

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

209310Orig1s000

OTHER REVIEW(S)

505(b)(2) ASSESSMENT

Application Information		
NDA # 209310	NDA Supplement #: S-	Efficacy Supplement Type SE-
Proprietary Name: Sinuva Sinus Implant Established/Proper Name: Mometasone furoate Dosage Form: Implant Strengths: 1350 mcg		
Applicant: Intersect ENT		
Date of Receipt: March 7, 2017		
PDUFA Goal Date: January 7, 2018		Action Goal Date (if different): December 8, 2017
RPM: Nina Ton		
Proposed Indication(s): Nasal polyps		

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)
NDA 021067 Asmanex Twisthaler (mometasone furoate)	FDA's previous finding of safety (nonclinical and clinical pharmacology)

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

- 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 literature¹. [See also Guidance for Industry Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products.](#)

Study R500-0513 was the only clinical pharmacology study conducted for NDA 209310. The applicant relies on FDA's previous findings for aspects of clinical pharmacology for the Asmanex Twisthaler, a mometasone furoate dry powder inhaler, approved for the treatment of asthma.

The bridge between the proposed product and Asmanex Twisthaler is based on a cross-study comparison of the systemic exposure for mometasone furoate (MF) from the proposed product (Sinuva Sinus Implant, Clinical Pharmacology Study 0513) and the reference product (NDA 021067 Asmanex Twisthaler). The cross-study comparison demonstrated that the systemic exposure for MF from the proposed drug product was generally comparable to that following administration of Asmanex Twisthaler's highest approved dose (440 µg, BID).

The cross-study comparison of PK is a very common approach in supporting the systemic safety profiles of drug products containing the same active ingredient across different indications, age groups, and administration routes. The direct bioavailability comparison study is not required and not necessary for this NDA from clinical pharmacology perspective. The results from this cross-study comparison sufficiently provided adequate basis for the applicant relying on FDA's previous findings for MF systemic safety from the Asmanex Twisthaler.

The clinical studies to support approval of the Sinuva Sinus Implant for the treatment of nasal polyps in patients 18 years of age and older who have had ethmoid sinus surgery consisted primarily of two randomized, single-blind, parallel group, concurrently-controlled, multicenter studies. Study 1 (RESOLVE) was 6 months' duration and Study 2 (RESOLVE II) was 90 days' duration. Safety was demonstrated based on data from

¹For 505(b)(2) applications that rely on a listed drug(s), bridging studies are often BA/BE studies comparing the proposed product to the listed drug(s). Other examples include: comparative physicochemical tests and bioassay; preclinical data (which may include bridging toxicology studies); pharmacokinetic/pharmacodynamic (PK/PD) data; and clinical data (which may include immunogenicity studies). A bridge may also be a scientific rationale that there is an adequate basis for reliance upon FDA's finding of safety and effectiveness of the listed drug(s). For 505(b)(2) applications that rely upon literature, the bridge is an explanation of how the literature is scientifically sound and relevant to the approval of the proposed 505(b)(2) product.

both studies, as well as the large breadth of clinical and historical experience with mometasone furoate. No new safety signals were noted in this development program. The efficacy of Sinuva Sinus Implant is based primarily on Study 2 which showed a statistically significant improvement from baseline in nasal obstruction/congestion score and bilateral polyp grade at day 90.

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?

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 ☐

¹For 505(b)(2) applications that rely on a listed drug(s), bridging studies are often BA/BE studies comparing the proposed product to the listed drug(s). Other examples include: comparative physicochemical tests and bioassay; preclinical data (which may include bridging toxicology studies); pharmacokinetic/pharmacodynamic (PK/PD) data; and clinical data (which may include immunogenicity studies). A bridge may also be a scientific rationale that there is an adequate basis for reliance upon FDA’s finding of safety and effectiveness of the listed drug(s). For 505(b)(2) applications that rely upon literature, the bridge is an explanation of how the literature is scientifically sound and relevant to the approval of the proposed 505(b)(2) product.

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)
Asmanex Twisthaler (mometasone furoate)	021067	Yes

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”).

This application provides for a new indication of treatment of nasal polyps in patients 18 years of age or older and also provides for a change in dosage form, from inhalation powder to drug eluting sinus implant.

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 ☐ NO ☒

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):

NDA 205641 Asmanex HFA (mometasone furoate) Inhalation Aerosol

NDA 019625 Elocon (mometasone furoate) Cream

NDA 019796 Elocon (mometasone furoate) Lotion

NDA 019543 Elocon (mometasone furoate) Ointment

NDA 021067 Asmanex Twisthaler (mometasone furoate)

NDA 020762 Nasonex (mometasone furoate) Nasal Spray

Approved generics are also listed in the Orange Book.

PATENT CERTIFICATION/STATEMENTS
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- 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): 6240918
6503537
8173172

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): 6240918

Expiry date(s): August 20, 2017

- ☒ 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): 6503537
8173172

(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): June 6, 2017

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 ☐

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

/s/

PHUONG N TON
12/08/2017



DEPARTMENT OF HEALTH AND HUMAN SERVICES

M E M O R A N D U M

Food and Drug Administration
Office of Device Evaluation
10903 New Hampshire Avenue
Silver Spring, MD 20993

To: Nina Ton, PharmD, Senior Regulatory Project Manager (CDER/OND/DPARP)

From: Joyce Lin, Ph.D., Materials Engineer (CDRH/ODE/DOED/ENTB)
Sunny Park, Ph.D., Microbiologist (CDRH/ODE/DOED/ENTB)

Through: Srinivas Nandkumar, Ph.D., ENTB Branch Chief (CDRH/ODE/DOED/ENTB)

Date: November 29, 2017

Subject: **NDA209310 – Device Engineering and Materials Review**

Device: Mometasone Furoate Sinus Implant
(Intersect ENT)

1 Purpose of Submission

Intersect ENT is hereby submitting an Original New Drug Application, NDA 209310, for the combination product, Mometasone Furoate Sinus Implant, 1350 mcg, also referred to as the S8 Sinus Implant or S8 Sinus Stent. The ODE/ENTB was asked to review the product from a device perspective. Below is a review of the submission covering the device design and materials, manufacturing process validation, sterilization, biocompatibility, packaging, and labeling.

