CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-122

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

1.3.5.2 PATENT CERTIFICATION

Novartis by this application submitted under 21 U.S.C. §355(b)(2) [Sec. 505(b)(2) of the Federal Food, Drug and Cosmetic Act, as amended through December 31, 2004], is requesting approval for diclofenac sodium topical gel, 1% (the "Novartis Product").

On information and belief, Bioglan Pharmaceuticals Corp. is the holder of Application No. 021005, approved October 16, 2000, for SOLARAZE® brand diclofenac sodium topical gel, 3%.

Novartis hereby states, on information and belief, that U.S. Patent Nos. 5,639,738; 5,792,753; 5,852,002; 5,914,322; 5,929,048 and 5,985,850, are listed in Approved Drug Products as covering SOLARAZE® or its use.

Paragraph IV Certification for
U.S. Patent Nos. 5,639,738, 5,792,753, 5,852,002, 5,914,322, 5,929,048, 5,985,850

Novartis submits the following certification with respect to the following U.S. patents:

U.S. Patent No.	Patent Owner	Patent Expiry
5,639,738	Jagotec AG	JUN 17,2014
5,792,753	Jagotec AG	AUG 11,2015
5,852,002	Jagotec AG	JUN 17,2014
5,914,322	Jagotec AG	AUG 11,2015
5,929,048	Jagotec AG	JUL 27,2016
5,985,850	Jagotec AG	NOV 16,2016

Novartis hereby certifies under 21 U.S.C. §355(b)(2)(A)(iv) [FDCA Sec. 505(b)(2)(A)(iv)]and 21 C.F.R. §314.50(i)(1)(i)(A)(4), that the claims of said U.S. Patent Nos.. 5,639,738, 5,792,753, 5,852,002, 5,914,322, 5,929,048, and 5,985,850 are invalid, unenforceable, or will not be infringed by the manufacture, use or sale of the Novartis Product.

Novartis will comply with the requirements of 21 U.S.C. §355(b)(3) and 21 C.F.R. §314.52(a) with respect to providing a notice to the patent owner or its representative, and to the holder of the approved application for SOLARAZE®, and with the requirements of 21 C.F.R. §314.52(c) with respect to the content of the notice.

Exclusivity Statement. Novartis also states on information and belief that there is no unexpired exclusivity for SOLARAZE® brand diclofenac sodium topical gel, 3%.

Very truly yours,

Drug Regulatory Affairs
Novartis Consumer Health
for
Diane Furman
Novartis Patent Counsel

Reference: Electronic Orange Book
(Current through October 2006)

Cross-reference to other applications

Reference is made to IND 64 334 for diclofenac sodium topical gel, 1%. Reference is also made to Novartis NDA 19-201 for Voltaren®□(diclofenac sodium) Enteric-coated tablets (and NDAs 20-254 and 20-142 as necessary).

Reference is also made to Solaraze NDA 21-005 via the 505(b)(2) route, for information and data pertaining to dermal carcinogenicity and photocodermal carcinogenicity.

EXCLUSIVITY SUMMARY

NDA # 22-122 SUPPL # HFD # 170

Trade Name Voltaren® Gel

Generic Name (diclofenac sodium topical gel) 1%

Applicant Name Novartis Consumer Health, Inc.

Approval Date, If Known

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES ☒ NO ☐

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

505(b)(2)

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

YES ☒ NO ☐

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

N/A

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

N/A

d) Did the applicant request exclusivity?

YES ☒ NO ☐

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

Applicant requested the period of marketing exclusivity under the privisons of CFR 314.108(b)(4) (3 years).

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

YES ☐ NO ☒

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

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

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

YES ☐ NO ☒

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

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

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

YES ☒ NO ☐

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

NOTE: See attachment from the Orange Book.

2. Combination product.

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

YES ☐ NO ☐

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

NDA#

NDA#

NDA#

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

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

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

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

YES ☒ NO ☐

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

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the

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

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

YES ☒ NO ☐

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

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

YES ☐ NO ☒

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

YES ☐ NO ☒

If yes, explain:

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

YES ☐ NO ☒

If yes, explain:

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

Phase 3 Pivotal Trials and the Safety Trial:
Investigation #1: VOSG-PN-310
Investigation #2: VOSG-PE-315
Investigation #3: VOSG-PN-309

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

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

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

Investigation #1	YES ☐	NO ☒
Investigation #2	YES ☐	NO ☒
Investigation #3	YES ☐	NO ☒

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

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

Investigation #1	YES ☐	NO ☒
Investigation #2	YES ☐	NO ☒
Investigation #3	YES ☐	NO ☒

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

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

Phase 3 Pivotal Trials and the Safety Trial:
Investigation #1: VOSG-PN-310
Investigation #2: VOSG-PE-315
Investigation #3: VOSG-PN-309

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

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

Investigation #1		!
		!
IND # 64,334	YES ☒	! NO ☐
		! Explain:
Investigation #2		!
		!
IND # 64,334	YES ☒	! NO ☐
		! Explain:
Investigation #3		!
		!
IND # 64,334	YES ☒	! NO ☐
		! Explain:

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

Investigation #1	!
	!
YES ☐	! NO ☐
Explain:	! Explain:

Investigation #2	!
	!
YES ☐	! NO ☐
Explain:	! Explain:

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

YES ☐ NO ☒

If yes, explain:

==========

Name of person completing form: Lauren Tornetta, M.S.
Title: Regulatory Project Manager
Date: October 17, 2007

Name of Office/Division Director signing form: Bob A. Rappaport. M.D.
Title: Director, Division of Anesthesia, Analgesia and Rheumatology Products

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA # : 22-122 Supplement Type (e.g. SE5): _____ Supplement Number: _____

Stamp Date: December 19, 2006 PDUFA Goal Date: October 20, 2007

HFD -170 Trade and generic names/dosage form: Voltaren® Gel (diclofenac sodium topical gel) 1%

Applicant: Novartis Consumer Health, Inc. Therapeutic Class: 503

Does this application provide for new active ingredient(s), new indication(s), new dosage form, new dosing regimen, or new route of administration? *

- X **Yes. Please proceed to th e next question.**
- ☐ **No. PREA does not apply. Skip to signature block.**

** SE5, SE6, and SE7 submissions may also trigger PREA. If there are questions, please contact the Rosemary Addy or Grace Carmouze.*

Indication(s) *previously approved* (please complete this section for supplements only):_____

Each indication covered by current application under review must have pediatric studies: *Completed, Deferred, and/or Waived.*

Number of indications for this application(s):__1_____

Indication #1: Relief of pain of osteoarthritis of joints amenable to topical treatment, such as the hands and knees.

Is this an orphan indication?

- ☐ **Yes. PREA does not apply. Skip to signature block.**
- X **No. Please proceed to the next question.**

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

- X **Yes: Please proceed to Section A.**
- ☐ **No: Please check all that apply: ____Partial Waiver ____Deferred ____Completed**

NOTE: More than one may apply

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

Section A: Fully Waived Studies

Reason(s) for full waiver:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- X **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 (fill in applicable criteria below):

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 (fill in applicable criteria below):

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 (fill in applicable criteria below):

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

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH STAFF at 301-796-0700

(Revised: 10/10/2006)

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

Indication #2: _____

Is this an orphan indication?

- ☐ **Yes. PREA does not apply. Skip to signature block.**
- ☐ **No. Please proceed to the next question.**

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 (fill in applicable criteria below)::

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 (fill in applicable criteria below): :

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 (fill in applicable criteria below):

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

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH STAFF at 301-796-0700

(Revised: 10/10/2006)

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

/s/

Lauren Tornetta
10/11/2007 01:15:45 PM

NDA No. 22-122

Diclofenac sodium topical gel, 1%

New Drug Application

NOVARTIS CERTIFICATION IN COMPLIANCE WITH THE GENERIC DRUG ENFORCEMENT ACT OF 1992

Novartis Consumer Health, Inc. 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.

Florian Bieber, M.D.

Date: November 13, 2006

Name: Florian Bieber, M.D.
Title: Head, Clinical Development & Drug Safety

ACTION PACKAGE CHECKLIST

Application Information			
BLA # NDA # 22-122	BLA STN# NDA Supplement #	If NDA, Efficacy Supplement Type	
Proprietary Name: Voltaren® Gel Established Name: diclofenac sodium Dosage Form: topical gel, 1%		Applicant: Novartis Consumer Health, Inc.	
RPM: Lauren P. Tornetta, M.S.		Division: Anesthesia, Analgesia and Rheumatology Products	Phone # 301-796-2246

NDAs:	505(b)(2) NDAs and 505(b)(2) NDA supplements:
NDA Application Type: ☐ 505(b)(1) ☒ 505(b)(2) Efficacy Supplement: ☐ 505(b)(1) ☐ 505(b)(2) (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). Consult page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)	Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s)): NDA 21-005: Solaraze™ (diclofenac sodium) 3% Gel / dermal carcinogencity and photocodermal carcinogenicity Provide a brief explanation of how this product is different from the listed drug. Different strength and indication. ☐ If no listed drug, check here and explain: **Review and confirm the information previously provided in Appendix B to the Regulatory Filing Review. Use this Checklist to update any information (including patent certification information) that is no longer correct.** ☒ Confirmed ☐ Corrected Date: October 9, 2007

❖ User Fee Goal Date ❖ Action Goal Date (if different)	October 20, 2007 October 17, 2007
❖ Actions	
• Proposed action	☒ AP ☐ TA ☐ AE ☐ NA ☐ CR
• Previous actions *(specify type and date for each action taken)*	☒ None
❖ Advertising *(approvals only)* Note: If accelerated approval (21 CFR 314.510/601.41), advertising must have been submitted and reviewed *(indicate dates of reviews)*	☒ Requested in AP letter ☐ Received and reviewed

❖ Application Characteristics

Review priority: ☒ Standard ☐ Priority
Chemical classification (new NDAs only): 3

NDAs, BLAs and Supplements:
☐ Fast Track
☐ Rolling Review
☐ CMA Pilot 1
☐ CMA Pilot 2

☐ Orphan drug designation

NDAs: Subpart H
☐ Accelerated approval (21 CFR 314.510)
☐ Restricted distribution (21 CFR 314.520)
Subpart I
☐ Approval based on animal studies

BLAs: Subpart E
☐ Accelerated approval (21 CFR 601.41)
☐ Restricted distribution (21 CFR 601.42)
Subpart H
☐ Approval based on animal studies

NDAs and NDA Supplements:
☐ OTC drug

Other:

Other comments:

❖ Application Integrity Policy (AIP)	
• Applicant is on the AIP	☐ Yes ☒ No
• This application is on the AIP	☐ Yes ☒ No
• Exception for review *(file Center Director's memo in* Administrative Documents *section)*	☐ Yes ☐ No
• OC clearance for approval *(file communication in* Administrative Documents *section)*	☐ Yes ☐ Not an AP action
❖ Public communications (approvals only)	
• Office of Executive Programs (OEP) liaison has been notified of action	☒ Yes ☐ No
• Press Office notified of action	☒ Yes ☐ No
• Indicate what types (if any) of information dissemination are anticipated	☒ None ☐ FDA Press Release ☐ FDA Talk Paper ☐ CDER Q&As ☐ Other

