CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-920

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

Department of Health and Human Services
Food and Drug Administration

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

Form Approved: OMB No. 0910-0513
Expiration Date: 07/31/06
See OMB Statement on Page 3.

NDA NUMBER

NAME OF APPLICANT / NDA HOLDER
Banner Pharmacaps 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)
Naproxen Sodium Capsules, 220 mg

ACTIVE INGREDIENT(S)	STRENGTH(S)
Naproxen Sodium	220 mg

DOSAGE FORM
Capsule (liquid filled soft gelatin)

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	b. Issue Date of Patent	c. Expiration Date of Patent

d. Name of Patent Owner	Address *(of Patent Owner)*	
	City/State	
	ZIP Code	FAX Number *(if available)*
	Telephone Number	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)	Address *(of agent or representative named in 1.e.)*	
	City/State	
	ZIP Code	FAX Number *(if available)*
	Telephone Number	E-Mail Address *(if available)*

f. Is 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

PSC Media Arts (301) 443-1090 EF

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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)*	Date Signed
Shelly K. Meachum	4/14/05

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.

☒ NDA Applicant/Holder	☐ NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
☐ Patent Owner	☐ Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name Banner Pharmacaps Inc.	
Address 4125 Premier Drive	City/State High Point, NC
ZIP Code 27265	Telephone Number 336-812-8700 extension 3312
FAX Number *(if available)* 336-812-9091	E-Mail Address *(if available)* skmeachum@banpharm.com

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Patent Certification

21 CFR 314.50(h)(ii), No Relevant Patents

In the opinion and to the best knowledge of Banner Pharmacaps Inc., there are no patents that claim the drug on which investigations that are relied upon in this application were conducted or that claim a use of such drug.

Shelly K Meachum
Shelly K. Meachum
Director, Regulatory Affairs

4-14-2005
Date

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In accordance with 21 CFR 314.50(j), Banner Pharmacaps Inc. does not believe that the proposed drug product is entitled to a period of marketing exclusivity.

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On Original

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA # :21-920 Supplement Type (e.g. SE5): _____ Supplement Number:

Stamp Date: 4/18/05 Action Date: 2/18/06

HFD 560 Trade and generic names/dosage form: naproxen sodium capsules

Applicant: Banner Pharmacaps, Inc. Therapeutic Class: 5030300 NSAID

Indication(s) previously approved:

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

Number of indications for this application(s):1

Indication #1: Relief of minor aches and pains due to: headache, backache, muscular aches, common cold, arthritis, toothache, menstrual cramps, fever.

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

- ☐ Yes: Please proceed to Section A.
- X No: Please check all that apply: X Partial Waiver X 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: Less than 6 months of age.

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
- X There are safety concerns
- ☐ Adult studies ready for approval
- ☐ Formulation needed
- X Other: The September 18, 1997, Nonprescription Drug Advisory Committee determined that labeling for pain/fever reducer products could safely include children down to 6 months of age, therefore the partial waiver is for ages less than 6 months of age.

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

omplete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred: 6 months to ~ years of age

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**
- X **Formulation needed**

Other:_____

Date studies are due (mm/dd/yy): February 18, 2009

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: None

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 21-920
HFD-960/ Grace Carmouze

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

(revised 12-22-03)

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:**_____

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 copy the fields above and complete pediatric information as directed. If there are no other 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

cc: NDA 21-920
HFD-960/ Grace Carmouze

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

(revised 10-14-03)

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

/s/

Laura Shay
2/16/2006 04:53:38 PM

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Debarment Certification Statement

Banner Pharmacaps Inc. 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 NDA.

Charles L. Ramsburg

Charles Ramsburg
Global Vice President
Human Resources

4/15/05
Date

Appears This Way
On Original

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

Form Approved: OMB No. 0910-0396
Expiration Date: February 28, 2006.

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	

☐ (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 any 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 it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
Shelly K. Meachum, B.Sc., RAC	Director, Regulatory Affairs
FIRM / ORGANIZATION: Banner Pharmacaps Inc.	
SIGNATURE: Shelly K. Meachum	DATE: 4/15/05

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 necessary 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

FORM FDA 3454 (2/03)

Created by: PSC Media Arts Branch (301) 443-1090 EF

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

Application Information			
NDA 21-920	Efficacy Supplement Type SE-	Supplement Number	
Drug: naproxen sodium 220 mg		Applicant: Banner Pharmacaps Inc.	
RPM: Laura Shay		HFD-560	Phone # 301-796-0994

Application Type: ( ) 505(b)(1) **X** 505(b)(2) (This can be determined by consulting page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.) **If this is a 505(b)(2) application, please review and confirm the information previously provided in Appendix B to the NDA Regulatory Filing Review. Please update any information (including patent certification information) that is no longer correct.** **X** Confirmed and/or corrected	Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s)): NDA 20-204 Aleve® (naproxen sodium 220 mg)

❖ Application Classifications:	
• Review priority	**X** Standard ( ) Priority
• Chem class (NDAs only)	
• Other (e.g., orphan, OTC)	
❖ User Fee Goal Dates	NA
❖ Special programs (indicate all that apply)	**X** None Subpart H ( ) 21 CFR 314.510 (accelerated approval) ( ) 21 CFR 314.520 (restricted distribution) ( ) Fast Track ( ) Rolling Review ( ) CMA Pilot 1 ( ) CMA Pilot 2
❖ User Fee Information	
• User Fee	( ) Paid UF ID number
• User Fee waiver	( ) Small business ( ) Public health ( ) Barrier-to-Innovation ( ) Other (specify)
• User Fee exception	( ) Orphan designation **X** No-fee 505(b)(2) (see NDA Regulatory Filing Review for instructions) ( ) Other (specify)
❖ Application Integrity Policy (AIP)	
• Applicant is on the AIP	( ) Yes **X** No

• This application is on the AIP	( ) Yes **X** No
• Exception for review (Center Director's memo)	
• 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.	**X** Verified
❖ Patent	
• Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought.	**X** Verified
• Patent certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent.	21 CFR 314.50(i)(1)(*i*)(A) **X** Verified 21 CFR 314.50(i)(1) ( ) (ii) ( ) (iii)
• [505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval).	
• [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). *(If the application does not include any paragraph IV certifications, mark "N/A" and skip to the next box below (Exclusivity)).*	**X** N/A (no paragraph IV certification) ( ) Verified
• [505(b)(2) applications] For each paragraph IV certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation. Answer the following questions for each paragraph IV certification: (1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification? (Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e))). *If "**Yes**," skip to question (4) below. If "**No**," continue with question (2).* (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)? *If "**Yes**," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).* *If "**No**," continue with question (3).* (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?	( ) Yes ( ) No ( ) Yes ( ) No ( ) Yes ( ) No

(Note: This can be determined by confirming whether the Division has received a written notice from the applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2))). *If "**No**," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.* (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)? *If "**Yes**," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).* *If "**No**," continue with question (5).* (5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification? (Note: This can be determined by confirming whether the Division has received a written notice from the applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period). *If "**No**," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).* *If "**Yes**," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007) and attach a summary of the response.*	( ) Yes ( ) No ( ) Yes ( ) No
❖ Exclusivity (approvals only)	
• Exclusivity summary • Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? (Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)	
• Is there existing orphan drug exclusivity protection for the "same drug" for the proposed indication(s)? *Refer to 21 CFR 316.3(b)(13) for the definition of "same drug" for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.*	( ) Yes, Application #_____ **X** No
❖ Administrative Reviews (Project Manager, ADRA) *(indicate date of each review)*	

❖ Actions	
• Proposed action	X AP ( ) TA ( ) AE ( ) NA
• Previous actions (specify type and date for each action taken)	
• Status of advertising (approvals only)	( ) 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)	
• Most recent applicant-proposed labeling	
• Original applicant-proposed labeling	
• Labeling reviews (including DDMAC, DMETS, DSRCS) and minutes of labeling meetings *(indicate dates of reviews and meetings)*	
• 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)	
• Applicant proposed	
• Reviews	X
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	
• Documentation of discussions and/or agreements relating to post-marketing commitments	
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	X
❖ Memoranda and Telecons	X
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	
• Pre-NDA meeting (indicate date)	
• Pre-Approval Safety Conference (indicate date; approvals only)	
• Other	
❖ Advisory Committee Meeting	
• Date of Meeting	
• 48-hour alert	
❖ Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)	

Summary Review	
❖ Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) *(indicate date for each review)*	1/31/06
Clinical Information	
❖ Clinical review(s) *(indicate date for each review)*	NA
❖ Microbiology (efficacy) review(s) *(indicate date for each review)*	NA
❖ Safety Update review(s) *(indicate date or location if incorporated in another review)*	1/6/06
❖ Risk Management Plan review(s) *(indicate date/location if incorporated in another rev)*	NA
❖ Pediatric Page(separate page for each indication addressing status of all age groups)	12/1/05
❖ Demographic Worksheet *(NME approvals only)*	NA
❖ Statistical review(s) *(indicate date for each review)*	NA
❖ Biopharmaceutical review(s) *(indicate date for each review)*	2/1/06
❖ Controlled Substance Staff review(s) and recommendation for scheduling *(indicate date for each review)*	NA
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	
• Bioequivalence studies	1/30/06
CMC Information	
❖ CMC review(s) *(indicate date for each review)*	2/16/06
❖ Environmental Assessment	
• Categorical Exclusion *(indicate review date)*	2/16/06
• Review & FONSI *(indicate date of review)*	
• Review & Environmental Impact Statement *(indicate date of each review)*	
❖ Microbiology (validation of sterilization & product sterility) review(s) *(indicate date for each review)*	NA
❖ Facilities inspection (provide EER report)	Date completed: NA ( ) Acceptable ( ) Withhold recommendation
❖ Methods validation	( ) Completed NA ( ) Requested ( ) Not yet requested
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	NA
❖ Nonclinical inspection review summary	NA
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	NA
❖ CAC/ECAC report	NA

Appendix A to NDA/Efficacy Supplement Action Package Checklist

An application is likely to be a 505(b)(2) application if:

(1) it relies on literature to meet any of the approval requirements (unless the applicant has a written right of reference to the underlying data)
(2) it relies on the Agency's previous approval of another sponsor's drug product (which may be evidenced by reference to publicly available FDA reviews, or labeling of another drug sponsor's drug product) to meet any of the approval requirements (unless the application includes a written right of reference to data in the other sponsor's NDA)
(3) it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)
(4) it seeks approval for a change from a product described in an OTC monograph and relies on the monograph to establish the safety or effectiveness of one or more aspects of the drug product for which approval is sought (see 21 CFR 330.11).