2 Indications For Use

The S8 Sinus Implant (mometasone furoate, 1350 mcg) is a corticosteroid-eluting implant indicated for the treatment of ^{(b) (4)} polyps, in patients ≥ 18 years of age who have had ethmoid sinus surgery.

3 Device Description

Device Components

The S8 Sinus Implant is a self-expanding, bioabsorbable, drug eluting implant (see Figure 1). The S8 Sinus Implant is provided with a single-use delivery system (see Figure 2) and crimpers (see Figure 3). The S8 implant is coated with mometasone furoate (MF; 1350 mcg total drug content)

embedded in a bioabsorbable polymer matrix containing (b) (4) poly(DL-lactide-co-glycolide) and polyethylene glycol (inactive ingredients) which provides for gradual release of the drug. The S8 Sinus Implant is packaged in a tray (see Figure 4) which is then sealed in a foil pouch and placed in the product carton. The S8 product is provided sterile.

Figure 1: Implant

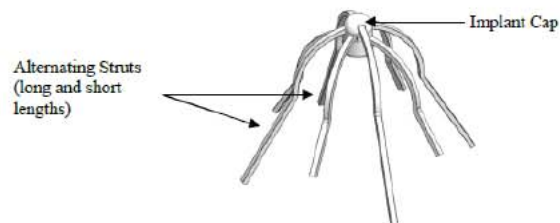


Figure 2: Delivery System

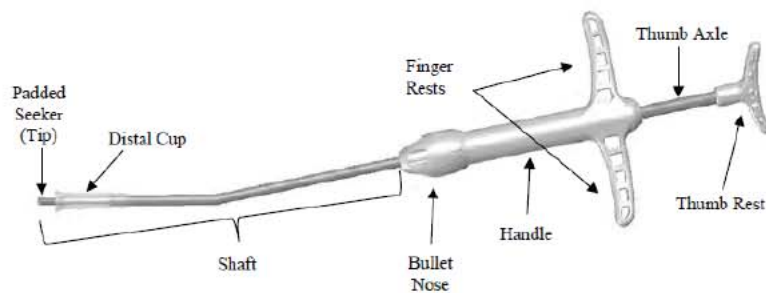


Figure 3: Crimper with Implant



(b) (4)

Table 1: Components of the S8 Sinus Implant

Component	Function
Drug Component	
Implant Coating	Provides controlled release of MF (b) (4) and polyps in the supported tissues.
Device Components	
Implant	Provides mechanical spacing to open obstructed sinus cavity.
Delivery System	<ul style="list-style-type: none"> Accesses the ethmoid sinus. Places the implant in the desired location.
Crimper	<ul style="list-style-type: none"> Holds the implant in the product packaging. Compresses the implant for loading into the delivery system.
Container Closure and Packaging Components	
Tray/Lid	Minimizes movement of the implant, delivery system, and desiccant box within the tray.
Pouch	Provides sterile barrier and barrier to moisture, light, and gas. (b) (4)
Package Insert	Provides product information. (b) (4)
Box Seal	Keeps product carton closed.
Product Label	Provides product traceability.

