

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPROVAL PACKAGE FOR:**

**APPLICATION NUMBER**

**NDA 21-530**

**Administrative/Correspondence Reviews**

**PATENT INFORMATION SUBMITTED WITH THE  
FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT**

**For Each Patent That Claims a Drug Substance  
(Active Ingredient), Drug Product (Formulation and  
Composition) and/or Method of Use**

NDA NUMBER

21-530

NAME OF APPLICANT / NDA HOLDER

Boehringer Ingelheim Pharmaceuticals, Inc.

*The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.*

TRADE NAME (OR PROPOSED TRADE NAME)

MOBIC®

ACTIVE INGREDIENT(S)

meloxicam

STRENGTH(S)

7.5 mg/5 mL

DOSAGE FORM

oral suspension

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4).

Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the only information relied upon by FDA for listing a patent in the Orange Book.

**For hand-written or typewriter versions (only) of this report:** If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

**FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.**

**For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.**

**1. GENERAL**

a. United States Patent Number

6,184,220

b. Issue Date of Patent

2/6/2001

c. Expiration Date of Patent

3/25/2019

d. Name of Patent Owner

Boehringer Ingelheim Pharma GmbH & Co. KG

Address (of Patent Owner)

Binger Strasse 173

City/State

Ingelheim, Federal Republic of Germany

ZIP Code

55216

FAX Number (if available)

Telephone Number

49-613277-0

E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

 **Boehringer Ingelheim Pharmaceuticals, Inc.**

Address (of agent or representative named in 1.e.)

900 Ridgebury Road/P.O. Box 368

City/State

Ridgefield, CT

ZIP Code

06877

FAX Number (if available)

203-798-4408

Telephone Number

203-798-9988

E-Mail Address (if available)

the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

**For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.**

**2. Drug Substance (Active Ingredient)**

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement?  Yes  No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement?  Yes  No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b).  Yes  No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.)  Yes  No

2.6 Does the patent claim only an intermediate?  Yes  No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)  Yes  No

**3. Drug Product (Composition/Formulation)**

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?  Yes  No

3.2 Does the patent claim only an intermediate?  Yes  No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)  Yes  No

**4. Method of Use**

**Sponsors must submit the information in section 4 separately for each patent claim claiming a method of using the pending drug product for which approval is being sought. For each method of use claim referenced, provide the following information:**

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes  No

4.2 Patent Claim Number (as listed in the patent) Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes  No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product. Use: (Submit indication or method of use information as identified specifically in the approved labeling.)

**5. No Relevant Patents**

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval 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.  Yes

**6. Declaration Certification**

**6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.**

**Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.**

**6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)**

*Timothy Witkowski*

Date Signed  
5/14/2004

**NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).**

**Check applicable box and provide information below.**

<input type="checkbox"/> NDA Applicant/Holder	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Timothy X. Witkowski, Esq.	
Address Boehringer Ingelheim Pharmaceuticals, Inc. 900 Ridgebury Road/P.O. Box 368	City/State Ridgefield, CT
ZIP Code 06877	Telephone Number 203-798-4310
FAX Number (if available) 203-798-4408	E-Mail Address (if available) twitkows@rdg.boehringer-ingelheim.com

The public reporting burden for this collection of information has been estimated to average 9 hours 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:

Food and Drug Administration  
CDER (HFD-007)  
5600 Fishers Lane  
Rockville, MD 20857

*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.*

EXCLUSIVITY SUMMARY FOR NDA 21-530 SUPPL # N/A

Trade Name Mobic® Oral Suspension Generic Name meloxicam oral suspension

Applicant Name Boehringer Ingelheim Pharmaceuticals, Inc. HFD-550

Approval Date If Known June 01, 2004

**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.

N/A  
\_\_\_\_\_

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:

N/A  
\_\_\_\_\_

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 //

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?

No

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 //

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 /\_\_\_/ NO //

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

NDA# 20-938 \_\_\_\_\_  
NDA# \_\_\_\_\_  
NDA# \_\_\_\_\_

2. Combination product. N/A

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 /\_\_\_/

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:

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(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:

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(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:

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(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:

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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.



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 Barbara Gould Date May 14, 2004  
Title: Regulatory Health Project Manager

Signature Brian E. Harvey, M.D., Ph.D. Date \_\_\_\_\_  
Acting Division Director

Form OGD-011347 Revised 05/10/2004

cc:  
Archival NDA 21-530  
HFD-550/Division File  
HFD-550/Barbara Gould  
HFD-610/Mary Ann Holovac  
HFD-104/PEDS/T.Crescenzi

**1. ADMINISTRATIVE INFORMATION AND LABELING**

**ITEM 16 – DEBARMENT CERTIFICATION**

Certification Requirement - Section 306(K)(L) of the Act 21 U.S.C. 355a(K)(L)

The undersigned certifies that **Boehringer Ingelheim Pharmaceuticals, Inc.** 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 Federal Food, Drug, and Cosmetic Act in connection with **MOBIC® (meloxicam) Oral Suspension 7.5 mg/5 mL**.