Products that may be likely to be described in a 505(b)(2) application include combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations), OTC monograph deviations, new dosage forms, new indications, and new salts.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, please consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

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/s/

Laura Shay
4/24/2006 05:14:00 PM

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OTC Drug Labeling Review for Naproxen Sodium Capsules, 220 mg (NDA 21-920) Addendum

Office of Nonprescription Products
Center for Drug Evaluation and Research • Food and Drug Administration

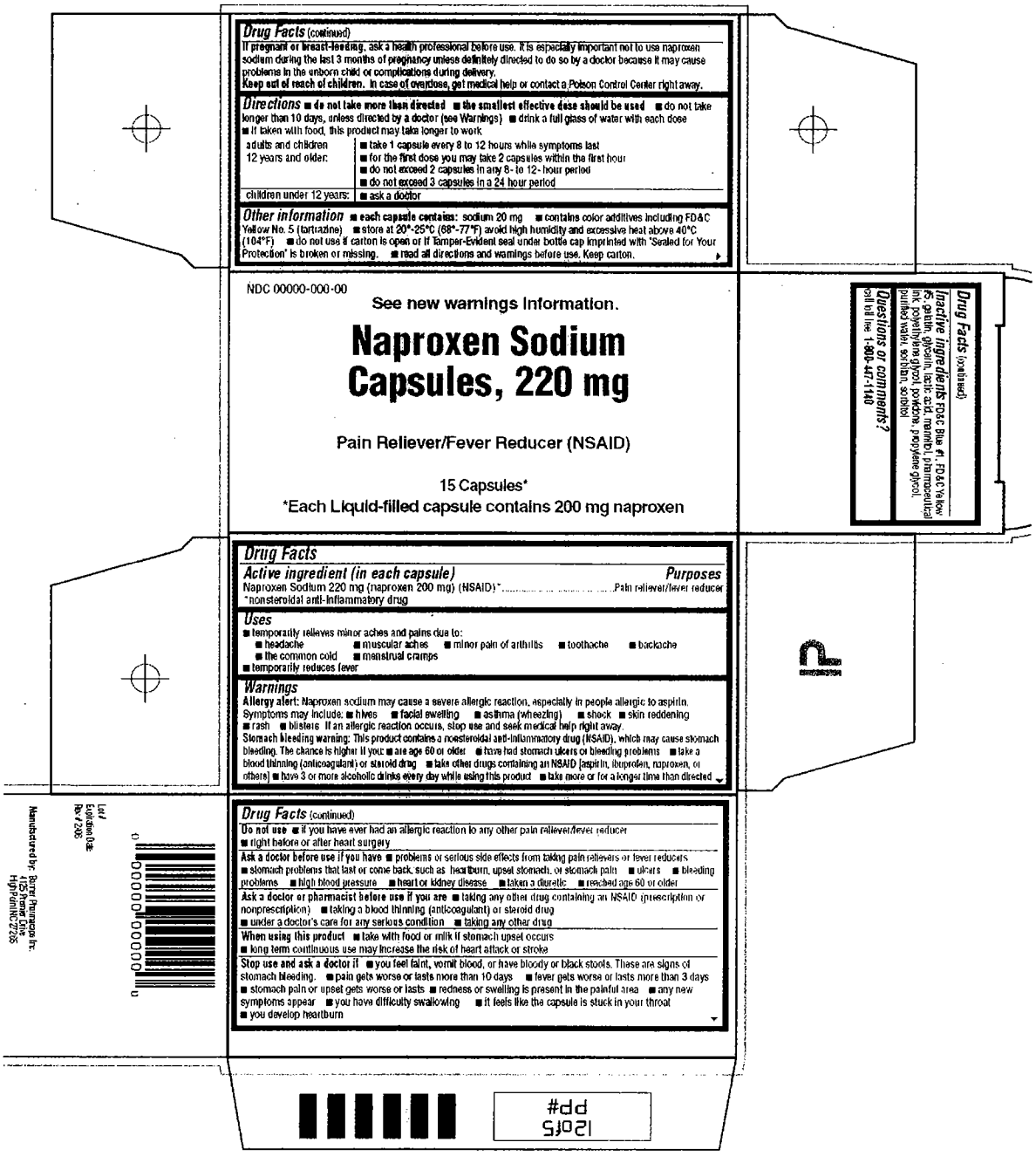
SUBMISSION DATE: February 9, 2006	**RECEIVED DATE:** February 10, 2006
REVIEW DATE:	February 14, 2006
NDA/SUBMISSION TYPE:	NDA 21-920 (N-000)
SPONSOR/CONTACT:	Shelly K. Meachum Director, Regulatory Affairs Banner Pharmacaps, Inc. 4125 Premier Drive High Point, NC 27265 336-812-8700 x-3312 FAX: 336-812-9091
DRUG PRODUCT:	Naproxen sodium capsules, 220 mg
ACTIVE INGREDIENT:	Naproxen sodium, 220 mg
INDICATIONS:	Pain reliever/fever reducer
PHARMACOLOGICAL CATEGORY:	Internal analgesic
LABELING SUBMITTED:	Carton and bottle, 15-count Bottle, 200-count
REVIEWER:	Michael L. Koenig, Ph.D.
TEAM LEADER:	Matthew Holman, Ph.D.

BACKGROUND

This is a second addendum to my review of labeling submitted with NDA 21-920. In response to my review and review addendum, both dated February 2, 2006, the sponsor submitted revised labeling on February 9, 2006.

REVIEWED LABELS

Carton, 15-count



Drug Facts (continued)

If **pregnant or breast-feeding**, ask a health professional before use. It is especially important not to use naproxen sodium during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery.

Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Directions ■ **do not take more than directed** ■ **the smallest effective dose should be used** ■ do not take longer than 10 days, unless directed by a doctor (see Warnings) ■ drink a full glass of water with each dose ■ if taken with food, this product may take longer to work

adults and children 12 years and older:	■ take 1 capsule every 8 to 12 hours while symptoms last ■ for the first dose you may take 2 capsules within the first hour ■ do not exceed 2 capsules in any 8- to 12- hour period ■ do not exceed 3 capsules in a 24 hour period
children under 12 years:	■ ask a doctor

Other information ■ **each capsule contains:** sodium 20 mg ■ contains color additives including FD&C Yellow No. 5 (tartrazine) ■ store at 20°-25°C (68°-77°F) avoid high humidity and excessive heat above 40°C (104°F) ■ do not use if carton is open or if Tamper-Evident seal under bottle cap imprinted with "Sealed for Your Protection" is broken or missing. ■ read all directions and warnings before use. Keep carton.

NDC 00000-000-00

See new warnings information.

Naproxen Sodium Capsules, 220 mg

Pain Reliever/Fever Reducer (NSAID)

15 Capsules*

*Each Liquid-filled capsule contains 200 mg naproxen

Drug Facts (continued)

Inactive ingredients FD&C Blue #1, FD&C Yellow #6, gelatin, glycerin, lactic acid, mannitol, pharmaceutical ink, polyethylene glycol, povidone, propylene glycol, purified water, sorbitan, sorbitol

Questions or comments? call toll free 1-800-447-1140

Drug Facts

Active ingredient (in each capsule) — **Purposes**

Naproxen Sodium 220 mg (naproxen 200 mg) (NSAID)* ..... Pain reliever/fever reducer

*nonsteroidal anti-inflammatory drug

Uses

■ temporarily relieves minor aches and pains due to:
■ headache ■ muscular aches ■ minor pain of arthritis ■ toothache ■ backache ■ the common cold ■ menstrual cramps
■ temporarily reduces fever

Warnings

Allergy alert: Naproxen sodium may cause a severe allergic reaction, especially in people allergic to aspirin. Symptoms may include: ■ hives ■ facial swelling ■ asthma (wheezing) ■ shock ■ skin reddening ■ rash ■ blisters If an allergic reaction occurs, stop use and seek medical help right away.