Principle of Operation

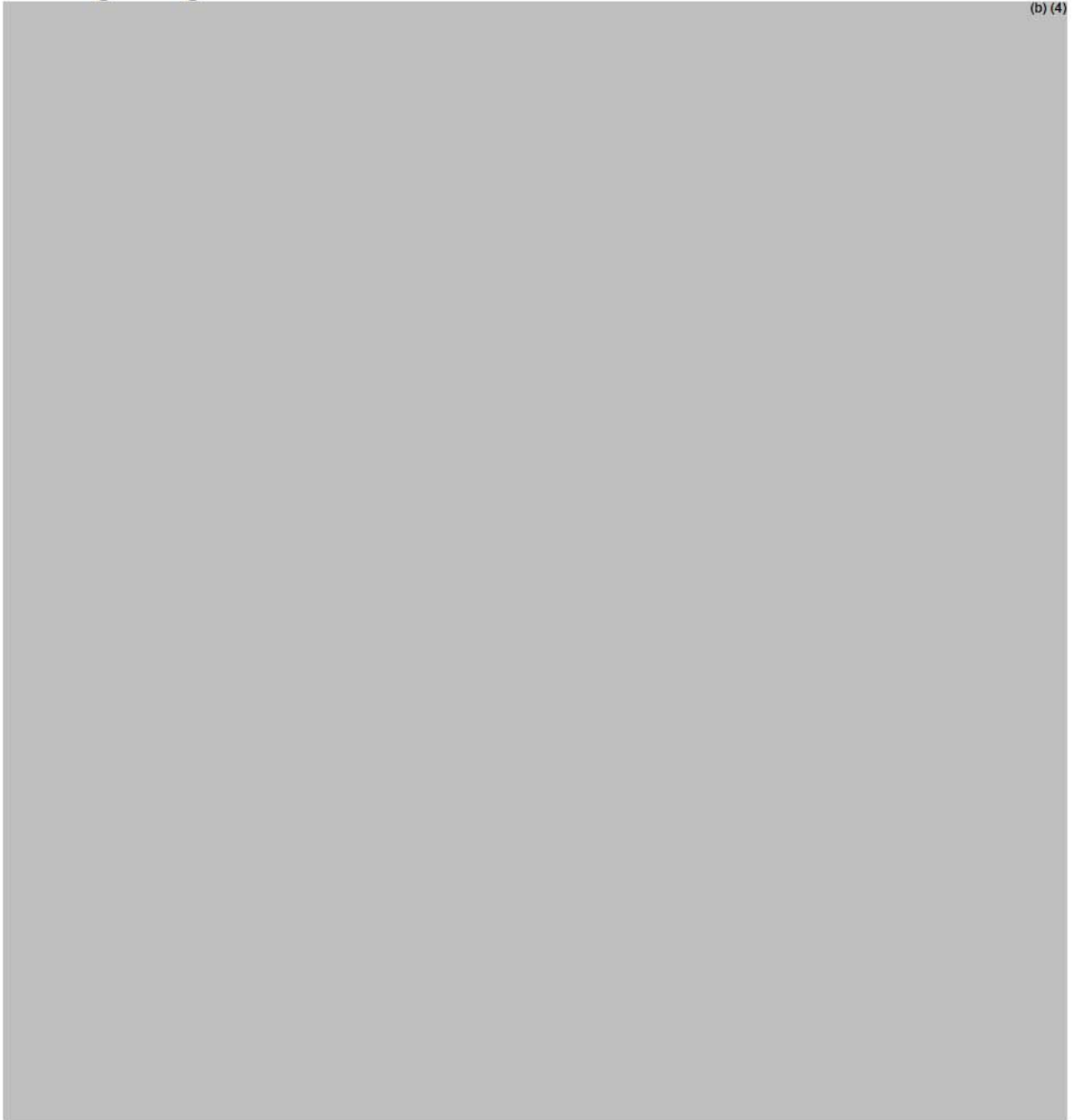
The S8 Sinus Implant is intended to be placed by a physician under endoscopic visualization. The implant is compressed using the crimper and loaded onto the delivery system (see Figure 5). The tip of the delivery system is inserted in the patient's nostril and advanced to the ethmoid sinus cavity under endoscopic visualization. The physician positions the distal tip of the delivery system in the desired location and depresses the thumb rest of the delivery system to deploy the implant. The delivery system is then retracted and discarded. The radial strength of the implant creates an opening in the obstructed ethmoid sinus while the drug is eluted from the implant to provide local anti-inflammatory activity to aid in minimizing (b) (4)/polypsis within the supported tissues. The coating provides controlled release of drug to the mucosal tissue.

Figure 5: Compressed Implant Loaded onto Tip of Delivery System



Component Materials

Drug Coating:

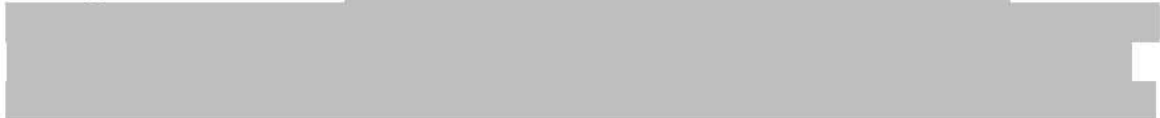


(b) (4)

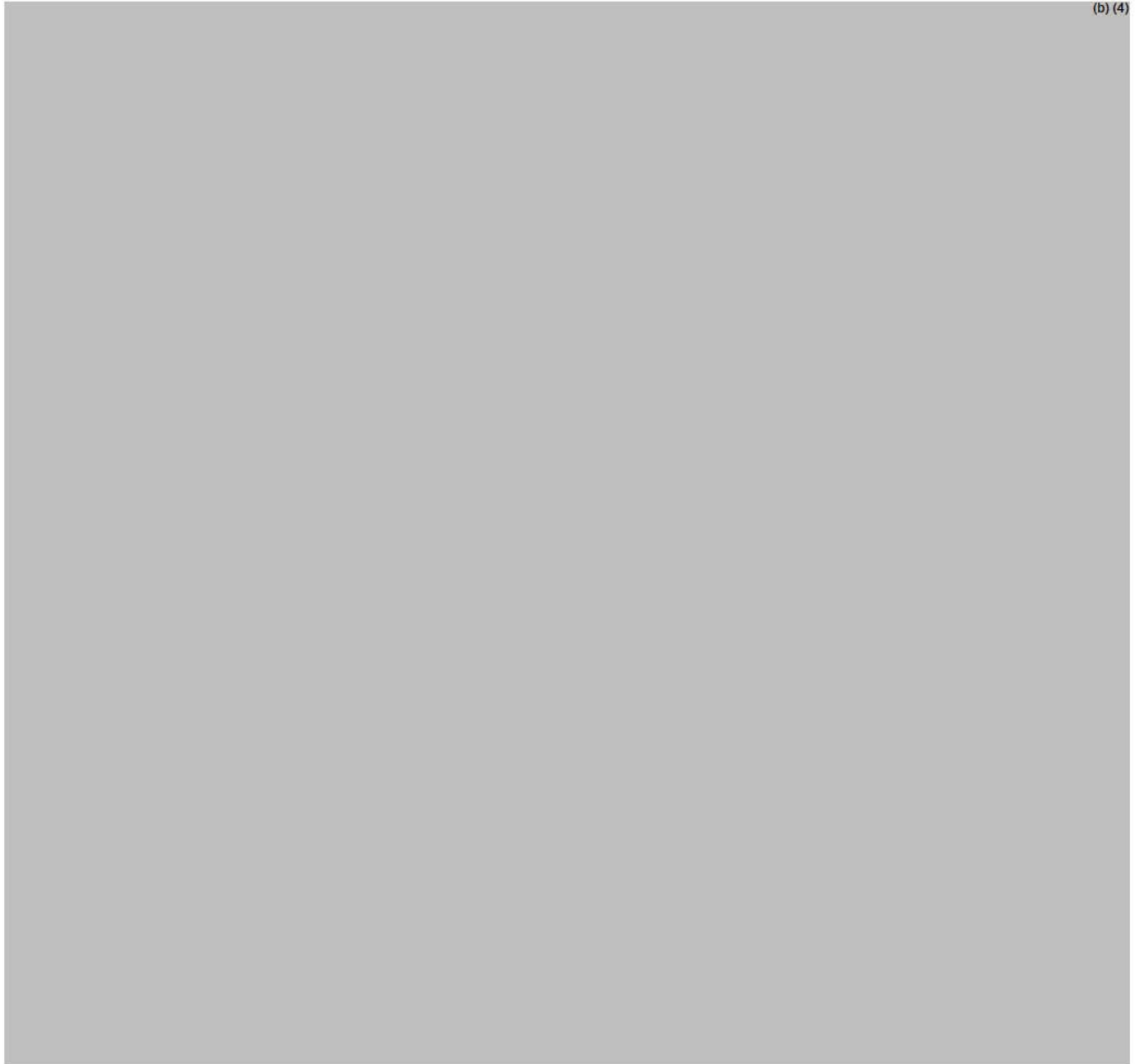
Implant:

The implant is manufacture

(b) (4)

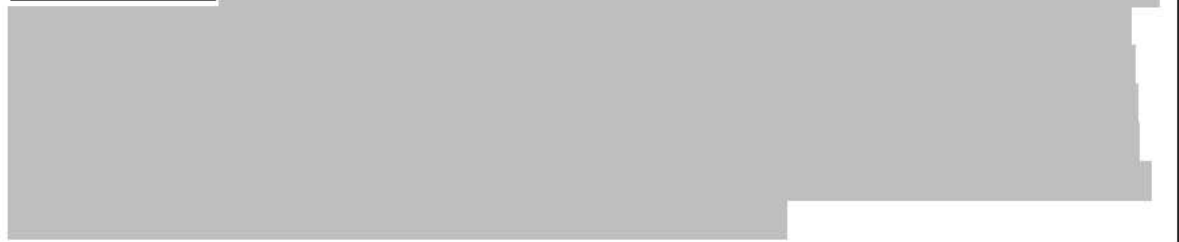


(b) (4)



Reviewer Notes:

(b) (4)



Delivery System:

The delivery system components and material descriptions are provided in Table 4.

(b) (4)

Crimper:

Prior to use, the crimper is used to compress the implant and load it into the delivery system. The crimper components and materials are provided in Table 5.

Table 5: Crimper Component List

Component	Material Description
Crimper	(b) (4)
Crimper Cap	

Reviewer Notes: The implant is

(b) (4)

The delivery system should be able to consistently deliver the implant in a controlled force and direction to the sinus where the struts open radially to their un-crimped positions.

4 Manufacturing Information

Product Development

(b) (4)

9 Conclusions

Intersect ENT has submitted a new drug application for the Mometasone Furoate Sinus Implant combination product, which is indicated for the treatment of (b) (4) polyps, in patients ≥ 18 years of age who have had ethmoid sinus surgery.

The product is a drug-eluting stent consisting of (b) (4)

(b) (4) and packaged within a foil pouch and carton.

The implant component consists of alternating struts connected via a cap. (b) (4)

(b) (4) he labeling instructions and recommendations were also consistent with the design verification testing showing that the implant could be deployed at least two times. The deployment device was also tested for mechanical strength to ensure that the implant could be loaded and deployed without damaging the implant, and to ensure that the tip of the deployment device remains intact throughout deployment of the implant. Additionally, the device functionality was maintained after accelerated aging simulating the labeled 24 month shelf life.

Biocompatibility testing was also performed for the implant and delivery device. The implant is considered a permanent (>30 days) surface device with mucosal membranes and breached or compromised surface contact, and was evaluated per ISO 10993 for cytotoxicity, sensitization, irritation, acute systemic toxicity, subchronic toxicity, and genotoxicity. The delivery device is considered a limited (< 24 hours) surface device with mucosal membranes and breached or compromised surface contact, and was evaluated per ISO 10993 for cytotoxicity, sensitization, and irritation. The results of these tests were found to be acceptable. Further toxicity testing to assess the long-term effects of material resorption were conducted in animals and assessed by CDER.

All of the components of the system have successfully passed sterilization validation. The packaging validation was also acceptable and included extreme conditioning (per ASTM D4332) and transportation simulation (per ASTM D4169). The packaging has also been tested to maintain sterility for the labeled shelf life of 24 months. Bacterial endotoxin testing was completed in accordance with USP<85> using the kinetic turbidimetric BET method, and was acceptable. The proposed labeling also contains adequate sterility information.

The manufacturing information and quality management system documentation of the implant and deployment device were summarized in the submission. The sponsor stated that they intend to [REDACTED] (b) (4)

From a device standpoint, the implant poses low risk in that it is not a permanent implant and is meant to resorb over a period of [REDACTED] (b) (4). It is also composed of similar materials as the sponsor's own Propel family of sinus implants, which have a well-characterized safety profile over several years of use on the market. The deployment device is also similar in materials and construction to those packaged with the Propel sinus implants. All new materials and compositions were evaluated for biocompatibility and found acceptable. Furthermore, the sponsor has completed design verification testing, biocompatibility, sterilization and packaging validation, and has committed to completing manufacturing process validation prior to commercialization. The completed device verification and validation testing has adequately demonstrated that the implant and delivery device can be produced consistently and can perform according to the device specifications defined for the proposed indications for use in the ethmoid sinus after sinus surgery.

