CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-472

ADMINISTRATIVE DOCUMENTS
CORRESPONDENCE

BANNER
PHARMACAPS

June 4, 2002
Re: NDA # 21-472, Paragraph I Certification

Dear Sir or Madam:

The purpose of this letter is to amend a patent certification under 21 CFR §314.50 (i) from a Paragraph IV Certification to a Paragraph I Certification. The reason for this amendment is that there is no patent information listed in the "Orange Book" for the reference listed drug (Whitehall-Robins' Ibuprofen Potassium, N 20402 001.) Additionally, the product covered by our pending application, and for which we seek approval, does not include a migraine headache indication and thus the three year non-patent exclusivity for Advil Migraine Liqui-gels does not apply.

Accordingly, pursuant to section 505 (b)(2)(A)(i) and 21 CFR section 314.50 (i)(1)(A)(i), I certify that to the best of my information and belief, there is no patent information with respect to the above reference listed drug that has been submitted to FDA.

Sincerely,

Donna S. Lee, R.Ph.
Director, Regulatory Affairs and Project Management

TOH/jdk

APPEARS THIS WAY
ON ORIGINAL

Banner Pharmacaps Inc. P.O. Box 2210 4125 Premier Drive High Point, NC 27261-2210 Phone: 336.812.8700 Fax: 336 812 8777
California North Carolina Canada Mexico Netherlands India

EXCLUSIVITY SUMMARY for NDA # 21-472 SUPPL # _____

Trade Name Ibuprofen 200mg Generic Name ibuprofen

Applicant Name Banner Pharmacaps HFD- 550
Approval Date 10/09/02

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete Parts II and III of this Exclusivity Summary only if you answer "YES" to one or more of the following questions about the submission.

   a) Is it an original NDA? YES/_x__/ NO /___/

   b) Is it an effectiveness supplement? YES /___/ NO /___/

      If yes, what type(SE1, SE2, etc.)? _____

   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 /x___/

      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.

      The sponsor was precluded from submitting an ANDA (there are 2 referenced products) based on the fact that this product's active ingredient is ibuprofen potassium. The sponsor believes the products should exhibit similar bioavailability since they are both soft gelatin capsules, section 505(j) of the Act prohibits the approval of an ANDA for a drug product that contains an active ingredient that is different from the listed drug. Therefore based on this the sponsor submitted this application with 2 bioavailability trials under 505(b)(2).

      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 /_x__/

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 YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use? (Rx to OTC Switches should be answered No - Please indicate as such).

YES /___/ NO /___/

If yes, NDA # _____ Drug Name _____

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

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

YES /___/ NO /___/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9 (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 # _____ _____

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 9. IF "YES," GO TO PART III.

PART III: <u>THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS</u>

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 9.

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.

For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

(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 9:**

_____

_____

(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:

Investigation #1, Study # _____

Investigation #2, Study # _____

Investigation #3, Study # _____

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 /___/

Investigation #3 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:

NDA # _____ Study # _____
NDA # _____ Study # _____
NDA # _____ Study # _____

(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 /___/

Investigation #3 YES /___/ NO /___/

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

NDA # _____ Study # _____

NDA # _____ Study # _____

NDA # _____ Study # _____

(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"):

Investigation #__, Study # _____

Investigation #__, Study # _____

Investigation #__, Study # _____

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 of Preparer — Date: 10/9/02

Title: CPMS

_____ _____

Signature of Office or Division Director — Date

cc:
Archival NDA
HFD- /Division File
HFD- /RPM
HFD-093/Mary Ann Holovac
HFD-104/PEDS/T.Crescenzi

Form OGD-011347
Revised 8/7/95; edited 8/8/95; revised 8/25/98, edited 3/6/00

PEDIATRIC PAGE

(Complete for all APPROVED original applications and efficacy supplements)

DA/BLA # : 21-472 **Supplement Type (e.g. SE5):** x **Supplement Number:** x

Stamp Date: 12/18/01 **Action Date:** 10/09/02

HFD 550 **Trade and generic names/dosage form:** Ibuprofen Capsules 200mg

Applicant: Banner Pharmaceuticals **Therapeutic Class:** 3S

Indication(s) previously approved: None

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

Number of indications for this application(s): 1

Indication #1: Temporarily relieves the minor aches and pains due to: headache, muscular aches, minor pain of arthritis, toothache, backache, the common cold, menstrual cramps, temporarily reduces fever.