Stomach bleeding warning: This product contains a nonsteroidal anti-inflammatory drug (NSAID), which may cause stomach bleeding. The chance is higher if you: ■ are age 60 or older ■ have had stomach ulcers or bleeding problems ■ take a blood thinning (anticoagulant) or steroid drug ■ take other drugs containing an NSAID (aspirin, ibuprofen, naproxen, or others) ■ have 3 or more alcoholic drinks every day while using this product ■ take more or for a longer time than directed

Drug Facts (continued)

Do not use ■ if you have ever had an allergic reaction to any other pain reliever/fever reducer ■ right before or after heart surgery

Ask a doctor before use if you have ■ problems or serious side effects from taking pain relievers or fever reducers ■ stomach problems that last or come back, such as heartburn, upset stomach, or stomach pain ■ ulcers ■ bleeding problems ■ high blood pressure ■ heart or kidney disease ■ taken a diuretic ■ reached age 60 or older

Ask a doctor or pharmacist before use if you are ■ taking any other drug containing an NSAID (prescription or nonprescription) ■ taking a blood thinning (anticoagulant) or steroid drug ■ under a doctor's care for any serious condition ■ taking any other drug

When using this product ■ take with food or milk if stomach upset occurs ■ long term continuous use may increase the risk of heart attack or stroke

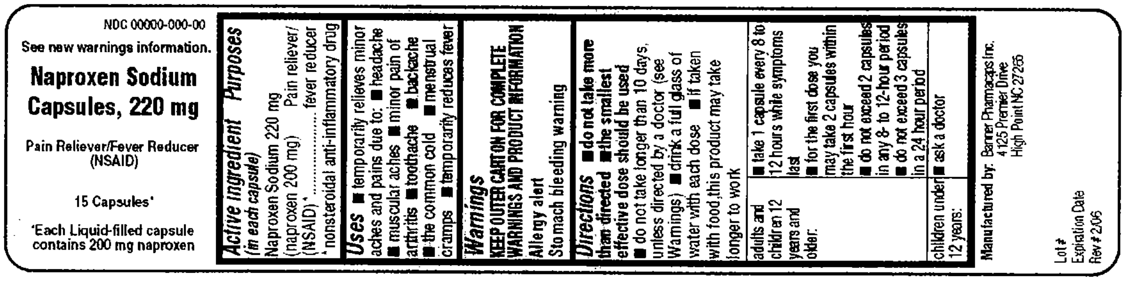
Stop use and ask a doctor if ■ you feel faint, vomit blood, or have bloody or black stools. These are signs of stomach bleeding. ■ pain gets worse or lasts more than 10 days ■ fever gets worse or lasts more than 3 days ■ stomach pain or upset gets worse or lasts ■ redness or swelling is present in the painful area ■ any new symptoms appear ■ you have difficulty swallowing ■ it feels like the capsule is stuck in your throat ■ you develop heartburn

Manufactured by: Barry Pharmaceuticals Inc. High Point, NC 27265

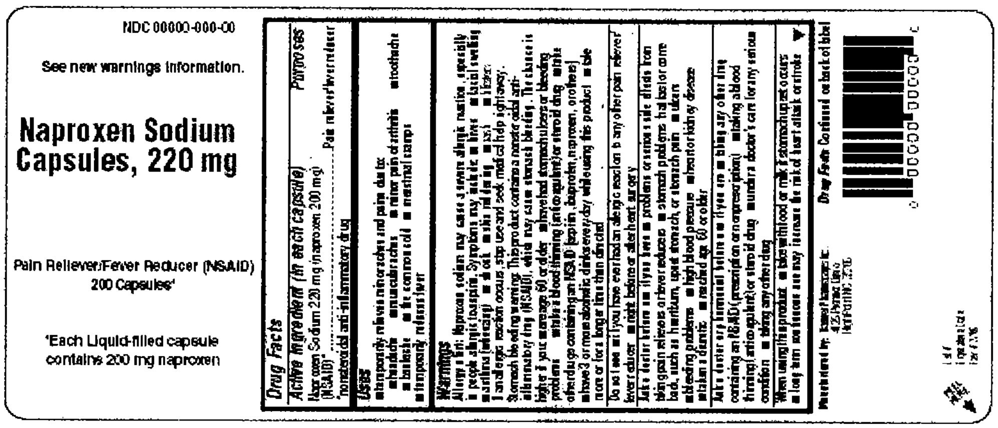
Lot / Expiration Date Rev # 2/05

#dd 12of5

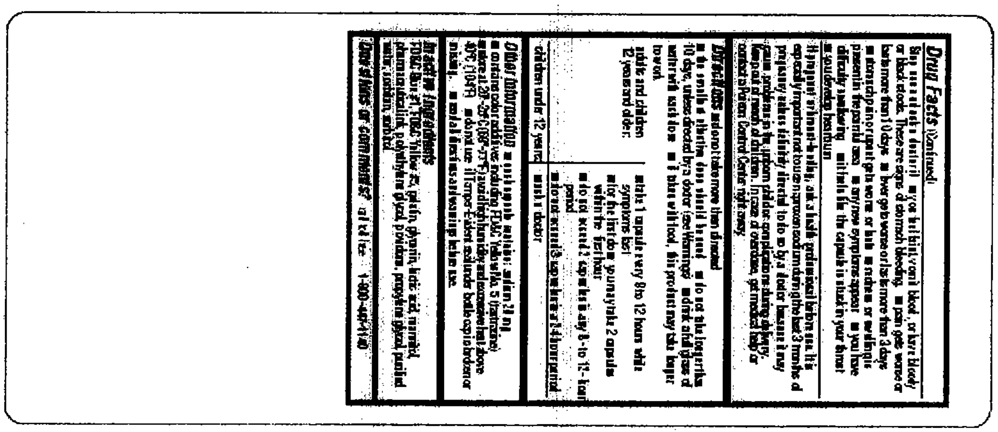
Bottle, 15-count



Bottle, 200-count



BACK



REVIEWER'S COMMENTS

The revised labeling submitted on February 9, 2006, adequately addresses all of the changes recommended in FDA's discipline review letter dated February 2, 2006. Label formatting complies with the regulations in §§ 201.61-62 (principal display panel) and 201.66(d) (Drug Facts).

RECOMMENDATION

Issue an **APPROVAL** letter for 15- and 200-count naproxen sodium capsules. The final printed labeling should be identical to the labeling submitted on February 9, 2006, and should be submitted when available.

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/s/

Michael Koenig
2/15/2006 08:09:39 AM
INTERDISCIPLINARY

Matthew Holman
2/15/2006 08:17:50 AM
INTERDISCIPLINARY

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-920

DISCIPLINE REVIEW LETTER

Banner Pharmacaps Inc.
Attention: Shelly Meachum
Director, Regulatory Affairs
4125 Premier Drive
High Point, NC 27265

Dear Ms. Meachum:

Please refer to your April 15, 2005 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for naproxen sodium 220 mg capsules.

Our review of the Labeling section of your submission is complete, and we have identified the following deficiencies in your April 15, and July 28, 2005 submissions:

1. Principal Display Panel (PDP)

   a. Add the following statement to the PDP, as indicated in the FDA's supplemental label request letters dated June 14, 2005, and July 15, 2005 requesting required warning language for all NSAID products: "See new warnings information". The statement should be fluorescent, in a contrasting color, or in bold type. The font size should be at least one-third the size of the most prominent printed matter on the PDP.

2. Drug Facts

   a. Add the following three bulleted statements under the **Stop use and ask a doctor if** subheading:
      - you have difficulty swallowing
      - it feels like the capsule is stuck in your throat
      - you develop heartburn

   b. Add a bulleted statement under ***Other information*** indicating that the product contains the color additive FD&C Yellow No. 5. According to § 201.20, the statement can be written either "contains color additives including FD&C Yellow No. 5 (tartrazine)."

   c. To be consistent with the most recently approved labeling for the reference listed drug, remove the dosing instructions for [redacted]

d. In accordance with 21 CFR 201.66(d)(5), revise the "front" Drug Facts label on the 200-count bottle to include a visual graphic (e.g., an arrow) at the bottom to indicate that the Drug fact label continues onto another panel.

e. On the 15-count carton label, under the **Stomach bleeding warning** and **Stop use and ask a doctor if** subheadings, avoid the continuation of information onto adjacent panels in order to reduce potential consumer confusion.

In addition, we have identified the need for additional language on your label based on the data from your pharmacokinetic study of drug absorption under fed conditions. According to the clinical pharmacology review of your study under fed conditions, the mean T_{max} value was increased by more than 2 hours relative to the value under fasting conditions. This delay in reaching therapeutic level (>15 µg/mL) is greater than that seen with the Reference Listed Product. FDA considers an analgesic effective if pain or fever reduction occurs within 1 hour of taking the drug. Based on this delay, you will need to add the following statement to Drug Facts under the ***Directions*** heading:

- If taken with food, this product may take longer to work

We are providing these comments to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

In order to ensure a timely action for this new drug application, we request that you respond to the issues listed above as soon as possible and submit a new label with these changes as an amendment to your April 15, 2005 new drug application.

Please cite the application number listed above at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Nonprescription Products
Division of Nonprescription Clinical Evaluation
5901-B Ammendale Road
Beltsville, MD 20705-1266

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If you have any questions you may contact Laura Shay, Regulatory Project Manager, at (301) 796-0994.

Sincerely,

{See appended electronic signature page}

Leah Christl, Ph.D.
Acting Chief, Project Management Staff
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research

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/s/

Leah Christl
2/2/2006 04:06:20 PM

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OTC Drug Labeling Review for Naproxen Sodium Capsules, 220 mg (NDA 21-920)

Office of Nonprescription Products
Center for Drug Evaluation and Research • Food and Drug Administration

SUBMISSION DATE: April 15, 2005	**RECEIVED DATE:** April 18, 2005
REVIEW DATE:	February 2, 2006
NDA/SUBMISSION TYPE:	NDA 21-920 (N-000)
SPONSOR/CONTACT:	Shelly K. Meachum Director, Regulatory Affairs Banner Pharmacaps, Inc. 4125 Premier Drive High Point, NC 27265 336-812-8700 x-3312 FAX: 336-812-9091
DRUG PRODUCT:	Naproxen sodium capsules, 220 mg
ACTIVE INGREDIENT:	Naproxen sodium, 220 mg
INDICATIONS:	Pain reliever/fever reducer
PHARMACOLOGICAL CATEGORY:	Internal analgesic
LABELING SUBMITTED:	Carton and bottle, 15-count Bottle, 200-count
REVIEWER:	Michael L. Koenig, Ph.D.
TEAM LEADER:	Matthew Holman, Ph.D.

BACKGROUND

Banner Pharmacaps, Inc. submitted NDA 21-920 for naproxen sodium capsules, 220 mg, on April 15, 2005. The NDA was submitted under section 505(b)(2) of the Federal Food Drug and Cosmetic Act. The reference listed drug (RLD) is Aleve® (NDA 20-204). Aleve is marketed as 220 mg naproxen sodium caplets.