❖ Exclusivity	
• NDAs: Exclusivity Summary (approvals only) *(file Summary in* Administrative Documents *section)*	☒ Included
• Is approval of this application blocked by any type of exclusivity?	☒ No ☐ Yes
• NDAs/BLAs: Is there existing orphan drug exclusivity for the "same" drug or biologic 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.*	☒ No ☐ Yes If, yes, NDA/BLA # and date exclusivity expires:
• NDAS: Is there remaining 5-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.)*	☒ No ☐ Yes If yes, NDA # and date exclusivity expires:
• NDAs: 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.)*	☒ No ☐ Yes If yes, NDA # and date exclusivity expires:
• NDAs: Is there remaining 6-month pediatric 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.)*	☒ No ☐ Yes If yes, NDA # and date exclusivity expires:
❖ Patent Information (NDAs and NDA supplements only)	
• Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions.	☒ Verified ☐ Not applicable because drug is an old antibiotic.
• 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) ☒ 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).	☐ No paragraph III certification Date patent will expire
• [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 section below (*Summary Reviews*)).*	☐ 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	☒ Yes ☐ No NOTE: SEE COMMENTS BELOW

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 section below (*Summary Reviews*).* *If "**No**," continue with question (3).*	☐ Yes ☐ No NOTE: SEE COMMENTS BELOW
(3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant? (Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) 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.*	☐ Yes ☐ No NOTE: SEE COMMENTS 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 section below (*Summary Reviews*).* *If "**No**," continue with question (5).*	☐ Yes ☐ No NOTE: SEE COMMENTS BELOW
(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) 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 (b)(2) 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	☐ Yes ☐ No NOTE: SEE COMMENTS BELOW

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 section below (*Summary Reviews*).* *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.*	Reference is made to a submission to NDA 22-122 on March 27, 2007, in which the Sponsor informed the FDA that Bioglan Pharmaceuticals Corp. (wholly owned subsidiary of Bradley Pharmaceuticals, Inc.) and Jagotec AG had filed a complaint for patent infringement against Novartis Consumer Health, Inc. Reference is also made to a subsequent submission to NDA 22-122 on August 2, 2007, in which the Sponsor notified the FDA that a "Notice of Voluntary Dismissal With Prejudice Pursuant to Federal Rule of Civil Procedure 41(a)," dismissing all claims against Novartis Consumer Health, Inc. with prejudice, was entered on the court's docket on July 26, 2007. This dismissal constitutes a full and final adjudication of the lawsuit, and operates as a final judgment. Thus, there is no stay of approval.
Summary Reviews	
❖ Summary Reviews (e.g., Office Director, Division Director) *(indicate date for each review)*	Division Director: 10/17/2007
❖ BLA approvals only: Licensing Action Recommendation Memo (LARM) *(indicate date)*	
Labeling	
❖ Package Insert	

• Most recent division-proposed labeling (only if generated after latest applicant submission of labeling)	
• Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)	10/17/2007
• Original applicant-proposed labeling • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable	12/19/2006
❖ Patient Package Insert	N/A
• Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling)	
• Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)	
• Original applicant-proposed labeling	
• Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable	
❖ Medication Guide	
• Most recent division-proposed labeling (only if generated after latest applicant submission of labeling)	
• Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)	10/17/2007
• Original applicant-proposed labeling	12/19/2006
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	
❖ Labels (**full color** carton and immediate-container labels)	
• Most-recent division-proposed labels (only if generated after latest applicant submission)	
• Most recent applicant-proposed labeling	10/11/2007
❖ Labeling reviews and minutes of any labeling meetings *(indicate dates of reviews and meetings)*	☒ DMETS 06/09/2007 04/17/2007 11/06/2006 ☐ DSRCS N/A ☒ DDMAC 03/26/2007 ☒ SEALD 10/05/2007 ☐ Other reviews ☒ Memos of Mtgs 10/11/2007 10/10/2007 10/03/2007 09/11/2007 08/28/2007 08/06/2007
❖	

Administrative Documents	
❖ Administrative Reviews (RPM Filing Review/Memo of Filing Meeting; ADRA) *(indicate date of each review)*	RPM Filing Review: 10/09/2007 Memo of Filing Mtg: 02/06/2007
❖ NDA and NDA supplement approvals only: Exclusivity Summary *(signed by Division Director)*	☒ Included
❖ AIP-related documents • Center Director's Exception for Review memo • If AP: OC clearance for approval	
❖ Pediatric Page (all actions)	☒ Included

❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent. *(Include certification.)*	☒ Verified, statement is acceptable
❖ Postmarketing Commitment Studies	☐ None
• Outgoing Agency request for post-marketing commitments *(if located elsewhere in package, state where located)*	10/15/2007
• Incoming submission documenting commitment	10/17/2007
❖ Outgoing correspondence (letters including previous action letters, emails, faxes, telecons)	Included
❖ Internal memoranda, telecons, email, etc.	Included
❖ Minutes of Meetings	
• Pre-Approval Safety Conference *(indicate date; approvals only)*	08/16/2007
• Pre-NDA/BLA meeting *(indicate date)*	☐ No mtg 07/21/2006
• EOP2 meeting *(indicate date)*	☐ No mtg 06/01/2005
• Other (e.g., EOP2a, CMC pilot programs) CMC EOP2	06/29/2004
❖ Advisory Committee Meeting	☒ No AC meeting
• Date of Meeting	
• 48-hour alert or minutes, if available	
❖ Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)	N/A
CMC/Product Quality Information	
❖ CMC/Product review(s) *(indicate date for each review)*	09/20/2007, 10/16/2007
❖ Reviews by other disciplines/divisions/Centers requested by CMC/product reviewer *(indicate date for each review)*	☒ None
❖ BLAs: Product subject to lot release (APs only)	☐ Yes ☐ No
❖ Environmental Assessment (check one) (original and supplemental applications)	
• ☐ Categorical Exclusion *(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)*	N/A
• ☐ Review & FONSI *(indicate date of review)*	N/A
• ☐ Review & Environmental Impact Statement *(indicate date of each review)*	N/A
❖ NDAs: Microbiology reviews (sterility & apyrogenicity) *(indicate date of each review)*	N/A ☐ Not a parenteral product
❖ Facilities Review/Inspection	
❖ NDAs: Facilities inspections (include EER printout)	Date completed: 10/05/2007 ☒ Acceptable ☐ Withhold recommendation

❖ BLAs: Facility-Related Documents • Facility review *(indicate date(s))* • Compliance Status Check (approvals only, both original and supplemental applications) *(indicate date completed, must be within 60 days prior to AP)*	☐ Requested ☐ Accepted ☐ Hold
❖ NDAs: Methods Validation	☐ Completed ☒ Requested ☐ Not yet requested ☐ Not needed

Nonclinical Information	
❖ Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	TL Memo: 10/15/2007 PTOX Review: 09/27/2007
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer *(indicate date for each review)*	☒ None
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	☐ No carc N/A
❖ ECAC/CAC report/memo of meeting	N/A
❖ Nonclinical inspection review Summary (DSI)	☒ None requested
Clinical Information	
❖ Clinical review(s) *(indicate date for each review)*	TL Memo: 10/02/2007 Clinical Review: 08/30/2007
❖ Financial Disclosure reviews(s) or location/date if addressed in another review	Included in clinical review
❖ Clinical consult reviews from other review disciplines/divisions/Centers *(indicate date of each review)*	☐ None Division of Dermatology and Dental Drug Products: 06/13/2007
❖ Microbiology (efficacy) reviews(s) *(indicate date of each review)*	☒ Not needed
❖ Safety Update review(s) *(indicate location/date if incorporated into another review)*	Included in clinical review
❖ Risk Management Plan review(s) (including those by OSE) *(indicate location/date if incorporated into another review)*	N/A
❖ Controlled Substance Staff review(s) and recommendation for scheduling *(indicate date of each review)*	☒ Not needed
❖ DSI Inspection Review Summary(ies) *(include copies of DSI letters to investigators)*	☐ None requested
• Clinical Studies	07/17/2007 (2) 06/21/2007 (2) 06/15/2007
• Bioequivalence Studies	
• Clin Pharm Studies	
❖ Statistical Review(s) *(indicate date for each review)*	☐ None 09/05/2007
❖ Clinical Pharmacology review(s) *(indicate date for each review)*	☐ None 09/12/2007

Appendix A to Action Package Checklist

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

(1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.

(2) **Or** it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.

(3) **Or** 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.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations(see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy 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).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

(1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).

(2) **And** no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.

(3) **And** all other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

(1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).

(2) **Or** the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.

(3) **Or** the applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's Office of Regulatory Policy representative.

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/s/

Lauren Tornetta
10/17/2007 07:09:18 PM

Sent: Wednesday, October 17, 2007 3:17 PM
To: Hertz, Sharon H; Wasserman, Adam
Subject: RE: RESPONSE NEEDED: PMCs

Adam,

Do the dates seem reasonable? Just one carc study?

Bob

From: Hertz, Sharon H
Sent: Wednesday, October 17, 2007 3:13 PM
To: Rappaport, Bob A
Subject: FW: RESPONSE NEEDED: PMCs

Sharon

Sharon Hertz, M.D.

Deputy Director, DAARP

(301) 796-2280

From: francis.barbone@novartis.com [mailto:francis.barbone@novartis.com]
Sent: Wednesday, October 17, 2007 3:11 PM
To: Hertz, Sharon H
Cc: Tornetta, Lauren
Subject: Re: RESPONSE NEEDED: PMCs

Dr Hertz,

Please see protocol submission, study start and final report dates for the PMCs. As always, please contact me if you need additional information.

Thanks,

Fran

Francis P. Barbone, Ph.D.
Regulatory Affairs
Novartis Consumer Health
200 Kimball Drive
Parsippany, NJ 07054-0622
973-503-7891

"Tornetta, Lauren" <Lauren.Tornetta@fda.hhs.gov>
10/16/2007 12:54 PM

To
francis.barbone@novartis.com
cc

Subject
RESPONSE NEEDED: PMCs

Hi Fran:
As per my voicemail, please let me know if NCH concurs with the proposed PMCs. Also, upon your concurrence provide the 3
dates referenced below for each PMC, including sub-parts. If you have any questions, please give me a call or email.

Thanks,
Lauren

1. Evaluation of the photo-contact allergic potential of Voltaren® Gel.

Protocol Submission: by March/2008
Study Start: by June/2008
Final Report Submission: by December/2009

2. The excipient cocoyl caprylocaprate contained in the Voltaren Gel formulation is considered novel by the Agency. Therefore, unless an adequate scientific rationale establishes this information is not necessary, the following safety information is requested as a post-marketing commitment consistent with FDA guidance "Nonclinical Studies for the Safety Evaluation of Pharmaceutical Excipients":

Response to Agency with rationale for use of cocoyl caprylocaprate January/2008

a. Provide a dermal carcinogenicity evaluation of cocoyl caprylocaprate in two species. One of these studies may be conduced in a transgenic mouse model with concurrence from the Agency. If needed,

Protocol Submission: by July/2008
Study Start: by April/2009
Final Report Submission: by April/2012

b. Provide a full reproductive toxicology evaluation of cocoyl caprylocaprate

consistent with ICH-S5A unless the topical route can be demonstrated to produce non-detectable systemic exposure.

Protocol Submission: by April/2008
Study Start: by June/2008
Final Report Submission: by June/2009

You may refer to the FDA guidance described above for suggested components of a justification that such data are necessary.

3. Provide a toxicological risk assessment of photo-degredants which are considered unique or are found at substantially greater levels when compared against a characterization of photo-degredants in the referenced drug Solaraze.