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

X **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:

X **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.

ection 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}

_____

Regulatory Project Manager

cc: NDA

HFD-950/ Terrie Crescenzi
HFD-960/ Grace Carmouze
(revised 9-24-02)

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT, PEDIATRIC TEAM, HFD-960
301-594-7337

Attachment A

(This attachment is to be completed for those applications with multiple indications only.)

Indication #2: _____

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:**_____

studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is mplete 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): _____

f 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:

f there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no ther indications, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

_____
Regulatory Project Manager

APPEARS THIS WAY
ON ORIGINAL

c: NDA
HFD-960/ Terrie Crescenzi
(revised 1-18-02)

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT, PEDIATRIC TEAM, HFD-960
301-594-7337

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: 3/31/02

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

(1)As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators		
	[redacted]	[redacted]
	[redacted]	
	[redacted]	

(2)As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in an financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

(3)As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and t was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
Donna Lee, R.Ph.	Director of Nutritional New Product Concepts.
FIRM/ORGANIZATION: Banner Pharmacaps Inc.	
SIGNATURE: Donna S Lee R.Ph	DATE: 4-16-01

Paperwork Reduction Act Statement

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. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessar data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

1 24aR

FORM FDA 3454 (3/99)

(301) 443-2454 XFT

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-472

Banner Pharmacaps
Attention: Dale A. Kruep, Ph.D.
Director, Regulatory Affairs
P.O. Box 2210
4125 Premier Drive
High Point, NC 27261

Dear Dr. Kruep:

We have received your new drug application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product:	ibuprofen capsule 200 mg
Review Priority Classification:	Standard (S)
Date of Application:	December 14, 2001
Date of Receipt:	December 18, 2001
Our Reference Number:	NDA 21-472

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b)(2) of the Act on February 18, 2002 in accordance with 21 CFR 314.101(a). If the application is filed, the primary user fee goal date will be October 18, 2002 and the secondary user fee goal date will be December 18, 2002.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). If you have not already fulfilled the requirements of 21 CFR 314.55 (or 601.27), please submit your plans for pediatric drug development within 120 days from the date of this letter unless you believe a waiver is appropriate. Within approximately 120 days of receipt of your pediatric drug development plan, we will review your plan and notify you of its adequacy.

APPEARS THIS WAY
ON ORIGINAL

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will make a determination whether to grant or deny a request for a waiver of pediatric studies during the review of the application. In no case, however, will the determination be made later than the date action is taken on the application. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov/cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" (PPSR) in addition to your plans for pediatric drug development described above. We recommend that you submit a Proposed Pediatric Study Request within 120 days from the date of this letter. If you are unable to meet this time frame but are interested in pediatric exclusivity, please notify the division in writing. FDA generally will not accept studies submitted to an NDA before issuance of a Written Request as responsive to a Written Request. Sponsors should obtain a Written Request before submitting pediatric studies to an NDA. If you do not submit a PPSR or indicate that you are interested in pediatric exclusivity, we will review your pediatric drug development plan and notify you of its adequacy. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application. All communications concerning this NDA should be addressed as follows:

U.S. Postal Service:

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

Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Anti-Inflammatory, Analgesic and
Ophthalmic Drug Products, HFD-550
Attention: Division Document Room
HFD-550
9201 Corporate Blvd.
Rockville, Maryland 20850-3202

If you have any questions, call Barbara Gould, Project Manager, at (301) 827-2090.

Sincerely,

{See appended electronic signature page}

Carmen DeBellas, R.Ph.
Chief, Project Management Staff
Division of Anti-Inflammatory, Analgesic and Ophthalmic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL

APPEARS THIS WAY
ON ORIGINAL

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

/s/

Barbara Gould
2/14/02 04:38:26 PM
for Carmen DeBellas

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-472

Banner Pharmacap, Inc.
Attention: Dale A. Kruep, Ph.D.
4125 Premier Drive
High Point, NC 27265

Dear Dr. Kruep:

Please refer to your submission dated January 25, 2002, requesting a waiver for pediatric studies for ibuprofen capsules 200 mg.

We have reviewed the submission and agree that a waiver is justified only for pediatric studies in patients up to 12 years of age for ibuprofen for the following indications:

> Temporary relief of minor aches and pains due to: headache, backache, muscular aches, common cold, minor pain [redacted] arthritis, toothache, menstrual cramps, and [redacted]

However, we do not agree that a waiver of pediatric studies in patients 12-17 is justified for ibuprofen.

