

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

***APPLICATION NUMBER:***

**206911Orig1s000**

**OTHER REVIEW(S)**

### 505(b)(2) ASSESSMENT

Application Information		
NDA 206911	NDA Supplement #: N/A	Efficacy Supplement Type: N/A
Proprietary Name: <b>Bromsite</b> Established/Proper Name: <b>bromfenac ophthalmic solution 0.075%</b> Dosage Form: topical <b>ophthalmic solution</b> Strengths: <b>0.075%</b>		
Applicant: <b>InSite Vision Incorporated</b>		
Date of Receipt: <b>June 10, 2015</b>		
PDUFA Goal Date: <b>April 10, 2016</b>		Action Goal Date (if different):
RPM: <b>Diana Willard</b>		
Proposed Indication(s): <b>treatment of postoperative inflammation and prevention of ocular pain in patients undergoing cataract surgery</b>		

### GENERAL INFORMATION

- 1) Is this application for a recombinant or biologically-derived product and/or protein or peptide product *OR* is the applicant relying on a recombinant or biologically-derived product and/or protein or peptide product to support approval of the proposed product?

YES ☐ NO ☒

*If "YES" contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.*

**INFORMATION PROVIDED VIA RELIANCE  
(LISTED DRUG OR LITERATURE)**

- 2) List the information essential to the approval of the proposed drug that is provided by reliance on our previous finding of safety and efficacy for a listed drug by reliance on published literature, or by reliance on a final OTC monograph. *(If not clearly identified by the applicant, this information can usually be derived from annotated labeling.)*

Source of information* (e.g., published literature, name of listed drug(s), OTC final drug monograph)	Information relied-upon (e.g., specific sections of the application or labeling)
NO published literature essential to approval	
NDA 21664 Xibrom/Bromday	FDA's previous finding of safety and effectiveness for pharmacology and for studies such as carcinogenicity, genotoxicity, reproductive toxicology, drug interaction, excretion, and metabolism to support labeling for Sections 8 and 13

\*each source of information should be listed on separate rows, however individual literature articles should not be listed separately

NOTE: For completeness of the administrative record, there is no reliance on NDA 203168/Prolensa.

- 3) The bridge in a 505(b)(2) application is information to demonstrate sufficient similarity between the proposed product and the listed drug(s) or to justify reliance on information described in published literature for approval of the 505(b)(2) product. Describe in detail how the applicant bridged the proposed product to the listed drug(s) and/or published literature<sup>1</sup>. [See also Guidance for Industry Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products.](#)

NDA 206911 (BromSite) relies on FDA's previous finding of safety for the listed drug Xibrom/Bromday (NDA 21664), specifically nonclinical information. The applicant conducted a nonclinical ocular toxicity study in rabbits to qualify impurities, and provide ocular toxicity bridging data. In this study, it was demonstrated that the plasma levels of bromfenac following topical ocular administration of BromSite were comparable to those obtained with the listed drug Xibrom. This supports reliance on the nonclinical data used to support approval of Xibrom to support the approval of BromSite.

### RELIANCE ON PUBLISHED LITERATURE

- 4) (a) Regardless of whether the applicant has explicitly stated a reliance on published literature to support their application, is reliance on published literature necessary to support the approval of the proposed drug product (i.e., the application *cannot* be approved as labeled without the published literature)?

YES ☐ NO ☒

If “NO,” proceed to question #5.

- (b) Does any of the published literature necessary to support approval identify a specific (e.g., brand name) *listed* drug product?

N/A ☒ YES ☐ NO ☐

If “NO,” proceed to question #5.

If “YES”, list the listed drug(s) identified by name and answer question #4(c).

- (c) Are the drug product(s) listed in (b) identified by the applicant as the listed drug(s)?

YES ☐ NO ☐

### RELIANCE ON LISTED DRUG(S)

*Reliance on published literature which identifies a specific approved (listed) drug constitutes reliance on that listed drug. Please answer questions #5-9 accordingly.*

- 5) Regardless of whether the applicant has explicitly cited reliance on listed drug(s), does the application **rely** on the finding of safety and effectiveness for one or more listed drugs (approved drugs) to support the approval of the proposed drug product (i.e., the application cannot be approved without this reliance)?

YES ☒ NO ☐

If “NO,” proceed to question #10.

- 6) Name of listed drug(s) relied upon, and the NDA #(s). Please indicate if the applicant explicitly identified the product as being relied upon (see note below):

Name of Listed Drug	NDA #	Did applicant specify reliance on the product? (Y/N)
<b>Bromday/Xibrom</b>	<b>21664</b>	<b>Yes</b>

*Applicants should specify reliance on the 356h, in the cover letter, and/or with their patent certification/statement. If you believe there is reliance on a listed product that has not been explicitly identified as such by the applicant, please contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.*

- 7) If this is a (b)(2) supplement to an original (b)(2) application, does the supplement rely upon the same listed drug(s) as the original (b)(2) application?  
N/A ☒ YES ☐ NO ☐

*If this application is a (b)(2) supplement to an original (b)(1) application or not a supplemental application, answer "N/A".*

*If "NO", please contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.*

- 8) Were any of the listed drug(s) relied upon for this application:

a) Approved in a 505(b)(2) application?

YES ☐ NO ☒

*If "YES", please list which drug(s).*

Name of drug(s) approved in a 505(b)(2) application:

b) Approved by the DESI process?

YES ☐ NO ☒

*If "YES", please list which drug(s).*

Name of drug(s) approved via the DESI process:

c) Described in a final OTC drug monograph?

YES ☐ NO ☒

*If "YES", please list which drug(s).*

Name of drug(s) described in a final OTC drug monograph:

d) Discontinued from marketing?

YES ☒ NO ☐

*If "YES", please list which drug(s) and answer question d) i. below.*

*If "NO", proceed to question #9.*

Name of drug(s) discontinued from marketing:

i) Were the products discontinued for reasons related to safety or effectiveness?

YES ☐ NO ☒

*(Information regarding whether a drug has been discontinued from marketing for reasons of safety or effectiveness may be available in the Orange Book. Refer to section 1.11 for an explanation, and section 6.1 for the list of discontinued drugs. If a determination of the reason for discontinuation has not been published in the Federal Register (and noted in the Orange Book), you will need to research the archive file and/or consult with the review team. Do not rely solely on any statements made by the sponsor.)*

- 9) Describe the change from the listed drug(s) relied upon to support 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 capsule to solution").

NDA 21664 was approved for Xibrom (bromfenac ophthalmic solution) 0.09% for the treatment of postoperative inflammation in patients who have undergone cataract extraction.

NDA 206911 for BromSite (bromfenac ophthalmic solution) 0.75%, a new strength and formula of bromfenac, will be indicated for the treatment of postoperative inflammation and prevention of ocular pain in patients undergoing cataract surgery.

*The purpose of the following two questions 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.*

*The assessment of pharmaceutical equivalence for a recombinant or biologically-derived product and/or protein or peptide product is complex. If you answered **YES to question #1**, proceed to question #12; if you answered **NO to question #1**, proceed to question #10 below.*

- 10) (a) Is there a pharmaceutical equivalent(s) to the product proposed in the 505(b)(2) application that is already approved (via an NDA or ANDA)?

*(**Pharmaceutical equivalents** are drug products in identical dosage forms intended for the same route of administration 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), FDA's "Approved Drug Products with Therapeutic Equivalence Evaluations" (the Orange Book)).*

***Note** that for proposed combinations of one or more previously approved drugs, a pharmaceutical equivalent must also be a combination of the same drugs.*

YES 0 NO X

*If "**NO**" to (a) proceed to question #11.  
If "**YES**" to (a), answer (b) and (c) then proceed to question #12.*

- (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 listed drug(s) referenced by the application a pharmaceutical equivalent?

N/A ☐ YES ☐ NO ☐

*If this application relies only on non product-specific published literature, answer "**N/A**"*

*If "**YES**" to (c) and there are no additional pharmaceutical equivalents listed, proceed to question #12.*

*If "**NO**" or if there are additional pharmaceutical equivalents that are not referenced by the application, list the NDA pharmaceutical equivalent(s); you do not have to individually list all of the products approved as ANDAs, but please note below if approved approved generics are listed in the Orange Book. Please also contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.*

Pharmaceutical equivalent(s):

11) (a) Is there a pharmaceutical alternative(s) already approved (via an NDA or ANDA)?

*(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.)*

*Note that for proposed combinations of one or more previously approved drugs, a pharmaceutical alternative must also be a combination of the same drugs.*

YES ☒ NO ☐

If "NO", proceed to question #12.

(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) referenced as the listed drug(s)?

N/A ☐ YES ☒ NO ☐

*If this application relies only on non product-specific published literature, answer "N/A"*

*If "YES" and there are no additional pharmaceutical alternatives listed, proceed to question #12.*

*If "NO" or if there are additional pharmaceutical alternatives that are not referenced by the application, list the NDA pharmaceutical alternative(s); you do not have to individually list all of the products approved as ANDAs, but please note below if approved generics are listed in the Orange Book. Please also contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.*

Pharmaceutical alternative(s):

#### PATENT CERTIFICATION/STATEMENTS

12) List the patent numbers of all unexpired patents listed in the Orange Book for the listed drug(s) for which our finding of safety and effectiveness is relied upon to support approval of the (b)(2) product.

Listed drug/Patent number(s):

No patents listed ☒ proceed to question #14

- 13) Did the applicant address (with an appropriate certification or statement) all of the unexpired patents listed in the Orange Book for the listed drug(s) relied upon to support approval of the (b)(2) product?

YES ☒ NO ☐

*If “NO”, list which patents (and which listed drugs) were not addressed by the applicant.*

Listed drug/Patent number(s):

- 14) 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.*)

- ☐ No patent certifications are required (e.g., because application is based solely on published literature that does not cite a specific innovator product)
- ☐ 21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA. (Paragraph I certification)
- ☐ 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):

Expiry date(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). *If Paragraph IV certification was submitted, proceed to question #15.*
- ☐ 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the NDA holder/patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above). *If the applicant has a licensing agreement with the NDA holder/patent owner, proceed to question #15.*

☒ **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):



Method(s) of Use/Code(s):

- 15) Complete the following checklist **ONLY** for applications containing Paragraph IV certification and/or applications in which the applicant and patent holder have a licensing agreement:

- (a) Patent number(s):
- (b) Did the applicant submit a signed certification stating that the NDA holder and patent owner(s) were notified that this b(2) application was filed [21 CFR 314.52(b)]? YES ☐ NO ☐

*If "NO", please contact the applicant and request the signed certification.*

- (c) Did the applicant submit documentation showing that the NDA holder and patent owner(s) received the notification [21 CFR 314.52(e)]? This is generally provided in the form of a registered mail receipt. YES ☐ NO ☐

*If "NO", please contact the applicant and request the documentation.*

- (d) What is/are the date(s) on the registered mail receipt(s) (i.e., the date(s) the NDA holder and patent owner(s) received notification):

Date(s):

***Note**, the date(s) entered should be the date the notification occurred (i.e., delivery date(s)), not the date of the submission in which proof of notification was provided*

- (e) Has the applicant been sued for patent infringement within 45-days of receipt of the notification listed above?