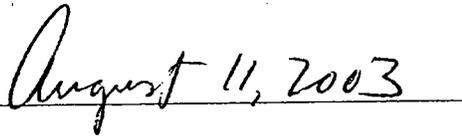
Signature:



Name of the Applicant:

Martin M. Kaplan, M.D., J.D.  
Vice President, Drug Regulatory Affairs  
Boehringer Ingelheim Pharmaceuticals, Inc.

Date:



Mailing Address:

Boehringer Ingelheim Pharmaceuticals, Inc.  
900 Ridgebury Road  
P.O. Box 368  
Ridgefield, CT 06877-0368

5 Page(s) Withheld

§ 552(b)(4) Trade Secret / Confidential

§ 552(b)(5) Deliberative Process

§ 552(b)(5) Draft Labeling

3 Page(s) Withheld

       § 552(b)(4) Trade Secret / Confidential

✓ § 552(b)(5) Deliberative Process

       § 552(b)(5) Draft Labeling



Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation ODE V

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**FACSIMILE TRANSMITTAL SHEET**

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**DATE:** May 7, 2004

**To:** Jeffrey R. Synder

**From:** Barbara Gould

**Company:** Boehringer Ingelheim Pharmaceuticals,  
Inc

Division of Anti-Inflammatory, Analgesic, and  
Ophthalmic Drug Products, HFD-550

**Fax number:** 203-791-6262

**Fax number:** 301-827-2531

**Phone number:** 203-778-7727

**Phone number:** 301 827-2090

**Subject:** Information Request Clinical Pharmacology

**Total no. of pages including cover:** 1

**Comments:**

Please provide statistical analysis data (90% confidence intervals and point estimate ratios) on the 0-6 hour Day 1 fasting stage  $C_{max_{0-6h}}$  and  $AUC_{0-6h}$  parameters for Study No. 107.172.

Thanks Carmen

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**Document to be mailed:**

YES

NO

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# Fax



**Division of Anti-Inflammatory, Analgesic,  
Ophthalmic Drug Products**  
Center for Drug Evaluation and Research, HFD-550  
Parklawn Building  
5600 Fishers Lane, Rockville, MD 20857

**To:** Charles Mazzarella

**From:** Barbara Gould

**Fax:** (203) 791-6262

**Fax:** (301) 827-2531

**Phone:** (203) 798-5462

**Phone:** (301) 827-2506

**Pages:** 20 (including cover)

**Date:** 28 April 2004

**Re:** NDA 21-530 FDA Proposed Draft Label

**Urgent**    **For Review**    **Please Comment**    **Please Reply**    **Please Recycle**

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● **Comments:**

Charlie,

Attached is the FDA proposed label w/key. Please let me know if you have any questions. Also the email version will have 1 less page than the fax. The difference is that the faxed label will have the electronic signature page included as well.

Regards,

BJ

# Fax



**Division of Anti-Inflammatory, Analgesic,  
Ophthalmic Drug Products**  
Center for Drug Evaluation and Research, HFD-550  
Parklawn Building  
5600 Fishers Lane, Rockville, MD 20857

**To:** Charles Mazzarella

**From:** Barbara Gould

**Fax:** (203) 791-6262

**Fax:** (301) 827-2531

**Phone:** (203) 798-5462

**Phone:** (301) 827-2506

**Pages:** 1 (including cover)

**Date:** 13 April 2004

**Re:** NDA 21-530 Mobic Suspension Information Request

**Urgent**    **For Review**    **Please Comment**    **Please Reply**    **Please Recycle**

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● **Comments:**

In Study 107.172 the meloxicam oral formulation is referred as a syrup where as in Study 107.254 the oral formulation is referred as a suspension. The sponsor needs to clarify whether the dosage form used in study 107.172 is a syrup or suspension?

Please call if you have any questions.

Thanks,

BJ Gould



NDA 21-530

**DISCIPLINE REVIEW LETTER**

Boehringer Ingelheim Pharmaceuticals, Inc.  
Attention: Charles R. Mazarella  
Manager, Drug Regulatory Affairs  
900 Ridgebury Road  
P.O. Box 368  
Ridgefield, CT 06877

Dear Mr. Mazarella:

Please refer to your August 18, 2003 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Mobic (meloxicam) Suspension 7.5 mg/5mL.