Accordingly, a waiver for pediatric studies for this application is denied under 21 CFR 314.55 at this time. Please submit your pediatric drug development plan.

If you have questions, please call Barbara Gould, Regulatory Project Manager, at 301 827-2090.

Sincerely,

{See appended electronic signature page}

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

APPEARS THIS WAY
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/s/

Lee Simon
5/2/02 12:46:49 PM

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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: Ms. Donna S. Lee	**From:** Ms. Jane A. Dean, RN, MSN
Fax: 336-812-9091	**Fax:** 301-827-2531
Phone: 336-812-8700	**Phone:** 301-827-2090
Pages: (including cover page) 1	**Date:** 6 September 2002
Re: NDA 21-472 Biopharm Request	

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

• **Comments:**

Dear Ms. Lee,

I am the project manager who is covering your IND for Barbara Gould while she is on a four month detail. Our biopharm reviewer has asked that I forward the following request to you.

- A relatively high agitation speed of [redacted] rpm was specified in your proposed dissolution method without any documentation on the rationale for this choice. Since the subject drug product contains solubilized active ingredients in a soft gelatin capsule, one would expect dissolution to be complete and rapid after the gelatin shell ruptures. The applicant should submit other data that they have generated at lower agitation speeds (e.g. 50, 75 and 100 rpm) that resulted in them concluding that an agitation speed of [redacted] rpm is the most appropriate.

Please feel free to call me at 301-827-2536 if you should have any questions. Thank you.

Sincerely,

Ms. Jane A. Dean
Project Manager

APPEARS THIS WAY
ON ORIGINAL

CC: NDA 21-472
HFD 560 Div file
Lumpkins
Ellenberg
Yoder
Draft to DL: 5-20-02; 9-11-02
Revised review 7-14-02, 8-27-02; 9-11-02 ;9-18-02
To M. Chang 9-18-02.
Revised per M. Chang comments 9-18-02; 9-23-02
Doc name: 21-472lbl.doc

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/s/

Jane Dean
9/26/02 11:02:39 AM
CSO

Carmen DeBellas
9/26/02 01:33:55 PM
CSO

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ON ORIGINAL

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:	Ms. Donna S. Lee	**From:**	Mr. Carmen DeBellas
Fax:	336-812-9091	**Fax:**	301-827-2531
Phone:	**336-812-8700**	**Phone:**	**301-827-2090**
Pages:	**2 (including cover page)**	**Date:**	**2 October 2002**
Re:	**NDA 21-472 Phase IV Biopharm study request**		

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

• **Comments:**

NDA 21-472 Biopharm Response to Sponsor

Please refer to your new drug application NDA 21-472 dated December 18t^{h}, 2001, submitted under section 505 (b) (2) of the Federal Food, Drug and Cosmetic Act for Ibuprofen Capsules, 200 mg, our faxed comments related to dissolution studies on September 6th, 2002, and your submission dated September 10th, 2002.

The September 10th response to the comment of the Agency's fax dated September 6th, 2002 was found inadequate to justify the choice of your speed of [redacted] for the following reasons:

1. Although this was the speed specified in the USP 23-1995 for ibuprofen tablets when the development of your project occurred, the speed specified in the current USP 25-2002 has been changed to 50 RPM. Also your dosage form is different from that stated in the USP, therefore the USP method should serve only as a guide.
2. We are unable to discuss the specifications of the other NDA's (# 20-402 and 18-989) that you referred to because it represents information on both test methods and specifications that are trade secret in nature.

Based on the aforementioned we are requesting that you conduct dissolution studies to evaluate the effect of the following lower agitation speeds, 50, 75 and 100 RPM. The results of these studies should be submitted by December 1st, 2002.

Please send a correspondence to the NDA indicating your agreement to provide this data by December 1st, 2002.

If you have any questions, or if for any reason you do not agree with this request, please promptly contact Carmen Debellas, Supervisory (CSO), at 301-827-2538.

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-472

Banner Pharmacap, Inc.
Attention: Dale A. Kruep, Ph.D.
4125 Premier Drive
High Point, NC 27265

Dear Dr. Kruep:

Please refer to your submission dated January 25, 2002, requesting a waiver for pediatric studies for ibuprofen capsules.