Protocol Submission: by June/2008
Study Start: by August/2008
Final Report Submission: by December/2008

From: francis.barbone@novartis.com [mailto:francis.barbone@novartis.com]
Sent: Tuesday, October 16, 2007 12:01 PM
To: Tornetta, Lauren
Subject: Comments on Draft labeling

Hi Lauren,

Enclosed is an updated Draft Label for Voltaren Gel. There are a few changes in addition to what we had discussed yesterday during the teleconference. The Instructions for use of the dosing card have been added to the end of the PI, but I have also included these instructions as a separate document, if that makes for an easier review.

Please contact me if you need additional information.

Thanks,

Fran

Francis P. Barbone, Ph.D.
Regulatory Affairs
Novartis Consumer Health
200 Kimball Drive
Parsippany, NJ 07054-0622
973-503-7891

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/s/

Lauren Tornetta
10/17/2007 05:17:00 PM
CSO

Tornetta, Lauren

From: Tornetta, Lauren
Sent: Monday, October 15, 2007 4:21 PM
To: 'francis.barbone@novartis.com'
Cc: Jani, Parinda
Subject: DMETS Comments/Voltaren Gel
Importance: High

Fran:

Per the discussion post-teleconference, DMETS has the following comments:

The dosing instructions should begin with information on the maximum amount of gel to be applied to an affected area/joint.

For the upper extremity dosing instructions -

The instructions imply [redacted]

The upper extremity dosing instructions should more clearly define the treatment sites that are to be treated with gel, and how much should be applied to each site.

DDMAC has determined that use of the word ← to describe a treatment site is not acceptable.

Kindly confirm receipt. Please incorporate the above-mentioned comments into the materials to be submitted tomorrow.

Thanks,
Lauren

Lauren P. Tornetta

Lauren P. Tornetta, M.S.
Regulatory Project Manager
Div. of Anesthesia, Analgesia & Rheum. Products
Phone: (301) 796-2246
Fax: (301) 796-9722 / 9723
Email: lauren.tornetta@fda.hhs.gov

Tornetta, Lauren

From: Tornetta, Lauren
Sent: Monday, October 15, 2007 3:53 PM
To: 'francis.barbone@novartis.com'
Cc: Jani, Parinda
Subject: Response Needed: PMCs & Question/Voltaren Gel
Importance: High

Fran:

As discussed in today's TCON, please see below Phase 4 / Post-Marketing Commitments; there are three in total.

PMC 1: An evaluation of the photocontact allergic potential of Voltaren Gel has not been performed. We request that you conduct this assessment as a post-marketing commitment.

PMC 2: The excipient cocoyl caprylocaprate contained in the Voltaren Gel formulation is considered *novel* by the Agency. Therefore, unless an adequate scientific rationale establishes this information is not necessary, the following safety information is requested as a post-marketing commitment consistent with FDA guidance "Nonclinical Studies for the Safety Evaluation of Pharmaceutical Excipients":

> 2A. Provide a dermal carcinogenicity evaluation of cocoyl caprylocaprate in two species. One of these studies may be conduced in a transgenic mouse model with concurrence from the Agency.
>
> 2B. Provide a full reproductive toxicology evaluation of cocoyl caprylocaprate consistent with ICH-S5A unless the topical route can be demonstrated to produce non-detectable systemic exposure.

You may refer to the FDA guidance described above for suggested components of a justification that such data are necessary.

PMC 3: Provide a toxicological risk assessment of photo-degredants which are considered unique or are found at substantially greater levels when compared against a characterization of photo-degredants in the referenced drug Solaraze.

It is our understanding that there will be no further submissions made by NCH during this review cycle. Please confirm if our understanding is correct.

Best Regards,
Lauren

Lauren P. Tornetta

Lauren P. Tornetta, M.S.

Regulatory Project Manager
Div. of Anesthesia, Analgesia & Rheum. Products
Phone: (301) 796-2246
Fax: (301) 796-9722 / 9723
Email: lauren.tornetta@fda.hhs.gov

APPEARS THIS WAY
ON ORIGINAL

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/s/

Lauren Tornetta
10/16/2007 10:52:13 AM
CSO

Tornetta, Lauren

From: francis.barbone@novartis.com
Sent: Thursday, October 11, 2007 8:10 AM
To: Tornetta, Lauren
Subject: RE: NDA 22-122
Attachments: emfalert.txt

Lauren,

Received. Apologies for any confusion on the wording.

Regards,

Fran

Francis P. Barbone, Ph.D.
Regulatory Affairs
Novartis Consumer Health
200 Kimball Drive
Parsippany, NJ 07054-0622
973-503-7891

"Tornetta, Lauren" <Lauren.Tornetta@fda.hhs.gov>
10/11/2007 08:05 AM

To
francis.barbone@novartis.com
cc
"Jani, Parinda" <parinda.jani@fda.hhs.gov>
Subject
RE: NDA 22-122

Fran:

Thank you for your below email.

To clarify, the Division did *not* state during the telecon that we are heading to an approval action.

What the Division did say is that we would not approve the proposed indication, but would consider an alternative indication, for the reasons outlined, pending completion of our reviews.

Thus, no action has been determined.

Regards,
Lauren

From: francis.barbone@novartis.com [mailto:francis.barbone@novartis.com]
Sent: Wednesday, October 10, 2007 5:01 PM
To: Tornetta, Lauren
Subject: NDA 22-122

Dear Lauren,

Reference is made to NDA 22-122 and to the teleconference on October 9, 2007 between FDA and Novartis Consumer Health (NCH). The FDA indicated, during this teleconference, that they would not be extending the review cycle for NDA 22-122 and are progressing toward an action on the PDUFA date of October 19, 2007. The Agency further indicated that they were willing to proceed with an Approval of NDA 22-1222 if NCH was willing to accept the FDA's revised indication.

The Division proposed the following indication for Voltaren Gel : "Voltaren Gel is a nonsteroidal anti-inflammatory drug indicated for the relief of the pain of osteoarthritis of joints amenable to topical

treatment,

such as the hands and knees"

NCH was offered the option to continue towards an Approval with the above indication or to decline this opportunity with the understanding that additional clincial data would needed for consideration of an expanded indication.
As discussed during teleconference, NCH committed to providing an answer to the Agency by COB on Wednesday, October 10, 2007.

NCH, through this communication, is hereby ACCEPTING the FDA's option to proceed with an Approval for Voltaren Gel on October 19, 2007, and further NCH accepts the indication proposed by the Agency.

In addition, NCH will provide, by noon on October 11, 2007, comments on the most recent version of the Label and packaging requests as provided to NCH on October 9, 2007.

NCH thanks the Division for affording us this opportunity and we look forward to finalizing the approval of Voltaren Gel.

Please confirm receipt of this email and contact me if you need additional information.

Thank you.

Best Regards,

Fran

Francis P. Barbone, Ph.D.
Regulatory Affairs
Novartis Consumer Health
200 Kimball Drive
Parsippany, NJ 07054-0622
973-503-7891

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/s/

Lauren Tornetta
10/12/2007 09:18:04 AM
CSO

NDA REGULATORY FILING REVIEW

(Including Memo of Filing Meeting)

NDA # 22-122 Supplement # N/A Efficacy Supplement Type SE- N/A

Proprietary Name: Voltaren® Gel
Established Name: diclofenac sodium topical gel
Strengths: 1%

Applicant: Novartis Consumer Health
Agent for Applicant (if applicable): N/A

Date of Application: 12/19/2006
Date of Receipt: 12/20/2006
Date clock started after UN:
Date of Filing Meeting: 02/06/2007
Filing Date: 02/18/2007
Action Goal Date (optional): 10/15/2007 User Fee Goal Date: 10/19/2007

Indication(s) requested: [redacted] joints amenable to [redacted] treatment such as the hands and knees.

Type of Original NDA: (b)(1) ☐ (b)(2) ☒
AND (if applicable)
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 or efficacy supplement is a (b)(2), complete Appendix B.

Review 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 by contacting the User Fee staff in the Office of Regulatory Policy. 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 any approved (b)(1) or (b)(2) application? YES ☐ NO ☒
  If yes, explain:

Note: If the drug under review is a 505(b)(2), this issue will be addressed in detail in appendix B.

- 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 ☐
  If no, explain:

- 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:

- Answer 1, 2, or 3 below (do not include electronic content of labeling as an partial electronic submission).

1. This application is a paper NDA YES ☐ NO ☒

2. This application is an eNDA or combined paper + eNDA YES ☒
   This application is: All electronic ☐ Combined paper + eNDA ☐
   This application is in: NDA format ☐ CTD format ☒
   Combined NDA and CTD formats ☐

   Does the eNDA, follow the guidance?
   (http://www.fda.gov/cder/guidance/2353fnl.pdf) YES ☐ NO ☐

   If an eNDA, all forms and certifications must be in paper and require a signature.

   If combined paper + eNDA, which parts of the application were submitted in electronic format?

   Additional comments:

3. This application is an eCTD NDA. YES ☒
   If an eCTD NDA, all forms and certifications must either be in paper and signed or be electronically signed.

Additional comments: This submission is provided in eCTD hybrid format.

- Patent information submitted on form FDA 3542a? YES ☒ NO ☐
- Exclusivity requested? YES ☒ Period of exclusivity not specified Years

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 . . . ."*

- Are the required pediatric assessment studies and/or deferral/partial waiver/full waiver of pediatric studies (or request for deferral/partial waiver/full waiver of pediatric studies) included? YES ☒ NO ☐
- If the submission contains a request for deferral, partial waiver, or full waiver of studies, does the application contain the certification required under FD&C Act sections 505B(a)(3)(B) and (4)(A) and (B)? YES ☒ NO ☐
- Is this submission a partial or complete response to a pediatric Written Request? YES ☐ NO ☒

  If yes, contact PMHT in the OND-IO
- Financial Disclosure forms included with authorized signature? YES ☒ NO ☐
  (Forms 3454 and/or 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) YES ☒ NO ☐
- PDUFA and Action Goal dates correct in tracking system? 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: IND 64,334
- Are the trade, established/proper, and applicant names correct in COMIS? YES ☒ NO ☐
  If no, have the Document Room make the corrections.
- End-of-Phase 2 Meeting(s)? Date(s) CMC-only EOP2: 6/01/2005
  EOP2: 6/29/2004 NO ☐

If yes, distribute minutes before filing meeting.

- Pre-NDA Meeting(s)? Date(s) 7/21/2006 NO ☐
  If yes, distribute minutes before filing meeting.

- Any SPA agreements? Date(s) Requested: 12/22/2004
  Response: 02/04/2005 NO ☐
  If yes, distribute letter and/or relevant minutes before filing meeting.

Project Management

- If Rx, was electronic Content of Labeling submitted in SPL format? YES ☒ NO ☐
  If no, request in 74-day letter.