Our reviews of the Biopharmaceutics and Chemistry, Manufacturing and Controls sections of your submission are complete, and we have identified the following deficiencies:

**BIOPHARMACEUTICS:**

- As there is not a direct comparison study linking the tablet to suspension, the Sponsor needs to reanalyze the combined results of studies 107.172 and 107.74 using the capsule legs which are in both studies as a scaling factor and construct a 90% confidence interval for a comparison of the tablet to suspension.

The Sponsor may refer to the following publication:

Zintzaras, E. and Bouka, P., *Bioequivalence studies: biometrical concepts of alternative design and pooled analysis*, **Eur. J. Metab. Pharmacokinet.** 1999, **24** (3):225-32.

**CHEMISTRY:**

- For the drug substance specification, it is not acceptable for the analytical procedures (section 3.2.S.4.2) and the validation of the procedures (section 3.2.S.4.3) to be referenced to DMF because the DMF analytical procedures are not regulatory analytical procedures. However, it would be acceptable to refer to NDA 20-938, because the approved NDA procedures are regulatory procedures. Please revise sections 3.2.S.4.2 and 3.2.S.4.3 accordingly. Please also revise section 3.2.S.4.1 to indicate that the drug substance specification is the same as that approved in NDA 20-938 (instead of the DMF, as shown in your submission) with the exception of the particle size test. Please provide the drug substance specification in the same format as was submitted to the approved NDA 20-938 (for example, under "method" column, indicate the specific USP tests).

Appears This Way  
On Original

# Fax



**Division of Anti-Inflammatory, Analgesic,  
Ophthalmic Drug Products**

Center for Drug Evaluation and Research, HFD-550  
Parklawn Building  
5600 Fishers Lane, Rockville, MD 20857

**To:** Jeffrey Synder

**From:** Barbara Gould

**Fax:** (203) 778-7357

**Fax:** (301) 827-2531

**Phone:** (203) 778-7727

**Phone:** (301) 827-2506

**Pages:** 1 (including cover)

**Date:** 28 November 2003

**Re:** NDA 20-938/S-004 & NDA 21-530 Safety Update Proposal

**Urgent**    **For Review**    **Please Comment**    **Please Reply**    **Please Recycle**

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● **Comments:**

Please refer to your submission dated November 13, 2003: Safety Update Proposal, received November 14, 2003. The DAAODP recommends that the Sponsor provide a complete safety update for **NDA 21-530** Mobic Suspension 7.5 mg/5 mL to include updated post marketing safety information for the tablet (NDA 20-938) and oral suspension for the period April 2000 to December 2003, in addition to the clinical trial information. The Division will accept a safety update of post marketing information for the tablet and oral suspension formulations for NDA 20-938/S-004 as a complete response to include the period of January 2004 to April 2004 (provided that the safety update for NDA 21-530 includes the above described information). This is subject to supplement 004 being submitted in January 2004 as planned.

Please call if you have any concerns.

Thanks,

BJ Gould

cc Charles Mazarella



**NO FILING REVIEW ISSUES IDENTIFIED**

NDA 21-530

Boehringer Ingelheim Pharmaceutical, Inc.  
Attention: Charles Mazzarella  
Manager, Drug Regulatory Affairs  
Ridgebury Road  
P.O. Box 368  
Ridgefield, CT 06877

Dear Mr. Mazzarella:

Please refer to your August 18, 2003 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Mobic<sup>®</sup> (meloxicam suspension) 7.5 mg/5 mL.

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 October 17, 2003 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 Barbara Gould, Regulatory Project Manager, at (301) 827-2506.

Sincerely,

*{See appended electronic signature page}*

Lee S. Simon, M.D.  
Director  
Division of Anti-Inflammatory, Analgesics,  
And Ophthalmic Drug Products  
Office of Drug Evaluation V  
Center for Drug Evaluation and Research



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-530

Boehringer Ingelheim Pharmaceutical, Inc.  
Attention: Charles Mazzarella  
Manager, Drug Regulatory Affairs  
Ridgebury Road  
P.O. Box 368  
Ridgefield, CT 06877

Dear Mr. Mazzarella:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Mobic<sup>®</sup> (meloxicam suspension) 7.5 mg/5 mL

Review Priority Classification: Standard

Date of Application: August 18, 2003

Date of Receipt: August 19, 2003

Our Reference Number: NDA 21-530

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on October 17, 2003 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be June 18, 2004.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application. Address all communications concerning this NDA as follows:

U.S. Postal Service:

Center for Drug Evaluation and Research  
Division of Anti-Inflammatory, Analgesics, and Ophthalmic Drug Products  
Attention: Division Document Room, HFD-550  
5600 Fishers Lane  
Rockville, Maryland 20857

NDA 21-530

Page 2

Courier/Overnight Mail:

Food and Drug Administration

Center for Drug Evaluation and Research

Division of Anti-Inflammatory, Analgesics, and Ophthalmic Drug Products, HFD-550

Attention: Document Room N115

9201 Corporate Blvd.

Rockville, Maryland 20856

If you have any questions, call Barbara Gould, Regulatory Project Manager, at (301) 827-2506.