We have reviewed the submission and agree that a waiver is justified for ibuprofen capsules, 200 mg indicated for temporary relief of minor aches and pains due to headache, backache, muscular aches, common cold, minor pain – arthritis, toothache, menstrual cramps, and — for the entire pediatric population.

Accordingly, a waiver for pediatric studies for your application is granted under 21 CFR 314.55 at this time.

If you have questions, please call Barbara Gould, Regulatory Project Manager, at 301 827-2090.

Sincerely,

{See appended electronic signature page}

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

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ON ORIGINAL

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/s/

Lee Simon
10/7/02 12:26:15 PM

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Number of Pages Redacted 4

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Draft Labeling
(not releasable,

LABELING REVIEW OF NDA

NDA: 21-472 and 21-472 BL

Labeling Amend (BL) Date: Oct 3, 2002
Received Date: Oct 7, 2002

Review Date: Oct 9, 2002

Applicant:

Banner Pharmacaps, Inc.
P.O. Box 2210
4125 Premier Drive
High Point, NC
27261-2210

Applicant's Representative:

Donna Lee, R.Ph.
Director, Regulatory Affairs and
Project Management
336-812-8700 ext. 3312

Drug:

Ibuprofen capsules (Softgels), 200 mg

Pharmacologic Category

Pain reliever/fever reducer

Submitted:

Proposed [redacted] (outer) label for 40- and 200-count

Color immediate container and outer carton labels for 40 and [redacted]

Reviewer:

Ida Yoder

Background: On September 23, 2002 the agency asked the sponsor to make the following labeling changes to their August 20th labeling submission:

1. The heading, [redacted], should be revised to the pleural "Purposes".
2. The line separating the "Alergy alert" warning and the "Alcohol warning" should be removed.
3. The storage statement under "Other information" should be revised from [redacted] "■ store at 20-25 °C (68-77 °F) ■ avoid excessive heat above 40 °C (104 °F)".
4. Based on the chemist's comments, in the list of inactive ingredients, the name [redacted] should be changed to "vitamin E polyethylene glycol succinate" or [redacted], and the ingredient names, "sorbitan" and "mannitol", should be added. The ingredients should appear in alphabetical order.
5. "Questions and comments" should be included in the Drug Facts labeling after "Inactive ingredients".
6. The bullets under "Uses", "Warnings", "Directions", and "Other information" should be spaced and aligned to comply with §201.66(d)(4).
7. Where the drug facts labeling is continued from one panel to the next, a visual graphic (e.g., an arrow) should be used to signal the continuation of the Drug Facts labeling from one panel to the next, to comply with §201.66(d)(4). The graphic should be inside the Drug Facts enclosure.

The agency also encouraged the sponsor to enhance the tamper-evident statement by specifically identifying the "tamper-evident seal", and said the statement may appear under "Other information", or alternatively, may appear elsewhere on the label. The sponsor was reminded that it will need to comply with the specifications as stated in the OTC Labeling Requirements final rule (64 FR 13254) and the technical amendment to the final rule (65 FR 7) that published in the FEDERAL REGISTER on March 17, 1999, and January 3, 2000, respectively. The sponsor was asked to resubmit draft labeling after making the changes. On October 3, 2002 the sponsor submitted revised

labeling for the 40 and [redacted]count packages. The submission also included labeling for [redacted] which is not reviewed here.

Reviewer's Comments:

The text of the labeling in this October 3 rd submission is acceptable, except as stated in number 8 below. The sponsor has made changes requested by the agency in numbers 1 through 5 and number 7 above. However, the formatting does not comply with §201.66(d), and the following revisions should be made to comply with the regulations.

1. Under "USES", the bullets should be vertically aligned to comply with §201.66(d)(4). (See number 5 below.)
2. Under "Other information" the tamper-evident statement should be preceded by a bullet as stated in §201.66(d)(4), and should not be bolded. All upper case letters in the words [redacted] if Tamper-Evident" (including the [redacted]) should be revised to lower case. The regulations in §201.66 do not provide for bolding except for headings, subheadings, telephone numbers when included under "Questions" or "Questions and comments", or if otherwise required in an approved drug application or OTC drug monograph. The regulations also do not provide for the use of upper case letters except in specific instances, such as in headings.
3. Under "Questions and comments" the telephone number should be bolded, as required in §201.66(d)(9).
4. The drug facts labeling should be continuous without interruption from panel to panel as required in §201.66(c)(5). Therefore, the [redacted] statement that appears immediately after the drug facts on the front side should be deleted, and the [redacted]

