A YES NO
- Has the Director, Div. of Regulatory Policy II, HFD-007, been notified of the existence of the (b)(2) application?
 YES NO

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Christy Cottrell
6/9/04 03:39:03 PM
CSO

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST		
NDA 21-759	Efficacy Supplement Type SE-	Supplement Number
Drug: Eloxatin (oxaliplatin) Injection		Applicant: Sanofi-Synthelabo, Inc.
RPM: Christy Cottrell		HFD-150 Phone # (301) 594-5761
<p>Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) (This can be determined by consulting page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)</p> <p>If this is a 505(b)(2) application, please review and confirm the information previously provided in Appendix B to the NDA Regulatory Filing Review. Please update any information (including patent certification information) that is no longer correct.</p> <p><input type="checkbox"/> Confirmed and/or corrected</p>		Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s):
❖ Application Classifications:		
• Review priority		<input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority
• Chem class (NDAs only)		5
• Other (e.g., orphan, OTC)		N/A
❖ User Fee Goal Dates		
		January 31, 2005
❖ Special programs (indicate all that apply)		
		<input checked="" type="checkbox"/> None Subpart H <input type="checkbox"/> 21 CFR 314.510 (accelerated approval) <input type="checkbox"/> 21 CFR 314.520 (restricted distribution) <input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review <input type="checkbox"/> CMA Pilot 1 <input type="checkbox"/> CMA Pilot 2
❖ User Fee Information		
• User Fee		<input checked="" type="checkbox"/> Paid UF ID number 4726
• User Fee waiver		<input type="checkbox"/> Small business <input type="checkbox"/> Public health <input type="checkbox"/> Barrier-to-Innovation <input type="checkbox"/> Other (specify)
• User Fee exception		<input type="checkbox"/> Orphan designation <input type="checkbox"/> No-fee 505(b)(2) (see NDA Regulatory Filing Review for instructions) <input type="checkbox"/> Other (specify)
❖ Application Integrity Policy (AIP)		
• Applicant is on the AIP		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

(Note: This can be determined by confirming whether the Division has received a written notice from the applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)).

If "No," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.

- (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).

If "No," continue with question (5).

- (5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?

Yes No

(Note: This can be determined by confirming whether the Division has received a written notice from the applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).

If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).

If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007) and attach a summary of the response.

❖ Exclusivity (approvals only)	
<ul style="list-style-type: none"> • Exclusivity summary • Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? (Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.) 	Included
<ul style="list-style-type: none"> • Is there existing orphan drug exclusivity protection for the "same drug" for the proposed indication(s)? Refer to 21 CFR 316.3(b)(13) for the definition of "same drug" for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification. 	<input type="checkbox"/> Yes, Application # _____ <input checked="" type="checkbox"/> No
❖ Administrative Reviews (Project Manager, ADRA) (indicate date of each review)	Filing review- 6/9/04

❖ Actions	
• Proposed action	(X) AP () TA () AE () NA
• Previous actions (specify type and date for each action taken)	N/A
• Status of advertising (approvals only)	(X) Materials requested in AP letter () Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	() Yes (X) Not applicable
• Indicate what types (if any) of information dissemination are anticipated	(X) None () Press Release () Talk Paper () Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable))	
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	Included
• Most recent applicant-proposed labeling	N/A
• Original applicant-proposed labeling	N/A
• Labeling reviews (including DDMAC, DMETS, DSRCs) and minutes of labeling meetings (indicate dates of reviews and meetings)	DMETS- 12/9/04
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	N/A
❖ Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	Included
• Applicant proposed	N/A
• Reviews	N/A
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	N/A
• Documentation of discussions and/or agreements relating to post-marketing commitments	N/A
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	Included
❖ Memoranda and Telecons	N/A
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	N/A
• Pre-NDA meeting (indicate date)	11/7/02
• Pre-Approval Safety Conference (indicate date; approvals only)	N/A
• Other	Filing mtg- 5/24/04
❖ Advisory Committee Meeting	
• Date of Meeting	N/A
• 48-hour alert	N/A
❖ Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)	N/A

❖ Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) (indicate date for each review)	N/A
❖ Clinical review(s) (indicate date for each review)	N/A
❖ Microbiology (efficacy) review(s) (indicate date for each review)	N/A
❖ Safety Update review(s) (indicate date or location if incorporated in another review)	N/A
❖ Risk Management Plan review(s) (indicate date/location if incorporated in another rev)	N/A
❖ Pediatric Page(separate page for each indication addressing status of all age groups)	Included
❖ Demographic Worksheet (NME approvals only)	N/A
❖ Statistical review(s) (indicate date for each review)	N/A
❖ Biopharmaceutical review(s) (indicate date for each review)	Included- 6/2/04
❖ Controlled Substance Staff review(s) and recommendation for scheduling (indicate date for each review)	N/A
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	N/A
• Bioequivalence studies	N/A
❖ CMC review(s) (indicate date for each review)	1/26/05
❖ Environmental Assessment	
• Categorical Exclusion (indicate review date)	1/26/05
• Review & FONSI (indicate date of review)	N/A
• Review & Environmental Impact Statement (indicate date of each review)	N/A
❖ Microbiology (validation of sterilization & product sterility) review(s) (indicate date for each review)	Included- 12/20/04
❖ Facilities inspection (provide EER report)	Date completed: 1/3/05 (X) Acceptable () Withhold recommendation
❖ Methods validation	() Completed (X) Requested () Not yet requested
❖ Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	Included- 7/12/04
❖ Nonclinical inspection review summary	N/A
❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)	N/A
❖ CAC/ECAC report	N/A

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Christy Cottrell
2/16/05 11:22:28 AM