***Note** that you may need to call the applicant (after 45 days of receipt of the notification) to verify this information **UNLESS** the applicant provided a written statement from the notified patent owner(s) that it consents to an immediate effective date of approval.*

YES ☐ NO ☐ Patent owner(s) consent(s) to an immediate effective date of approval ☐

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/s/  
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DIANA M WILLARD  
04/08/2016

RENATA ALBRECHT  
04/08/2016

**Department of Health and Human Services  
Public Health Service  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Medical Policy**

**PATIENT LABELING REVIEW**

Date: March, 4, 2016

To: Renata Albrecht, M.D.  
Director  
**Division of Transplant and Ophthalmology Products (DTOP)**

Through: LaShawn Griffiths, MSHS-PH, BSN, RN  
Associate Director for Patient Labeling  
**Division of Medical Policy Programs (DMPP)**

Shawna Hutchins, MPH, BSN, RN  
Team Leader, Patient Labeling  
**Division of Medical Policy Programs (DMPP)**

From: Sharon W. Williams, MSN, BSN, RN  
Patient Labeling Reviewer  
**Division of Medical Policy Programs (DMPP)**

Subject: Review of Patient Labeling: Instructions for Use (IFU)

Drug Name (established name): BromSite (bromfenac) 0.075%

Dosage Form and Route: ophthalmic solution

Application Type/Number: NDA 206911

Applicant: InSite Vision, Inc.

## 1 INTRODUCTION

On June 10, 2015, InSite Vision, Inc. submitted for the Agency's review an Original New Drug Application for bromfenac ophthalmic solution, 0.075%. On October 15, 2015, the propriety name BromSite was approved. BromSite (bromfenac) 0.075% ophthalmic solution is indicated for the treatment of postoperative inflammation and the prevention of ocular pain in patients undergoing cataract surgery.

This review is written in response by the Division of Medical Policy Programs (DMPP) in response to a request by the Division of Transplant and Ophthalmic Products (DTOP) on February 29, 2016, to review the Applicant's proposed Instructions for Use (IFU) for BromSite (bromfenac) 0.075% ophthalmic solution.

## 2 MATERIAL REVIEWED

- Draft BromSite (bromfenac) 0.075% ophthalmic solution IFU received on June 10, 2015, and received by DMPP on February 29, 2016.
- Draft BromSite (bromfenac) 0.075% ophthalmic solution Prescribing Information (PI) received on June 10, 2015, revised by the Review Division throughout the review cycle, and received by DMPP on February 29, 2016.

## 3 REVIEW METHODS

To enhance patient comprehension, materials should be written at a 6<sup>th</sup> to 8<sup>th</sup> grade reading level, and have a reading ease score of at least 60%. A reading ease score of 60% corresponds to an 8<sup>th</sup> grade reading level. In our review of the IFU the target reading level is at or below an 8<sup>th</sup> grade level.

Additionally, in 2008 the American Society of Consultant Pharmacists Foundation (ASCP) in collaboration with the American Foundation for the Blind (AFB) published *Guidelines for Prescription Labeling and Consumer Medication Information for People with Vision Loss*. The ASCP and AFB recommended using fonts such as Verdana, Arial or APhont to make medical information more accessible for patients with vision loss. We have reformatted the IFU document using the Arial font, size 10.

In our review of the IFU we have:

- simplified wording and clarified concepts where possible
- ensured that the IFU is consistent with the Prescribing Information (PI)
- ensured that the IFU meets the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006)

## 4 CONCLUSIONS

The IFU is acceptable with our recommended changes.

## **5 RECOMMENDATIONS**

- Please send these comments to the Applicant and copy DMPP on the correspondence.
- Our review of the IFU is appended to this memorandum. Consult DMPP regarding any additional revisions made to the PI to determine if corresponding revisions need to be made to the IFU.

Please let us know if you have any questions.

5 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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/s/  
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SHARON W WILLIAMS  
03/04/2016

SHAWNA L HUTCHINS  
03/04/2016

LASHAWN M GRIFFITHS  
03/04/2016

**FOOD AND DRUG ADMINISTRATION  
Center for Drug Evaluation and Research  
Office of Prescription Drug Promotion**

**\*\*\*\*Pre-decisional Agency Information\*\*\*\***

## Memorandum

**Date:** March 1, 2016

**To:** Diana Willard, Chief Project Management Staff  
Division of Transplant and Ophthalmology Products (DTOP)

**From:** Meena Ramachandra PharmD, Regulatory Review Officer  
Office of Prescription Drug Promotion (OPDP)

**Subject:** BromSite (bromfenac ophthalmic solution) 0.075%  
**NDA 206911**

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As requested in DTOP's consult dated August 5, 2015, OPDP has reviewed the draft PI and proposed carton and container labeling for BromSite (bromfenac ophthalmic solution) 0.075%.

OPDP reviewed the proposed substantially complete version of the PI titled, "Labeling text from 6.10.15 submission.doc" received via the DTOP SharePoint website on February 23, 2016. OPDP's comments are provided in the attached clean version of the substantially complete labeling.

OPDP has no comments on the version of the proposed carton and container labeling titled "BromSite Foil (b) (4).docx", "BromSite Container Label.docx" and "BromSite Carton.docx" accessed on the DTOP SharePoint website on February 23, 2016.

Thank you for the opportunity to review and provide comments on this proposed labeling. If you have any questions please contact Meena Ramachandra (240) 402-1348 or Meena.Ramachandra@fda.hhs.gov.

9 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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/s/  
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MEENA RAMACHANDRA  
03/01/2016



**MEMORANDUM**

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

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**CLINICAL INSPECTION SUMMARY**

**DATE:** January 7, 2016

**TO:** Diana Willard, Regulatory Project Manager  
Sonal Wadhwa, M.D., Medical Officer  
William Boyd, M.D., Medical Team Leader  
Division of Transplantation and Ophthalmology Products

**FROM:** Roy Blay, Ph.D.  
Good Clinical Practice Assessment Branch  
Division of Clinical Compliance Evaluation  
Office of Scientific Investigations

**THROUGH:** Janice Pohlman, M.D., M.P.H.  
Team Leader  
Good Clinical Practice Assessment Branch  
Division of Clinical Compliance Evaluation  
Office of Scientific Investigations

Susan D. Thompson, M.D. for  
Kassa Ayalew, M.D., M.P.H.  
Branch Chief  
Good Clinical Practice Assessment Branch  
Division of Clinical Compliance Evaluation  
Office of Scientific Investigations

**SUBJECT:** Evaluation of Clinical Inspections

**NDA:** 206911

**APPLICANT:** InSite Vision

**DRUG:** ISV-303, BromSite (bromfenac ophthalmic solution)

**NME:** No

**THERAPEUTIC CLASSIFICATION:** Standard Review

**INDICATION:** Treatment of postoperative inflammation and (b) (4) of ocular pain in patients (b) (4) cataract surgery

CONSULTATION REQUEST DATE: June 24, 2015  
CLINICAL INSPECTION SUMMARY DATE: January 15, 2016  
DIVISION ACTION GOAL DATE: February 1, 2016  
PDUFA DATE: April 10, 2016

## I. BACKGROUND:

The Applicant submitted this NDA to support the use of ISV-303, BromSite (bromfenac ophthalmic solution) for the treatment of postoperative inflammation and (b) (4) of ocular pain in patients (b) (4) cataract surgery

The identical pivotal studies, “C-11-303-003 and C-12-303-004 entitled, “A Randomized Double-masked Study to Compare the Ocular Safety, Tolerability, and Efficacy of ISV-303 (0.075% bromfenac in Durasite®) to Durasite® Vehicle in Cataract Surgery Subjects”, were inspected in support of this application.

The sites of Drs. Berdy, Walters, DaVanzo, and McLaurin were chosen because of their relatively large enrollment numbers.

## II. RESULTS (by Site):

Name of CI, Location	Protocol #/ Site #/ # of Subjects (enrolled)	Inspection Dates	Final Classification
Gregg Jonathan Berdy, M.D. Ophthalmology Associates 12990 Manchester Road, Suite 200 St. Louis, MO 63131	C-11-303-003/ 105/ 22	9-10 Sep 2015	NAI
Thomas R. Walters, M.D. Texan Eye, PA / Keystone Research, Ltd. 5717 Balcones Drive Austin, TX 78731	C-11-303-003/ 6/ 30	30 Oct-3 Nov 2015	NAI
Robert J. DaVanzo, M.D. Cornerstone Health Care 307 North Lindsay Street High Point, NC 27262	C-12-303-004/ 321/ 34	27 Jul-3 Aug 2015	NAI
Eugene B. McLaurin, M.D. Total Eye Care, P.A. 6060 Primacy Parkway, Suite 200 Memphis, TN 38119	C-12-303-004/ 264/ 21	21-23 Sep 2015	NAI

### Key to Classifications

NAI = No deviation from regulations.

VAI = Deviation(s) from regulations.

OAI = Significant deviations from regulations. Data unreliable.

Pending = Preliminary classification based on information in Form FDA 483 or preliminary communication with the field; EIR has not been received from the field or complete review of EIR is pending.

1. Gregg Jonathan Berdy, M.D.

Ophthalmology Associates  
12990 Manchester Road, Suite 200  
St. Louis, MO 63131

- a. **What was inspected:** At this site for Protocol C-11-303-003, 22 subjects were screened, 22 subjects were enrolled, and 13 subjects completed the study. The records of all subjects were reviewed and included, but were not limited to, informed consent forms, training records, delegation of responsibilities, protocol deviations, IRB and monitor documentation, inclusion/exclusion criteria, primary efficacy data, adverse event reporting, concomitant medications, and drug accountability.
- b. **General observations/commentary:** Signed informed consent was obtained from all screened subjects prior to study entry. A Form FDA 483 was not issued at the conclusion of the inspection. Review of the records noted above revealed no significant discrepancies or regulatory violations.
- c. **Assessment of data integrity:** The study appears to have been conducted adequately, and the data generated by this site appear acceptable in support of the respective indication.

2. Thomas R. Walters, M.D.

Texan Eye, PA  
5717 Balcones Drive  
Austin, TX 78731-4203

- a. **What was inspected:** At this site for Protocol C-11-303-003, 30 subjects were screened, all 30 subjects were enrolled, and 22 subjects completed the study. The records of 15 subjects were reviewed. Records reviewed included, but were not limited to, informed consent forms, financial disclosure, IRB and sponsor correspondence, medical histories, concomitant medications, inclusion/exclusion criteria, primary and secondary efficacy endpoints, drug accountability, and adverse events.
- b. **General observations/commentary:** Signed informed consent was obtained from all enrolled subjects prior to study entry. A Form FDA 483 was not issued at the conclusion of the inspection. Review of the records noted above revealed no significant discrepancies or regulatory violations.
- c. **Assessment of data integrity:** The study appears to have been conducted adequately, and the data generated by this site appear acceptable in support of the respective indication.