2 Page(s) Withheld

_____ Trade Secret / Confidential

✓ Draft Labeling

_____ Deliberative Process

Withheld Track Number: Administrative- A

5. [redacted]

6. In accordance with § 201.66(d)(5), the sponsor must revise the "front" label of the 200-count bottle to include a visual graphic (e.g., an arrow) at the bottom of the Drug Facts box.

7. On the 15-count carton label, the information under a single subheading in the Drug Facts box is split between two adjacent panels. This occurs for two ***Warnings*** subheadings: **Stomach bleeding warning** and **Stop use and ask a doctor if**. The sponsor is strongly encouraged to avoid this situation, as it may be confusing to consumers.

RECOMMENDATIONS

Communicate the following comments regarding the proposed labeling to the sponsor prior to the PDUFA goal date:

1. You are strongly encouraged to add the following statement to the PDP, as indicated in FDA's supplemental label request letters dated June 14, 2005, and July 15, 2005: "See new warnings information." If the statement is added, it should be fluorescent, in a contrasting color, or in bold type, and the font size should be at least one-third the size of the most prominent printed matter on the PDP.

2. To be consistent with the last approved RLD labeling (and your original proposed labeling), add the following three bulleted statements under the **Stop use and ask a doctor if** subheading in the Drug Facts box:
   - you have difficulty swallowing
   - it feels like the capsule is stuck in your throat
   - you develop heartburn

3. Add the following statement under ***Directions*** in the Drug Facts box:
   - if you take it with food, this product may take longer to work.

4. Add a bulleted statement in the ***Other information*** section of the Drug Facts box indicating that the product contains the color additive FD&C Yellow No. 5. According to § 201.20, the statement can be written either "contains FD&C Yellow No. 5 (tartrazine) as a color additive" or "contains color additives including FD&C Yellow No. 5(tartrazine)."

5. [redacted]

6. In accordance with 21 CFR 201.66(d)(5), revise the "front" label of the 200-count bottle to include a visual graphic (e.g., an arrow) at the bottom of the Drug Facts box.

7. If possible, avoid the continuation of information included under the **Stomach bleeding warning** and **Stop use and ask a doctor if** subheadings onto adjacent panels of the 15-count carton label. This could reduce potential consumer confusion.

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/s/

Michael Koenig
2/2/2006 09:10:41 AM
INTERDISCIPLINARY

Matthew Holman
2/2/2006 09:28:11 AM
INTERDISCIPLINARY

OTC Drug Labeling Review for Naproxen Sodium Capsules, 220 mg (NDA 21-920) - Addendum

Office of Nonprescription Products
Center for Drug Evaluation and Research • Food and Drug Administration

SUBMISSION DATE: April 15, 2005	**RECEIVED DATE:** April 18, 2005
REVIEW DATE:	February 2, 2006
NDA/SUBMISSION TYPE:	NDA 21-920 (N-000)
SPONSOR/CONTACT:	Shelly K. Meachum Director, Regulatory Affairs Banner Pharmacaps, Inc. 4125 Premier Drive High Point, NC 27265 336-812-8700 x-3312 FAX: 336-812-9091
DRUG PRODUCT:	Naproxen sodium capsules, 220 mg
ACTIVE INGREDIENT:	Naproxen sodium, 220 mg
INDICATIONS:	Pain reliever/fever reducer
PHARMACOLOGICAL CATEGORY:	Internal analgesic
LABELING SUBMITTED:	Carton and bottle, 15-count Bottle, 200-count
REVIEWER:	Michael L. Koenig, Ph.D.
TEAM LEADER:	Matthew Holman, Ph.D.

REVIEWER'S COMMENTS

This is an addendum to my original review.

1. The labeling reviewed in the original review was submitted on July 28, 2005. This labeling differed from the labeling included in the original NDA (submitted on April 15, 2005). The reviewed labeling addressed issues raised in FDA's supplemental labeling request letters dated June 14 and July 15, 2005.

2. The bulleted statement in comment 3 of my original review should be changed as follows:
   - if taken with food, this product may take longer to work

RECOMMENDATIONS

Communicate the comments listed in my original review to the sponsor prior to the PDUFA goal date. Change recommendation #3 to read:

3. Add the following statement under ***Directions*** in the Drug Facts box:
   - if taken with food, this product may take longer to work.

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/s/

Michael Koenig
2/2/2006 03:12:01 PM
INTERDISCIPLINARY

Matthew Holman
2/2/2006 03:31:01 PM
INTERDISCIPLINARY

MEMORANDUM OF TELECON

DATE: January 30, 2006

APPLICATION NUMBER: NDA 21-290

BETWEEN:

Name: Shelly Meachum, Leonard Baum, and Steve Zolnick
Phone: (866) 606-4717
Representing: Banner Pharmacaps Inc. and Bayer Consumer Healthcare

AND

Name: Office of Nonprescription Products
Division of Nonprescription Clinical Evaluation
Laura Shay, Project Manager
Leah Christl, Acting Chief Regulatory Project Management Staff
Andrea Leonard-Segal, Acting Division Director
Daiva Shetty, Acting Medical Team Leader
Karen Feibus, Medical Officer
Office of Counter-Terrorism and Pediatrics
Division of Pediatric Drug Development
Lisa Mathis, Acting Division Director
Rosemary Addy, Project Manager

SUBJECT: Clarification on Pediatric Post-marketing Commitment

Pending the upcoming PUDFA action letter date of February 18, 2006, Banner requested a T-con to clarify the requirements and timing of the post marketing pediatric studies under PREA. FDA stated that under PREA, they are required to conduct clinical trials that address safety and efficacy of naproxen sodium for pediatric OTC NSAID indications in children ages 6 months to [redacted] years. FDA stated that Banner will need to submit their proposed pediatric plan 120 days after the receipt of an approval letter.

SIGNER'S NAME
TITLE

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/s/

Laura Shay
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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

PREA PARTIAL WAIVER GRANTED

NDA 21-920

Banner Pharmacaps Inc.
Attention: Shelly Meachum
Director, Regulatory Affairs
4125 Premier Drive
High Point, NC 27265

Dear Ms. Meachum:

Please refer to your submission dated April 15, 2005, requesting a full waiver under 505B(a) of the Federal Food, Drug, and Cosmetic Act (the Act) for pediatric studies for naproxen sodium (220mg) capsules.

We have reviewed your submission and agree that a partial waiver is justified for pediatric studies in patients younger than 6 months of age for naproxen sodium for the temporary relief of fever and minor aches and pains due to the common cold, flu, headache, sore throat, and toothache. The reason for granting the partial waiver is that an OTC naproxen product would offer an additional option for treatment of pain and fever in the pediatric population between the ages of six months and

Accordingly, a full waiver for pediatric studies for this application is denied at this time. We are deferring submission of your pediatric studies for ages 6 months to [redacted] years until February 18, 2009. The requirements for your deferred pediatric studies will be fully addressed upon approval of this product. Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are required postmarketing study commitments. The status of these postmarketing studies shall be reported annually according to 21 CFR 314.81.

If you have questions, please call Laura Shay, Regulatory Project Manager, at (301) 796-0094.

Sincerely,

Andrea Leonard-Segal, M.D.
Acting Director
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research

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/s/

Andrea Segal
12/2/2005 03:05:27 PM

MEMORANDUM

Department Of Health and Human Services
Food and Drugs Administration
Center For Drug Evaluation and Research
Office of Nonprescription Products
Division of Nonprescription Clinical Evaluation

Date: **December 2, 2005**

From: **Andrea Leonard-Segal, M.D.**
Acting Director, DNCE

Subject: **NDA 21-920**
Naproxen sodium 220 mg capsules
Pediatric Waiver

Sponsor: **Banner Pharmacaps, Inc.**

Recommendation:
The sponsor should be granted a partial waiver for pediatric studies in children younger than 6 months of age for naproxen sodium capsules, 220 mg for the temporary relief of fever and minor aches and pains due to the common cold, flu, headache, sore throat, and toothache.

Discussion:
I concur with the reasoning and recommendations in a November 30, 2005 memorandum from Dr. Lisa Mathis, Acting Director, Division of Pediatric Drug Development on the need for pediatric studies in children $\geq$ 6 months of age. The nonprescription pain reliever/fever reducer armamentarium for children is limited, consisting of acetaminophen, ibuprofen, and aspirin. Acetaminophen is labeled down to the age of 2 years. Ibuprofen is labeled down to the age of 6 months. Aspirin is labeled down to the age of 3 years; however, because of the risk of Reye's Syndrome, aspirin use is discouraged in children and teenagers. Given the potential need for an alternative medication by some children, it would be beneficial to have pediatric study information for naproxen sodium for the pain reliever/fever reducer claim. At its September 18, 1997 meeting, the Nonprescription Drug Advisory Committee determined that labeling for pain reliever/fever reducers could safely include children down to 6 months of age.

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/s/

Andrea Segal
12/2/2005 09:51:35 AM
MEDICAL OFFICER

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DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Division of Pediatric Drug Development
Office of Counter-Terrorism and Pediatrics
Center for Drug Evaluation and Research
Food and Drug Administration
Rockville MD 20857

Tel 301-827-7777
FAX 301-827-7738

M E M O R A N D U M

Date: November 30, 2005

From: Lisa Mathis, M.D.
Acting Director, Division of Pediatric Drug Development
Office of Counter-Terrorism and Pediatric Drug Development

To: Andrea Leonard Segal, M.D.
OND/ONP/DNCE

Re: Naproxen Sodium pediatric studies

Naproxen sodium, 220 mg is an over-the counter drug, approved for marketing by the FDA for various companies including Roche (Aleve®, NDA 20-204) and Perrigo (ANDA 74-661). They state that naproxen sodium "Temporarily relieves minor aches and pains due to headache, muscular aches, backache, toothache, common cold, menstrual cramps and minor pain due to arthritis. Temporarily reduces fever." It is approved for use in children 12 years old and older for these indications. Naproxen sodium is approved for treatment of pediatric patients with Juvenile Rheumatoid Arthritis (JRA) down to 2 years of age.