Sincerely,

*{See appended electronic signature page}*

Carmen DeBellas, R.Ph.

Chief Project Management Staff

Division of Anti-Inflammatory, Analgesics,  
And Ophthalmic Drug Products

Office of Drug Evaluation V

Center for Drug Evaluation and Research

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/s/

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Barbara Gould  
10/5/03 02:38:17 PM  
for Carmen DeBellas, R.Ph.

# MEETING MINUTES

**MEETING DATE:** July 19, 2001    **TIME:** 1:00 PM    **LOCATION:** Corp S300

**IND 51,268**

**Meeting Request Submission Date:** June 01, 2001

**Briefing Document Submission Date:** June 05, 2001

**DRUG:** Meloxicam Oral Suspension

**SPONSOR/APPLICANT:** Boehringer Ingelheim

**TYPE of MEETING:** PreNDA

**FDA PARTICIPANTS:**    **Division of Anti-Inflammatory, Analgesic & Ophthalmic Drug Product**

Jonca C. Bull, MD	Acting Division Director
Wiley Chambers, MD	Deputy Division Director
Joel Schifffenbauer	Medical Reviewer
Dennis Bashaw, Pharm. D.	Biopharmaceutical Team Leader
Veneeta Tandon, Ph.D.	Biopharm Reviewer
Frank Pelsor, Ph.D.	Clinical Pharmacologist
Barbara Gould	Project Manager

**INDUSTRY PARTICIPANTS:**

	<b>Boehringer Ingelheim</b>
Robert Menge	Director, Regulatory Affairs
Hiroshi Ueko	Director, Regulatory Affairs
Martin Kaplan	VP, Director, Regulatory Affairs
Jeff Synder	Director, Regulatory Affairs
Stefan Schuerer	Pharmacokinetics.

**BACKGROUND INFORMATION:**

Solid oral formulations of meloxicam (Mobic NDA 20-938, 7.5 mg and 15 mg tablets) are approved in the US for use in treating the signs and symptoms of osteoarthritis (OA). The primary focus of this NDA submission will be to establish the bioequivalence of the oral suspension formulation of meloxicam to the solid oral dosage forms, particularly the 7.5 mg and 15 mg tablets. Support for the bioequivalence of the oral suspension to the solid oral dosage is based primarily on the results of Study 107.172. Additional clinical evidence will be provided to support the oral suspension's comparable symptomatic relief of OA to the tablet formulation.

**QUESTIONS for DISCUSSION with FDA RESPONSE and DECISIONS REACHED:**

**General:**

1. We intend to follow the format described for the Common Technical Document for this submission (see next page). Does the Division have any comments on this proposal?

FDA Response:

Yes.

2. **At this time, we do not plan to file this submission electronically. We will provide any CRFs for deaths and discontinuations due to AEs from Study 107.179 and we will provide electronic copies of all Clinical Trial Reports referenced in the submission as aides to the reviewers. All electronic components will follow current guidances. Does the Division have any comments or suggestions regarding this proposal?**

FDA Response:

We strongly encourage you to file the submission electronically, however your proposal is acceptable.

**Chemistry:**

3. **Does the FDA agree that for post-approval annual stability batches of meloxicam oral suspension, anti-microbial preservative efficacy no longer needs to be tested, but that chemical testing of the preservative will suffice?**

FDA Response:

Upon demonstration of chemical content commensurate with antimicrobial effectiveness in the primary stability batches, chemical assays of preservatives should be adequate for post-approval annual batches.

During product development, large bottles containing suspensions should be tested to demonstrate the microbial effectiveness of the preservative system in contact with replacement container components L

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4. **Based on the outcome of on-going investigations, we may propose to test particle size in lieu of dissolution testing for control of the suspension, according to ICH Guideline "Q6A Specification: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances". In this way, dissolution testing would be deleted from the regulatory specifications for meloxicam oral suspension. Would the FDA comment on this approach?**

FDA Response:

The FDA's current thinking is that dissolution test can not be deleted from regulatory specifications. Particle size measurements can not replace dissolution test for suspensions.

**Additional CMC Comments:**

- A. Page 16: The inactive ingredients for which monographs exist in the USP/NF should comply with the requirements of the current USP/NF.
- B. Page 16: Please clarify that the information for Citric Acid and Raspberry Flavor in Table 4
- C. Page 20: Uniformity of Dosage Units (Uniformity of Fill) should be included in the specification. Add,  $\left[ \begin{array}{l} \text{ } \\ \text{ } \end{array} \right]$  to the Microbial limits.
- D. Please specify how you plan to measure the dose?  $\left[ \begin{array}{l} \text{ } \\ \text{ } \end{array} \right]$

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**Pre-Clinical Pharmacology/Toxicology**

5. We believe that no additional preclinical pharmacology or toxicology information for the oral suspension is necessary for the NDA to be fileable, does the Division concur?