The agency is also requesting the following revisions:

5. Under "USES", the first bullet ("temporarily relieves minor aches and pains due to:") and last bullet ("temporarily reduces fever") should be far left justified and vertically aligned. Bullet numbers 2 through 7 are sub-bullets of the first bullet and, for clarity, should be indented and vertically aligned with the sub-bullet(s) on the previous line(s). (See mockup and §201.66(d)(4).)
6. Under "Do not use" the period after "reducer" should be removed.
7. Under "Directions" the first two and the last bullet should be far left justified and vertically aligned. Bullet numbers 3 through 6 are sub-bullets of number 2 and, for clarity, should be indented and vertically aligned with the sub-bullet(s) on the previous line(s). (See attached mockup.)
8. Under "Inactive ingredients" the name [redacted] should be revised to use the more common term "povidone" and the period should be removed after the last ingredient.
9. The USP officially recognizes solid oral dosage forms as capsules and tablets. The word "Softgels" is not officially recognized. The word "Softgels" may be used only if defined in the net quantity of content declaration on the principle display panel. "Softgel(s)" must be followed by an asterisk and a footnote defining "Softgels" ([redacted]

It is noted that the PDP submitted provides little detail and the sponsor should verify that this is the PDP that will be used.

The sponsors proposed arrangement of bullets under "USES" would be acceptable under §201.66(d)(10)(iv). However, the sponsor has not given any justification to support the use of a modified format. Thus, the label will need to comply with the standard format described in §201.66(d)(4).

Recommendations: The sponsor should be advised that the labeling is approvable, providing changes 1 through 8 under "Reviewer's Comments" are made and providing the PDP submitted is the PDP that will be used. The attached mockup label should be included with the recommendations to the sponsor. The sponsor should also be informed that if the any other PDP labeling is used, a prior approval supplement, as opposed to a CBE, will be necessary.

Ida Yoder
Interdisciplinary Scientist

Debbie Lumpkins.
Team Leader

APPEARS THIS WAY
ON ORIGINAL

CC: NDA 21-472
HFD 560 Div file
Debellas
Ellenberg
Draft to DL: 10-08-02
Final 10-9-02
Doc name: 21-472lbl10-3-2.doc

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/s/

Ida Yoder
10/10/02 11:13:42 AM
INTERDISCIPLINARY

please sign document

Debbie Lumpkins
10/10/02 11:23:23 AM
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Number of Pages Redacted 2

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Draft Labeling
(not releasable,

LABELING REVIEW OF NDA

NDA: 21-472 BL

Labeling Amend (BL) Date: Oct 15, 2002
Received Date: Oct 15, 2002 (via FAX)

Review Date: Oct 16, 2002

Applicant:

Banner Pharmacaps, Inc.
P.O. Box 2210
4125 Premier Drive
High Point, NC
27261-2210

Applicant's Representative:

Donna Lee, R.Ph.
Director, Regulatory Affairs and
Project Management
336-812-8700 ext. 3312

Drug:

Ibuprofen capsules (Softgels), 200 mg

Pharmacologic Category

Pain reliever/fever reducer

Submitted:

Proposed [redacted] (outer) label for 40- and 200-count

Reviewer:

Ida Yoder

Background: On September 23, 2002 the agency asked the sponsor to make labeling changes to meet the requirements of § 201.66(d) and also encouraged the sponsor to make certain additional changes to their August 20th labeling submission. The sponsor was asked to resubmit draft labeling after making the changes. On October 3, 2002 the sponsor submitted revised labeling for the 40 and [redacted] packages. The submission also included labeling for [redacted] In a telecon and FAX dated 10-9-02 the agency advised the sponsor that certain changes (mainly formatting) needed to be made to the labeling in their October 3, 2002 submission.