Other similar products available over-the-counter are acetaminophen, labeled for children 2 years old and older, aspirin, labeled for children 3 years old and older, and ibuprofen, labeled for children 6 months old and older. Aspirin use in children is discouraged because of the risk of Reyes Syndrome. There are patients who are allergic to ibuprofen. This may leave a pediatric patient with only one OTC medication to treat pain and fever.

Naproxen does appear in handbooks frequently used for dosing medications in pediatrics (Harriet Lane Handbook). The dose referenced for the treatment of pain/fever is 5-7 mg/kg Q8-12 hours. The approved dose for JRA is 10-20 mg/kg Q12 hours.

Recommendation:

Given the potential need for alternatives by some patients, and the lack of dosing information in labeling for over-the-counter indications (other than JRA), it would be beneficial to have pediatric study information for this drug.

OTC antipyretics do not having labeling under 6 months based on safety, and it is recommended that a partial waiver be granted for patients under 6 months.

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/s/

Lisa Mathis
12/1/2005 09:48:06 AM
MEDICAL OFFICER

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Food and Drug Administration
Center for Drug Evaluation and Research
Division of OTC Drug Products
Office of Drug Evaluation V

FACSIMILE TRANSMITTAL SHEET

DATE: July 12, 2005

To: Shelly K. Meachum	**From:** Laura Shay, MS, RN, C-ANP Regulatory Project Manager
Company: Banner	Division of Over-the-Counter Drug Products
Fax number: 336-812-9091	**Fax number:** (301) 827-2315
Phone number:336-812-8700	**Phone number:** (301) 827-2274

Subject: Request for data

Total no. of pages including cover: 2

Document to be mailed: ☐ YES ☑ NO

Please refer to your new drug application NDA 21-920 submitted April 18, 2005 under section 505(b) of the Federal Food, Drug, and Cosmetic Act for 220 mg naproxen sodium capsules.

Below is a list of items requested by the chemistry reviewer. Please submit the following information as an amendment to your NDA as soon as possible so that the reviewer can complete the review. If you have any questions you may call Laura Shay, regulatory project manager, at (301) 827-2274.

1. [redacted]

2. Please provide the quantitative composition of sorbitol [redacted] along with compendial status of the components.

3. Please provide the composition of [redacted]

4. Please provide a complete list of materials of construction used in each primary packaging component with names of suppliers. Provide DMF references if applicable, or a statement of compliance with appropriate CFR sections for suitability.

5. Please provide updated stability data, with statistical analysis if appropriate, justifying the proposed expiration dating period.

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We request that you submit the following information:

1. A pharmacokinetic study of drug absorption under fed conditions versus fasting conditions.

2. A color-mock up of the to-be-marketed package label with a listing of the graphic specifications. We remind you to incorporate the new cardiovascular, gastrointestinal and Steven Johnson Syndrome warnings listed in the OTC NSAID templates available at: http://www.fda.gov/cder/drug/infopage/COX2/default.htm.

3. As part of your NDA submission safety update, we request that you review, summarize, and analyze the cardiovascular and cerebrovascular adverse events associated with ibuprofen use from the published literature and any in-house data you may have.

In addition, please include the following items in electronic form:

- an alphabetized listing (by author) of abstracts;
- a tabular summary of individual adverse events by article;
- copies of the articles; and
- an alphabetized table of contents for articles.

A template for the adverse event table will be provided. Please group article listings by study type (e.g.: clinical trials, meta-analyses, case-control, cohort, and case reports). Within each study group listing, list articles in alphabetical order by first author.

The following adverse events should be included: cardiovascular death, myocardial infarction, stroke, hospitalization for congestive heart failure.

Please respond only to the above requests for additional information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

If you have any questions, call Laura Shay, Regulatory Project Manager, at (301) 827-2274.

Sincerely,

[See appended electronic signature page]

Leah Christl, Ph.D.
Acting Chief, Project Management Staff
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research

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/s/

Leah Christl
6/30/05 08:18:28 AM

NDA FILEABILITY CHECKLIST (CMC)

NDA Number: 21-920 **Applicant:** Banner Pharmacaps Inc. **Stamp Date:** 4/18/05
Drug Name: Naproxen Sodium Capsules, 220 mg

IS THE CMC SECTION OF THE APPLICATION FILABLE? Yes

The following parameters are necessary in order to initiate a full review, i.e., complete enough to review but may have deficiencies.

	Parameter	Yes	No	Comment
1	On its face, is the section organized adequately?	✓		
2	Is the section indexed and paginated adequately?	✓		
3	On its face, is the section legible?	✓		
4	Are ALL of the facilities (including contract facilities and test laboratories) identified with full street addresses and CFNs?	✓		Volume 1, pages 105, 347-348
5	Is a statement provided that all facilities are ready for GMP inspection?	✓		Volume 1, page 4
6	Has an environmental assessment report or categorical exclusion been provided?	✓		Volume 1, page 77
7	Does the section contain controls for the drug substance?	✓		Volume 1, pages 107
8	Does the section contain controls for the drug product?	✓		Volume 2, page 357
9	Has stability data and analysis been provided to support the requested expiration date?	✓		12 months of stability data at 25°C/60%RH and 30°C/65%RH on two pilot scale and one smaller batches of drug product each in 15 count and 200 count bottles was provided. 24 months expiration dating period proposed
10	Has all information requested during the IND phase, and at the pre-NDA meetings been included?			N/A
11	Have draft container labels been provided?	✓		Volume 1, Pages 87 - 91
12	Has the draft package insert been provided?		✓	N/A (OTC drug product)
13	Has an investigational formulations section been provided?		✓	
14	Is there a Methods Validation package?	✓		
15	Is a separate microbiological section included?		✓	Drug product specification includes testing for microbial limits

If the NDA is not fileable from a manufacturing and controls perspective state why it is not.

Reviewing Chemist: Rao Puttagunta, Ph.D. Date: 6/01/05

NDA FILEABILITY CHECKLIST

NDA Number: 21-920 **Applicant**: Banner Pharmacaps Inc., **Drug Name**: Naproxen Sodium Capsules, 220 mg

Have all DMF References been Identified? YES

DMF Number	Type	Holder	Description	LOA
11940	II	Albemarle Corporation	Naproxen Sodium	9/22/04
14194	IV	Banner Pharmacaps Inc.	Gel Mass	4/15/05
				10/13/04
				10/13/04
				10/13/04
				9/30/04
				10/04/04
				10/01/04
				4/05/05

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/s/

Rao Puttagunta
6/1/05 08:54:10 AM
CHEMIST

John Smith
6/1/05 09:28:42 AM
CHEMIST

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NDA 45 Day Fileability Meeting Checklist

NDA#: 21-920
Product Name: Naproxen sodium capsules, 220 mg
Sponsor: Banner
Reviewer: Karen B. Feibus, M.D.
Date: May 31, 2005

Item	Yes	No
1. Is the clinical section of the NDA organized in a manner to allow substantive review to begin?	x	
2. Is the clinical section of the NDA indexed and paginated in a manner to allow substantive review to begin?	x	
3. Is the clinical section of the NDA legible so that substantive review can begin?	x	
4. If needed, has the sponsor made an appropriate attempt to determine the most appropriate dosage and schedule for this product through appropriately designed dose-ranging studies?	NA	
5. Do there appear to be the requisite number of adequately and well-controlled studies in the application?	NA	
6. Are the pivotal efficacy studies of appropriate design to meet basic requirements for approvability of this product based on proposed draft labeling?	NA	
7. Are all data sets for pivotal efficacy studies complete for all indications requested?	NA	
8. Do all pivotal studies appear to be adequate and well-controlled within current divisional policies (or to the extent agreed to previously with the applicant by the Division) for approvability of this product based on proposed draft labeling?	x	
9. Has the applicant submitted line listings in a format to allow reasonable review of the patient data and in the format agreed to previously by the Division?	x	
10. Has the application submitted a rationale for the applicability of foreign data (disease specific, microbiologic specific) in the submission to the U.S. population?	NA	
11. Has the applicant submitted all additional required case record forms, in addition to deaths and drop-outs, previously requested by the Division?	x	
12. Has the applicant presented the safety data in a manner consistent with Center guidelines and/or in a manner previously agreed to by the Division?		x
13. Has the applicant presented the safety assessment based on all current world-wide knowledge regarding this product?		x
14. Has the applicant submitted adequate and well-controlled actual usage trial(s) within current divisional policies (or to the extent agreed to previously with the applicant by the Division) for approvability of this product based on proposed draft labeling?	NA	
15. Has the applicant submitted adequate and well-controlled labeling comprehension trial(s) within current divisional policies (or to the extent agreed to previously with the applicant by the Division) for approvability of this product based on proposed draft labeling?	NA	

Item	Yes	No
16. Has the applicant submitted draft labeling consistent with 201.5 and 201.56, current divisional policies, and the design of the development package?	x	
17. Has the applicant submitted all special studies/data requested by the Division during pre-submission discussions with the sponsor?	NA	
18. Has PREA been addressed?	x	
19. From a clinical perspective, is this NDA file-able? In no, please explain below.	x	

Reviewer Comments:

✓ Consistent with requests being made for all NSAID applications, FDA requests that Banner, Inc. submit a safety update on cardiovascular and cerebrovascular adverse events associated with naproxen sodium use.