3. Robert J. DaVanzo, M.D.  
Cornerstone Health Care  
307 North Lindsay Street  
High Point, NC 27262

- a. **What was inspected:** At this site for Protocol C-12-303-004, 34 subjects were screened, 34 subjects were enrolled, and 26 subjects completed the study. Signed informed consent was obtained from all screened subjects prior to study entry. The records of all 34 subjects were reviewed. Source records were compared against data listings. Records reviewed included, but were not limited to, financial disclosure, IRB and monitoring correspondence, inclusion/exclusion criteria, primary efficacy data, concomitant medications, and drug accountability and storage.
- b. **General observations/commentary:** A Form FDA 483 was not issued at the conclusion of the inspection. Review of the records noted above revealed no significant discrepancies or regulatory violations.
- c. **Assessment of data integrity:** The study appears to have been conducted adequately, and the data generated by this site appear acceptable in support of the respective indication.

4. Eugene B. McLaurin, M.D.  
Total Eye Care, P.A.  
6060 Primacy Parkway, Suite 200  
Memphis, TN 38119

- a. **What was inspected:** At this site for Protocol C-12-303-004, 21 subjects were screened, 21 subjects were enrolled, and 15 subjects completed the study. The records of all 21 screened subjects were reviewed. Source records were compared against data listings. Records reviewed included, but were not limited to, informed consent forms, financial disclosure, training records, delegation of responsibilities, sponsor, monitor, and IRB communications, eligibility criteria, subject randomization, primary efficacy data, safety endpoints, adverse events, protocol deviations, subject discontinuations, and drug accountability.
- b. **General observations/commentary:** Signed informed consent was obtained from all enrolled subjects prior to study entry. A Form FDA 483 was not issued at the conclusion of the inspection. Review of the records noted above revealed no significant discrepancies or regulatory violations.
- c. **Assessment of data integrity:** The study appears to have been conducted adequately, and the data generated by this site appear acceptable in support of the respective indication.

### III. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

The clinical sites of Drs. Berdy, Walters, DaVanzo, and McLaurin were inspected in support of this NDA. None of these sites were issued a Form FDA 483. The final classification of each of these inspections was No Action Indicated (NAI). The studies appear to have been conducted adequately, and the data generated by these sites appear acceptable in support of the respective indication.

*{See appended electronic signature page}*

Roy Blay, Ph.D.  
Good Clinical Practice Assessment Branch  
Division of Clinical Compliance Evaluation  
Office of Scientific Investigations

CONCURRENCE:

*{See appended electronic signature page}*

Janice Pohlman, M.D., M.P.H.  
Team Leader  
Good Clinical Practice Assessment Branch  
Division of Clinical Compliance Evaluation  
Office of Scientific Investigations

*{See appended electronic signature page}*

Susan D. Thompson, M.D. for  
Kassa Ayalew, M.D., M.P.H.  
Branch Chief  
Good Clinical Practice Assessment Branch  
Division of Clinical Compliance Evaluation  
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ROY A BLAY  
01/07/2016

JANICE K POHLMAN  
01/07/2016

SUSAN D THOMPSON  
01/08/2016

## RPM FILING REVIEW

(Including Memo of Filing Meeting)

**To be completed for all new NDAs, BLAs, and Efficacy Supplements [except SE8 (labeling change with clinical data) and SE9 (manufacturing change with clinical data)]**

Application Information		
<b>NDA 206911</b>	NDA Supplement – N/A	<b>Efficacy Supplement Category:</b> <input type="checkbox"/> New Indication (SE1) <input type="checkbox"/> New Dosing Regimen (SE2) <input type="checkbox"/> New Route Of Administration (SE3) <input type="checkbox"/> Comparative Efficacy Claim (SE4) <input type="checkbox"/> New Patient Population (SE5) <input type="checkbox"/> Rx To OTC Switch (SE6) <input type="checkbox"/> Accelerated Approval Confirmatory Study (SE7) <input type="checkbox"/> Labeling Change With Clinical Data (SE8) <input type="checkbox"/> Manufacturing Change With Clinical Data (SE9) <input type="checkbox"/> Animal Rule Confirmatory Study (SE10)
Proposed Proprietary Name: <b>BromSite</b> Established/Proper Name: <b>bromfenac sodium sesquihydrate</b> Dosage Form: <b>ophthalmic solution</b> Strengths: <b>0.075%</b>		
Applicant: <b>InSite Vision Incorporated</b> Agent for Applicant (if applicable): <b>N/A</b>		
Date of Application: <b>June 10, 2015</b> Date of Receipt: <b>June 10, 2015</b> Date clock started after UN: <b>N/A</b>		
PDUFA Goal Date: <b>April 10, 2016</b>		Action Goal Date (if different):
Filing Date: <b>August 9, 2015</b>		Date of Filing Meeting: <b>July 27, 2015</b>
<b>Chemical Classification (original NDAs only) :</b> <input type="checkbox"/> Type 1- New Molecular Entity (NME); NME and New Combination <input type="checkbox"/> Type 2- New Active Ingredient; New Active Ingredient and New Dosage Form; New Active Ingredient and New Combination <input type="checkbox"/> Type 3- New Dosage Form; New Dosage Form and New Combination <input type="checkbox"/> Type 4- New Combination <input checked="" type="checkbox"/> <b>Type 5- New Formulation or New Manufacturer – check with reviewer at Filing Meeting</b> <input type="checkbox"/> Type 7- Drug Already Marketed without Approved NDA <input type="checkbox"/> Type 8- Partial Rx to OTC Switch		
<b>Proposed indication: treatment of postoperative inflammation and prevention of ocular pain in patients undergoing cataract surgery</b>		
Type of Original NDA: AND (if applicable) Type of NDA Supplement: <b>N/A</b>		<input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> <b>505(b)(2)</b> <hr/> <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)
<b>If 505(b)(2): Draft the “505(b)(2) Assessment” review found at:</b> <a href="http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/UCM027499">http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/UCM027499</a> .		



Type of BLA	<input type="checkbox"/> 351(a) <input type="checkbox"/> 351(k)
<b>If 351(k), notify the OND Therapeutic Biologics and Biosimilars Team</b>	
Review Classification:	<input checked="" type="checkbox"/> <b>Standard</b> <input type="checkbox"/> Priority  <input type="checkbox"/> Pediatric WR <input type="checkbox"/> QIDP <input type="checkbox"/> Tropical Disease Priority Review Voucher <input type="checkbox"/> Pediatric Rare Disease Priority Review Voucher
<i>The application will be a priority review if:</i> <ul style="list-style-type: none"> <li>• A complete response to a pediatric Written Request (WR) was included (a partial response to a WR that is sufficient to change the labeling should also be a priority review – check with DPMH)</li> <li>• The product is a Qualified Infectious Disease Product (QIDP)</li> <li>• A Tropical Disease Priority Review Voucher was submitted</li> <li>• A Pediatric Rare Disease Priority Review Voucher was submitted</li> </ul>	
Resubmission after withdrawal? <b>NO</b>	Resubmission after refuse to file? <b>NO</b>
Part 3 Combination Product? <b>NO</b>	<input type="checkbox"/> Convenience kit/Co-package <input type="checkbox"/> Pre-filled drug delivery device/system (syringe, patch, etc.) <input type="checkbox"/> Pre-filled biologic delivery device/system (syringe, patch, etc.) <input type="checkbox"/> Device coated/impregnated/combined with drug <input type="checkbox"/> Device coated/impregnated/combined with biologic <input type="checkbox"/> Separate products requiring cross-labeling <input type="checkbox"/> Drug/Biologic <input type="checkbox"/> Possible combination based on cross-labeling of separate products <input type="checkbox"/> Other (drug/device/biological product)
<i>If yes, contact the Office of Combination Products (OCP) and copy them on all Inter-Center consults</i>	

<input type="checkbox"/> Fast Track Designation <input type="checkbox"/> Breakthrough Therapy Designation <i>(set the submission property in DARRTS and notify the CDER Breakthrough Therapy Program Manager)</i> <input type="checkbox"/> Rolling Review <input type="checkbox"/> Orphan Designation  <input type="checkbox"/> Rx-to-OTC switch, Full <input type="checkbox"/> Rx-to-OTC switch, Partial <input type="checkbox"/> Direct-to-OTC  Other:	<input type="checkbox"/> PMC response <input type="checkbox"/> PMR response: <input type="checkbox"/> FDAAA [505(o)] <input type="checkbox"/> PREA deferred pediatric studies (FDCA Section 505B) <input type="checkbox"/> Accelerated approval confirmatory studies (21 CFR 314.510/21 CFR 601.41) <input type="checkbox"/> Animal rule postmarketing studies to verify clinical benefit and safety (21 CFR 314.610/21 CFR 601.42)
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Collaborative Review Division (if OTC product):				
List referenced IND Number(s): <b>No IND(s) listed on 356h; however, PIND, EOP2, and pre-NDA meetings for this product were held under IND 107723, for which InSite Vision Inc. is the sponsor</b>				
<b>Goal Dates/Product Names/Classification Properties</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
PDUFA/BsUFA and Action Goal dates correct in tracking system?	X	<input type="checkbox"/>		
<i>If no, ask the document room staff to correct them immediately. These are the dates used for calculating inspection dates.</i>				
Are the established/proper and applicant names correct in tracking system?	X	<input type="checkbox"/>		
<i>If no, ask the document room staff to make the corrections. Also,</i>				



ask the document room staff to add the established/proper name to the supporting IND(s) if not already entered into tracking system.					
Is the review priority (S or P) and all appropriate classifications/properties entered into tracking system (e.g., chemical classification, combination product classification, orphan drug)? <i>Check the New Application and New Supplement Notification Checklists for a list of all classifications/properties at:</i> <a href="http://inside.fda.gov:9003/CDER/OfficeofBusinessProcessSupport/ucm163969.htm">http://inside.fda.gov:9003/CDER/OfficeofBusinessProcessSupport/ucm163969.htm</a>  <i>If no, ask the document room staff to make the appropriate entries.</i>		X	<input type="checkbox"/>	<input type="checkbox"/>	
<b>Application Integrity Policy</b>		<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
Is the application affected by the Application Integrity Policy (AIP)? <i>Check the AIP list at:</i> <a href="http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm">http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm</a>		<input type="checkbox"/>	X		
If yes, explain in comment column.					
If affected by AIP, has OC been notified of the submission? If yes, date notified:		<input type="checkbox"/>	<input type="checkbox"/>		
<b>User Fees</b>		<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
Is Form 3397 (User Fee Cover Sheet)/Form 3792 (Biosimilar User Fee Cover Sheet) included with authorized signature?		X	<input type="checkbox"/>		
<u>User Fee Status</u>  <i>If a user fee is required and it has not been paid (and it is not exempted or waived), the application is unacceptable for filing following a 5-day grace period. Review stops. Send Unacceptable for Filing (UN) letter and contact user fee staff.</i>		Payment for this application (check daily email from <a href="mailto:UserFeeAR@fda.hhs.gov">UserFeeAR@fda.hhs.gov</a> ):  X Paid <input type="checkbox"/> Exempt (orphan, government) <input type="checkbox"/> Waived (e.g., small business, public health) <input type="checkbox"/> Not required			
<i>If the firm is in arrears for other fees (regardless of whether a user fee has been paid for this application), the application is unacceptable for filing (5-day grace period does not apply). Review stops. Send UN letter and contact the user fee staff.</i>		Payment of other user fees:  X Not in arrears <input type="checkbox"/> In arrears			
<u>User Fee Bundling Policy</u>  <i>Refer to the guidance for industry, Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees at:</i> <a href="http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079320.pdf">http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079320.pdf</a>		Has the user fee bundling policy been appropriately applied? <i>If no, or you are not sure, consult the User Fee Staff.</i>  X Yes <input type="checkbox"/> No			