- If Rx, for all new NDAs/efficacy supplements submitted on or after 6/30/06:
  Was the PI submitted in PLR format? YES ☒ NO ☐

  If no, explain. Was a waiver or deferral requested before the application was received or in the submission? If before, what is the status of the request:

- If Rx, all labeling (PI, PPI, MedGuide, carton and immediate container labels) has been consulted to DDMAC? YES ☒ NO ☐

- If Rx, trade name (and all labeling) consulted to OSE/DMETS? YES ☒ NO ☐

- If Rx, MedGuide and/or PPI (plus PI) consulted to ODE/DSRCS?
  N/A ☒ YES ☐ NO ☐

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

- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling submitted? NA ☒ YES ☐ NO ☐

If Rx-to-OTC Switch or OTC application:

- Proprietary name, all OTC labeling/packaging, and current approved PI consulted to OSE/DMETS? YES ☐ NO ☐

- If the application was received by a clinical review division, has DNPCE been notified of the OTC switch application? Or, if received by DNPCE, has the clinical review division been notified? YES ☐ NO ☐

Clinical

- If a controlled substance, has a consult been sent to the Controlled Substance Staff?
  NA ☒ 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 EA officer, OPS?	YES ☐		NO ☐	
•	Establishment Evaluation Request (EER) submitted to DMPQ?	YES ☒		NO ☐	
•	If a parenteral product, consulted to Microbiology Team?	N/A X	YES ☐	NO	☐

ATTACHMENT

MEMO OF FILING MEETING

DATE: February 6, 2007

NDA #: 22-122

DRUG NAMES: Voltaren Gel (diclofenac sodium topical gel) 1%

APPLICANT: Novartis Consumer Health

BACKGROUND: Reference is made to Novartis NDA 19-201 for Voltaren® (diclofenac sodium) enteric-coated tablets (and NDAs 20-254 & 20-142) for which a letter of authorization is included in this application. As requested in the pre-NDA meeting, the nonclinical legacy documents from NDA 19-201 have been included. Diclofenac sodium topical gel, 1% was studied under IND 64,334. This application is submitted under 505(b)(2). Therefore, in line with discussions held during the pre-NDA meeting, reference is made to Solaraze™ Gel (NDA 21-005) for information and data pertaining to dermal carcinogenicity and photocodermal carcinogenicity.

ATTENDEES: Sharon Hertz, M.D., Deputy Director
Ellen Fields, M.D., Medical Team Leader
Neville Gibbs, M.D., Medical Officer
Ali Al-Hakim, Ph.D., Pharmaceutical Assessment Lead
Sue-Ching Lin, Ph.D., Chemistry Reviewer
Adam Wasserman, Ph.D., Pharmacology/Toxicology Supervisor
Lawrence (Steve) Leshin, Ph.D., Pharmacology/Toxicology Reviewer
David Lee, Ph.D., Clinical Pharmacology Reviewer
Dionne Price, Ph.D., Statistical Team Leader
Lauren Tornetta, M.S., Project Manager

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

Discipline/Organization	**Reviewer**
Medical:	Neville Gibbs, M.D.
Secondary Medical:	Ellen Fields, M.D.
Statistical:	Ruthana Davi, Ph.D.
Pharmacology:	Lawrence (Steve) Leshin, Ph.D.
Statistical Pharmacology:	N/A
Chemistry:	Sue-Ching Lin, Ph.D.
Environmental Assessment (if needed):	
Biopharmaceutical:	David Lee, Ph.D.
Microbiology, sterility:	N/A
Microbiology, clinical (for antimicrobial products only):	N/A
DSI:	Sherbert Samuels

OPS:
Regulatory Project Management: Lauren Tornetta, M.S.
Other Consults: DMETS
DDMAC
ORP: Janice Weiner, J.D., MPH

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

CLINICAL FILE ☒ REFUSE TO FILE ☐

- Clinical site audit(s) needed? YES ☒ NO ☐
  If no, explain:
- 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. study site audits(s) needed? YES ☐ NO ☒

PHARMACOLOGY/TOX N/A ☐ FILE ☒ REFUSE TO FILE ☐

- GLP audit needed? YES ☐ NO ☒

CHEMISTRY FILE ☒ REFUSE TO FILE ☐

- Establishment(s) ready for inspection? YES ☒ NO ☐
- Sterile product? YES ☐ NO ☒
  If yes, was microbiology consulted for validation of sterilization? YES ☐ NO ☐

ELECTRONIC SUBMISSION:
Any comments: This submission is provided in eCTD hybrid formt.

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.☒ Ensure that the review and chemical classification codes, as well as any other pertinent classification codes (e.g., orphan, OTC) are correctly entered into COMIS.

2. ☐ If RTF, notify everybody who already received a consult request of RTF action. Cancel the EER.

3.☐ 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.

4. ☒ If filed, complete the Pediatric Page at this time. (If paper version, enter into DFS.)

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

Lauren P. Tornetta, M.S.
Regulatory Project Manager

Appendix A to NDA Regulatory Filing Review

NOTE: The term "original application" or "original NDA" as used in this appendix denotes the NDA submitted. It does not refer to the reference drug product or "reference listed drug."

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

(1) it relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application,
(2) it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval, or
(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.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations(see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy 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).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

(1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies),

(2) No additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application, and.

(3) All other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

(1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the

original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2),

(2) The applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement, or

(3) The applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's Office of Regulatory Policy representative.

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):

   NDA 21-005: Solaraze™ (diclofenac sodium) 3% Gel / Dermal carcinogencity and photocodermal carcinogenicity.

   Note:

   Reference is made to a submission to NDA 22-122 on March 27, 2007, in which the Sponsor informed the FDA that Bioglan Pharmaceuticals Corp. (wholly owned subsidiary of Bradley Pharmaceuticals, Inc.) and Jagotec AG had filed a complaint for patent infringement against Novartis Consumer Health, Inc.

   Reference is also made to a subsequent submission to NDA 22-122 on August 2, 2007, in which the Sponsor notified the FDA that a "Notice of Voluntary Dismissal With Prejudice Pursuant to Federal Rule of Civil Procedure 41(a)," dismissing all claims against Novartis Consumer Health, Inc. with prejudice, was entered on the court's docket on July 26, 2007. This dismissal constitutes a full and final adjudication of the lawsuit, and operates as a final judgment.

3. Is this application for a drug that is an "old" antibiotic (as described in the draft guidance implementing the 1997 FDAMA provisions? (Certain antibiotics are not entitled to Hatch-Waxman patent listing and exclusivity benefits.)

   YES ☐ NO ☒

*If "**Yes**," skip to question 7.*

4. Is this application for a recombinant or biologically-derived product?

   YES ☐ NO ☒

*If "**Yes** "contact your ODE's Office of Regulatory Policy representative.*

5. The purpose of the questions below (questions 5 to 6) is to determine if there is an approved drug product that is equivalent or very similar to the product proposed for approval 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**," to (a) skip to question 6. Otherwise, answer part (b and (c)).*

(b) Is the pharmaceutical equivalent approved for the same indication for which the 505(b)(2) application is seeking approval? YES ☐ NO ☐

(c) Is the approved pharmaceutical equivalent(s) cited as the listed drug(s)? YES ☐ NO ☐

*If "**Yes**," (c), list the pharmaceutical equivalent(s) and proceed to question 6.*

*If "**No**," to (c) list the pharmaceutical equivalent and contact your ODE's Office of Regulatory Policy representative.*
Pharmaceutical equivalent(s):

6. (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**," to (a) skip to question 7. Otherwise, answer part (b and (c)).*

(b) Is the pharmaceutical alternative approved for the same indication for which the 505(b)(2) application is seeking approval? YES ☐ NO ☒

(c) Is the approved pharmaceutical alternative(s) cited as the listed drug(s)? YES ☒ NO ☐

*If "**Yes**," to (c), proceed to question 7.*

***NOTE:** If there is more than one pharmaceutical alternative approved, consult your ODE's Office of Regulatory Policy representative to determine if the appropriate pharmaceutical alternatives are referenced.*

*If "**No**," to (c), list the pharmaceutical alternative(s) and contact your ODE's Office of Regulatory Policy representative. Proceed to question 7.*

Pharmaceutical alternative(s):

7. (a) Does the application rely on published literature necessary to support the proposed approval of the drug product (i.e. is the published literature necessary for the approval)? YES ☐ NO ☒

*If "**No**," skip to question 8. Otherwise, answer part (b).*

(b) Does any of the published literature cited reference a specific (e.g. brand name) product? Note that if yes, the applicant will be required to submit patent certification for the product, see question 12.

8. 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"). This application provides for a new indication, treatment of osteoarthritis of joints amenable to superficial treatment, such as the hands and knees. This application provides for a change in dosage strength, 1% topical gel.

9. Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? (Normally, FDA may refuse-to-file such NDAs (see 21 CFR 314.101(d)(9)). YES ☐ NO ☒

10. Is the application for a duplicate of a listed drug whose only difference is that 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 may be refused for filing under 21 CFR 314.101(d)(9)). YES ☐ NO ☒

11. Is the application for a duplicate of a listed drug whose only difference is that the rate at which the product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the RLD (see 21 CFR 314.54(b)(2))? If yes, the application may be refused for filing under 21 CFR 314.101(d)(9). YES ☐ NO ☒

12. Are there certifications for each of the patents listed in the Orange Book for the listed drug(s) referenced by the applicant (see question #2)? (This is different from the patent declaration submitted on form FDA 3542 and 3542a.) YES ☒ NO ☐

13. 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.)

☐ Not applicable (e.g., solely based on published literature. See question # 7

☐ 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): See below

Novartis hereby states, on information and belief, that U.S. Patent Nos. 5,639,738; 5,792,753; 5,852,002; 5,914,322; 5,929,048 and 5,985,850, are listed in Approved Drug Products as covering SOLARAZE® or its use.

Paragraph IV Certification for
U.S. Patent Nos. 5,639,738, 5,792,753, 5,852,002, 5,914,322, 5,929,048, 5,985,850

Novartis submits the following certification with respect to the following U.S. patents:

U.S. Patent No.	Patent Owner	Patent Expiry
5,639,738	Jagotec AG	JUN 17,2014
5,792,753	Jagotec AG	AUG 11,2015
5,852,002	Jagotec AG	JUN 17,2014
5,914,322	Jagotec AG	AUG 11,2015
5,929,048	Jagotec AG	JUL 27,2016
5,985,850	Jagotec AG	NOV 18,2015

Novartis hereby certifies under 21 U.S.C. §355(b)(2)(A)(iv) [FDCA Sec. 505(b)(2)(A)(iv)]and 21 C.F.R. §314.50(i)(1)(i)(A)(4), that the claims of said U.S. Patent Nos., 5,639,738, 5,792,753, 5,852,002, 5,914,322, 5,929,048, and 5,985,850 are invalid, unenforceable, or will not be infringed by the manufacture, use or sale of the Novartis Product.

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)]. OND will contact you to verify that this documentation was received.*

☐ 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):

☐ 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):

14. Did the applicant:

- Identify which parts of the application rely on the finding of safety and effectiveness for a listed drug or published literature describing a listed drug or both? For example, pharm/tox section of application relies on finding of preclinical safety for a listed drug.

YES ☒ NO ☐

*If "**Yes**," what is the listed drug product(s)* Solaraze™ *and which sections of the 505(b)(2) application rely on the finding of safety and effectiveness or on published literature about that listed drug* Reference is made to Solaraze NDA 21-005 via the 505(b)(2) route, for information and data pertaining to dermal carcinogencity and photocodermal carcinogenicity.

Was this listed drug product(s) referenced by the applicant? (see question # 2)

YES ☒ NO ☐

- Submit a bioavailability/bioequivalence (BA/BE) study comparing the proposed product to the listed drug(s)?

N/A ☐ YES ☒ NO ☐

15. (a) Is there unexpired exclusivity on this listed drug (for example, 5 year, 3 year, orphan or pediatric exclusivity)? Note: this information is available in the Orange Book.