✓ A request for waiver of pediatric studies was filed by the sponsor. This issue was addressed by The Pediatric Committee, the Division of Pediatrics, the Division of Over-the Counter Drug Products, and the Division of Anti-inflammatory, Analgesic and Ophthalmologic Drug Products

NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA # 21-920 Supplement # Efficacy Supplement Type SE-

Trade Name:
Established Name: naproxen sodium
Strengths: 220 mg

Applicant: Banner Pharmacaps Inc.
Agent for Applicant: Shelly K. Meachum, Director, Regulatory

Date of Application: April 15, 2005
Date of Receipt: April 18, 2005
Date clock started after UN:
Date of Filing Meeting: May 31, 2005
Filing Date: June 17, 2005
Action Goal Date (optional): February 18, 2006 User Fee Goal Date: NA 505b(2)

Indication(s) requested: relief of minor aches & pains due to; headache, backache, muscular aches, common cold, arthritis, toothache, menstrual cramps and fever

Type of Original NDA: (b)(1) ☐ (b)(2) ☒
OR
Type of Supplement: (b)(1) ☐ (b)(2) ☐

NOTE:

(1) If you have questions about whether the application is a 505(b)(1) or 505(b)(2) application, see Appendix A. 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), complete Appendix B.

(2) If the application is a supplement to an NDA, please indicate whether the NDA is a (b)(1) or a (b)(2) application:

☐ NDA is a (b)(1) application OR ☒ NDA is a (b)(2) application

Therapeutic Classification: S ☒ P ☐
Resubmission after withdrawal? ☐ Resubmission after refuse to file? ☐
Chemical Classification: (1,2,3 etc.) 3
Other (orphan, OTC, etc.)

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

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

NOTE: *If the NDA is a 505(b)(2) application, and the applicant did not pay a fee in reliance on the 505(b)(2) exemption (see box 7 on the User Fee Cover Sheet), confirm that a user fee is not required. The applicant is required to pay a user fee if: (1) the product described in the 505(b)(2) application is a new molecular entity or (2) the applicant claims a new indication for a use that that has not been approved under section 505(b). Examples of a new indication for a use include a new indication, a new dosing regime, a new patient population, and an Rx-to-OTC switch. The best way to determine if the applicant is claiming a new indication for a use is to compare the applicant's proposed labeling to labeling that has already been approved for the*

product described in the application. Highlight the differences between the proposed and approved labeling. If you need assistance in determining if the applicant is claiming a new indication for a use, please contact the user fee staff.

- Is there any 5-year or 3-year exclusivity on this active moiety in an approved (b)(1) or (b)(2) application? YES ☐ NO ☒
  If yes, explain:

- 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 ☒

  If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

- Is the application affected by the Application Integrity Policy (AIP)? YES ☐ NO ☒
  If yes, explain:

- 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 forms and certifications must be in paper and require a signature.
  Which parts of the application were submitted in electronic format?

  Additional comments:

- If an electronic NDA in Common Technical Document format, does it follow the CTD guidance? N/A ☒ YES ☐ NO ☐

- Is it an electronic CTD (eCTD)? N/A ☒ YES ☐ NO ☐
  If an electronic CTD, all forms and certifications must either be in paper and signed or be electronically signed.

  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 included and must be signed by the APPLICANT, not an agent.)
  NOTE: *Financial disclosure is required for bioequivalence studies that are the basis for approval.*

- Field Copy Certification (that it is a true copy of the CMC technical section)? Y ☒ NO ☐

- 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 and applicant name correct in COMIS? If not, have the Document Room make the corrections. Ask the Doc Rm to add the established name to COMIS for the supporting IND if it is not already entered.

- List referenced IND numbers: 71,161

- End-of-Phase 2 Meeting(s)? Date(s) _____ NO ☐
  If yes, distribute minutes before filing meeting.

- Pre-NDA Meeting(s)? Date(s) _____ NO ☐
  If yes, distribute minutes before filing meeting.

Project Management

- Was electronic "Content of Labeling" submitted? YES ☐ NO ☒
  If no, request in 74-day letter.

- All labeling (PI, PPI, MedGuide, carton and immediate container labels) consulted to DDMAC?
  YES ☐ NO ☒

- Risk Management Plan consulted to ODS/IO? N/A ☒ YES ☐ NO ☐

- Trade name (plus PI and all labels and labeling) consulted to ODS/DMETS? Y ☐ 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 Florian Zielinski (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 ☒

ATTACHMENT

MEMO OF FILING MEETING

DATE: May 31, 2005

BACKGROUND: Banner Pharmacaps Inc., submitted a 505b(2) application for naproxen sodium capsules 220 mg relieing on the the Agency's finding of sagety and effectiveness of the reference listed drug Aleve®tablets, 220 mg. The porposed product difers from the RLD in dosage form: a liquid filled sof gelatin capsule vs. a tablet. Data provided included bioavailability/bioequivalence studies.
(Provide a brief background of the drug, e.g., it is already approved and this NDA is for an extended-release formulation; whether another Division is involved; foreign marketing history; etc.)

ATTENDEES: Cutis Rosebraugh, Leah Christl, John Smith, Rao Puttagunta, Dennis Bashaw, Lei Zhang, Andrea Leonard-Segal, Karen Feibus, Mathew Holman, Mike koneig,

ASSIGNED REVIEWERS (including those not present at filing meeting) :

Discipline	**Reviewer**
Medical:	Andrea Leonard-Segal
Secondary Medical:	Karen Feibus
Statistical:	
Pharmacology:	
Statistical Pharmacology:	
Chemistry:	Rao Puttagunta
Environmental Assessment (if needed):	
Biopharmaceutical:	Lei Zhang
Microbiology, sterility:	
Microbiology, clinical (for antimicrobial products only):	
DSI:	
Regulatory Project Management:	Laura Shay
Other Consults:	Elaine Tseng

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

CLINICAL FILE ☒ REFUSE TO FILE ☐

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

CLINICAL MICROBIOLOGY N/A ☒ FILE ☐ REFUSE TO FILE ☐

STATISTICS N/A ☒ FILE ☐ REFUSE TO FILE ☐

BIOPHARMACEUTICS		FILE ☒	REFUSE TO FILE ☐
• Biopharm. inspection needed?			YES ☐ NO ☒
PHARMACOLOGY	N/A ☒	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:
(Refer to 21 CFR 314.101(d) for filing requirements.)

☐ 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 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. ☒ Convey document filing issues/no filing issues to applicant by Day 74.

laura Shay
Regulatory Project Manager, HFD-560

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Appendix A to NDA Regulatory Filing Review

An application is likely to be a 505(b)(2) application if:

(1) it relies on literature to meet any of the approval requirements (unless the applicant has a written right of reference to the underlying data)
(2) it relies on the Agency's previous approval of another sponsor's drug product (which may be evidenced by reference to publicly available FDA reviews, or labeling of another drug sponsor's drug product) to meet any of the approval requirements (unless the application includes a written right of reference to data in the other sponsor's NDA)
(3) it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)
(4) it seeks approval for a change from a product described in an OTC monograph and relies on the monograph to establish the safety or effectiveness of one or more aspects of the drug product for which approval is sought (see 21 CFR 330.11).

Products that may be likely to be described in a 505(b)(2) application include combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations), OTC monograph deviations, new dosage forms, new indications, and new salts.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, please consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

Appendix B to NDA Regulatory Filing Review
Questions for 505(b)(2) Applications

1. Does the application reference a listed drug (approved drug)? YES ☒ NO ☐

   *If "**No**," skip to question 3.*

2. Name of listed drug(s) referenced by the applicant (if any) and NDA/ANDA #(s): Aleve® N20-204

3. The purpose of this and the questions below (questions 3 to 5) is to determine if there is an approved drug product that is equivalent or very similar to the product proposed for approval and that should be referenced as a listed drug in the pending application.

   (a) Is there a pharmaceutical equivalent(s) to the product proposed in the 505(b)(2) application that is already approved?

   YES ☐ NO ☒

   (***Pharmaceutical equivalents*** are drug products in identical dosage forms that: **(1)** contain identical amounts of the identical active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety, or, in the case of modified release dosage forms that require a reservoir or overage or such forms as prefilled syringes where residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; **(2)** do not necessarily contain the same inactive ingredients; **and** **(3)** meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates. (21 CFR 320.1(c))

   *If "**No**," skip to question 4. Otherwise, answer part (b).*

   (b) Is the approved pharmaceutical equivalent(s) cited as the listed drug(s)? YES ☐ NO ☐
   (The approved pharmaceutical equivalent(s) should be cited as the listed drug(s).)

   *If "**Yes**," skip to question 6. Otherwise, answer part (c).*

   (c) Have you conferred with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (ORP) (HFD-007)? YES ☐ NO ☐

   *If "**No**," please contact the Director, Division of Regulatory Policy II, ORP. Proceed to question 6.*

4. (a) Is there a pharmaceutical alternative(s) already approved? YES ☒ NO ☐

   (***Pharmaceutical alternatives*** are drug products that contain the identical therapeutic moiety, or its precursor, but not necessarily in the same amount or dosage form or as the same salt or ester. Each such drug product individually meets either the identical or its own respective compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times and/or dissolution rates. (21 CFR 320.1(d)) Different dosage forms and strengths within a product line by a single manufacturer are thus pharmaceutical alternatives, as are extended-release products when compared with immediate- or standard-release formulations of the same active ingredient.)

   *If "**No**," skip to question 5. Otherwise, answer part (b).*

   (b) Is the approved pharmaceutical alternative(s) cited as the listed drug(s)? YES ☒ NO ☐
   (The approved pharmaceutical alternative(s) should be cited as the listed drug(s).)

NOTE: *If there is more than one pharmaceutical alternative approved, consult the Director, Division of*

Regulatory Policy II, Office of Regulatory Policy (ORP) (HFD-007) to determine if the appropriate pharmaceutical alternatives are referenced.

*If "**Yes**," skip to question 6. Otherwise, answer part (c).*

(c) Have you conferred with the Director, Division of Regulatory Policy II, ORP? YES ☒ NO ☐

*If "**No**," please contact the Director, Division of Regulatory Policy II, ORP. Proceed to question 6.*

5. (a) Is there an approved drug product that does not meet the definition of "pharmaceutical equivalent" or "pharmaceutical alternative," as provided in questions 3(a) and 4(a), above, but that is otherwise very similar to the proposed product?