505(b)(2) (NDAs/NDA Efficacy Supplements only)		YES	NO	NA	Comment																
Is the application a 505(b)(2) NDA? (Check the 356h form, cover letter, and annotated labeling). <b>If yes, answer the bulleted questions below:</b>		<input checked="" type="checkbox"/>	<input type="checkbox"/>																		
• Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA?		<input type="checkbox"/>	<input checked="" type="checkbox"/>																		
• 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 is less than that of the reference listed drug (RLD)? [see 21 CFR 314.54(b)(1)].		<input type="checkbox"/>	<input checked="" type="checkbox"/>																		
• Is the application for a duplicate of a listed drug whose only difference is that the rate at which the proposed product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the listed drug [see 21 CFR 314.54(b)(2)]?		<input type="checkbox"/>	<input checked="" type="checkbox"/>																		
<p><i>If you answered yes to any of the above bulleted questions, the application may be refused for filing under 21 CFR 314.101(d)(9). Contact the 505(b)(2) review staff in the Immediate Office of New Drugs for advice.</i></p>																					
• Is there unexpired exclusivity on another listed drug product containing the same active moiety (e.g., 5-year, 3-year, orphan, or pediatric exclusivity)? <b>Check the Electronic Orange Book at:</b> <a href="http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm">http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm</a>		<input checked="" type="checkbox"/>	<input type="checkbox"/>																		
<p><b>If yes, please list below:</b></p> <table border="1"> <thead> <tr> <th>Application No.</th> <th>Drug Name</th> <th>Exclusivity Code</th> <th>Exclusivity Expiration</th> </tr> </thead> <tbody> <tr> <td>NDA 203168</td> <td>Prolensa</td> <td>NP (New Product)</td> <td>April 5, 2006</td> </tr> <tr> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td></td> <td></td> <td></td> <td></td> </tr> </tbody> </table>						Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration	NDA 203168	Prolensa	NP (New Product)	April 5, 2006								
Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration																		
NDA 203168	Prolensa	NP (New Product)	April 5, 2006																		
<p><i>If there is unexpired, 5-year exclusivity remaining on another listed drug product containing the same active moiety, a 505(b)(2) application cannot be submitted until the period of exclusivity expires (unless the applicant provides paragraph IV patent certification; then an application can be submitted four years after the date of approval.) Pediatric exclusivity will extend both of the timeframes in this provision by 6 months. 21 CFR 314.108(b)(2). Unexpired, 3-year exclusivity may block the approval but not the submission of a 505(b)(2) application.</i></p>																					
Exclusivity		YES	NO	NA	Comment																
Does another product (same active moiety) have orphan exclusivity for the same indication? <b>Check the Orphan Drug Designations and Approvals list at:</b> <a href="http://www.accessdata.fda.gov/scripts/opdlisting/ood/index.cfm">http://www.accessdata.fda.gov/scripts/opdlisting/ood/index.cfm</a>		<input type="checkbox"/>	<input checked="" type="checkbox"/>																		
<b>If another product has orphan exclusivity, is the product considered to be the same product according to the orphan drug definition of sameness [see 21 CFR 316.3(b)(13)]?</b>  <i>If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy</i>		<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>																	
<b>NDAs/NDA efficacy supplements only:</b> Has the applicant requested 5-year or 3-year Waxman-Hatch exclusivity?		<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																	

<b>If yes, # years requested: 3 years</b>				
<i>Note: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.</i>				
<b>NDAs only:</b> Is the proposed product a single enantiomer of a racemic drug previously approved for a different therapeutic use?	<input type="checkbox"/>	<b>X</b>	<input type="checkbox"/>	
<b>If yes, did the applicant:</b> (a) elect to have the single enantiomer (contained as an active ingredient) not be considered the same active ingredient as that contained in an already approved racemic drug, and/or (b): request exclusivity pursuant to section 505(u) of the Act (per FDAAA Section 1113)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<i>If yes, contact the Orange Book Staff (CDER-Orange Book Staff).</i>				
<b>BLAs only:</b> Has the applicant requested 12-year exclusivity under section 351(k)(7) of the PHS Act?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<i>If yes, notify Marlene Schultz-DePalo, CDER Purple Book Manager</i>				
<i>Note: Exclusivity requests may be made for an original BLA submitted under Section 351(a) of the PHS Act (i.e., a biological reference product). A request may be located in Module 1.3.5.3 and/or other sections of the BLA and may be included in a supplement (or other correspondence) if exclusivity has not been previously requested in the original 351(a) BLA. An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.</i>				

Format and Content				
<i>Do not check mixed submission if the only electronic component is the content of labeling (COL).</i>	<input type="checkbox"/> All paper (except for COL) <b>X All electronic</b> <input type="checkbox"/> Mixed (paper/electronic)			
	<input type="checkbox"/> CTD <input type="checkbox"/> Non-CTD <input type="checkbox"/> Mixed (CTD/non-CTD)			
<b>If mixed (paper/electronic) submission, which parts of the application are submitted in electronic format?</b>				
<b>Overall Format/Content</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
<b>If electronic submission, does it follow the eCTD guidance?<sup>1</sup></b> <b>If not, explain (e.g., waiver granted).</b>	<b>X</b>	<input type="checkbox"/>	<input type="checkbox"/>	
<b>Index:</b> Does the submission contain an accurate comprehensive index?	<b>X</b>	<input type="checkbox"/>		
Is the submission complete as required under 21 CFR 314.50	<b>X</b>	<input type="checkbox"/>		

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<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072349.pdf>

<p>(NDAs/NDA efficacy supplements) or under 21 CFR 601.2 (BLAs/BLA efficacy supplements) including:</p> <p><input type="checkbox"/> legible</p> <p><input type="checkbox"/> English (or translated into English)</p> <p><input type="checkbox"/> pagination</p> <p><input type="checkbox"/> navigable hyperlinks (electronic submissions only)</p> <p><b>If no, explain.</b></p>				
<p><b>BLAs only:</b> Companion application received if a shared or divided manufacturing arrangement?</p> <p><b>If yes, BLA #</b></p>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<b>Forms and Certifications</b>				
<p><i>Electronic forms and certifications with electronic signatures (scanned, digital, or electronic – similar to DARRTS, e.g., /s/) are acceptable. Otherwise, <b>paper</b> forms and certifications with hand-written signatures must be included. <b>Forms</b> include: user fee cover sheet (3397/3792), application form (356h), patent information (3542a), financial disclosure (3454/3455), and clinical trials (3674); <b>Certifications</b> include: debarment certification, patent certification(s), field copy certification, and pediatric certification.</i></p>				
<b>Application Form</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
Is form FDA 356h included with authorized signature per 21 CFR 314.50(a)?	X	<input type="checkbox"/>		
<i>If foreign applicant, a U.S. agent must sign the form [see 21 CFR 314.50(a)(5)].</i>				
Are all establishments and their registration numbers listed on the form/attached to the form?	X	<input type="checkbox"/>	<input type="checkbox"/>	
<p><b>NOTE: The establishments and their registration numbers were listed on the 356h. However, the applicant did not provide site-specific data listings. Mr. Roy Blay in the Office of Scientific Investigations contacted the applicant on July 10, 2015, and requested this information be submitted to the NDA. This information was submitted on</b></p>				
<b>Patent Information</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
<b>(NDAs/NDA efficacy supplements only)</b>				
Is patent information submitted on form FDA 3542a per 21 CFR 314.53(c)?	X	<input type="checkbox"/>	<input type="checkbox"/>	
<b>Financial Disclosure</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
Are financial disclosure forms FDA 3454 and/or 3455 included with authorized signature per 21 CFR 54.4(a)(1) and (3)?	X	<input type="checkbox"/>		
<i>Forms must be signed by the APPLICANT, not an Agent [see 21</i>				

<b>CFR 54.2(g)].</b>				
<i>Note: Financial disclosure is required for bioequivalence studies that are the basis for approval.</i>				
<b>Clinical Trials Database</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
Is form FDA 3674 included with authorized signature?	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
<i>If yes, ensure that the application is also coded with the supporting document category, "Form 3674."</i>				
<i>If no, ensure that language requesting submission of the form is included in the acknowledgement letter sent to the applicant</i>				
<b>Debarment Certification</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
Is a correctly worded Debarment Certification included with authorized signature?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<i>Certification is not required for supplements if submitted in the original application; If foreign applicant, <u>both</u> the applicant and the U.S. Agent must sign the certification [per Guidance for Industry: Submitting Debarment Certifications].</i>				
<i>Note: Debarment Certification should use wording in FD&amp;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..."</i>				
<b>Field Copy Certification (NDAs/NDA efficacy supplements only)</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
<b>For paper submissions only:</b> Is a Field Copy Certification (that it is a true copy of the CMC technical section) included?	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<b>Electronic Only Submission</b>
<i>Field Copy Certification is not needed if there is no CMC technical section or if this is an electronic submission (the Field Office has access to the EDR)</i>				
<i>If maroon field copy jackets from foreign applicants are received, return them to CDR for delivery to the appropriate field office.</i>				
<b>Controlled Substance/Product with Abuse Potential</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
<u>For NMEs:</u> Is an Abuse Liability Assessment, including a proposal for scheduling, submitted per 21 CFR 314.50(d)(5)(vii)?	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
<i>If yes, date consult sent to the Controlled Substance Staff:</i>				
<u>For non-NMEs:</u> Date of consult sent to Controlled Substance Staff:				
<b>Pediatrics</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>



<b><u>PREA</u></b>				
Does the application trigger PREA?  <i>If yes, notify <a href="mailto:PeRC@fda.hhs.gov">PeRC@fda.hhs.gov</a> to schedule required PeRC meeting<sup>2</sup></i>  <i>Note: NDAs/BLAs/efficacy supplements for new active ingredients (including new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration trigger PREA. All waiver &amp; deferral requests, pediatric plans, and pediatric assessment studies must be reviewed by PeRC prior to approval of the application/supplement.</i>	<input type="checkbox"/>	<b>X</b>		
<b>If the application triggers PREA</b> , is there an agreed Initial Pediatric Study Plan (iPSP)?  <i>If no, may be an RTF issue - contact DPMH for advice.</i>	<input type="checkbox"/>	<input type="checkbox"/>	<b>X</b>	
<b>If required by the agreed iPSP</b> , are the pediatric studies outlined in the agreed iPSP completed and included in the application?  <i>If no, may be an RTF issue - contact DPMH for advice.</i>	<input type="checkbox"/>	<input type="checkbox"/>	<b>X</b>	
<b><u>BPCA:</u></b>  Is this submission a complete response to a pediatric Written Request?  <i>If yes, notify Pediatric Exclusivity Board RPM (pediatric exclusivity determination is required)<sup>3</sup></i>	<input type="checkbox"/>	<b>X</b>		
<b>Proprietary Name</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
Is a proposed proprietary name submitted?  <i>If yes, ensure that the application is also coded with the supporting document category, "Proprietary Name/Request for Review."</i>	<b>X</b>	<input type="checkbox"/>	<input type="checkbox"/>	Proprietary name submission received July 20, 2015
<b>REMS</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
Is a REMS submitted?  <i>If yes, send consult to OSE/DRISK and notify OC/OSI/DSC/PMSB via the CDER OSI RMP mailbox</i>	<input type="checkbox"/>	<b>X</b>	<input type="checkbox"/>	
<b>Prescription Labeling</b>	<input type="checkbox"/> Not applicable			
Check all types of labeling submitted.	<input checked="" type="checkbox"/> <b>Package Insert (PI)</b> <input type="checkbox"/> Patient Package Insert (PPI) <input type="checkbox"/> Instructions for Use (IFU) <input type="checkbox"/> Medication Guide (MedGuide) <input checked="" type="checkbox"/> <b>Carton labels</b> <input checked="" type="checkbox"/> <b>Immediate container labels</b>			