Recommendation: Approval

Joyce C. Lin -S
2017.11.29 12:13:13 -05'00'

Sunny Park -S
2017.11.29 12:19:31 -05'00'

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

/s/

PHUONG N TON

11/30/2017

Administratively checked into DARRTS by Project Manager on behalf of the reviewer



**Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research| Office of Surveillance and Epidemiology (OSE)**

Epidemiology: ARIA Sufficiency Memo

Date: 11/28/2017

Reviewer(s): Efe Eworuke, PhD, Epidemiologist
Division of Epidemiology II

Team Leader: Margie Goulding, PhD, Epidemiologist
Division of Epidemiology II

Deputy Division Director: Lock Taylor, PhD, Deputy Director
Division of Epidemiology II

Subject: ARIA Sufficiency Memo

Drug Name(s): S8 Mometasone Sinus Implant

Application Type/Number: NDA 209310

Applicant/sponsor: Intersect

OSE RCM #: 2017-1875



EXECUTIVE SUMMARY (*place "X" in appropriate boxes*)

Memo type	
-Initial	X
-Interim	
-Final	
Source of safety concern	
-Peri-approval	X
-Post-approval	
Is ARIA sufficient to help characterize the safety concern?	
-Yes	X
-No	
If "No", please identify the area(s) of concern.	
-Surveillance or Study Population	
-Exposure	
-Outcome(s) of Interest	
-Covariate(s) of Interest	
-Surveillance Design/Analytic Tools	



1. BACKGROUND INFORMATION

Medical Product

The proposed product, S8 – a sinus stent impregnated with mometasone to be used in patients with recurrent nasal polyposis, is currently under review by the FDA (under NDA 209310). There are three currently marketed stents – Propel (approved: 08/11/2011), Propel Mini (approved: 03/23/2016) and Propel Contour (approved: 02/23/2017) used in patients following endoscopic ethmoid sinus surgery or frontal sinus surgery. After surgery, these drug-eluting sinus implants are used primarily to control hemorrhage, prevent adhesion formation and promote the drainage of sinus mucosa, thereby promoting wound healing. All these currently marketed sinus stent products were approved as devices by the Center for Devices and Radiological Health (CDRH). Due to the increased dose of Mometasone (from 370 mcg to 1350 mcg) in the proposed S8 sinus implant, its review is being conducted by the CDER's Division of Pulmonary, Allergy and Rheumatology Products (DPAAP).

The sinus implant, S8, is proposed for use (b) (4)

S8 stent has a higher mometasone dose compared to the marketed propel implants. The stent is placed endoscopically and then left in place for the steroid to slowly be released over time (90 days or earlier).

1.1. Describe the Safety Concern

FDA is concerned about the potential adverse effects of repeat use of the new high dose stent. The potential Adverse Events (AEs) of concern include nasal septal perforation, cataracts and glaucoma. Although the S8's clinical development program did not show a problem, long term use of oral or intranasal steroids has been previously linked to the development of cataracts (posterior subcapsular cataracts)^{1,2}, and intranasal steroids have been linked to increased intraocular pressure. The route of administration (endoscopically), location (nasal), and drug (corticosteroids) raised the possibility of an increased risk of these AEs with S8 implants. There are no published studies that have examined the use of sinus stent implants in US claims data or the incidence of these adverse outcomes with their use. There were no cases of glaucoma or cataract reported in the pivotal trial (RESOLVE II: A Clinical Evaluation of the Safety and Efficacy of the Steroid-Releasing S8 Sinus Implant in Chronic Sinusitis Patients with Recurrent Sinus Obstruction). It is important to note that patients were only followed for 90 days which is relatively short for the manifestation of the cataract and glaucoma.

All three events are labeled in sections 5 (warnings and precautions) and 6 (Adverse Reactions) of the proposed draft labeling as follows:

WARNINGS AND PRECAUTIONS

5.1 Local Effects

Monitor nasal mucosa adjacent to the <PROPRIETARY NAME> Sinus Implant for any signs of



bleeding (epistaxis), irritation, infection or perforation. Avoid use in patients with nasal ulcers, or trauma.

5.2 Ocular Effects

Glaucoma, cataracts, and clinically significant elevation of intraocular pressure were not observed in patients from the treatment group of one randomized controlled clinical study (N = 53) who underwent bilateral placement of <PROPRIETARY NAME> Sinus Implants.

Close monitoring is warranted in patients with a change in vision or with a history of increased intraocular pressure, glaucoma, and/or cataracts.

ADVERSE REACTIONS

The following adverse reactions are discussed in more detail in other sections of the labeling:

- Local effects including epistaxis, irritation, infection, or perforation [see Warnings and Precautions (5.1)]
- Cataracts and glaucoma (see Warnings and Precautions (5.2))
- Hypersensitivity Reactions (see Warnings and Precautions (5.3))
- Immunosuppression (see Warnings and Precautions (5.4))
- Hypothalamic-pituitary-adrenal (HPA) axis effects (see Warnings and Precautions (5.4))

1.2. FDAAA Purpose (per Section 505(o)(3)(B))

Purpose (place an "X" in the appropriate boxes; more than one may be chosen)	1	2	3
Assess a known serious risk	X	X	X
Assess signals of serious risk			
Identify unexpected serious risk when available data indicate potential for serious risk			

1= Nasal Septal Perforation

2= Glaucoma

3= Cataracts

1.3. Statement of Purpose

The objective of the safety assessment will be to provide rates of the above-listed AEs among patients who had a single implant of the S8 and separately for patients who had repeat S8 implants. At this time, DPARP is only interested in receiving crude incidence rates for the two (single implant and repeated implant) exposure groups.

Effect Size of Interest or Estimated Sample Size Desired

Given only crude incidence rates are to be produced by the assessment, a desired sample size is not relevant.