YES ☐ NO ☒

*If "**No**," skip to question 6.*

*If "**Yes**," please describe how the approved drug product is similar to the proposed one and answer part (b) of this question. Please also contact the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007), to further discuss.*

(b) Is the approved drug product cited as the listed drug? YES ☐ NO ☐

6. 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"). change in dosage form from tablet to liquid filled soft gelatin capsules

7. 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 (see 21 CFR 314.101(d)(9)). YES ☐ NO ☒

8. 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 21 CFR 314.101(d)(9)). YES ☐ NO ☒

9. 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 21 CFR 314.54(b)(2))? If yes, the application should be refused for filing under 21 CFR 314.101(d)(9). YES ☐ NO ☒

10. Are there certifications for each of the patents listed for the listed drug(s)? YES ☒ NO ☐

11. Which of the following patent certifications does the application contain? (Check all that apply and identify the patents to which each type of certification was made, as appropriate.)

☐ 21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA. (Paragraph I certification)
Patent number(s):

☐ 21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired. (Paragraph II certification)
Patent number(s):

☐ 21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire. (Paragraph III certification)
Patent number(s):

☐ 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. (Paragraph IV certification)
Patent number(s):

NOTE: *IF FILED, and if the applicant made a "Paragraph IV" certification [21 CFR 314.50(i)(1)(i)(A)(4)], the applicant must* ***subsequently*** *submit a signed certification stating that the NDA holder and patent owner(s) were notified the NDA was filed [21 CFR 314.52(b)]. The applicant must also submit documentation showing that the NDA holder and patent owner(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 as described in the corresponding use code in the Orange Book. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications. (Section viii statement)
Patent number(s):

☐ 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).
Patent number(s):

☐ Written statement from patent owner that it consents to an immediate effective date upon approval of the application.
Patent number(s):

12. Did the applicant:

- Identify which parts of the application rely on information (e.g. literature, prior approval of another sponsor's application) that 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 ☐

13. If the (b)(2) applicant is requesting 3-year exclusivity, did the applicant submit the following information required by 21 CFR 314.50(j)(4):

- Certification that at least one 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 the NDA sponsor provided substantial support for the clinical investigation(s) essential to approval if it was not the sponsor of the IND under which those clinical studies were conducted?

  YES ☐ NO ☐

14. Has the Associate Director for Regulatory Affairs, OND, been notified of the existence of the (b)(2) application?

YES ☒ NO ☐

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/s/

Laura Shay
1/5/2006 12:26:10 PM
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Food and Drug Administration
Center for Drug Evaluation and Research
Division of OTC Drug Products
Office of Drug Evaluation V

FACSIMILE TRANSMITTAL SHEET

DATE: October 3, 20050

To: Shelly K. Meachum	**From:** Laura Shay, MS, RN, C-ANP Regulatory Project Manager
Company: Banner	Office of Nonprescription Products
Fax number: 336-812-9091	**Fax number:**
Phone number:336-812-8700	**Phone number:** (301)769-0994

Subject: Request for data

Total no. of pages including cover: 2

Document to be mailed: ☐ YES ☑ NO

Please refer to your new drug application NDA 21-920 submitted April 18, 2005 under section 505(b) of the Federal Food, Drug, and Cosmetic Act for 220 mg naproxen sodium capsules.

Below is a list of items requested by the chemistry reviewer.

1. The in-process specification should include tests for hardness and moisture content with appropriate acceptance criteria. These controls should also be incorporated into the master batch records.

2. Clarify whether the [redacted] in the in-process specification is [redacted] or [redacted] or both.

3. The information provided on the container closure materials is confusing. Specify the materials used in each container closure system configuration.

Per our conversation on September 28, 2005, it has been determined that you are required to submit additional safety information for naproxen sodium. To date, you have provided safety data for the fasting and fed PK studies in addition to cardiovascular data requested in the 74 day filing letter. Please provide a general summary of the safety data on naproxen sodium found in the literature. You should include a list of the references, copies of the references, and a summary and analysis of the safety data.

Please submit the following information as an amendment to your NDA as soon as possible so that the reviewers can complete the review. If you have any questions you may call Laura Shay, regulatory project manager, at (301) 796-0994.

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

/s/

Laura Shay
10/3/2005 01:03:19 PM

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Addendum (pg. 8)

NDA REGULATORY FILING REVIEW

(Including Memo of Filing Meeting)

NDA # 21-920 Supplement # Efficacy Supplement Type SE-

Trade Name:
Established Name: naproxen sodium
Strengths: 220 mg

Applicant: Banner Pharmacaps Inc.
Agent for Applicant: Shelly K. Meachum, Director, Regulatory

Date of Application: April 15, 2005
Date of Receipt: April 18, 2005
Date clock started after UN:
Date of Filing Meeting: May 31, 2005
Filing Date: June 17, 2005
Action Goal Date (optional): February 18, 2006 User Fee Goal Date: NA 505b(2)

Indication(s) requested: relief of minor aches & pains due to; headache, backache, muscular aches, common cold, arthritis, toothache, menstrual cramps and fever

Type of Original NDA: (b)(1) ☐ (b)(2) ☒
OR
Type of Supplement: (b)(1) ☐ (b)(2) ☐

NOTE:

(1) If you have questions about whether the application is a 505(b)(1) or 505(b)(2) application, see Appendix A. 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), complete Appendix B.

(2) If the application is a supplement to an NDA, please indicate whether the NDA is a (b)(1) or a (b)(2) application:

☐ NDA is a (b)(1) application OR ☒ NDA is a (b)(2) application

Therapeutic Classification: S ☒ P ☐
Resubmission after withdrawal? ☐ Resubmission after refuse to file? ☐
Chemical Classification: (1,2,3 etc.) 3
Other (orphan, OTC, etc.)

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

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

NOTE: *If the NDA is a 505(b)(2) application, and the applicant did not pay a fee in reliance on the 505(b)(2) exemption (see box 7 on the User Fee Cover Sheet), confirm that a user fee is not required. The applicant is required to pay a user fee if: (1) the product described in the 505(b)(2) application is a new molecular entity or (2) the applicant claims a new indication for a use that that has not been approved under section 505(b). Examples of a new indication for a use include a new indication, a new dosing regime, a new patient population, and an Rx-to-OTC switch. The best way to determine if the applicant is claiming a new indication for a use is to compare the applicant's proposed labeling to labeling that has already been approved for the*

product described in the application. Highlight the differences between the proposed and approved labeling. If you need assistance in determining if the applicant is claiming a new indication for a use, please contact the user fee staff.

- Is there any 5-year or 3-year exclusivity on this active moiety in an approved (b)(1) or (b)(2) application? YES ☐ NO ☒
  If yes, explain:

- 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 ☒

  If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

- Is the application affected by the Application Integrity Policy (AIP)? YES ☐ NO ☒
  If yes, explain:

- 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 forms and certifications must be in paper and require a signature.
  Which parts of the application were submitted in electronic format?

  Additional comments:

- If an electronic NDA in Common Technical Document format, does it follow the CTD guidance? N/A ☒ YES ☐ NO ☐

- Is it an electronic CTD (eCTD)? N/A ☒ YES ☐ NO ☐
  If an electronic CTD, all forms and certifications must either be in paper and signed or be electronically signed.

  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 included and must be signed by the APPLICANT, not an agent.)
  NOTE: *Financial disclosure is required for bioequivalence studies that are the basis for approval.*

- Field Copy Certification (that it is a true copy of the CMC technical section)? Y ☒ NO ☐

- 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 and applicant name correct in COMIS? If not, have the Document Room make the corrections. Ask the Doc Rm to add the established name to COMIS for the supporting IND if it is not already entered.

- List referenced IND numbers: 71,161

- End-of-Phase 2 Meeting(s)? Date(s) _____ NO ☐
  If yes, distribute minutes before filing meeting.

- Pre-NDA Meeting(s)? Date(s) _____ NO ☐
  If yes, distribute minutes before filing meeting.

Project Management

- Was electronic "Content of Labeling" submitted? YES ☐ NO ☒
  If no, request in 74-day letter.

- All labeling (PI, PPI, MedGuide, carton and immediate container labels) consulted to DDMAC?
  YES ☐ NO ☒

- Risk Management Plan consulted to ODS/IO? N/A ☒ YES ☐ NO ☐

- Trade name (plus PI and all labels and labeling) consulted to ODS/DMETS? Y ☐ 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 Florian Zielinski (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 ☒

ATTACHMENT

MEMO OF FILING MEETING

DATE: May 31, 2005

BACKGROUND: Banner Pharmacaps Inc., submitted a 505b(2) application for naproxen sodium capsules 220 mg relieing on the the Agency's finding of sagety and effectiveness of the reference listed drug Aleve®tablets, 220 mg. The porposed product difers from the RLD in dosage form: a liquid filled sof gelatin capsule vs. a tablet. Data provided included bioavailability/bioequivalence studies.
(Provide a brief background of the drug, e.g., it is already approved and this NDA is for an extended-release formulation; whether another Division is involved; foreign marketing history; etc.)

ATTENDEES: Cutis Rosebraugh, Leah Christl, John Smith, Rao Puttagunta, Dennis Bashaw, Lei Zhang, Andrea Leonard-Segal, Karen Feibus, Mathew Holman, Mike koneig,

ASSIGNED REVIEWERS (including those not present at filing meeting) :

Discipline	**Reviewer**
Medical:	Andrea Leonard-Segal
Secondary Medical:	Karen Feibus
Statistical:	
Pharmacology:	
Statistical Pharmacology:	
Chemistry:	Rao Puttagunta
Environmental Assessment (if needed):	
Biopharmaceutical:	Lei Zhang
Microbiology, sterility:	
Microbiology, clinical (for antimicrobial products only):	
DSI:	
Regulatory Project Management:	Laura Shay
Other Consults:	Elaine Tseng

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

CLINICAL FILE ☒ REFUSE TO FILE ☐

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

CLINICAL MICROBIOLOGY N/A ☒ FILE ☐ REFUSE TO FILE ☐

STATISTICS N/A ☒ FILE ☐ REFUSE TO FILE ☐

BIOPHARMACEUTICS FILE ☒ REFUSE TO FILE ☐

- Biopharm. inspection needed? YES ☐ NO ☒

PHARMACOLOGY N/A ☒ 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:
(Refer to 21 CFR 314.101(d) for filing requirements.)