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<http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/PediatricandMaternalHealthStaff/ucm027829.htm>

3

<http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/PediatricandMaternalHealthStaff/ucm027837.htm>

	<input type="checkbox"/> Diluent <input checked="" type="checkbox"/> Other (specify) – Foil (b) (4)			
	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
Is Electronic Content of Labeling (COL) submitted in SPL format?	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
<i>If no, request applicant to submit SPL before the filing date.</i>				
Is the PI submitted in PLR format? <sup>4</sup>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
<b>If PI not submitted in PLR format</b> , was a waiver or deferral requested before the application was received or in the submission? <b>If requested before application was submitted</b> , what is the status of the request?	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
<i>If no waiver or deferral, request applicant to submit labeling in PLR format before the filing date.</i>				
<b>For applications submitted on or after June 30, 2015:</b> Is the PI submitted in PLLR format? <sup>5</sup>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Submitted June 10, 2015
<b>For applications submitted on or after June 30, 2015: If PI not submitted in PLLR format</b> , was a waiver or deferral requested before the application was received or in the submission? <b>If requested before application was submitted</b> , what is the status of the request?	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
<i>If no waiver or deferral, request applicant to submit labeling in PLR/PLLR format before the filing date.</i>				
All labeling (PI, PPI, MedGuide, IFU, carton and immediate container labels) consulted to OPDP?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Consult Request dated August 5, 2015
MedGuide, PPI, IFU (plus PI) consulted to OSE/DRISK? (send WORD version if available)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Carton and immediate container labels, PI, PPI sent to OSE/DMEPA and appropriate CMC review office in OPQ (OBP or ONDP)?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<b>OTC Labeling</b>	<b>X Not Applicable</b>			
Check all types of labeling submitted.	<input type="checkbox"/> Outer carton label <input type="checkbox"/> Immediate container label <input type="checkbox"/> Blister card <input type="checkbox"/> Blister backing label <input type="checkbox"/> Consumer Information Leaflet (CIL) <input type="checkbox"/> Physician sample <input type="checkbox"/> Consumer sample			

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<http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/StudyEndpointsandLabelingDevelopmentTeam/ucm025576.htm>

5

<http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/StudyEndpointsandLabelingDevelopmentTeam/ucm025576.htm>

	<input type="checkbox"/> Other (specify)			
	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
Is electronic content of labeling (COL) submitted?	<input type="checkbox"/>	<input type="checkbox"/>		
<i>If no, request in 74-day letter.</i>				
Are annotated specifications submitted for all stock keeping units (SKUs)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<i>If no, request in 74-day letter.</i>				
If representative labeling is submitted, are all represented SKUs defined?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<i>If no, request in 74-day letter.</i>				
All labeling/packaging sent to OSE/DMEPA?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<b>Other Consults</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
Are additional consults needed? (e.g., IFU to CDRH; QT study report to QT Interdisciplinary Review Team)	<input type="checkbox"/>	<b>X</b>	<input type="checkbox"/>	<b>At date of Filing Meeting, no known need for other consults</b>
<i>If yes, specify consult(s) and date(s) sent:</i>				
<b>Meeting Minutes/SPAs</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
End-of Phase 2 meeting(s)? <b>Date: February 17, 2012</b>	<b>X</b>	<input type="checkbox"/>		
<i>If yes, distribute minutes before filing meeting</i>				
Pre-NDA/Pre-BLA/Pre-Supplement meeting(s)? <b>Dates: January 13, 2014</b> <b>April 22, 2014 CMC</b>	<b>X</b>	<input type="checkbox"/>		
<i>If yes, distribute minutes before filing meeting</i>				
Any Special Protocol Assessments (SPAs)? <b>Date(s):</b>	<input type="checkbox"/>	<b>X</b>		
<i>If yes, distribute letter and/or relevant minutes before filing meeting</i>				



ATTACHMENT

**MEMO OF FILING MEETING**

**DATE:** July 27, 2015

**BACKGROUND:** NDA was submitted on June 10, 2015, for treatment of postoperative inflammation and prevention of ocular pain in patients undergoing cataract surgery.

**REVIEW TEAM:**

<b>Discipline/Organization</b>	<b>Names</b>		<b>Present at filing meeting? (Y or N)</b>
Regulatory Project Management	RPM:	<b>Diana Willard</b>	<b>Y</b>
	CPMS/TL:	<b>Diana Willard</b>	<b>Y</b>
Cross-Discipline Team Leader (CDTL)	<b>William Boyd, M.D.</b>		<b>Y</b>
Division Director/Deputy	<b>Director: Renata Albrecht, M.D.</b> <b>Deputy: Wiley A. Chambers, M.D.</b>		<b>Y</b> <b>Y</b>
Office Director/Deputy	<b>N/A</b>		
Clinical	Reviewer:	<b>Sonal Wadhwa, M.D.</b>	<b>N</b>
	TL:	<b>William Boyd, M.D.</b>	<b>Y</b>
Clinical Pharmacology	Reviewer:	<b>Yongheng Zhang, Ph.D.</b>	<b>Y</b>
	TL:	<b>Philip Colangelo, Pharm.D., Ph.D.</b>	<b>Y</b>
Biostatistics	Reviewer:	<b>Yunfan Deng, Ph.D.</b>	<b>Y</b>
	TL:	<b>Yan Wang, Ph.D.</b>	<b>Y</b>

Nonclinical (Pharmacology/Toxicology)	Reviewer:	<b>Aaron Ruhland, Ph.D.</b>	<b>Y</b>
	TL:	<b>Lori Kotch, Ph.D.</b>	<b>Y</b>
Product Quality (CMC) Review Team:	Branch Chief:	<b>Bala Shanmugam, Ph.D.</b>	<b>N</b>
	ATL:	<b>Jean Tang, Ph.D.</b>	<b>N</b>
	ATL:	<b>Anamitro Banerjee, Ph.D.</b>	<b>Y</b>
	RBPM:	<b>Navi Bhandari, Pharm.D.</b>	<b>N</b>
• Drug Substance	Team Leader: Reviewer:	<b>Kasturi Srinivasachar, Ph.D.</b> <b>Katherine Windsor, Ph.D.</b>	<b>N</b>
• Drug Product	Team Leader: Reviewer:	<b>Shrikant Pagay, Ph.D.</b>	<b>N</b>
• Process	Team Leader: Reviewer:	<b>Upinder Atwal, Ph.D.</b> <b>Dave Anderson, Ph.D.</b>	<b>N</b>
• Microbiology	Team Leader: Reviewer:	<b>Vera Viehmann, Ph.D.</b> <b>Jonathan Swoboda, Ph.D.</b>	<b>N</b> <b>N</b>
• Facility	Team Leader: Reviewer:	<b>Mahesh Ramanadham, Ph.D.</b> <b>Frank Wackes, Ph.D.</b>	<b>N</b> <b>N</b>
• Biopharmaceutics	Team Leader: Reviewer:	<b>Om Anand, Ph.D.</b>	<b>N</b>
• Immunogenicity	Reviewer:		
• Other (e.g., Branch Chiefs, EA Reviewer)			
OMP/OMPI/DMPP (Patient labeling: MG, PPI, IFU)	Reviewer:		
	TL:		
OMP/OPDP (PI, PPI, MedGuide, IFU, carton and immediate container labels)	Reviewer:		
	TL:		
OSE/DMEPA (proprietary name, carton/container labels)	Reviewer:	<b>Michelle Rutledge, Ph.D.</b>	<b>N</b>
	TL:	<b>Yelena Maslov, Ph.D.</b>	<b>Y</b>
OSE/DRISK (REMS)	Reviewer:		
	TL:		
OC/OSI/DSC/PMSB (REMS)	Reviewer:		
	TL:		

**FILING MEETING DISCUSSION:**

<p><b>GENERAL</b></p> <ul style="list-style-type: none"><li>• 505(b)(2) filing issues:<ul style="list-style-type: none"><li>○ Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA?</li><li>○ Did the applicant provide a scientific “bridge” demonstrating the relationship between the proposed product and the referenced product(s)/published literature?</li></ul></li></ul> <p>Describe the scientific bridge (e.g., BA/BE studies):</p>	<p><input type="checkbox"/> Not Applicable</p> <p><input type="checkbox"/> YES   <input checked="" type="checkbox"/> NO</p> <p><input checked="" type="checkbox"/> YES   <input type="checkbox"/> NO</p> <p><b>InSite Vision conducted a nonclinical bridging study in rabbits that the applicant states demonstrated that the plasma levels of bromfenac following topical ocular administration of ISV-303 were comparable to those obtained with the listed drug Bromday.</b></p>
<ul style="list-style-type: none"><li>• Per reviewers, are all parts in English or English translation?</li></ul> <p><b>If no, explain:</b></p>	<p><input checked="" type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>
<ul style="list-style-type: none"><li>• Electronic Submission comments</li></ul> <p><b>List comments:</b></p>	<p><input type="checkbox"/> Not Applicable</p> <p><input checked="" type="checkbox"/> No comments</p>