2. SURVEILLANCE OR DESIRED STUDY POPULATION

2.1. Population

The surveillance population will include patients with a diagnosis of nasal polyps. Nasal polyps are benign lesions arising from the mucosa of the nasal sinuses (commonly at the outflow tract of one or more of the sinuses) or from the mucosa of the nasal cavity. In the general population, the prevalence of NP is considered to be around 4%. Nasal polyps predominantly affect adults and usually present in patients older than 20 years old. Corticosteroids are the mainstay therapy option for nasal polyps. Patients would commence first on topical nasal steroids and then oral steroids for advanced and refractory cases when allergy is present. Surgery is reserved for refractory cases. The currently marketed propel implants are indicated for patients following ethmoid/frontal sinus surgery to maintain patency of the ethmoid sinus or frontal sinus opening. The new S8 implant will be used in patients who may not want/be a candidate for surgery. Therefore, the utilization of S8 implant will likely be higher than the currently marketed stents. The proposed analyses in Sentinel should examine patients (18 years and older) with nasal polyp diagnosis in the 183 days prior to any study drug implant exposure. Nasal polyps will be identified using ICD-10 codes J33.x.

2.2. Is ARIA sufficient to assess the intended population?

Yes. The diagnosis of chronic rhinosinusitis (J32.x and J33.x) which includes nasal polyps has been validated in a Canadian database with a positive predictive value (PPV) of 93.3%.³ Although the authors do not provide the performance metrics for nasal polyps alone, we anticipate similar performance. We deem ARIA to be sufficient to identify the target population.

3. EXPOSURES

3.1. Treatment Exposure(s)

The exposure of interest will be the new S8 sinus implant. To inform decisions on the exposure, we examined the current coding system for the propel implants in the Sentinel system using summary tables and an L1 modular program (completed 11/7/2017). The S1090 (Mometasone, 370mcg) is considered the most specific code for the propel implants. Medicare and some payors will use the J3490 code which is a CPT procedure code for use of any unclassified drug. To make this specific, we can require an NDC for the sinus implant on the same day as the J3490 code. Discussions with the sponsor on 11/14/2017 suggest that there is very likely going to be an assigned J code for S8 implant (that will be analogous to the S1090 code for the other propel sinus implants). The J code will be the supply code for surgeries and outpatient procedures associated with the use of the implant. There will also be a new NDC for the S8 sinus implant. For Medicare patients, the sponsor states that the C2625 and J3490 codes will likely be used for S8 implant procedures. As stated above, the requirement of the NDC and non-specific codes should be sufficient for identifying S8 exposure in Medicare claims.

3.2. Comparator Exposure(s)

There will be no comparator exposure since the objective of the study will be to provide incidence rates for the listed outcomes. There will be a group with repeated S8 implant exposure, but no formal comparison of its outcome rates with that of the single exposure group will be done.

3.3. Is ARIA sufficient to identify the exposure of interest?

Yes. The new S8 implant can be accurately identified in the ARIA system using the anticipated J code. For other payors who do not accept J codes, exposure can be identified using non-specific procedure codes – J3490 or C2625 and NDC. We deem ARIA to be sufficient to identify the exposure of interest.

4. OUTCOME(S)

4.1. Outcomes of Interest

FDA is interested in evaluating the risk of the following outcomes: nasal septal perforation, glaucoma and cataracts.

Glaucoma:

Glaucoma (ICD-9 code: 365.1x to 365.9x (types of glaucoma) and 365.0x (borderline glaucoma or glaucoma suspect and one pharmacy claim) have been validated in two Medicare-choice databases with a sensitivity of 78% and specificity of 92%.⁴ The authors do not report the positive predictive value of this definition. However, another study reported that 97% out of the 200 charts reviewed for glaucoma were correctly classified using the ICD9 codes.⁵ The same definitions have also been used in other claims-based studies that examined the prevalence of longitudinal eye diseases.^{6,7} A trend analysis in the Sentinel System reveals a stable transition between the ICD-9 and ICD-10 coding eras. Therefore, ARIA is deemed sufficient to identify the outcome of glaucoma.

Cataracts:

Cataracts (ICD-9 code: 366-366.4) have been validated in a study that included records from 67 health care providers (incl. ophthalmologists, optometrists and generalists) and two institutions. Out of the 220 verified charts, 100% of cases were correctly identified by the ICD-9 code.⁵ Another study examined the validity of cataract extraction procedure codes in Medicare data and found a PPV of 99%.⁸ A trend analysis in the Sentinel System reveals a stable transition between the ICD-9 and ICD-10 coding eras. Therefore, ARIA is deemed sufficient to identify the outcome of cataracts and cataract extraction.

Nasal septal perforation:

A published validation study for nasal septal perforation could not be found. However, discussions with medical officers (DPARP) indicate that most, if not all, nasal septal perforation patients will undergo a repair procedure. Using the nasal septal perforation diagnoses (ICD 10: J34.89 and Q30.3) and a

requirement of a procedure code (HCPCS code: 30630) for the repair should improve the accuracy of identifying this outcome with relatively low bias. We deem ARIA sufficient to identify the outcome of nasal septal perforation with repair.

4.2. Is ARIA sufficient to assess the outcome of interest?

Yes, based on the discussions above, ARIA is sufficient to assess the outcomes of interest.

5. COVARIATES

Since the analyses will only provide crude rates for the outcomes of interest, covariates that may be prognostic for the study outcomes, i.e. measures of health (including number of outpatient, inpatient or emergency visits) and number of prescribed medications, will be used to describe the study population, but not used for risk adjustment.

6. SURVEILLANCE DESIGN / ANALYTIC TOOLS

6.1. Surveillance or Study Design

We propose a cohort study design comprised of patients with a nasal polyp diagnoses who received the new S8 implant. Patients with a diagnosis of glaucoma, cataracts, blindness or nasal septal perforation during the baseline period will be excluded. The following drugs will be used to exclude patients who received treatment during the baseline period for any of these conditions: latanoprost, bimatoprost, timolol, betaxolol, apraclonidine, brimonidine, dorzolamide, brinzolamide, pilocarpine (eye drop formulations only). Also, patients with evidence of eye laser surgery, trabeculectomy or cataract surgery during the baseline period will be excluded.