YES ☐ NO ☒

If "**Yes**," please list:

Application No.	Product No.	Exclusivity Code	Exclusivity Expiration

---

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

/s/

Lauren Tornetta
10/5/2007 01:56:03 PM
CSO

Please sign

Parinda Jani
10/9/2007 01:51:19 PM
CSO

Tornetta, Lauren

From: Delasko, Jeanne
Sent: Friday, October 05, 2007 3:38 PM
To: Tornetta, Lauren
Cc: Jani, Parinda; Kashoki, Mwango; Hertz, Sharon H; Burke, Laurie B
Subject: RE: DRAFT Label/NDA 22122/Voltaren Gel/Novartis
Attachments: LabelingReviewJMDelasko.10.05.07.doc

Lauren - Here are SEALD's comments. Let me know if you have questions.

From: Tornetta, Lauren
Sent: Thursday, October 04, 2007 9:58 AM
To: Delasko, Jeanne
Cc: Jani, Parinda; Kashoki, Mwango; Hertz, Sharon H
Subject: DRAFT Label/NDA 22122/Voltaren Gel/Novartis
Importance: High

Hi Jeanne:

Here is a DRAFT, working version of the label for NDA 22-122 (Voltaren Gel). Please review/revise, as needed.

Our next internal labeling meeting is on 10/10 (Wednesday). If possible, it would be great to have your comments in advance of this meeting.

Please contact me with any questions/concersn.

Just a few PLR Questions:

1. What is the preferred way to write the tradname in the label? (Voltaren Gel OR Voltaren(R) Gel)

2. Under Section 4/Contradinications, what is the preferred wording for hypersensitivity statements?

3. What is the preferred location for Laboratory Tests?

Thanks,

Lauren

Lauren P. Tornetta

Lauren P. Tornetta, M.S.
Regulatory Project Manager
Div. of Anesthesia, Analgesia & Rheum. Products
Phone: (301) 796-2246
Fax: (301) 796-9722 / 9723
Email: lauren.tornetta@fda.hhs.gov

APPEARS THIS WAY
ON ORIGINAL

Tornetta, Lauren

From: francis.barbone@novartis.com
Sent: Tuesday, September 25, 2007 12:33 PM
To: Tornetta, Lauren
Subject: RE: New Info.Request/CMC/NDA 22122 (9/14/07)

Hi Lauren,

Thanks very much!

I will confirm our NDA Amendment submission with you on Thursday.

Thanks,

Fran

Francis P. Barbone, Ph.D.
Regulatory Affairs
Novartis Consumer Health
200 Kimball Drive
Parsippany, NJ 07054-0622
973-503-7891

"Tornetta, Lauren" <Lauren.Tornetta@fda.hhs.gov>

09/25/2007 12:27 PM

To francis.barbone@novartis.com
cc
Subject RE: New Info.Request/CMC/NDA 22122 (9/14/07)

Hi Fran:

In response to your below question, the CMC reviewer has the following response:

Please update the relevant sections (individual modules) of the electronic NDA submission with the revised drug product specifications. A submission of the full method validation package is not needed.

If you have any further questions/concerns, please contact me.

Best,
Lauren

From: francis.barbone@novartis.com [mailto:francis.barbone@novartis.com]
Sent: Monday, September 24, 2007 3:29 PM

Tornetta, Lauren

From: francis.barbone@novartis.com
Sent: Monday, September 24, 2007 3:29 PM
To: Tornetta, Lauren
Subject: Fw: New Info.Request/CMC/NDA 22122 (9/14/07)
Importance: High
Attachments: TM-III-J-1_09-Oct-03.pdf.zip

Hi Lauren,

I hope you had a good weekend!

Our submission for September 27th remains on track, however our CMC colleagues have a question regarding the CMC content of the submission as related to the FDA CMC reviewer's comments of September 14th. NCH is planning to submit the revised specifications for release, stability etc., as recommended below, however NCH also recognizes that a change to these specifications can impact documents previously submitted in the original NDA 22-122. Can the revised specifications (individual modules) be submitted alone or does NCH need to also submit the full methods validation package on September 27th? Alternatively, can the full methods validation package be submitted later?

Thank you.

Regards,

Fran

Andras:

The CMC reviewer has the following information request:

Revise the – acceptance criteria

Please provide a response to the above request as soon as possible, but no later then C.O.B. Monday, September 17, 2007.

Kindly confirm receipt of this request.

Best Regards,

Lauren

Francis P. Barbone, Ph.D.
Regulatory Affairs
Novartis Consumer Health
200 Kimball Drive
Parsippany, NJ 07054-0622
973-503-7891

----- Forwarded by Francis Barbone/CH/Novartis on 09/24/2007 03:05 PM -----

Francis Barbone/CH/Novartis

09/17/2007 04:46 PM

To "Tornetta, Lauren" <Lauren.Tornetta@fda.hhs.gov>

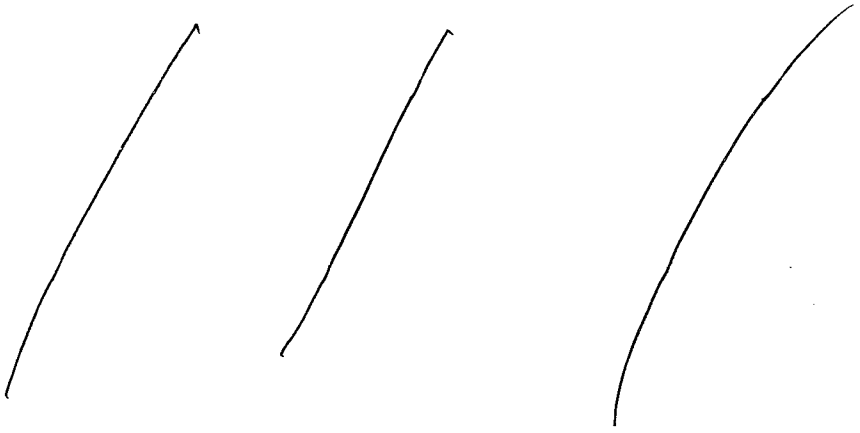
cc Andras Megyeri/CH/Novartis@PH, Kim Stranick/CH/Novartis@PH

Subject Re: FW: New Info.Request/CMC/NDA 22122 (9/14/07) Link

Dear Lauren,

As discussed earlier today, NCH is responding to the FDA CMC requests sent Friday September 14th and Monday September 17th, 2007 regarding NDA 22-122.

NCH agrees to revise the [redacted] acceptance criteria [redacted]



NCH will provide the revised drug product specifications in the NDA Amendment of September 27, 2007.

Please confirm receipt of this email and contact me if you need additional information. Thank you.

Best Regards,

Fran

Francis P. Barbone, Ph.D.
Drug Regulatory Affairs
Novartis Consumer Health
200 Kimball Drive
Parsippany, NJ 07054-0622
973-503-7891

Dear Fran:

As a follow-up to our phone conversation, the CMC reviewer has requested the following:

Please provide the revised drug product specifications [redacted] as soon as possible. While it may not be possible to provide the revised specifications today (as you indicated in our phone conversation), please provide the [redacted], COB today.

Kindly confirm receipt of this request and deadline.

Best,
Lauren

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Mbvsf o! Upsof uub
210303118! 22; 33; 17! BN
DTP

Tornetta, Lauren

From: Tornetta, Lauren
Sent: Friday, September 14, 2007 8:08 AM
To: andras.megyeri@novartis.com
Subject: New Info.Request/CMC/NDA 22122 (9/14/07)
Importance: High

Andras:

The CMC reviewer has the following information request:

Revise the — acceptance criteria

Please provide a response to the above request as soon as possible, but no later then C.O.B. Monday, September 17, 2007.

Kindly confirm receipt of this request.

Best Regards,
Lauren

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/s/

Lauren Tornetta
9/14/2007 08:15:08 AM
CSO

Tornetta, Lauren

From: francis.barbone@novartis.com
Sent: Friday, September 14, 2007 3:03 PM
To: Tornetta, Lauren
Cc: andras.megyeri@novartis.com; fiona.gardiner@novartis.com; kim.stranick@novartis.com; Jani, Parinda
Subject: Fw: Response Needed: Status update on 2 outstanding issues/NDA 22-122

Dear Lauren,

As Andras Megyeri has communicated I have been given responsibilty for NDA 21-122.

With regard to the questions asked in your email of today (September 14, 2007) I can confirm the following:

In addition, an updated PI (and SPL) and PPI will be be included with this submission.
The carton labels were submitted by Nicholas Romano (NCH) by email on September 7, 2007.
The PTOX results are planned to be submitted on October 15, 2007.

Please confirm receipt of this message and contact me if you need additional information. Thank you.

Best Regards,

Fran

Francis P. Barbone, Ph.D.
Novartis Consumer Health

----- Original Message -----
From: Andras Megyeri
Sent: 09/14/2007 12:39 PM EDT
To: Tornetta, Lauren" <Lauren.Tornetta@fda.hhs.gov>
Cc: Jani, Parinda" <parinda.jani@fda.hhs.gov>; Francis Barbone; Fiona Gardiner
Subject: Re: Response Needed: Status update on 2 outstanding issues/NDA 22-122

Dear Lauren,
I am traveling and received your e-mail through my Blackberry.

I am confirming the receipt of the e mail regarding of the 2 outstanding issues of NDA 22-122.
I am confirming that NCH is planning to submit

I can also confirm the submission of the study related to the PTOX request of August 27, 2007.

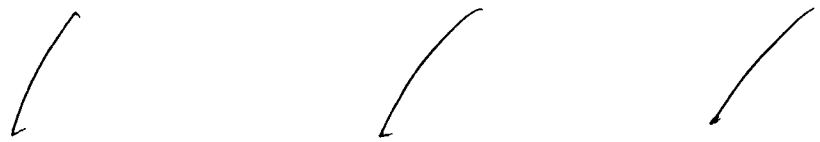
The exact submission dates will be communicated by Francis Barbone, associate director RA. Francis will be responsible in the future for NDA 22-122.
Regards
Andras

Sent from my BlackBerry Wireless Handheld.

----- Original Message -----
From: "Tornetta, Lauren" [Lauren.Tornetta@fda.hhs.gov]
Sent: 09/14/2007 10:11 AM AST
To: Andras Megyeri
Cc: Jani, Parinda" <parinda.jani@fda.hhs.gov>
Subject: Response Needed: Status update on 2 outstanding issues/NDA 22-122

Andras:

Please provide a status update on the following two outstanding items for NDA 22-122:



Response to PTOX request of August 15, 2007:
As relayed in your August 27, 2007, email: "In accordance with the Agency's request of August 15, 2007, Novartis Consumer Health, Inc. (NCH) will conduct a study to demonstrate the degradant profiles between diclofenac sodium topical gel, 1% and Solaraze by comparing the identities and amounts of degradants formed over time from solar or simulated solar exposure. NCH will submit the results of this study to the NDA, first half October 2007. "

Provide both an update on this study and an estimated submission date to FDA.

Kindly confirm receipt of this email and provide responses to the two items outlined above by C.O.B., Friday, September 14, 2007, if possible. I look forward to hearing from you.