The agency requested the following changes to comply with § 201.66:

1. Under "USES", the bullets should be vertically aligned to comply with §201.66(d)(4). (See number 5 below.)
2. Under "Other information" the tamper-evident statement should be preceded by a bullet as stated in §201.66(d)(4), and should not be bolded. All upper case letters in the words [redacted] (including the [redacted] should be revised to lower case. The regulations in §201.66 do not provide for bolding except for headings, subheadings, telephone numbers when included under "Questions" or "Questions and comments", or if otherwise required in an approved drug application or OTC drug monograph. The regulations also do not provide for the use of upper case letters except in specific instances, such as in headings.
3. Under "Questions and comments" the telephone number should be bolded, as required in §201.66(d)(9).
4. The Drug Facts labeling should be continuous without interruption from panel to panel as required in §201.66(c)(5). Therefore, the [redacted] statement that appears immediately after the drug facts on the front side should be deleted, and the [redacted]

The agency also requested the following revisions:

5. Under "USES", the first bullet ("temporarily relieves minor aches and pains due to:") and last bullet ("temporarily reduces fever") should be far left justified and vertically aligned. Bullet numbers 2 through 7 are sub-bullets of the first bullet and, for clarity, should be indented and vertically aligned with the sub-bullet(s) on the previous line(s). (See mockup and §201.66(d)(4).)

6. Under "Do not use" the period after "reducer" should be removed.
7. Under "Directions" the first two and the last bullet should be far left justified and vertically aligned. Bullet numbers 3 through 6 are sub-bullets of number 2 and, for clarity, should be indented and vertically aligned with the sub-bullet(s) on the previous line(s). (See attached mockup.)
8. Under "Inactive ingredients" the name [redacted] should be revised to use the more common term "povidone" and the period should be removed after the last ingredient.

The agency noted that the sponsor's proposed arrangement of bullets under "USES" would be acceptable under §201.66(d)(10)(iv) in a modified format. However, the sponsor did not give any justification to support the use of a modified format and stated that they intend to use the standard format rather than the modified format.

In a second telephone conversation with the sponsor, on the same date (October 9, 2002) the agency also informed the sponsor the the word "Softgels" is not an officially recognized dosage form and that it may be used only if defined in the net quantity of content declaration on the principle display panel.

In a submission dated October 10, 2002 the sponsor submitted revised labeling that included the changes requested above, except that requested in number 4. [redacted]

On October 15, 2002, the agency phoned the sponsor and relayed the deficiencies in their October 10th submission ([redacted]). On the same day (October 15th) the sponsor submitted revised labeling.

Reviewer's Comments:

The labeling submitted on October 15, 2002 is acceptable. The text of the Drug Facts labeling is the same as the mockup attached. The PDP of the labeling includes the following information on separate lines:
NDC number
Tamper-Evident
Ibuprofen Capsules, 200 mg
Pain Reliever/Fever Reducer
200 *(or 40)* Softgels*
*Liquid filled capsules

Recommendations: The sponsor should be informed that the labeling submitted on October 15, 2002, is acceptable. The sponsor should also be informed that if the any other PDP labeling is used, a prior approval supplement, as opposed to a CBE, will be necessary.

Ida Yoder
Interdisciplinary Scientist

Debbie Lumpkins.
Team Leader

CC: NDA 21-472
HFD 560 Div file
Debellas
Ellenberg
Draft to DL: 10-16-02
Final 10-16-02 (entered DFS)
Doc name: 21-472lbl10-15-2.doc

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/s/

Ida Yoder
10/16/02 02:48:20 PM
INTERDISCIPLINARY

please sign

Debbie Lumpkins
10/16/02 02:54:28 PM
INTERDISCIPLINARY

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LABELING REVIEW OF NDA

NDA: 21-472 and 21-472 BL	**Submission Date: December 14, 2001** **Received Date: December 20, 2001** **Labeling Amend (BL) Date: July 10, 2002** **Received Date: July 12, 2002** **Labeling Amend (BL) Date: July 18, 2002** **Received Date: July 19, 2002** **Labeling Amend (BL) (with font specifications) Date: Aug 20, 2002** **Received Date: Aug 21, 2002** **Review Dates:** 5-02-02, 7-14-02; 8-27-02
Applicant:	Banner Pharmacaps, Inc. P.O. Box 2210 4125 Premier Drive High Point, NC 27261-2210 336-812-8700
Applicant's Representative:	Donna Lee, R.Ph. Director, Regulatory Affairs and Project Management
Drug:	Ibuprofen capsules (Softgels), 200 mg
Pharmacologic Category	Pain reliever/fever reducer
Submitted:	Proposed bottle (outer) label for 40- and 200-count
Reviewer:	Ida Yoder

Background: Label text was provided for Ibuprofen capsules (Softgels), 200 mg with the January 18, 2002 submission. The agency requested that actual samples be submitted, and later asked the sponsor to submit specifications for the labeling (e.g., font, etc). The sponsor submitted draft labeling (hard copy and diskette) on July 10, 2002, and stated that actual labels would be submitted when samples are ready. The sponsor subsequently submitted revised labeling on July 18, and labeling with font size designation on August 20, 2002. The sponsor has not submitted final printed labels.