FDA Response:

The Division does concur.

**Biopharmaceutics:**

6. Does the Division agree that the bioequivalence of the oral suspension to the capsule formulation at steady-state (107.172<sup>1</sup>) adequately establishes the bioequivalence of the oral suspension for registration purposes?

FDA Response:

Yes, dependent on the review and acceptability of the study report. The sponsor should also provide additional bioequivalence analysis by pooling the data from Study 107.172 (BE between suspension and capsules) and Study 107.082 (BE between tablets and capsules) and by dose normalizing the capsule arm.

7. Does the Division agree that the proposed design of the dose-proportionality/food-effect study (107.243) is adequate to answer any additional bioavailability issues that need to be addressed for the oral suspension (particularly information regarding the 22.5mg dose of the oral suspension)?

FDA Response:

Yes.

**Clinical:**

8. The primary source of information regarding the safety and efficacy of meloxicam in treating the signs and symptoms of OA is NDA 20-938. We do not propose to write a

separate ISS or ISE for the oral suspension NDA nor do we propose to provide a separate Statistical section for the NDA. Does the Division concur?

FDA Response:

An ISE is not required; however, please submit a safety summary including all safety data on studies not included in the original NDA and a current review of the literature.

9. We believe that no additional clinical studies (other than the proposed 107.243 trial) are necessary to provide a fileable NDA for the oral suspension. Does the Division agree?

FDA Response:

Yes, provided that there is bioequivalence to the clinically studied formulation.

10. Pediatric studies using the oral suspension formulation have been addressed in separate proposals in conjunction with the rheumatoid arthritis (RA) supplement (NDA 20-938/S004) that is currently under review at the FDA. Because OA is a disease of adults, we are formally requesting a waiver of the requirement to provide pediatric information or plans with regards to this NDA. Does the Division agree?

FDA Response:

If the pediatric suspension and the oral suspension formulation under review are identical, the requirement to provide pediatric information for the present NDA may be waived.

**Additional FDA Comments:**

**Financial Disclosure:**

We remind you of the requirement to collect the information on all studies that the FDA relies on to establish that the product is effective, or that makes a significant contribution to demonstration of safety. Please refer to "Financial Disclosure by Clinical Investigators" Final Rule February 2, 1998.

**Pediatric Rule:**

Please note that you will need to address the December 2, 1998 Pediatric Rule (63 FR 66632) when you submit your NDA (or sNDA).

**Pediatric Exclusivity:**

Under the Food and Drug Administration Modernization Act, an approved application may have the opportunity for an exclusivity extension based on the completion of pediatric studies. If you choose to pursue pediatric exclusivity, your plans for pediatric drug development, in the form of a Proposed Pediatric Study Requirement (PPRS), should be submitted so that we can consider issuing a Written Request. For complete

information, please refer to the FDA/CDER web page, <http://www.fda.gov/cder/guidance/index.htm>. "Guidance for Industry: Qualifying for Pediatric Exclusivity Under Section 505 A of the Federal Food, Drug and Cosmetic Act".

**ACTION ITEMS:**

1. Chemistry reviewers were not present for the meeting. It was suggest that the sponsor review the chemistry comments and if necessary a teleconference will be arranged to clarify comments.
2. The sponsor will provide raw data of study background information in excel format for the simulation studies submitted in April 24, 2001 briefing document.
3. Minutes will be conveyed within 30 days.

\_\_\_\_\_  
Barbara Gould      Date  
Project Manager

Concurrence Chair:

\_\_\_\_\_  
Wiley Chambers, MD Date  
Deputy Division Director

IND 51,268 Meloxicam Oral Suspension  
Mtg. Date: 19-Jul-01 Boehringer Ingelheim  
EOP2  
Page 6

Initialed by: JSchiffenbauer/25-Jul-01  
VTandon/DBashaw/25-Jul-01  
WChambers/

**MEETING MINUTES**

*Minutes faxed and DFS'ed* \_\_\_\_\_

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/s/

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Wiley Chambers

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## NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