Regards,
Lauren

From: filomena.gesek@novartis.com [mailto:filomena.gesek@novartis.com]
Sent: Monday, August 27, 2007 10:47 AM
To: Tornetta, Lauren
Cc: andras.megyeri@novartis.com; kim.stranick@novartis.com; fiona.gardiner@novartis.com
Subject: Re: Response Needed: Status update on 2 outstanding IRs/NDA 22-122

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/s/

Lauren Tornetta
10/2/2007 11:20:36 AM
CSO

Tornetta, Lauren

From: francis.barbone@novartis.com
Sent: Wednesday, September 19, 2007 12:23 PM
To: Tornetta, Lauren
Cc: andras.megyeri@novartis.com; kim.stranick@novartis.com
Subject: Re: New Info.Request/CMC & PTOX /NDA 22122 (9/18/07)

Dear Lauren,

NCH has reviewed the FDA CMC and PTOX requests of Tuesday, September 19th regarding NDA 22-122. We agree to the Agency's requests and have the following comments:

- A footnote will be added to the product specification stating that once reduced testing is implemented for [redacted], if a test fails under the reduced testing schedule full testing for that test will be re-implemented until root cause analysis is competed and the adequate controls re-established in the manufacturing process.

- Acceptance criteria for [redacted] will be tightened to nmt [redacted] in the product specification. To support this tighter degradation limit [redacted] will be tightened in the specification appropriately. Justification will be provided in the updated Justification of Specifications section 3.2.P.5.6.

Please confirm receipt of this email and contact me if you need additional information. Thank you.

Best Regards,

Fran

Francis . Barbone, Ph.D.
Regulatory Affairs
Novartis Consumer Health
200 Kimball Drive
Parsippany, NJ 07054-0622
973-503-7891

"Tornetta, Lauren" <Lauren.Tornetta@fda.hhs.gov>

09/18/2007 08:18 PM

To francis.barbone@novartis.com
cc
Subject New Info.Request/CMC & PTOX /NDA 22122 (9/18/07)

Fran:

The review team has the following CMC and PTOX comments/requests. Please provide a response to me via email by noon on Wednesday, September 19th, if possible. We request that in your email response, please confirm that you agree to include the below comments in the revised specifications for the drug product to be submitted on September 27, 2007.

1. Reduced testing frequency proposed for [redacted] in the drug product is acceptable with a caveat that if a test fails under this schedule, it will be implemented on all batches until root cause analysis is completed and adequate controls are reestablished in the manufacturing controls. Please include this provision in a footnote to the specification sheet.

2. Tighten the acceptance criteria for [redacted] to NMT [redacted], the qualification threshold for impurities based on the maximum daily dose of Voltaren Gel. Note that this impurity is not considered qualified at the proposed limit of NMT [redacted] in the drug product.

Best Regards,
Lauren

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/s/

Lauren Tornetta
9/20/2007 09:53:39 AM
CSO

Tornetta, Lauren

From: Tornetta, Lauren
Sent: Tuesday, August 28, 2007 8:04 AM
To: 'Filomena_Gesek/PH/Novartis@ah.novartis.com'
Cc: andras.megyeri@novartis.com; Malandro, Lisa
Subject: New Info.Request/NDA 22122 (8/28/07)
Importance: High

Filomena and Andras:

The chemistry reviewer has requested the following information in response to your 8/27/02 email for NDA 22-122:

1. Please explain why the ___ is not included in #16 "How supplied/storage and handling" section of the package insert that was submitted on 8/27/07.

2. Submit the revised container label and carton labeling as soon as possible. We appreciate that NCH is diligently working on making the required revisions; however, this information is pertinent to the continued review and is requested by noon on August 31th, if possible. Kindly confirm this deadline and *if* not possible, provide a date.

Since I will be on leave starting C.O.B., August 29th, please respond to Lisa Malandro at lisa.malandro@fda.hhs.gov if response is sent post-Augsut 29th.

Regards,
Lauren

From: filomena.gesek@novartis.com [mailto:filomena.gesek@novartis.com] **On Behalf Of** Filomena_Gesek/PH/Novartis@ah.novartis.com
Sent: Monday, August 27, 2007 5:16 PM
To: Tornetta, Lauren
Cc: andras.megyeri@novartis.com
Subject: RE: Response Needed: Status update on 2 outstanding IRs/NDA 22-122

Lauren,

In response to your telephone request to Andras Meygeri, attached is the PI in track changes.

Regards,
Filomena Gesek
Regulatory Affairs
Novartis Consumer Health
973-503-7645

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/s/

Lauren Tornetta
8/28/2007 08:49:36 AM
CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-122

DISCIPLINE REVIEW LETTER

Novartis Consumer Health, Inc.
200 Kimball Drive
Parsippany, New Jersey 07054-0622

Attention: Filomena Gesek
Director, Regulatory Affairs, U.S., Therapeutic Areas

Dear Ms. Gesek:

Please refer to your December 19, 2006, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Voltaren® Gel (diclofenac sodium topical gel).

The Division of Drug Marketing, Advertising and Communication (DDMAC) and the Division of Medication Errors and Technical Support (DMETS) have completed the review of the labeling and find the name Voltaren® Gel acceptable. However, the name will be re-reviewed prior to the NDA approval to rule out any objections based upon approvals of other similar look alike/sound alike proprietary or established names.

In the review of the container labels and carton labeling of Voltaren® Gel, DMETS has focused on safety issues relating to possible medication errors. DMETS has identified the following areas of improvement, in the interest of minimizing potential user error and maximizing patient safety.

1. GENERAL COMMENTS

a. Remove or decrease the prominence of the graphic located to the right of the tradename. As currently presented, it is distracting and draws attention away from important information such as the tradename, established name, and product strength.

b. The presentation of the proprietary name and established name should be as follows:

Voltaren® Gel
(diclofenac sodium topical gel) 1%.

2. CONTAINER and CARTON LABELING

a. See GENERAL COMMENTS 1a-1b.

b. The statement ___ should be changed to read "For topical use only".

3. PHYSICIAN SAMPLE CONTAINER LABEL

a. See GENERAL COMMENTS 1a-1b.

b. Revise ___ ' to read "Physician's Sample". Additionally, increase the prominence of this statement.

4. DOSING CARDS

a. DMETS acknowledges that the printed instructions on the dosing cards provided by the Sponsor are in draft form. However, after reviewing the dosing cards from a safety perspective, DMETS has the following comments and recommendations.

DMETS recommends that each dosing card provide only one designated area on which to apply Voltaren Gel to avoid dosing errors. Using a single application area which is clearly demarcated to show measured dosing amounts of 2 grams vs. 4 grams, similar to a measuring tape, may be more effective for patients to use correctly.

ii. Include more specific instructions for patients to consistently dispense the correct dose using the dosing card.

iii. Provide instructions for how patients are to apply the gel to the affected area.

iv. The dosing card instructions state, "

The sponsor should consider ways to make it more apparent to all patients, which side of each dosing sheet is the printed side.

v. DMETS questions whether enough dosing sheets will be enclosed in each package for a patient to apply Voltaren Gel four times a day for the prescribed treatment period. Patients may have more than one affected area on which to apply Voltaren Gel and may need more than one dosing card for each prescribed treatment area.

vi. Include

vii. Include instructions for discarding used dosing cards in a safe place out of the reach of children and pets.

5. PACKAGE INSERT LABELING

DMETS recommends including a Patient Package Insert which gives clear and detailed instructions for how to use the dosing card to optimize treatment. Instructions with diagrams would be very useful for patients to maximize effective administration and minimize medication errors.

If you have any questions, call Lauren Tornetta, Regulatory Project Manager, at (301) 796-2246.

Sincerely,

{See appended electronic signature page}

Parinda Jani
Chief, Project Management Staff
Division of Anesthesia, Analgesia
and Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

Parinda Jani
8/15/2007 01:39:24 PM

Tornetta, Lauren

From: Tornetta, Lauren
Sent: Wednesday, August 15, 2007 9:21 AM
To: 'filomena.gesek@novartis.com'
Subject: PTOX Response to your 6/26 Request/NDA 22122
Importance: High

Filomena:

In response to your June 26, 2007, request for further clarification regarding Comment #4 of the June 15, 2007, information request letter, please see the below Pharmacology/Toxicology comments:

> **Your proposal to rely on a short-term comparative phototoxicity study of Diclofenac Sodium Gel and Solaraze to serve as a bridge to utilize the Solaraze photococarcinogenicity data is not acceptable. We are requesting that you compare the identities and amounts of degradants formed over time from solar or simulated solar exposure of Diclofenac sodium 1% gel and Solaraze.**
>
> **A short-term toxicity study as proposed, may not accurately predict comparability to a 2-year dermal photococarcinogenicity bioassay. Thus, we are requesting the demonstration of degradant profiles between your drug product and Solaraze.**

Kindly confirm receipt of this email. Should you have any additional questions/concerns, please do not hesitate to contact me.

Regards,

Lauren

Lauren P. Tornetta

Lauren P. Tornetta, M.S.
Regulatory Project Manager
Div. of Anesthesia, Analgesia & Rheum. Products
Phone: (301) 796-2246
Fax: (301) 796-9722 / 9723
Email: lauren.tornetta@fda.hhs.gov

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/s/

Lauren Tornetta
8/15/2007 11:21:56 AM
CSO

MEMORANDUM

Date:	August 14, 2007
From:	L.S. Leshin
Through:	A. Wasserman, Pharm/Tox Supervisor
Subject:	**Response to Request for Clarification of Comment #4 of the June 15, 2007 PTOX/CMC IR letter**
Submission:	**NDA 22-122** (June 26, 2007 email; no submission code)
Sponsor:	**Novartis Consumer Health**
Drug:	**Diclofenac Topical Gel, 1%**

Background:

The following comment was sent to the Sponsor on June 15, 2007 to request additional information in External Comments to Sponsor:

> During the review of your product, Diclofenac Sodium Topical Gel, 1%, the following issues have been identified for which we are requesting further information:
>
> 4. Provide information that the photodegradants for which you are relying on the Agency's prior findings of safety are the same and do not exceed the levels of those produced by the 505(b)(2) reference compound, Solaraze.

The Sponsor then submitted the following response via email on June 26, 2007 requesting clarification of our request:

> Comment No. 4
> A phototoxicity study comparing the effects of Diclofenac sodium 1% gel and Solaraze may be performed. Similar responses from the diclofenac sodium 1% gel and Solaraze or lower phototoxicity from diclofenac sodium 1% gel indicate that the level of toxic photodegradants in diclofenac sodium 1% gel do not exceed those in Solaraze. This information is sufficient to justify the use of prior findings of safety of Solaraze to Diclofenac sodium 1% gel. Does the Agency agree?

Recommendations and External Comments to Sponsor

Your proposal to rely on a short-term comparative phototoxicity study of Diclofenac Sodium Gel and Solaraze to serve as a bridge to utilize the Solaraze photococarcinogenicity data is not acceptable. We are requesting that you compare the identities and amounts of degradants formed over time from solar or simulated solar exposure of Diclofenac sodium 1% gel and Solaraze.

A short-term toxicity study as proposed, may not accurately predict comparability to a 2-year dermal photococarcinogenicity bioassay. Thus, we are requesting the demonstration of degradant profiles between your drug product and Solaraze.

Novartis Consumer Health, Inc.
200 Kimball Drive
Parsippany, NJ 07054-0622

Fax 973 503 8428

NOVARTIS

Bob Rappaport, MD - Division Director
Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705

NDA 22-122
Diclofenac Sodium Gel, 1%

Dismissal of Patent Infringement Suit

August 2, 2007 *(via overnight mail)*

Dear Dr. Rappaport:

Reference is made to the submission of NDA 22-122 of December 19, 2006 for approval of diclofenac sodium topical gel, 1%. Reference is also made to Novartis Consumer Health, Inc. (NCH) correspondences of March 27 and May 17, 2007.