Reviewer's Comments: The text of the labeling in the original submission of January 16, 2002 and the three amendments submitted on July 10, July 18, and August 20, 2002, is similar, but not exactly the same. The labeling is generally consistent with currently approved labeling for ibuprofen. The amended labeling submitted on August 20, is the same as that submitted on July 18, but includes font specifications. This review is based on the latest submission dated August 20, 2002. The earlier amendment submissions will not be reviewed.

For the labeling text submitted August 20, 2002:

1. The heading, [redacted] should be revised to the pleural "Purposes".
2. The line separating the "Alergy alert" warning and the "Alcohol warning" should be removed.
3. The storage statement under "Other information" should be revised from [redacted] to: "■ store at 20-25 °C (68-77 °F) ■ avoid excessive heat above 40 °C (104 °F)".

4. Based on the chemist's comments, in the list of inactive ingredients, the name [redacted] should be changed to "vitamin E polyethylene glycol succinate" or [redacted] and the ingredient names, "sorbitan" and "mannitol", should be added. The ingredients should appear in alphabetical order.
5. "Questions and comments" should be included in the Drug Facts labeling after "Inactive ingredients".
6. The bullets under "Uses", "Warnings", "Directions", and "Other information" should be spaced and aligned to comply with §201.66(d)(4).
7. Where the drug facts labeling is continued from one panel to the next, a visual graphic (e.g., an arrow) should be used to signal the continuation of the Drug Facts labeling from one panel to the next, to comply with §201.66(d)(4). The graphic should be inside the Drug Facts enclosure.
8. The tamper-evident statement could be enhanced by specifically identifying the "tamper-evident seal". For instance, if the seal is imprinted with specific wording and is placed around the neck of the bottle, the statement should include that wording, and the placement of the seal, so that the consumer can readily identify whether or not the seal has been broken.
9. The tamper-evident statement may appear under "Other information", or alternatively, may appear elsewhere on the label.
10. The bottle label submitted is the outer label. The sponsor stated that there is no carton.

Recommendations: The sponsor should be advised to make the changes outlined in numbers 1 through 7 and encouraged to make the change suggested in number 8. The sponsor should be reminded that it will need to comply with the specifications as stated in the OTC Labeling Requirements final rule (64 FR 13254) and the technical amendment to the final rule (65 FR 7) that published in the FEDERAL REGISTER on March 17, 1999, and January 3, 2000, respectively. The sponsor should be asked to resubmit draft labeling after making the changes.

Ida Yoder
Interdisciplinary Scientist

Marina Chang, R.Ph.
Team Leader

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/s/

Ida Yoder
9/23/02 11:15:06 AM
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please sign

Marina Chang
9/23/02 01:13:46 PM
INTERDISCIPLINARY

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ON ORIGINAL

BANNER
PHARMACAPS

Regulatory Affairs

FAX

Date: 10/03/02 1:23 pm
Number of pages including cover sheet: 5

To:
Mr. Carmen DeBellas
FDA

Phone:
Fax phone: 301-827-2531
CC:

From:
Donna S. Lee

Phone: 336-812-8700 x3312
Fax phone: 336-812-9091

REMARKS: ☐ Urgent ☒ For your review ☐ Reply ASAP ☐ Please comment

Dear Mr. DeBellas,

Attached please find our amendment response to your fax dated 10/2/02 pertaining to NDA #21-472. Hard copies of this amendment will be sent via overnight delivery.

Thank you for your time and we look forward to your reply.

APPEARS THIS WAY ON ORIGINAL

BANNER
PHARMACAPS

October 3, 2002

Dr. Lee Simon
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Anti-Inflammatory, Analgesic and
Ophthalmic Drug Products, HFD-550
9201 Corpórate Blvd
Rockville, MD 20857-3302

RE: NDA 21-472: Ibuprofen Capsules, 200 mg CMC Amendment
Banner Pharmacaps Inc.