Application Information		
NDA 21-530	Efficacy Supplement Type SE-N/A	Supplement Number N/A
Drug: <b>Mobic® Oral Suspension (meloxicam oral suspension)</b> 7.5 mg/5 mL		Applicant: <b>Boehringer Ingelheim Pharmaceuticals, Inc.</b>
RPM: <b>Barbara Gould</b>		HFD-550      Phone # 301 827-2506
Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)		Reference Listed Drug (NDA #, Drug name):
❖ Application Classifications:		
• Review priority		<input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority
• Chem class (NDAs only)		<b>3 New formulation</b>
• Other (e.g., orphan, OTC)		N/A
❖ User Fee Goal Dates		<b>18 June 2004</b>
❖ 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
• User Fee waiver		<input type="checkbox"/> Small business <input type="checkbox"/> Public health <input type="checkbox"/> Barrier-to-Innovation <input type="checkbox"/> Other
• User Fee exception		<input type="checkbox"/> Orphan designation <input type="checkbox"/> No-fee 505(b)(2) <input type="checkbox"/> Other
❖ Application Integrity Policy (AIP)		
• Applicant is on the AIP		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• This application is on the AIP		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• Exception for review (Center Director's memo)		N/A
• OC clearance for approval		
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification & certifications from foreign applicants are cosigned by US agent.		<input checked="" type="checkbox"/> Verified
❖ Patent		
• Information: Verify that form FDA-3542a was submitted.		<input checked="" type="checkbox"/> Verified
• Patent certification [505(b)(2) applications]: Verify type of certifications submitted.		21 CFR 314.50(i)(1)(i)(A) <input type="checkbox"/> I <input type="checkbox"/> II <input type="checkbox"/> III <input type="checkbox"/> IV  21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii)
• For paragraph IV certification, verify that the applicant notified the patent holder(s) of their certification that the patent(s) is invalid, unenforceable, or will not be infringed (certification of notification and documentation of receipt of notice).		(N/A) Verified

❖ Exclusivity (approvals only)	
• Exclusivity summary	(X)
• Is there an existing orphan drug exclusivity protection for the active moiety for the proposed indication(s)? Refer to 21 CFR 316.3(b)(13) for the definition of sameness for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification!	( ) Yes, Application # _____ (X) No
❖ Administrative Reviews (Project Manager, ADRA) (indicate date of each review)	15 October 2003
<b>General Information</b>	
❖ 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)	N/A
• Most recent applicant-proposed labeling	10 May 2004
• Original applicant-proposed labeling	18 August 2004
• Labeling reviews (including DDMAC, DMETS, DSRCS) and minutes of labeling meetings (indicate dates of reviews and meetings)	24 March 2004
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	
❖ Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	(X)
• Applicant proposed	18 August 2004
• Reviews	24 March 2004
❖ 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)	14 Nov. 2003 IR Fax 31 Oct. 2003 Advice Fax 05 Oct. 2003 Ack. Letter 25 Feb. 2004 AD/IR Letter 13 Apr. 2004 IR Fax 07 May 2004 IR Fax 29 Oct. 2003 Filling Letter
❖ Memoranda and Telecons	N/A
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	N/A
• Pre-NDA meeting (indicate date)	19 July 2001

• Pre-Approval Safety Conference (indicate date; approvals only)	N/A
• Other	N/A
❖ 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
<b>Summary Application Review</b>	
❖ Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) (indicate date for each review)	28 May 2004
<b>Clinical Information</b>	
❖ Clinical review(s) (indicate date for each review)	24 May 2004
❖ Microbiology (efficacy) review(s) (indicate date for each review)	N/A
❖ Safety Update review(s) (indicate date or location if incorporated in another review)	See the Clinical Review Page 20
❖ 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)	14 May 2004
❖ 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)	27 May 2004
❖ 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	22 March 2004/DFS'ed 26 May 2004
<b>CMC Information</b>	
❖ CMC review(s) (indicate date for each review)	07 May 2004
❖ Environmental Assessment	
• Categorical Exclusion (indicate review date)	07 May 2004
• 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)	N/A
❖ Facilities inspection (provide EER report)	Date completed: 20 October 2003 (X) Acceptable ( ) Withhold recommendation
❖ Methods validation	( ) Completed ( ) Requested (X) Not yet requested
<b>Nonclinical Pharm/Tox Information</b>	
❖ Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	20 January 2004
❖ Nonclinical inspection review summary	N/A
Statistical review(s) of carcinogenicity studies (indicate date for each review)	N/A
CAC/ECAC report	N/A

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/s/

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Barbara Gould

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**NDA REGULATORY FILING REVIEW**  
(Including Memo of Filing Meeting)

NDA 21-530

Supplement # N/A

SE1 SE2 SE3 SE4 SE5 SE6 SE7 SE8

Trade Name: **Mobic®**  
Generic Name: **meloxicam suspension**  
Strengths: **7.5 mg/5 mL**

Applicant: **Boehringer Ingelheim Pharmaceutical, Inc.**

Date of Application: **August 18, 2003**

Date of Receipt: **August 19, 2003**

Date clock started after UN:

Date of Filing Meeting: **October 07, 2003**

Filing Date: **October 17, 2003**

Action Goal Date (optional):

User Fee Goal Date: **June 19, 2004**

Indication(s) requested: **Indicated for the signs and symptoms of osteoarthritis**

Type of Original NDA: (b)(1)  (b)(2) \_\_\_\_\_

OR

Type of Supplement: (b)(1) \_\_\_\_\_ (b)(2) \_\_\_\_\_

NOTE: A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). If the application is a (b)(2) application, complete the (b)(2) section at the end of this review.