Patients will be followed from the date of their index exposure after meeting study entry and exclusion criteria until the occurrence of any of the study outcomes, disenrollment from their health plan, evidence of death or the end of the study period, whichever comes first.

The incidence of the study outcomes (per 1000 person-years) will be calculated and stratified by number of S8 implants during follow-up.

6.2. Is ARIA sufficient with respect to the design/analytic tools available to assess the question of interest?

The L1 Sentinel program will be sufficient for providing crude rates for the study outcomes. No adjustments with patient characteristics will be needed.



7. NEXT STEPS

ARIA is considered sufficient to assess the risk of cataracts, glaucoma and nasal septal perforation with repair because the outcomes are either well-validated in the claims data or qualified to improve accuracy of the codes. The next steps will be to write a planning brief after the S8 implant is approved, then monitor the S8 implant's uptake and conduct a feasibility analysis once sufficient uptake is established. The feasibility study will specifically examine the market uptake and numbers of patients with single and repeat S8 implant use.



References

1. Cumming RG, Mitchell P, Leeder SR. Use of Inhaled Corticosteroids and the Risk of Cataracts. *New England Journal of Medicine*. 1997;337(1):8-14.
2. Garbe E, Suissa S, LeLorier J. Association of inhaled corticosteroid use with cataract extraction in elderly patients. *JAMA*. 1998;280(6):539-543.
3. Macdonald KI, Kilty SJ, van Walraven C. Development and validation of an administrative data algorithm to identify adults who have endoscopic sinus surgery for chronic rhinosinusitis. *J Otolaryngol Head Neck Surg*. 2017;46.
4. Rector TS, Wickstrom SL, Shah M, et al. Specificity and sensitivity of claims-based algorithms for identifying members of Medicare+Choice health plans that have chronic medical conditions. *Health Serv Res*. 2004;39(6 Pt 1):1839-1857.
5. Muir KW, Gupta C, Gill P, Stein JD. Accuracy of international classification of diseases, ninth revision, clinical modification billing codes for common ophthalmic conditions. *JAMA Ophthalmology*. 2013;131(1):119-120.
6. Ellwein LB, Urato CJ. Use of eye care and associated charges among the medicare population: 1991-1998. *Archives of Ophthalmology*. 2002;120(6):804-811.
7. Lee PP, Feldman ZW, Ostermann J, Brown DS, Sloan FA. Longitudinal prevalence of major eye diseases. *Archives of Ophthalmology*. 2003;121(9):1303-1310.
8. Javitt JC, McBean A, Sastry SS, DiPaolo F, Jr. Accuracy of coding in medicare part b claims: Cataract as a case study. *Archives of Ophthalmology*. 1993;111(5):605-607.

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/s/

EFE EWORUKE
11/28/2017

MARGIE R GOULDING
11/28/2017

LOCKWOOD G TAYLOR
11/28/2017

MICHAEL D BLUM
11/28/2017

MICHAEL D NGUYEN
11/28/2017

ROBERT BALL
11/28/2017

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

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

Memorandum

Date: November 16, 2017

To: Miya Okada Paterniti, M.D.
Clinical Reviewer
Division of Pulmonary, Allergy, and Rheumatology Products (DPARP)

Nina Ton, Pharm.D.
Regulatory Project Manager (DPARP)

From: Kyle Snyder, Pharm.D.
Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Kathleen Klemm
Team Leader (OPDP)

Subject: OPDP Labeling Comments for Sinuva (mometasone furoate) sinus implant

NDA: 209310

In response to DPARP's consult request dated March 22, 2017, OPDP has reviewed the proposed prescribing information (PI) for NDA 209310, Sinuva (mometasone furoate) sinus implant.

PI: OPDP's comments on the proposed labeling are based on the draft PI received by electronic mail from DPARP on November 14, 2017. Comments on the proposed PI are provided below.

Carton and Container Labeling: Per email communication from DPARP on November 14, 2017, carton and container labels are currently undergoing revisions. OPDP will review proposed carton and container labels at a later date.

Thank you for your consult. If you have any questions, please contact Kyle Snyder at (240) 402-8796 or kyle.snyder@fda.hhs.gov.

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/s/

KYLE SNYDER
11/16/2017

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*****

Date of This Review:	October 30, 2017
Requesting Office or Division:	Division of Pulmonary, Allergy, and Rheumatology Products (DPARP)
Application Type and Number:	NDA 209310
Product Name and Strength:	Sinuva (Mometasone Furoate) Sinus Implant, 1350 mcg
Product Type:	Single-ingredient Combination Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Intersect ENT
Submission Date:	March 7, 2017
OSE RCM #:	2017-528
DMEPA Primary Reviewer:	Lissa C. Owens, PharmD
DMEPA Team Leader:	Sarah K. Vee, PharmD

1 REASON FOR REVIEW

This review evaluates the proposed labels and labeling Sinuva (Mometasone Furoate) Sinus Implant for areas of vulnerability that could lead to medication errors. The Division of Pulmonary, Allergy and Rheumatology Products (DPARP) requested this review as part of their evaluation of NDA 209310.

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.

Table 1. Materials Considered for this Label and Labeling Review	
Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B-N/A
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 our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

3 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

Intersect ENT submitted a 505(b)(2) NDA 209310 on March 7, 2017, with the proposed indication of (b) (4) polyps, in patients 18 years of age and older who have had ethmoid sinus surgery. DMEPA evaluated the proposed Prescribing Information (PI), container label, and carton labeling to determine whether there are any vulnerabilities that may lead to medication errors.

We note that the proprietary name, Sinuva, was found conditionally acceptable under IND 116042^a and recommend that the name be included on the labels and labeling. Additionally, we note that the symbol “≥” is utilized in the prescribing information which may be misinterpreted. We make recommendations in section 4.1 and 4.2.