Dear Dr. Simon:

In response to the fax sent by Mr. Carmen DeBellas on 10/2/02 at the request of the biopharm reviewer, we agree to conduct dissolution studies to evaluate the effect of lower agitation speeds (50, 75 & 100 RPMs). It is our intention to use [redacted] capsules at each agitation speed. All other conditions of the method will remain the same as those used at the [redacted] speed. We will report the results to the agency by 12/1/02.

If the reviewer requests dissolution profiles or additional information be included, please notify me.

Thank you for your cooperation and guidance.

BPI is confident that this amendment represents a complete response to your request for information. If you have any additional questions, please feel free to contact me by telephone at (336) 812-8700, ext. 3312.

APPEARS THIS WAY
ON ORIGINAL

We hereby certify that a true copy of the information contained within this amendment has been submitted to the Atlanta district office.

Please acknowledge receipt of this submission by signing and dating the enclosed copy of the cover letter and return it in the self-addressed, stamped envelope.

Sincerely,

Donna S. Lee, R.Ph.
Director, Regulatory Affairs &
Project Management

Enclosures:
Two copies of submission
One Copy of cover letter & One Self-addressed, stamped envelope

APPEARS THIS WAY ON ORIGINAL

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, Parts 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: March 31, 2003
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Banner Pharmacaps Inc.	10/03/02
TELEPHONE NO. *(Include Area Code)*	**FACSIMILE** *(FAX)* **Number** *(Include Area Code)*
336-812-8700 ext. 3312	336-812-9091
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):*	**AUTHORIZED U.S. AGENT NAME & ADDRESS** *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE
4125 Premier Drive High Point, NC 27265	

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER *(If previously issued)* 21-472

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
Ibuprofen Capsules, 200 mg	

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*	CODE NAME *(If any)*
(±)-2-(p-isobutylphenyl) propionic acid	IBU-1

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
Capsule	200 mg	Oral

(PROPOSED) INDICATION(S) FOR USE:

Temporary relief of minor aches and pains due to: headache, backache, muscular aches, common cold, minor pain of arthritis, toothache, mestrual cramps, [redacted]

PRODUCT DESCRIPTION

APPLICATION TYPE *(check one)* ☒ NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) ☐ BIOLOGICS LICENSE APPLICATION (21 CFR Part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☐ 505 (b)(1) ☒ 505 (b)(2)

IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION

Name of Drug Advil Liqui-Gels Holder of Approved Application Whitehall-Robbins

TYPE OF SUBMISSION *(check one)* ☐ ORIGINAL APPLICATION ☒ AMENDMENT TO APENDING APPLICATION ☐ RESUBMISSION ☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ EFFICACY SUPPLEMENT ☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☐ OTHER

IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____

IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY ☐ CBE ☐ CBE-30 ☐ Prior Approval (PA)

REASON FOR SUBMISSION

Response to FDA request for additional information

PROPOSED MARKETING STATUS *(check one)* ☐ PRESCRIPTION PRODUCT (Rx) ☒ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED [redacted] THIS APPLICATION IS ☒ PAPER ☐ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)
Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

Refer to original application (submitted 12/17/01)

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

Refer to original application (submitted 12/17/01)

This application contains the following items: *(Check all that apply)*	
☐	1. Index
☐	2. Labeling *(check one)* ☐ Draft Labeling ☐ Final Printed Labeling
☐	3. Summary (21 CFR 314.50 (c))
☒	4. Chemistry section
☒	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
☐	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
☐	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
☐	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)
☐	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)
☐	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
☐	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
☐	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
☐	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
☐	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
☐	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)
☐	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
☐	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))
☐	15. Establishment description (21 CFR Part 600, if applicable)
☐	16. Debarment certification (FD&C Act 306 (k)(1))
☒	17. Field copy certification (21 CFR 314.50 (l)(3))
☐	18. User Fee Cover Sheet (Form FDA 3397)
☐	19. Financial Information (21 CFR Part 54)
☐	20. OTHER *(Specify)*

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660, and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.
5. Regulations on making changes in application in FD&C Act Section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE:
Donna Lee	Donna S. Lee, R.Ph. Director, Regulatory Affairs & Project Mgmt.	10/3/02

ADDRESS *(Street, City, State, and ZIP Code)*	Telephone Number
4125 Premier Drive High Point, NC 27265	(336) 812-8700 ext. 3312

APPEARS THIS WAY ON ORIGINAL