Therapeutic Classification: S  P \_\_\_\_\_  
Resubmission after withdrawal? N/A Resubmission after refuse to file? N/A  
Chemical Classification: (1,2,3 etc.) 3  
Other (orphan, OTC, etc.) N/A

User Fee Status: Paid  Exempt (orphan, government) \_\_\_\_\_  
Waived (e.g., small business, public health) \_\_\_\_\_

Form 3397 (User Fee Cover Sheet) submitted: YES NO

User Fee ID # 4581

Clinical data? YES \_\_\_\_\_ NO, Referenced to NDA 20-938

Is there any 5-year or 3-year exclusivity on this active moiety in either a (b)(1) or a (b)(2) application?

**YES** NO

If yes, explain:

Appl No	Prod No	Exclusivity Code	Exclusivity Expiration
020938	001	NCE	APR 13, 2005

Does another drug have orphan drug exclusivity for the same indication? YES **NO**

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)]?

YES NO

Is the application affected by the Application Integrity Policy (AIP)?  
 If yes, explain.

YES  NO

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

YES NO

• Does the submission contain an accurate comprehensive index?

YES NO

• Was form 356h included with an authorized signature?

YES NO

**If foreign applicant, both the applicant and the U.S. agent must sign.**

• Submission complete as required under 21 CFR 314.50?

YES NO

If no, explain:

• If an electronic NDA, does it follow the Guidance?

N/A YES

NO

**If an electronic NDA, all certifications must be in paper and require a signature.**

Which parts of the application were submitted in electronic format?

Additional comments:

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

YES NO

• Is it an electronic CTD?

N/A YES  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  NO

• Exclusivity requested?

YES, \_\_\_\_\_ years  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 NO

**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?  YES NO  
 (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 NO

**Refer to 21 CFR 314.101(d) for Filing Requirements**

- PDUFA and Action Goal dates correct in COMIS?  YES NO  
 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.
- List referenced IND numbers:
- End-of-Phase 2 Meeting(s)? Date(s) \_\_\_\_\_  NO  
 If yes, distribute minutes before filing meeting.
- Pre-NDA Meeting(s)? Date July 19, 2001 NO  
 If yes, distribute minutes before filing meeting.

**Project Management**

- All labeling (PI, PPI, MedGuide, carton and immediate container labels) consulted to DDMAC?  YES NO
- Trade name (plus PI and all labels and labeling) consulted to ODS/DMETS? YES  NO
- MedGuide and/or PPI (plus PI) consulted to ODS/DSRCS? N/A YES  NO
- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling, submitted?  N/A YES NO

**If Rx-to-OTC Switch application:**

- OTC label comprehension studies, all OTC labeling, and current approved PI consulted to ODS/DSRCS? N/A YES NO
- Has DOTCDP been notified of the OTC switch application? YES NO

**Clinical**

- If a controlled substance, has a consult been sent to the Controlled Substance Staff? YES  NO

**Chemistry**

- Did applicant request categorical exclusion for environmental assessment?  YES NO
- If no, did applicant submit a complete environmental assessment? YES NO
- If EA submitted, consulted to Nancy Sager (HFD-357)? YES  NO
- Establishment Evaluation Request (EER) submitted to DMPQ?  YES NO
- If a parenteral product, consulted to Microbiology Team (HFD-805)? YES  NO

**If 505(b)(2) application, complete the following section:** N/A

- 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

ATTACHMENT

MEMO OF FILING MEETING

DATE: October 07, 2003

**BACKGROUND:**

Meloxicam, an oxicam derivative, is a member of the enolic acid group of non steroidal anti-inflammatory drugs (NSAIDs). The safe and effective use of Mobic 7.5 and 15 mg tablet in treating the signs and symptoms of osteoarthritis has been established through NDA 20-938, which was submitted on December 15, 1998 and approved on April 13, 2000. The primary focus of this application is to establish the bioequivalence of the oral suspension formulation of meloxicam to the solid oral dosage forms, particularly the 7.5 mg and 15 mg tablets.