The May 17 correspondence informed the FDA that Bioglan Pharmaceuticals Corp. (wholly owned subsidiary of Bradley Pharmaceuticals, Inc.) and Jagotec AG had filed a complaint for patent infringement against Novartis Consumer Health, Inc (NCH). The complaint (case number 2:07-cv-02075-HAA-ES) was filed with the United States District Court, District of New Jersey on May 3, 2007.

21 CFR 314.107(e) states that a 505(b) (2) or 505(j) applicant shall "submit a copy of the entry of the order or judgment to the Office of Generic Drugs (HFD–600), or to the appropriate division in the Office of Drug Evaluation I (HFD–100) or Office of Drug Evaluation II (HFD–500), whichever is applicable, within 10 working days of a final judgment."

Accordingly, as required by 21 CFR § 314.107(e), NCH hereby notifies the FDA that a "Notice of Voluntary Dismissal With Prejudice Pursuant to Federal Rule of Civil Procedure 41(a)," dismissing all claims against NCH with prejudice, was entered on the court's docket on July 26, 2007. This dismissal constitutes a full and final adjudication of the lawsuit, and operates as a final judgment. A copy of the Notice is appended.

This submission is being provided on 1 Compact Disk (CD), is less than 1MB in size, was scanned for viruses using McAfee VirusScan Enterprise 7.1.0., and is virus free.

Bob Rapp port, MD
NDA 22-122
August 2, 2007

Should any additional information be needed, please contact the undersigned at (973) 503-7645.

Regards,

Filomena Gesek
Director US Regulatory Affairs-
Therapeutic Categories

William H. Trousdale
TOMPKINS MCGUIRE WACHENFELD & BARRY
Four Gateway Center
100 Mulberry Street
Newark, New Jersey 07102
Tel: (973) 623-7893
Fax: (973) 623-7682

Anthony Herman
COVINGTON & BURLING LLP
1201 Pennsylvania Avenue, NW
Washington, D.C. 20004
Tel: (202) 662-5280
Fax: (202) 662-6291

Attorneys for Plaintiffs

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

BIOGLAN PHARMACEUTICALS CORP. and JAGOTEC AG, Plaintiffs, v. NOVARTIS CONSUMER HEALTH, INC., Defendant.	No. 07-CV-2075 (DMC)(PS)

NOTICE OF VOLUNTARY DISMISSAL WITH PREJUDICE PURSUANT TO FEDERAL RULE OF CIVIL PROCEDURE 41(a)

Plaintiffs Bioglan Pharmaceuticals Corp. and Jagotec AG and Defendant Novartis Consumer Health, Inc. hereby notify the Court that they have resolved this matter. Accordingly, pursuant to Federal Rule of Civil Procedure 41(a), Plaintiffs dismiss all claims against Defendant with prejudice, with each side to bear its own costs. Defendant consents to this dismissal.

This dismissal with prejudice shall constitute a full and final adjudication of this lawsuit and shall operate as a final judgment to be submitted to the proper Office of the Department of Health and Human Services, Food and Drug Administration, within ten (10) working days of its entry pursuant to 21 C.F.R. § 314.107(e).

Respectfully Submitted

William H. Trousdale
TOMPKINS MCGUIRE WACHENFELD & BARRY
Four Gateway Center
100 Mulberry Street
Newark, New Jersey 07102
Tel: (973) 623-7893
Fax: (973) 623-7682

Anthony Herman
COVINGTON & BURLING LLP
1201 Pennsylvania Avenue, NW
Washington, D.C. 20004
Tel: (202) 662-5280
Fax: (202) 662-6291

Attorneys for Plaintiffs

Dated: July 26, 2007

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

CLINICAL INSPECTION SUMMARY

DATE: July 12, 2007

TO: Lauren Tornetta, Regulatory Project Manager
Neville Gibbs, M.D., Medical Officer
Bob Rappaport, M.D., Director
Division of Anesthesia, Analgesia, and Rheumatology Products, HFD-170

THROUGH: Constance Lewin, M.D., M.P.H., Branch Chief
Good Clinical Practice Branch I, HFD-46
Division of Scientific Investigations

FROM: Sheryl Gunther, Pharm.D.
Good Clinical Practice Branch I, HFD-46
Division of Scientific Investigations

SUBJECT: Evaluation of Clinical Inspections

NDA: 22-122

SPONSOR: Novartis Consumer Health, Inc.

DRUG: Voltaren AT® (diclofenac sodium topical gel), 1%

THERAPEUTIC CLASSIFICATION: Standard

INDICATION: [redacted] joints amenable to [redacted] treatment, such as the hands and knees

CONSULTATION REQUEST DATE: February 28, 2007

DIVISION ACTION GOAL DATE: October 15, 2007

PDUFA GOAL DATE: October 19, 2007

I. BACKGROUND

Diclofenac sodium topical gel, 1%, is a non-selective, non-steroidal anti-inflammatory drug (NSAID) product being evaluated under NDA 22-122 as a topical agent for [redacted], amenable to [redacted] treatment, such as the hands and knees.

Diclofenac sodium, the active ingredient for this NDA, has been used in various formulations in many approved drug products. Clinical investigator inspections were conducted at five clinical sites (Drs. Cohen, Chase, Champlin, Barthel, and Savage) submitting data in support of NDA 22-122. These sites were inspected because: 1) they have a significant impact on the efficacy results for studies VOSG-PN-310, VOSG-PN-315, and VOSG-PN-309; and 2) these sites enrolled a large number of study subjects. The goals of inspection included validation of submitted data and compliance of study activities with FDA regulations. Among the elements reviewed for compliance were subject record accuracy, informed consent, protocol inclusion/exclusion criteria, adherence to protocol, randomization procedures, documentation of adverse events, and protection of subjects' rights, safety, and welfare.

The inspections covered studies performed under the following protocols:
- Protocol VOSG-PE-310, entitled "A 12-week, randomized, double-blind, multi-center, vehicle-controlled, parallel group study to assess the efficacy and safety of diclofenac sodium gel, 1% for the relief of signs and symptoms in patients with osteoarthritis of the knee"
- Protocol VOSG-PE-315, entitled "An 8-week, multi-center, randomized, double-blind, placebo-controlled, parallel group trial of diclofenac sodium gel, 1% in patients with primary osteoarthritis of the hand"
- Protocol VOSG-PE-309, entitled "An uncontrolled long-term safety trial of diclofenac sodium gel, 1% in patients with osteoarthritis of the knee"

Protocols VOSG-PE-310 and 315 were prospective, randomized, double-blind, multi-center, parallel group studies in subjects with OA of the knee (VOSG-PE-310) and hand (VOSG-PE-315). The primary objectives of Protocols VOSG-PE-310 and 315 were to compare the efficacy of four-times daily topical applications of diclofenac sodium topical gel, 1%, with vehicle in subjects with OA of the knee and hand, respectively.

Protocol VOSG-PE-309 was a multi-center, open-label, single-arm, long-term safety study that included subjects with knee OA who had completed either the VOSG-PN-304 or the VOSG-PN-310 double-blind studies, as well as naïve subjects. The primary objective was to determine the long-term safety of diclofenac sodium topical gel, 1% when applied four-times daily for up to 12 months as measured by rates of clinical adverse events and monitoring of laboratory values.

II. RESULTS (by site):

Clinical Investigator/Site	Protocol(s)	Inspection Date	EIR Received Date	Final Classification
Dr. Selwyn A. Cohen, Site #309 Clinical Research Consultants 2590 Main Street Stratford, CT 06615	VOSG-PE-315	6/19/2007- 6/20/2007	7/6/2007	NAI
Dr. Walter F. Chase, Site #211 1301 W. 38th St., Suite 609 Austin, TX 78705-1015	VOSG-PE-310	5/1/2007- 5/7/2007	5/24/2007	VAI

Dr. John Champlin, Site #209 6651 Madison Ave. Carmichael, CA 95608	VOSG-PE-309 and VOSG-PE-310	7/6/2007- presently ongoing	pending	pending (NAI)
Dr. H. Richard Barthel, Site #224 2403 Castillo St., Suite 205 Santa Barbara, CA 93105	VOSG-PE-310	5/29/2007- 6/7/2007	6/19/2007	NAI
Dr. P. Lauren Savage, Site #233 Alabama Clinical Therapeutics 52 Medical Park Drive East, Suite 214 Birmingham, AL 35235-3423	VOSG-PE-310	5/23/2007- 5/24/2007	6/8/2007	NAI

Key to Classifications
NAI - No deviation from regulations. Data acceptable.
VAI - No Response Requested= Deviations(s) from regulations. Data acceptable.
VAI - Response Requested = Deviation(s) from regulations.
OAI - Significant deviations from regulations. Data unreliable.

(1) Dr. Selwyn A. Cohen, Site #309
Stratford, CT

a. What was inspected?

Fifty-six subjects consented to participate in the study. Of these, 24 subjects were enrolled and randomized, and 23 subjects completed the study. The FDA investigator performed a complete review of 15 subjects' records. The review included subject eligibility, source documents, case report forms, and data listings of efficacy endpoints. An audit of all 56 informed consent forms was conducted.

b. Limitations of inspection: None.

c. General observations/commentary:

Data in sponsor-provided data listings, including efficacy and safety endpoints, were supported by data in source documents and case report forms. There were no significant inspectional findings that would adversely impact data acceptability. No underreporting of adverse events was noted.

Recommendation: Data from this clinical site appear acceptable for use in support of this NDA.

(2) Dr. Walter F. Chase, Site #211
Austin, TX

a. What was inspected?

Forty-nine subjects were screened, 29 subjects were enrolled and randomized, and 23 subjects completed the study. A complete review of records was performed for all 29 enrolled subjects. The review included consent forms, source documents, case report forms, data listings of efficacy endpoints, drug accountability records, and correspondence with the IRB and sponsor. Additionally, the inspection encompassed an audit of all subjects' consent forms.

b. Limitations of inspection: None.

c. General observations/commentary:

Except for a deficiency related to protocol compliance in ensuring that weekly subject diaries were complete and signed and dated by subjects, there were no significant inspectional findings that would adversely impact data acceptability. No underreporting of adverse events was noted. Data in sponsor-provided data listings were supported by data in source documents and case report forms.

Recommendation: Data from this clinical site appear acceptable for use in support of this NDA.

(3) Dr. John Champlin, Site #209
Carmichael, CA

a. What was inspected?

For Protocol VOSG-PN-309, 22 subjects were screened, 20 subjects were randomized, and 10 subjects completed the study. The FDA investigator reviewed the records for all 10 subjects who completed the study, and conducted an audit of consent forms for all of the 22 subjects who were screened. For Protocol VOSG-PN-310, 39 subjects were screened, 28 subjects were randomized, and 24 subjects completed the study. A review of 12 subjects' records was performed, and an audit of consent forms was conducted for all of the 39 subjects who were screened. For both of these protocols, the FDA investigator reviewed the source documents and CRFs, and compared them with data listings provided by the sponsor as part of the NDA submission. Additional records reviewed included drug accountability records and communication with the IRB and sponsor.

b. Limitations of inspection: Unknown at this time, as the investigation is ongoing and the Establishment Inspection Report (EIR) is not available at this time.

c. General observations/commentary:

For Protocols VOSG-PN-309 and VOSG-PN-310, data in sponsor-provided data listings, including efficacy and safety endpoints, were supported by data in source documents and case report forms. No underreporting of adverse events was noted. Except for minor deficiencies related to protocol compliance, there were no significant inspectional findings that would adversely impact data acceptability.