<p><b>CLINICAL</b></p> <p><b>Comments:</b></p>	<p><input type="checkbox"/> Not Applicable  <input checked="" type="checkbox"/> <b>FILE</b>  <input type="checkbox"/> REFUSE TO FILE</p> <p><b>Review issues for 74-day letter - NONE</b></p>
<ul style="list-style-type: none"> <li>Clinical study site(s) inspections(s) needed?</li> </ul> <p><b>If no, explain:</b></p>	<p><input checked="" type="checkbox"/> <b>YES</b>  <input type="checkbox"/> NO</p>
<ul style="list-style-type: none"> <li>Advisory Committee Meeting needed?</li> </ul> <p><b>Comments:</b></p> <p><i>If no, for an NME NDA or original BLA, include the reason. For example:</i></p> <ul style="list-style-type: none"> <li><i>this drug/biologic is not the first in its class</i></li> <li><i>the clinical study design was acceptable</i></li> <li><i>the application did not raise significant safety or efficacy issues</i></li> <li><i>the application did not raise significant public health questions on the role of the drug/biologic in the diagnosis, cure, mitigation, treatment or prevention of a disease</i></li> </ul>	<p><input type="checkbox"/> YES  Date if known: <input type="text"/>  <input checked="" type="checkbox"/> <b>NO (at date of Filing Meeting)</b>  <input type="checkbox"/> To be determined</p> <p>Reason:</p>
<ul style="list-style-type: none"> <li>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?</li> </ul> <p><b>Comments:</b></p>	<p><input checked="" type="checkbox"/> <b>Not Applicable</b>  <input type="checkbox"/> YES  <input type="checkbox"/> NO</p>
<p><b>CONTROLLED SUBSTANCE STAFF</b></p> <ul style="list-style-type: none"> <li>Abuse Liability/Potential</li> </ul> <p><b>Comments:</b></p>	<p><input checked="" type="checkbox"/> <b>Not Applicable</b>  <input type="checkbox"/> FILE  <input type="checkbox"/> REFUSE TO FILE</p> <p><input type="checkbox"/> Review issues for 74-day letter</p>
<p><b>CLINICAL MICROBIOLOGY</b></p> <p><b>Comments:</b></p>	<p><input checked="" type="checkbox"/> <b>Not Applicable</b>  <input type="checkbox"/> FILE  <input type="checkbox"/> REFUSE TO FILE</p> <p><input type="checkbox"/> Review issues for 74-day letter</p>

<b>CLINICAL PHARMACOLOGY</b>  <b>Comments:</b>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> <b>FILE</b> <input type="checkbox"/> REFUSE TO FILE  <b>Review issues for 74-day letter - NONE</b>
<ul style="list-style-type: none"> <li>Clinical pharmacology study site(s) inspections(s) needed?</li> </ul>	<input type="checkbox"/> YES <input checked="" type="checkbox"/> <b>NO</b>
<b>BIOSTATISTICS</b>  <b>Comments:</b>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> <b>FILE</b> <input type="checkbox"/> REFUSE TO FILE  <b>Review issues for 74-day letter - NONE</b>
<b>NONCLINICAL (PHARMACOLOGY/TOXICOLOGY)</b>  <b>Comments:</b>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> <b>FILE</b> <input type="checkbox"/> REFUSE TO FILE  <b>Review issues for 74-day letter - NONE</b>
<b>PRODUCT QUALITY (CMC)</b>  <b>Comments:</b>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> <b>FILE</b> <input type="checkbox"/> REFUSE TO FILE  <b>Review issues for 74-day letter - NONE</b>
<u><b>New Molecular Entity (NDAs only)</b></u>  <ul style="list-style-type: none"> <li>Is the product an NME?</li> </ul>	<input type="checkbox"/> YES <input checked="" type="checkbox"/> <b>NO</b>
<u><b>Environmental Assessment</b></u>  <ul style="list-style-type: none"> <li>Categorical exclusion for environmental assessment (EA) requested?</li> </ul> <p><b>If no</b>, was a complete EA submitted?</p> <b>Comments:</b>	<input checked="" type="checkbox"/> <b>YES</b> <input type="checkbox"/> NO  <input type="checkbox"/> YES <input type="checkbox"/> NO

<p><b><u>Facility Inspection</u></b></p> <ul style="list-style-type: none"> <li>Establishment(s) ready for inspection?</li> </ul> <p><b>Comments:</b></p>	<p><input type="checkbox"/> Not Applicable</p> <p><input checked="" type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>
<p><b><u>Facility/Microbiology Review (BLAs only)</u></b></p> <p><b>Comments:</b></p>	<p><input type="checkbox"/> Not Applicable</p> <p><input type="checkbox"/> FILE</p> <p><input type="checkbox"/> REFUSE TO FILE</p> <p><input type="checkbox"/> Review issues for 74-day letter</p>
<p><b><u>CMC Labeling Review (BLAs only)</u></b></p> <p><b>Comments:</b></p>	<p><input type="checkbox"/> Review issues for 74-day letter</p>
<p><b>APPLICATIONS IN THE PROGRAM (PDUFA V) (NME NDAs/Original BLAs)</b></p> <ul style="list-style-type: none"> <li>Were there agreements made at the application's pre-submission meeting (and documented in the minutes) regarding certain late submission components that could be submitted within 30 days after receipt of the original application?</li> <li>If so, were the late submission components all submitted within 30 days?</li> </ul>	<p><input type="checkbox"/> N/A</p> <p><input type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p> <p><input type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>
<ul style="list-style-type: none"> <li>What late submission components, if any, arrived after 30 days?</li> </ul>	
<ul style="list-style-type: none"> <li>Was the application otherwise complete upon submission, including those applications where there were no agreements regarding late submission components?</li> </ul>	<p><input type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>
<ul style="list-style-type: none"> <li>Is a comprehensive and readily located list of all clinical sites included or referenced in the application?</li> </ul>	<p><input type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>

<ul style="list-style-type: none"><li>• Is a comprehensive and readily located list of all manufacturing facilities included or referenced in the application?</li></ul>	<input type="checkbox"/> YES <input type="checkbox"/> NO
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REGULATORY PROJECT MANAGEMENT	
<b>Signatory Authority:</b> Renata Albrecht, M.D.  <b>Date of Mid-Cycle Meeting:</b> At date of Filing Meeting, scheduled for November 17, 2015  <b>Comments:</b>	
REGULATORY CONCLUSIONS/DEFICIENCIES	
<input type="checkbox"/>	The application is unsuitable for filing. Explain why:
<input checked="" type="checkbox"/>	The application, on its face, appears to be suitable for filing.  <u>Review Issues:</u>  <input checked="" type="checkbox"/> <b>No review issues have been identified for the 74-day letter.</b> <input type="checkbox"/> Review issues have been identified for the 74-day letter.  <u>Review Classification:</u> <input checked="" type="checkbox"/> <b>Standard Review</b> <input type="checkbox"/> Priority Review
ACTION ITEMS - <u>NONE</u>	
<input type="checkbox"/>	Ensure that any updates to the review priority (S or P) and classifications/properties are entered into the electronic archive (e.g., chemical classification, combination product classification, orphan drug).
<input type="checkbox"/>	If RTF, notify everyone who already received a consult request, OSE PM, and RBPM
<input type="checkbox"/>	If filed, and the application is under AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
<input type="checkbox"/>	If priority review, notify applicant in writing by day 60 (see CST for choices)
<input type="checkbox"/>	Send review issues/no review issues by day 74
<input type="checkbox"/>	Conduct a PLR format labeling review and include labeling issues in the 74-day letter
<input type="checkbox"/>	Update the PDUFA V DARRTS page (for applications in the Program)
<input type="checkbox"/>	Other

Annual review of template by OND ADRAAs completed: September 2014



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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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DIANA M WILLARD  
08/18/2015

**REGULATORY PROJECT MANAGER  
PHYSICIAN'S LABELING RULE (PLR) FORMAT REVIEW  
OF THE PRESCRIBING INFORMATION**

**Application:** NDA 206911

**Application Type:** New NDA

**Name of Drug/Dosage Form:** BromSite (bromfenac ophthalmic solution) 0.075%

**Applicant:** InSite Vision Incorporated

**Receipt Date:** June 10, 2015

**Goal Date:** April 10, 2016

### **1. Regulatory History and Applicant's Main Proposals**

This NDA was dated and received June 10, 2015. The proposed indication is for the treatment of postoperative inflammation and prevention of ocular pain in patients undergoing cataract surgery.

### **2. Review of the Prescribing Information**

This review is based on the applicant's June 10, 2015, submitted Word format of the prescribing information (PI). The applicant's proposed PI was reviewed in accordance with the labeling format requirements listed in the "Selected Requirements for Prescribing Information (SRPI)" checklist (see the Appendix).

### **3. Conclusions/Recommendations**

SRPI format deficiencies were identified in the review of this PI. For identified deficiencies see below.

All SRPI format deficiencies of the PI will be conveyed to the applicant in an advice letter.

# Selected Requirements of Prescribing Information

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## Appendix

The Selected Requirement of Prescribing Information (SRPI) is a 42-item, drop-down checklist of important format elements of the prescribing information (PI) based on labeling regulations (21 CFR 201.56 and 201.57) and guidances.

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## Highlights

See Appendix A for a sample tool illustrating the format for the Highlights.

### HIGHLIGHTS GENERAL FORMAT

- NO** 1. Highlights (HL) must be in a minimum of 8-point font and should be in two-column format, with ½ inch margins on all sides and between columns.  
***Comment:** There appears to be less than 1/2 inch between columns.*
- YES** 2. The length of HL must be one-half page or less unless a waiver has been granted in a previous submission. The HL Boxed Warning does not count against the one-half page requirement.  
Instructions to complete this item: If the length of the HL is one-half page or less, select “YES” in the drop-down menu because this item meets the requirement. However, if HL is longer than one-half page, select “NO” unless a waiver has been granted.  
***Comment:***
- YES** 3. A horizontal line must separate HL from the Table of Contents (TOC). A horizontal line must separate the TOC from the FPI.  
***Comment:***
- YES** 4. All headings in HL must be **bolded** and presented in the center of a horizontal line (each horizontal line should extend over the entire width of the column as shown in Appendix A). The headings should be in UPPER CASE letters.  
***Comment:***
- NO** 5. White space should be present before each major heading in HL. There must be no white space between the HL Heading and HL Limitation Statement. There must be no white space between the product title and Initial U.S. Approval. See Appendix A for a sample tool illustrating white space in HL.  
***Comment:** There is white space present between the product title and Initial U.S. Approval. There is a dotted line above the "HIGHLIGHTS OF PRESCRIBING INFORMATION" wording that should not be there. It appears that there is "extra" white space between "WARNINGS AND PRECAUTIONS" and "ADVERSE REACTIONS."*
- YES** 6. Each summarized statement or topic in HL must reference the section(s) or subsection(s) of the

## Selected Requirements of Prescribing Information

Full Prescribing Information (FPI) that contain more detailed information. The preferred format is the numerical identifier in parenthesis [e.g., (1.1)] at the end of each summarized statement or topic.

**Comment:**

- YES** 7. Section headings must be presented in the following order in HL:

Section	Required/Optional
• Highlights Heading	Required
• Highlights Limitation Statement	Required
• Product Title	Required
• Initial U.S. Approval	Required
• Boxed Warning	Required if a BOXED WARNING is in the FPI
• Recent Major Changes	Required for only certain changes to PI*
• Indications and Usage	Required
• Dosage and Administration	Required
• Dosage Forms and Strengths	Required
• Contraindications	Required (if no contraindications must state "None.")
• Warnings and Precautions	Not required by regulation, but should be present
• Adverse Reactions	Required
• Drug Interactions	Optional
• Use in Specific Populations	Optional
• Patient Counseling Information Statement	Required
• Revision Date	Required

\* RMC only applies to the BOXED WARNING, INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, and WARNINGS AND PRECAUTIONS sections.

**Comment:**

### HIGHLIGHTS DETAILS

#### Highlights Heading

- YES** 8. At the beginning of HL, the following heading must be **bolded** and should appear in all UPPER CASE letters: "**HIGHLIGHTS OF PRESCRIBING INFORMATION**".