**ATTENDEES:**

Jonca Bull, M.D.  
Brian Harvey, M.D., Ph.D.  
Leslie Vaccari

Lee Simon, M.D.  
James Witter, M.D., Ph.D.  
Joel Schiffenbauer, M.D.  
John Smith, Ph.D.  
Sue Ching Lin, MS  
Annis Bashaw, PharmD  
Stan Lin, Ph.D.  
Yongman Kim, Ph.D.  
Conrad Chen, Ph.D.  
Carmen DeBellis, R.Ph.  
Barbara Gould

Martin K. Yau, Ph.D.

**Office of Drug Evaluation V**

Director  
Deputy Director  
Project Manager

**Division of Anti-Inflammatory, Analgesic, & Ophthalmic Drug Product**

Director  
Medical Team Leader  
Medical Team Leader  
Chemistry Team Leader  
Chemistry Reviewer  
Biopharmaceutical Team Leader  
Statistical Team Leader  
Statistical Reviewer  
Pharmacology/Toxicology Reviewer  
Chief Project Management Staff  
Project Manager

**Division of Scientific Investigations**

GLP and Bioequivalence Branch (HFD-48)

**ASSIGNED REVIEWERS:**

**Discipline**

Medical:  
Secondary Medical:  
Statistical:  
Pharmacology:  
Statistical Pharmacology:  
Chemistry:  
Environmental Assessment (if needed):  
Biopharmaceutical:  
Microbiology, sterility:  
Microbiology, clinical (for antimicrobial products only):  
Regulatory Project Management:  
Other Consults:

**Reviewer**

Tatiana Oussova, M.D.  
James Witter, M.D., Ph.D.  
Yongman Kim, Ph.D.  
Conrad Chen, Ph.D.  
N/A  
Sue Ching Lin, MS  
  
Chandra Chaurasia, Ph.D.  
N/A  
N/A  
Martin K. Yau, Ph.D.  
Barbara Gould

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

YES      NO

CLINICAL

FILE  \_\_\_\_\_

REFUSE TO FILE \_\_\_\_\_

- Clinical site inspection needed: YES  NO
- Advisory Committee Meeting needed? YES, date if known \_\_\_\_\_
- 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 YES NO

CLINICAL MICROBIOLOGY

NA  \_\_\_\_\_

FILE \_\_\_\_\_

REFUSE TO FILE \_\_\_\_\_

STATISTICS

FILE  \_\_\_\_\_

REFUSE TO FILE \_\_\_\_\_

BIOPHARMACEUTICS

FILE  \_\_\_\_\_

REFUSE TO FILE \_\_\_\_\_

- Biopharm. inspection needed: YES NO

PHARMACOLOGY

NA \_\_\_\_\_

FILE  \_\_\_\_\_

REFUSE TO FILE \_\_\_\_\_

- GLP inspection needed: YES NO

CHEMISTRY

FILE  \_\_\_\_\_

REFUSE TO FILE \_\_\_\_\_

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

ELECTRONIC SUBMISSION:

Any comments:

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:**

1. If RTF, notify everybody who already received a consult request of the RTF action. Cancel the EER.
2. If filed and the application is under the AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
3. Document filing issues/no filing issues conveyed to applicant by Day 74.

**Barbara Gould 15 October 2003**  
Regulatory Project Manager, HFD-550

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

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Barbara Gould  
5/30/04 08:22:35 PM  
CSO

51 Page(s) Withheld

\_\_\_\_\_ § 552(b)(4) Trade Secret / Confidential

\_\_\_\_\_ § 552(b)(5) Deliberative Process



\_\_\_\_\_ § 552(b)(5) Draft Labeling

5 Page(s) Withheld

       § 552(b)(4) Trade Secret / Confidential

✓ § 552(b)(5) Deliberative Process

✓ § 552(b)(5) Draft Labeling

# PRESCRIPTION DRUG USER FEE COVER SHEET

### See Instructions on Reverse Side Before Completing This Form

The 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>

<b>1. APPLICANT'S NAME AND ADDRESS</b> Boehringer Ingelheim Pharmaceuticals, Inc. 900 Ridgebury Road P.O. Box 368 Ridgefield, CT 06877	<b>4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER</b> NDA 21-530
<b>2. TELEPHONE NUMBER (include Area Code)</b>  ( 203 ) 798-7727	<b>5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?</b> <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 type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:  _____ (APPLICATION NO. CONTAINING THE DATA).
<b>3. PRODUCT NAME</b> Meloxicam Oral Suspension	<b>6. USER FEE I.D. NUMBER</b> 4581

**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 9/1/92 (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 736(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	Food and Drug Administration CDER, HFD-94 and 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 displays a currently valid OMB control number.
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<b>SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE</b> 	<b>TITLE</b> Jeffrey Snyder, Senior Associate Director Drug Regulatory Affairs	<b>DATE</b> 7/29/2003
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