The observations noted above are based on verbal communications with the field investigator. If significant problems are noted and/or conclusions change upon receipt and review of the EIR, an inspection summary addendum will be generated.

Recommendation: Data from this clinical site appear acceptable for use in support of this NDA.

(4) Dr. H. Richard Barthel, Site #224
Santa Barbara, CA

b. What was inspected?

Thirty-five subjects were screened, and 27 subjects passed screening criteria and were enrolled. Nine subjects withdrew or were discontinued during the study, and 18 subjects completed the study. The FDA investigator audited all 35 subjects' records. Records reviewed included source documents, case report forms, informed consent documents, drug accountability records, and communication with the IRB and sponsor.

b. Limitations of inspection: None.

c. General observations/commentary:

Data in sponsor-provided data listings, including efficacy and safety endpoints, were supported by data in source documents and case report forms. No underreporting of adverse events was noted. There were no significant inspectional findings that would adversely impact data acceptability.

Recommendation: Data from this clinical site appear acceptable for use in support of this NDA.

(5) **Dr. P. Lauren Savage, Site #233**
Birmingham, AL

c. What was inspected?

Thirty-six subjects were screened, and 14 subjects completed the study. The FDA investigator reviewed the source documents and CRFs for all subjects, and compared them with data listings provided by the sponsor as part of the NDA submission. Additionally, an audit of all 36 subjects' records was conducted.

b. Limitations of inspection: None.

c. General observations/commentary:

Data in sponsor-provided data listings, including efficacy and safety endpoints, were supported by data in source documents and case report forms. No underreporting of adverse events was noted. There were no significant inspectional findings that would adversely impact data acceptability.

Recommendation: Data from this clinical site appear acceptable for use in support of this NDA.

III. OVERALL ASSESSMENT OF FINDINGS AND GENERAL RECOMMENDATIONS

In general, for the five clinical investigator sites inspected, there was sufficient documentation to assure that all audited subjects did exist, fulfilled the eligibility criteria, received the assigned study medication, and had their primary efficacy endpoint captured as specified in the protocol. No underreporting of adverse events was noted. Overall, data generated for Protocols VOSG-PN-309, VOSG-PN-310, and VOSG-PN-315 at these clinical sites appear acceptable for use in support of NDA 22-122.

Observations noted above for Dr. John Champlin are based on communications from the field investigator. An inspection summary addendum will be generated if conclusions change significantly upon receipt and review of the final EIR.

{See appended electronic signature page}

Sheryl Gunther, Pharm.D.
Good Clinical Practice Branch I, HFD-46
Division of Scientific Investigations

CONCURRENCE:

{See appended electronic signature page}

Constance Lewin, M.D., M.P.H.
Branch Chief
Good Clinical Practice Branch I
Division of Scientific Investigations

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

/s/

Sheryl Gunther
7/17/2007 04:40:28 PM
PHARMACOLOGIST

Constance Lewin
7/17/2007 04:50:32 PM
MEDICAL OFFICER

Tornetta, Lauren

From: Tornetta, Lauren
Sent: Thursday, July 12, 2007 9:38 AM
To: 'filomena.gesek@novartis.com'
Cc: 'andras.megyeri@novatis.com'
Subject: NEW CMC Info.Request/NDA 22-122/12Jul07

Filomena-

The chemistry reviewer has a NEW information request. The following comments pertain to your labeling section of the NDA. Additional comments based on the DMETS review may be forthcoming.

1. Package insert:

   (a) #11 Description:

   - Revise the chemical structure by ——
   - Revise the chemical name to read 2-[(2,6-dichlorophenyl)amino]benzeneacetic acid, monosodium salt
   - Use lower case for carbomer homopolymer to read "carbomer homopolymer Type C."

   (b) #16 How supplied section:

   - Provide strength of the dosage form (21CFR 201.57(c)(17)
   - Names and addresses of manufacturer and distributor (21CFR 201.1 and 201.100(e))
   - It is noted that only —— and 100-gram tubes are included in this section. Explain why the 20-gram tube is not included.
   - Change the storage temperatures to the following:
     Store at 25°C (77°F); excursions permitted to 15-30°C (59-86 °F)
     [see USP Controlled Room Temperature]

2. Structured Product Labeling (SPL) Data Elements:

   (a) Revise the nonproprietary name to read "diclofenac sodium topical gel."
   (b) Revise the pharmacological class to nonsteroidal anti-inflammatory drug (NSAID).

3. Container and carton labeling:

   (a) Increase the prominence of the nonproprietary name to at least half that of the proprietary name. Please note that prominence includes a combination of font shape, size, font color, and overall visual appeal.
   (b) Change the storage temperatures to either of the following:
   Store at 25°C (77 °F); excursions 15-30°C (59-86 °F), or
   Store at 25°C (77°F) (see insert)
   (c) Correct the spelling for "Not for ophthalmic use" for all labeling.
   (d) Provide lot number and expiration date on the physician sample.

Please provide a response to the above-mentioned requests by C.O.B., July 19, 2007, if possible. Provide a response to me via email followed with an official submission to the NDA. This information is pertinent to the continued review of your NDA and your prompt attention is appreciated.

Kindly confirm receipt of this July 12, 2007, request.

Best,
Lauren

Lauren P. Tornetta, M.S.
Regulatory Project Manager
Div. of Anesthesia, Analgesia & Rheum. Products
Phone: (301) 796-2246
Fax: (301) 796-9722 / 9723
Email: lauren.tornetta@fda.hhs.gov

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/s/

Lauren Tornetta
7/12/2007 09:52:12 AM
CSO

Tornetta, Lauren

From: Tornetta, Lauren
Sent: Monday, July 02, 2007 11:02 AM
To: 'filomena.gesek@novartis.com'
Cc: Tornetta, Lauren
Subject: New/CMC Info.Request/NDA 22122
Importance: High

Filomena:

The Chemistry Reviewer has the following information requests for NDA 22-122:

1. Provide the following information for the container closure systems:

   a. Authorization letter for DMF — with specific reference to the amendment numbers and their submission dates for the packaging materials used in this NDA.
   b. A table listing the materials of construction for the tubes — including appropriate references to the indirect food additive regulations (21 CFR 174-186) for the packaging materials that are in contact with the drug product.

2. It is noted that a reduced testing frequency is proposed for the annual stability batches (refer to section 3.2.P.8.2, Production Batches). Revise the stability protocol by including a statement indicating that the proposed reduced testing frequency will be applied only if satisfactory stability data are obtained from the first three production batches.

3. The following comments pertain to the proposed comparability protocol (section 3.2.R.3):

   (a) An in-vitro release test should be included in the comparability protocol (CP) for the proposed changes. The in-vitro release rate of a lot of the drug product prepared with the proposed changes should be compared with the release rate of a recent lot of comparable age of the product prepared by the prechange process. The median in-vitro release rates of the lots prepared by the two processes should be demonstrated to be within acceptable limits, using the testing procedure described in section VII of the "Guidance for Industry, SUPAC-SS Nonsterile Semisolid Dosage Forms, Scale-Up and Postapproval Changes: Chemistry, Manufacturing, and Controls; in Vitro Release Testing and In Vivo Bioequivalence Documentation."

   (b) Provided the in-vitro release test is included in the CP, the changes proposed in the CP can be submitted in an annual report.

   (c) Include in the CP the steps you will take in cases the postchange product cannot be demonstrated to be equivalent to the prechange product without more extensive physicochemical or PK/PD testing, or the postchange product does not meet the prescribed acceptance criteria in the protocol.

Your prompt response to these requests is appreciated and pertinent to the review of your NDA. Please provide responses to me via email (followed by an official submission to the NDA) by C.O.B. Friday, July 6.

Kindly confirm receipt of this request.

Lauren

Lauren P. Tornetta, M.S.
Regulatory Project Manager
Div. of Anesthesia, Analgesia and Rheum. Products
Phone: (301) 796-2246
Fax: (301) 796-9722 / 9723
Email: lauren.tornetta@fda.hhs.gov

APPEARS THIS WAY

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

/s/

Lauren Tornetta
7/2/2007 11:06:45 AM
CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-122

INFORMATION REQUEST LETTER

Novartis Consumer Health, Inc.
200 Kimball Drive
Parsippany, New Jersey 07054-0622

Attention: Filomena Gesek
Director, U.S. Regulatory Affairs, Therapeutic Areas

Dear Ms. Gesek:

Please refer to your December 20, 2006, New Drug Application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for diclofenac sodium, topical gel, 1%.

We are reviewing the Chemistry, Manufacturing and Controls (CMC) and the nonclinical sections of your submission and have the following comments and information requests. We request a prompt written response, within 30 days, in order to continue our evaluation of your NDA.

1. Cocoyl caprylocaprate is a novel excipient for drug products marketed in the United States. As a novel excipient, the safety of cocoyl caprylocaprate should be established for use according to the following Guidance for Industry: ***Nonclinical Studies for the Safety Evaluation of Pharmaceutical Excipients*** which may be found at http://www.fda.gov/cder/guidance. Provide toxicological information about cocoyl caprylocaprate, especially genetic, dermal, photodermal, and systemic toxicology. Alternatively, provide support from published literature or the use of topical products containing similar or greater amounts of cocoyl caprylocaprate that this compound meets FDA criteria of safety.

2. The list of components of [redacted] comprises only those that are equal or greater than 5% of the total composition. This only totals to 78% of the [redacted] composition by weight. There is no threshold for reporting excipients or excipient components. Provide the entire composition for [redacted]

3. Impurities and degradants appear incompletely qualified and/or controlled. Since Voltaren® was approved in 1988, the Agency's chemistry and toxicology guidelines have been updated to ensure the safety of marketed products. In particular, these now include qualification of impurities containing structural alerts for genotoxicity [see FDA position paper *Regulation of genotoxic and carcinogenic impurities in drug substances and products* (McGovern and Jacobson-Kram; Trends in Analytical

Chemistry, 2006)] and the qualification of degradants observed in stability testing as described below.

[redacted] and contain structural alerts for genotoxicity. According to current Agency policy, such impurities must be controlled to [redacted] total daily intake or be toxicologically qualified consisting of negative findings in two in vitro genotoxicity studies (point mutation and clastogenicity assays). [redacted] while not containing a structural alert, exceeds the threshold for qualification (NMT [redacted] on stability and requires a similar genotoxicity evaluation unless levels can be reduced. Review of submitted studies present in the NDA does not identify evaluations of these impurities in both assays. Furthermore, impurities have not been toxicologically qualified in repeat-dose studies, up to 3 months duration, recommended to support a chronic indication. Provide further data and/or information to support the safety of the identified impurities at the levels proposed.

4. Provide information that the photodegradants for which you are relying on the Agency's prior findings of safety are the same and do not exceed the levels of those produced by the 505(b)(2) reference compound, Solaraze.

5. Submit to the NDA the 12-week rabbit dermal study using Voltaren Emulgel which was submitted to IND 64,334 in Jan 2004 to support the safety of clinical studies longer than 4 weeks. Also, provide the concentrations of impurities in the formulation used in this study, if available.

If you have any questions, call Lauren Tornetta, Regulatory Project Manager, at (301) 796-2246.

Sincerely,

Parinda Jani
Chief, Project Management Staff
Division of Anesthesia, Analgesia
and Rheumatology Products, HFD-170
Office of Drug Evaluation II
Center for Drug Evaluation and Research