**Comment:**

#### Highlights Limitation Statement

- NO** 9. The **bolded** HL Limitation Statement must include the following verbatim statement: "**These highlights do not include all the information needed to use (insert name of drug product) safely and effectively. See full prescribing information for (insert name of drug product).**" The name of drug product should appear in UPPER CASE letters.

**Comment:** Both the proposed trade name and established name are included: only the proposed trade name should be listed.

#### Product Title in Highlights

## Selected Requirements of Prescribing Information

- YES** 10. Product title must be **bolded**.

**Comment:**

### Initial U.S. Approval in Highlights

- YES** 11. Initial U.S. Approval in HL must be **bolded**, and include the verbatim statement “**Initial U.S. Approval:**” followed by the **4-digit year**.

**Comment:**

### Boxed Warning (BW) in Highlights

- N/A** 12. All text in the BW must be **bolded**.

**Comment:**

- N/A** 13. The BW must have a heading in UPPER CASE, containing the word “**WARNING**” (even if more than one warning, the term, “**WARNING**” and not “**WARNINGS**” should be used) and other words to identify the subject of the warning (e.g., “**WARNING: SERIOUS INFECTIONS and ACUTE HEPATIC FAILURE**”). The BW heading should be centered.

**Comment:**

- N/A** 14. The BW must always have the verbatim statement “*See full prescribing information for complete boxed warning.*” This statement should be centered immediately beneath the heading and appear in *italics*.

**Comment:**

- N/A** 15. The BW must be limited in length to 20 lines (this includes white space but does not include the BW heading and the statement “*See full prescribing information for complete boxed warning.*”).

**Comment:**

### Recent Major Changes (RMC) in Highlights

- N/A** 16. RMC pertains to only the following five sections of the FPI: BOXED WARNING, INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, and WARNINGS AND PRECAUTIONS. RMC must be listed in the same order in HL as the modified text appears in FPI.

**Comment:**

- N/A** 17. The RMC must include the section heading(s) and, if appropriate, subsection heading(s) affected by the recent major change, together with each section’s identifying number and date (month/year format) on which the change was incorporated in the PI (supplement approval date). For example, “Warnings and Precautions, Acute Liver Failure (5.1) --- 9/2013”.

## Selected Requirements of Prescribing Information

### Comment:

- N/A** 18. The RMC must list changes for at least one year after the supplement is approved and must be removed at the first printing subsequent to one year (e.g., no listing should be one year older than revision date).

### Comment:

### Indications and Usage in Highlights

- YES** 19. If a product belongs to an established pharmacologic class, the following statement is required under the Indications and Usage heading in HL: “(Product) is a (name of established pharmacologic class) indicated for (indication)”.

### Comment:

### Dosage Forms and Strengths in Highlights

- N/A** 20. For a product that has several dosage forms (e.g., capsules, tablets, and injection), bulleted subheadings or tabular presentations of information should be used under the Dosage Forms and Strengths heading.

### Comment:

### Contraindications in Highlights

- YES** 21. All contraindications listed in the FPI must also be listed in HL or must include the statement “None” if no contraindications are known. Each contraindication should be bulleted when there is more than one contraindication.

### Comment:

### Adverse Reactions in Highlights

- YES** 22. For drug products other than vaccines, the verbatim **bolded** statement must be present: “**To report SUSPECTED ADVERSE REACTIONS, contact (insert name of manufacturer) at (insert manufacturer’s U.S. phone number) or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch)**”.

### Comment:

### Patient Counseling Information Statement in Highlights

- YES** 23. The Patient Counseling Information statement must include one of the following three **bolded** verbatim statements that is most applicable:

If a product **does not** have FDA-approved patient labeling:

## Selected Requirements of Prescribing Information

- “See 17 for PATIENT COUNSELING INFORMATION”

If a product **has** FDA-approved patient labeling:

- “See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling”
- “See 17 for PATIENT COUNSELING INFORMATION and Medication Guide”

*Comment:*

### Revision Date in Highlights

- YES** 24. The revision date must be at the end of HL, and should be **bolded** and right justified (e.g., “**Revised: 9/2013**”).

*Comment:*

## Selected Requirements of Prescribing Information

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### Contents: Table of Contents (TOC)

See Appendix A for a sample tool illustrating the format for the Table of Contents.

- YES** 25. The TOC should be in a two-column format.  
*Comment:*
- YES** 26. The following heading must appear at the beginning of the TOC: **“FULL PRESCRIBING INFORMATION: CONTENTS”**. This heading should be in all UPPER CASE letters and **bolded**.  
*Comment:*
- N/A** 27. The same heading for the BW that appears in HL and the FPI must also appear at the beginning of the TOC in UPPER CASE letters and **bolded**.  
*Comment:*
- YES** 28. In the TOC, all section headings must be **bolded** and should be in UPPER CASE.  
*Comment:*
- YES** 29. In the TOC, all subsection headings must be indented and not bolded. The headings should be in title case [first letter of all words are capitalized except first letter of prepositions (through), articles (a, an, and the), or conjunctions (for, and)].  
*Comment:*
- YES** 30. The section and subsection headings in the TOC must match the section and subsection headings in the FPI.  
*Comment:*
- YES** 31. In the TOC, when a section or subsection is omitted, the numbering must not change. If a section or subsection from 201.56(d)(1) is omitted from the FPI and TOC, the heading “FULL PRESCRIBING INFORMATION: CONTENTS” must be followed by an asterisk and the following statement must appear at the end of TOC: “\*Sections or subsections omitted from the full prescribing information are not listed.”  
*Comment:* .



## Selected Requirements of Prescribing Information

### Full Prescribing Information (FPI)

#### FULL PRESCRIBING INFORMATION: GENERAL FORMAT

- YES** 32. The **bolded** section and subsection headings in the FPI must be named and numbered in accordance with 21 CFR 201.56(d)(1) as noted below (section and subsection headings should be in UPPER CASE and title case, respectively). If a section/subsection required by regulation is omitted, the numbering must not change. Additional subsection headings (i.e., those not named by regulation) must also be **bolded** and numbered.

<b>BOXED WARNING</b>
<b>1 INDICATIONS AND USAGE</b>
<b>2 DOSAGE AND ADMINISTRATION</b>
<b>3 DOSAGE FORMS AND STRENGTHS</b>
<b>4 CONTRAINDICATIONS</b>
<b>5 WARNINGS AND PRECAUTIONS</b>
<b>6 ADVERSE REACTIONS</b>
<b>7 DRUG INTERACTIONS</b>
<b>8 USE IN SPECIFIC POPULATIONS</b>
8.1 Pregnancy
8.2 Labor and Delivery
8.3 Nursing Mothers
8.4 Pediatric Use
8.5 Geriatric Use
<b>9 DRUG ABUSE AND DEPENDENCE</b>
9.1 Controlled Substance
9.2 Abuse
9.3 Dependence
<b>10 OVERDOSAGE</b>
<b>11 DESCRIPTION</b>
<b>12 CLINICAL PHARMACOLOGY</b>
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
12.4 Microbiology (by guidance)
12.5 Pharmacogenomics (by guidance)
<b>13 NONCLINICAL TOXICOLOGY</b>
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
13.2 Animal Toxicology and/or Pharmacology
<b>14 CLINICAL STUDIES</b>
<b>15 REFERENCES</b>
<b>16 HOW SUPPLIED/STORAGE AND HANDLING</b>
<b>17 PATIENT COUNSELING INFORMATION</b>

**Comment:**

- N/A** 33. The preferred presentation for cross-references in the FPI is the section (not subsection) heading followed by the numerical identifier. The entire cross-reference should be in *italics* and enclosed within brackets. For example, “[see *Warnings and Precautions (5.2)*]” or “[see *Warnings and Precautions (5.2)*]”.

## Selected Requirements of Prescribing Information

### Comment:

- N/A** 34. If RMCs are listed in HL, the corresponding new or modified text in the FPI sections or subsections must be marked with a vertical line on the left edge.

### Comment:

## FULL PRESCRIBING INFORMATION DETAILS

### FPI Heading

- YES** 35. The following heading must be **bolded** and appear at the beginning of the FPI: “**FULL PRESCRIBING INFORMATION**”. This heading should be in UPPER CASE.

### Comment:

### BOXED WARNING Section in the FPI

- N/A** 36. In the BW, all text should be **bolded**.

### Comment:

- N/A** 37. The BW must have a heading in UPPER CASE, containing the word “**WARNING**” (even if more than one Warning, the term, “**WARNING**” and not “**WARNINGS**” should be used) and other words to identify the subject of the Warning (e.g., “**WARNING: SERIOUS INFECTIONS and ACUTE HEPATIC FAILURE**”).

### Comment:

### CONTRAINDICATIONS Section in the FPI

- YES** 38. If no Contraindications are known, this section must state “None.”

### Comment:

### ADVERSE REACTIONS Section in the FPI

- N/A** 39. When clinical trials adverse reactions data are included (typically in the “Clinical Trials Experience” subsection of ADVERSE REACTIONS), the following verbatim statement or appropriate modification should precede the presentation of adverse reactions:

“Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.”

### Comment:

- N/A** 40. When postmarketing adverse reaction data are included (typically in the “Postmarketing Experience” subsection of ADVERSE REACTIONS), the following verbatim statement or appropriate modification should precede the presentation of adverse reactions:

## Selected Requirements of Prescribing Information

“The following adverse reactions have been identified during post-approval use of (insert drug name). Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.”

**Comment:**

### PATIENT COUNSELING INFORMATION Section in the FPI

- NO** 41. Must reference any FDA-approved patient labeling in Section 17 (PATIENT COUNSELING INFORMATION section). The reference should appear at the beginning of Section 17 and include the type(s) of FDA-approved patient labeling (e.g., Patient Information, Medication Guide, Instructions for Use).

**Comment:** *A statement regarding FDA-approved labeling is present in Section 17 of the labeling. However, a period should be placed at the end of the sentence.*

- YES** 42. FDA-approved patient labeling (e.g., Medication Guide, Patient Information, or Instructions for Use) must not be included as a subsection under section 17 (PATIENT COUNSELING INFORMATION). All FDA-approved patient labeling must appear at the end of the PI upon approval.

**Comment:**

# Selected Requirements of Prescribing Information

## Appendix A: Format of the Highlights and Table of Contents

### HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use [DRUG NAME] safely and effectively. See full prescribing information for [DRUG NAME].

[DRUG NAME (nonproprietary name) dosage form, route of administration, controlled substance symbol]

Initial U.S. Approval: [year]

#### WARNING: [SUBJECT OF WARNING]

*See full prescribing information for complete boxed warning.*

- [text]
- [text]

#### RECENT MAJOR CHANGES

[section (X.X)]  
[section (X.X)]

[m/year]  
[m/year]

#### INDICATIONS AND USAGE

[DRUG NAME] is a [name of pharmacologic class] indicated for [text]

#### DOSAGE AND ADMINISTRATION

- [text]
- [text]

#### DOSAGE FORMS AND STRENGTHS

[text]

#### CONTRAINDICATIONS

- [text]
- [text]

#### WARNINGS AND PRECAUTIONS

- [text]
- [text]

#### ADVERSE REACTIONS

Most common adverse reactions (incidence > x%) are [text].