☐ 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 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. ☒ Convey document filing issues/no filing issues to applicant by Day 74.

laura Shay
Regulatory Project Manager, HFD-560

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Appendix A to NDA Regulatory Filing Review

An application is likely to be a 505(b)(2) application if:

(1) it relies on literature to meet any of the approval requirements (unless the applicant has a written right of reference to the underlying data)
(2) it relies on the Agency's previous approval of another sponsor's drug product (which may be evidenced by reference to publicly available FDA reviews, or labeling of another drug sponsor's drug product) to meet any of the approval requirements (unless the application includes a written right of reference to data in the other sponsor's NDA)
(3) it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)
(4) it seeks approval for a change from a product described in an OTC monograph and relies on the monograph to establish the safety or effectiveness of one or more aspects of the drug product for which approval is sought (see 21 CFR 330.11).

Products that may be likely to be described in a 505(b)(2) application include combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations), OTC monograph deviations, new dosage forms, new indications, and new salts.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, please consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

Appendix B to NDA Regulatory Filing Review
Questions for 505(b)(2) Applications

1. Does the application reference a listed drug (approved drug)? YES ☒ NO ☐

   *If "**No**," skip to question 3.*

2. Name of listed drug(s) referenced by the applicant (if any) and NDA/ANDA #(s): Aleve® N20-204

3. The purpose of this and the questions below (questions 3 to 5) is to determine if there is an approved drug product that is equivalent or very similar to the product proposed for approval and that should be referenced as a listed drug in the pending application.

   (a) Is there a pharmaceutical equivalent(s) to the product proposed in the 505(b)(2) application that is already approved? YES ☐ NO ☒

   (***Pharmaceutical equivalents*** are drug products in identical dosage forms that: **(1)** contain identical amounts of the identical active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety, or, in the case of modified release dosage forms that require a reservoir or overage or such forms as prefilled syringes where residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; **(2)** do not necessarily contain the same inactive ingredients; **and** **(3)** meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates. (21 CFR 320.1(c))

   *If "**No**," skip to question 4. Otherwise, answer part (b).*

   (b) Is the approved pharmaceutical equivalent(s) cited as the listed drug(s)? YES ☐ NO ☐
   (The approved pharmaceutical equivalent(s) should be cited as the listed drug(s).)

   *If "**Yes**," skip to question 6. Otherwise, answer part (c).*

   (c) Have you conferred with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (ORP) (HFD-007)? YES ☐ NO ☐

   *If "**No**," please contact the Director, Division of Regulatory Policy II, ORP. Proceed to question 6.*

4. (a) Is there a pharmaceutical alternative(s) already approved? YES ☐ NO ☐

   (***Pharmaceutical alternatives*** are drug products that contain the identical therapeutic moiety, or its precursor, but not necessarily in the same amount or dosage form or as the same salt or ester. Each such drug product individually meets either the identical or its own respective compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times and/or dissolution rates. (21 CFR 320.1(d)) Different dosage forms and strengths within a product line by a single manufacturer are thus pharmaceutical alternatives, as are extended-release products when compared with immediate- or standard-release formulations of the same active ingredient.)

   *If "**No**," skip to question 5. Otherwise, answer part (b).*

   (b) Is the approved pharmaceutical alternative(s) cited as the listed drug(s)? YES ☐ NO ☐
   (The approved pharmaceutical alternative(s) should be cited as the listed drug(s).)

NOTE: *If there is more than one pharmaceutical alternative approved, consult the Director, Division of*

Regulatory Policy II, Office of Regulatory Policy (ORP) (HFD-007) to determine if the appropriate pharmaceutical alternatives are referenced.

*If "**Yes**," skip to question 6. Otherwise, answer part (c).*

(c) Have you conferred with the Director, Division of Regulatory Policy II, ORP? YES ☒ NO ☐

*If "**No**," please contact the Director, Division of Regulatory Policy II, ORP. Proceed to question 6.*

5. (a) Is there an approved drug product that does not meet the definition of "pharmaceutical equivalent" or "pharmaceutical alternative," as provided in questions 3(a) and 4(a), above, but that is otherwise very similar to the proposed product?

YES ☐ NO ☒

*If "**No**," skip to question 6.*

*If "**Yes**," please describe how the approved drug product is similar to the proposed one and answer part (b) of this question. Please also contact the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007), to further discuss.*

(b) Is the approved drug product cited as the listed drug? YES ☐ NO ☐

6. 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"). change in dosage form from tablet to liquid filled soft gelatin capsules

7. 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 (see 21 CFR 314.101(d)(9)). YES ☐ NO ☒

8. 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 21 CFR 314.101(d)(9)). YES ☐ NO ☒

9. 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 21 CFR 314.54(b)(2))? If yes, the application should be refused for filing under 21 CFR 314.101(d)(9). YES ☐ NO ☒

10. Are there certifications for each of the patents listed for the listed drug(s)? YES ☒ NO ☐

11. Which of the following patent certifications does the application contain? (Check all that apply and identify the patents to which each type of certification was made, as appropriate.)

☐ 21 CFR 314.50(i)(1)(i)(A)(1). The patent information has not been submitted to FDA. (Paragraph I certification)
Patent number(s):

☐ 21 CFR 314.50(i)(1)(i)(A)(2). The patent has expired. (Paragraph II certification)
Patent number(s):

☐ 21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire. (Paragraph III certification)
Patent number(s):

☐ 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. (Paragraph IV certification)
Patent number(s):

NOTE: *IF FILED, and if the applicant made a "Paragraph IV" certification [21 CFR 314.50(i)(1)(i)(A)(4)], the applicant must* ***subsequently*** *submit a signed certification stating that the NDA holder and patent owner(s) were notified the NDA was filed [21 CFR 314.52(b)]. The applicant must also submit documentation showing that the NDA holder and patent owner(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 as described in the corresponding use code in the Orange Book. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications. (Section viii statement)
Patent number(s):

☐ 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).
Patent number(s):

☐ Written statement from patent owner that it consents to an immediate effective date upon approval of the application.
Patent number(s):

12. Did the applicant:

- Identify which parts of the application rely on information (e.g. literature, prior approval of another sponsor's application) that 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 ☐

13. If the (b)(2) applicant is requesting 3-year exclusivity, did the applicant submit the following information required by 21 CFR 314.50(j)(4):

- Certification that at least one 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 the NDA sponsor provided substantial support for the clinical investigation(s) essential to approval if it was not the sponsor of the IND under which those clinical studies were conducted?

  YES ☐ NO ☐

14. Has the Associate Director for Regulatory Affairs, OND, been notified of the existence of the (b)(2) application?

YES ☒ NO ☐

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

/s/

Laura Shay
7/1/05 03:01:39 PM
CSO

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BANNER™
A SOBEL COMPANY

Banner Pharmacaps Inc.
4125 Premier Drive
High Point, NC 27265

PHONE 336.812.8700
FAX 336.812.8798

Asia/Pacific

Canada

Europe

India

Mexico/Latin America

➢ United States

April 15, 2005

Field Copy
Original 505(b)(2) NDA

Mary Woleske, District Director
Atlanta District Office (HFR-SE100)
Food and Drug Administration
60 Eighth Street NE
Atlanta, Georgia 30309

RE: Naproxen Sodium Capsules, 220 mg

Dear Ms. Woleske:

Banner Pharmacaps Inc. (BPI) has submitted a New Drug Application (NDA) for Naproxen Sodium Capsules, 220 mg to the Office of Drug Evaluation V, CDER/FDA.

In accordance with 21 CFR 314.54(a)(4), BPI is submitting herein to the FDA district office in Atlanta, a true copy of the technical sections of the NDA. BPI certifies that the enclosed Field Copy is a true copy of the technical sections of the NDA submitted to the Office of Drug Evaluation V, CDER/FDA.

If you have any questions, comments or require any additional information in regard to this application, please feel free to contact me by telephone at (336) 812-8700, extension 3312, by fax at (336) 812-9091, or in writing at the address upon this letterhead.

Sincerely,

Shelly K. Meachum

Shelly K. Meachum, B.Sc., RAC
Director, Regulatory Affairs

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

PRESCRIPTION DRUG USER FEE COVER SHEET

Form Approved: OMB No. 0910-0297
Expiration Date: December 31, 2006.

See Instructions on Reverse Side Before Completing This Form

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

1. APPLICANT'S NAME AND ADDRESS
Banner Pharmacaps Inc.
4125 Premier Drive
High Point, NC 27265

2. TELEPHONE NUMBER *(Include Area Code)*
(336) 812-8700 extension 3312

3. PRODUCT NAME
Naproxen Sodium Capsules, 220 mg

4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER

5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?
☒ YES ☐ 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:

☐ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☒ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:

20-204
(APPLICATION NO. CONTAINING THE DATA).

6. USER FEE I.D. NUMBER

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

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92
(Self Explanatory)

☒ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE
(See item 7, reverse side before checking box.)

☐ 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.)

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY
(Self Explanatory)

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FORTHIS 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
CBER, HFM-99
1401 Rockville Pike
Rockville, MD 20852-1448

and

Food and Drug Administration
CDER, HFD-94
12420 Parklawn Drive, Room 3046
Rockville, MD 20852

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
Shelly K Meachum	Director, Regulatory Affairs	4/15/2005

FORM FDA 3397 (12/03)

PSC Media Arts (301) 443-1090 EF

43 Page(s) Withheld

✓ Trade Secret / Confidential

✓ Draft Labeling

✓ Deliberative Process

Withheld Track Number: Administrative- B