To report SUSPECTED ADVERSE REACTIONS, contact [name of manufacturer] at [phone #] or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

#### DRUG INTERACTIONS

- [text]
- [text]

#### USE IN SPECIFIC POPULATIONS

- [text]
- [text]

See 17 for PATIENT COUNSELING INFORMATION [and FDA-approved patient labeling OR and Medication Guide].

Revised: [m/year]

### FULL PRESCRIBING INFORMATION: CONTENTS\*

WARNING: [SUBJECT OF WARNING]

#### 1 INDICATIONS AND USAGE

#### 2 DOSAGE AND ADMINISTRATION

- 2.1 [text]
- 2.2 [text]

#### 3 DOSAGE FORMS AND STRENGTHS

#### 4 CONTRAINDICATIONS

#### 5 WARNINGS AND PRECAUTIONS

- 5.1 [text]
- 5.2 [text]

#### 6 ADVERSE REACTIONS

- 6.1 [text]
- 6.2 [text]

#### 7 DRUG INTERACTIONS

- 7.1 [text]
- 7.2 [text]

#### 8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy
- 8.2 Labor and Delivery
- 8.3 Nursing Mothers
- 8.4 Pediatric Use
- 8.5 Geriatric Use

#### 9 DRUG ABUSE AND DEPENDENCE

- 9.1 Controlled Substance
- 9.2 Abuse
- 9.3 Dependence

#### 10 OVERDOSAGE

#### 11 DESCRIPTION

#### 12 CLINICAL PHARMACOLOGY

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics
- 12.4 Microbiology
- 12.5 Pharmacogenomics

#### 13 NONCLINICAL TOXICOLOGY

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
- 13.2 Animal Toxicology and/or Pharmacology

#### 14 CLINICAL STUDIES

- 14.1 [text]
- 14.2 [text]

#### 15 REFERENCES

#### 16 HOW SUPPLIED/STORAGE AND HANDLING

#### 17 PATIENT COUNSELING INFORMATION

\*Sections or subsections omitted from the full prescribing information are not listed.

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/s/  
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DIANA M WILLARD  
08/05/2015

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## **LABEL AND LABELING REVIEW**

Division of Medication Error Prevention and Analysis (DMEPA)  
Office of Medication Error Prevention and Risk Management (OMEPRM)  
Office of Surveillance and Epidemiology (OSE)  
Center for Drug Evaluation and Research (CDER)

**\*\*\* This document contains proprietary information that cannot be released to the public\*\*\***

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<b>Date of This Review:</b>	September 14, 2015
<b>Requesting Office or Division:</b>	Division of Transplant and Ophthalmology Products (DTOP)
<b>Application Type and Number:</b>	NDA 206911
<b>Product Name and Strength:</b>	Bromfenac Ophthalmic Solution, 0.075%
<b>Product Type:</b>	Single Ingredient Product
<b>Rx or OTC:</b>	Rx
<b>Applicant/Sponsor Name:</b>	Insite Vision, Inc
<b>Submission Date:</b>	June 15, 2015
<b>OSE RCM #:</b>	2015-1359
<b>DMEPA Primary Reviewer:</b>	Nicole Garrison, PharmD, BCPS
<b>DMEPA Team Leader:</b>	Yelena Maslov, PharmD

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## 1 REASON FOR REVIEW

This review evaluates the proposed labels and labeling for Bromsite ophthalmic solution, 0.075% (NDA 206911) for areas of vulnerability that could lead to medication errors. The Division of Transplant and Ophthalmology requested this review as part of their evaluation to the 505(b) (2) submission for Bromsite. The reference listed drug (Bromday, NDA 021664) was approved in March 2005.

## 2 MATERIALS REVIEWED

We considered the materials listed in Table 1 for this review. The Appendices provide the methods and results for each material reviewed.

<b>Table 1. Materials Considered for this Label and Labeling Review</b>	
<b>Material Reviewed</b>	<b>Appendix Section (for Methods and Results)</b>
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B
Human Factors Study	C-N/A
ISMP Newsletters	D-N/A
FDA Adverse Event Reporting System (FAERS)*	E-N/A
Other	F-N/A
Labels and Labeling	G

N/A=not applicable for this review

\*We do not typically search FAERS for label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

## 3 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

Insite Vision submitted a 505 (b)(2) NDA to obtain marketing approval of Bromsite for the treatment of post-operative inflammation and prevention of ocular pain in patients undergoing cataract surgery. The applicant referenced Bromday in the June 15, 2015 submission for Bromsite. The reference listed drug (RLD) has a different strength and frequency of administration than Bromsite. Our review identified the information contained in the proposed Bromsite prescribing information (PI) is inconsistent with Bromday's PI in reference to section 17, Patient Counseling Information.

We reviewed the proposed container labels, carton labeling, overwrap labeling and Instructions for Use and identified the following areas of vulnerability to error:

- The carton labeling does not provide the route of administration on the principal display panel.



- The lot number and expiration date are omitted from the carton labeling. We recommend adding the lot number and expiration date to ensure this critical information is available and to minimize the risk of the patient taking expired medications.
- The Instruction for Use contains small illustrations in black and white. The instructions are also complicated and error prone.
- The proprietary name includes tall man lettering.
- The established name on the overwrap labeling is crowded and difficult to read.

Therefore, we conclude that the proposed PI, container labels, carton labeling, and Instructions for Use can be improved to increase clarity and prominence of important information to promote safe use of the product.

## 4 CONCLUSION & RECOMMENDATIONS

We determined that the proposed PI, container labels, carton labeling, and Instructions for Use is vulnerable to confusion that can lead to medication errors. We provide recommendations in sections 4.1 and 4.2 below and advise they are implemented prior to approval of the application.

### 4.1 RECOMMENDATIONS FOR THE DIVISION

#### A. Prescribing Information

##### 1. In section 16 (Storage)

- a. Since water loss can occur, we recommend the addition of a cautionary statement regarding protection against moisture loss under storage conditions.

##### 2. In section 17 (Patient Counseling Information)

- a. We recommend the addition of sub- headings that are consistent with the reference listed product, Bromday.

##### i. 17.3 Concomitant Use of Contact Lenses

Advise patients not to wear contact lenses during (b) (4) administration of (b) (4). The preservative in (b) (4), benzalkonium chloride, may be absorbed by soft contact lenses.

##### ii. 17.4 Sterility of Dropper Tip

Advise patients to replace the bottle cap after use and do not touch the dropper tip to any surface as this may contaminate the contents.

- b. Please consider to list the following information under the sub-heading *Product Use*:

- i. Advise patients to thoroughly wash hands prior to using Bromsite

- ii. Advise patients that a single bottle of Bromsite should be used to treat only one eye.

## 4.2 RECOMMENDATIONS FOR INSITE VISION, INC

We recommend the following be implemented prior to approval of this NDA:

### A. Carton Labeling

1. The proprietary name BromSITE is presented with the letters 'SITE' capitalized. This mixed case type of presentation is typically reserved for differentiating known look-alike and sound-alike established name pairs or in rare circumstances for proprietary names to help reduce the risk of wrong drug name errors. Since Bromsite is not a name that has been involved in drug name confusion or wrong drug errors, the capitalization of the letters "SITE" is inappropriately applied.
2. Relocate the statement "For Topical Application in the Eye" to the principal display panel (PDP) following the statement of strength to increase its prominence and ensure proper administration of this product.
3. Provide adequate space between strength statement and established name on the PDP for increased readability and clarity by either inserting a space between established name and strength or placing the strength immediately underneath the established name.
4. Please indicate where the required lot number and expiration date will appear on the outer carton as required per 21 CFR 201.17.
5. Consider moving the (b) (4) company logo to the lower third of the PDP for increased prominence and help with identification of the drug.
6. Consider changing the font color of the proprietary name to one color to increase readability of this important information. For example, using different colors for one name may make the proprietary name appear like two names<sup>1</sup>.
7. Since water loss can occur, we recommend the addition of a cautionary statement regarding protection against moisture loss under storage conditions.

### B. Container Labeling

1. See A.1 and A.6 and revise container labeling accordingly.
2. Reorient the barcode to a vertical position to improve the scannability of the barcode. Barcodes placed in a horizontal position may not scan due to curvature of the bottle.

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<sup>1</sup> DMEPA Guidance for Industry. Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors. 2013 [cited 2015 Aug 17].

3. Consider placing the route of administration on the principle display panel if space permits.

C. Overwrap Labeling

1. See A.1, A.6 and A.7, and revise overwrap labeling accordingly.
2. The established name on the overwrap labeling is crowded and difficult to read. We recommend increasing the font of the established name on the overwrap to improve readability.

D. Instructions for Use

1. Increase the size of the illustrations and provide them in color to help demonstrate each instruction for use. We recommend this revision to help prevent wrong administration technique.
2. In step 5, you state to keep the bottle upside down and remove the gray cap. As stated, this sequence may produce dripping of the medication which could lead to in advert loss of the medication.
3. The directions are overly complicated. Since the directions differ from other products used post-operative for cataract surgery, this may introduce wrong administration technique. Consider revising the directions to simplify and eliminate unnecessary steps to help prevent medication errors during use of the product.

## APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

### APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Bromsite that Insite Vision submitted on June 15, 2015.

Table 2. Relevant Product Information for Bromsite	
Initial Approval Date	N/A
Active Ingredient	Bromfenac
Indication	This product is indicated for the treatment of postoperative inflammation and prevention of ocular pain in patients undergoing cataract surgery.
Route of Administration	Ophthalmic
Dosage Form	Solution
Strength	0.075%
Dose and Frequency	Instill one drop to the affected area twice daily 1 day prior to surgery, the day of surgery, and 14 days post-surgery
How Supplied	5 mL in a 7.5 mL container
Storage	Store at 15°C to 25°C (59°F to 77°F)
Container Closure	Stored in a white opaque low density polyethylene (LDPE) plastic bottle and translucent dropper tips, and gray high density polyethylene (HDPE) eyedropper caps. The gray color is consistent with the American Academy of Ophthalmology's policy statement "Color Codes for Topical Ocular Medications" which recommends the gray cap color for nonsteroidal anti-inflammatories (NSAIDS).

## **APPENDIX B. PREVIOUS DMEPA REVIEWS**

### **B. Methods**

On August 3, 2015, we searched the L: drive and AIMS using the terms, Bromsite to identify reviews previously performed by DMEPA.

### **B.2 Results**

Our search identified no previous label and labeling reviews, only one proprietary name review.

## **APPENDIX G. LABELS AND LABELING**

### **G.1 List of Labels and Labeling Reviewed**

Using the principles of human factors and Failure Mode and Effects Analysis,<sup>2</sup> along with postmarket medication error data, we reviewed the following Bromsite labels and labeling submitted by InSite Vision on June 15, 2015.

- Carton labeling
- Container label
- Overwrap labeling
- Instructions for Use

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<sup>2</sup> Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

## G.2 Label and Labeling Images

(b) (4)



3 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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/s/  
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09/14/2015

YELENA L MASLOV  
09/14/2015