4 CONCLUSION & RECOMMENDATIONS

^a Owens, L Proprietary Name Reconsideration Review for Sinuva IND 116042. Silver Spring (MD): Food and Drug Administration, Center for Drug Evaluation and Research, Office of Surveillance and Epidemiology, Division of Medication Error Prevention and Analysis (US); 2017 MAY 11. Panorama No. 2017-12759066

DMEPA identified areas in the label, labeling, and prescribing information that can be improved to promote the safe use of the product. We provide our recommendations in Section 4.1 and 4.2.

4.1 RECOMMENDATIONS FOR THE DIVISION

A. Prescribing Information

1. Consider replacing the symbols “≥” with its intended meaning to prevent misinterpretation and confusion^b.

4.2 RECOMMENDATIONS FOR INTERSECT ENT

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

A. All Label and Labeling

1. Update the placeholder on the labels and labeling to include the conditionally acceptable proprietary name, ‘Sinuva’.
2. Ensure that the established name is at least ½ the size of the proprietary name and in accordance with 21 CFR 201.10(g)(2).

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

^b <http://www.ismp.org/tools/errorproneabbreviations.pdf>

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Sinuva that Intersect ENT submitted on March 7, 2017.

Table 2. Relevant Product Information for Sinuva	
Initial Approval Date	N/A
Active Ingredient	Mometasone Furoate
Indication	Treatment of (b) (4) polyps, in patients 18 years of age and older who have had ethmoid sinus surgery
Route of Administration	Ethmoid sinuses
Dosage Form	Sinus Implant
Strength	1350 mcg
Dose and Frequency	Single-use
How Supplied	The Sinus Implant kit consists of an individual inside of a crimper and one Disposable delivery system packaged in a foil pouch
Storage	20°C –25°C (68°F –77°F); excursions permitted at 15°C – 30°C (59°F –86°F) [see USP Controlled Room Temperature].

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,^c along with postmarket medication error data, we reviewed the following Sinuva labels and labeling submitted by Intersect ENT on March 7, 2017.

- Container label
- Carton labeling
- Prescribing Information (Image not shown)

G.2 Label and Labeling Images

(b) (4)



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^c Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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/s/

LISSA C OWENS
10/30/2017

SARAH K VEE
11/08/2017

CLINICAL INSPECTION SUMMARY

Date	August 30, 2017
From	Min Lu, M.D., M.P.H., Medical Officer Janice Pohlman, M.D., M.P.H., Team Leader Kassa Ayalew, M.D., M.P.H., Branch Chief Good Clinical Practice Assessment Branch (GCPAB) Division of Clinical Compliance Evaluation (DCCE) Office of Scientific Investigations (OSI)
To	Miya Paterniti, M.D., Medical Officer Banu Karimi-Shah, M.D., Clinical Team Leader Nina Ton, Pharm. D., Regulatory Project Manager Division of Pulmonary, Allergy, and Rheumatology Products (DPARP)
NDA	NDA 209310
Applicant	Intersect ENT, Inc.
Drug	Mometasone Furoate Sinus Implant
NME	No
Therapeutic Classification	Combination product of corticosteroid and device
Proposed Indication	Treatment of (b) (4) polyps, in patients ≥ 18 years of age who have had ethmoid sinus surgery
Consultation Request Date	May 4, 2017
Summary Goal Date	September 5, 2017
Action Goal Date	January 5, 2018
PDUFA Date	January 7, 2018

1. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

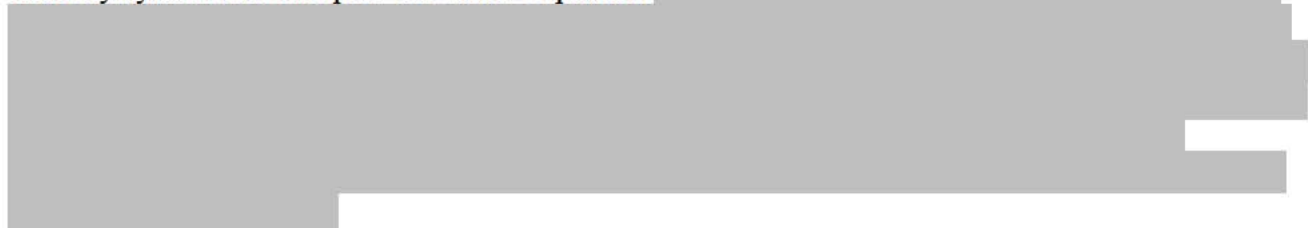
Two clinical sites (Drs. Silvers and Gould) were selected for inspection for Protocol P500-1113, a Phase 3, multicenter, randomized, single-blind, parallel-group study to evaluate the safety and efficacy of Mometasone Furoate Sinus Implant in adult patients with chronic sinusitis and recurrent sinus obstruction. The study data derived from these clinical sites, based on the inspections, are considered acceptable in support of the requested indication under this NDA.

The final classification for inspection for Dr. Gould's site is No Action Indicated (NAI). The preliminary classification of Dr. Silvers's site is NAI. Preliminary classifications are based on communications with the ORA investigator. Inspection classification becomes final when the Establishment Inspection Report is received from the field, has been reviewed, and a letter is issued to the inspected entity. A clinical inspection summary addendum will be provided if

review of the inspection report(s) indicates significant change in the classification for the inspection.

2. BACKGROUND

Mometasone Furoate Sinus Implant (S8 Sinus Implant) is a combination product (drug/device), comprised of a self-expanding, bioabsorbable, drug eluting implant, and is provided with a single-use delivery system and crimper. The sinus implant is (b) (4)



The sponsor submitted this NDA as a 505(b)(2) application for Mometasone Furoate Sinus Implant for the indication for the treatment of (b) (4) polyps, in adult patients who have had ethmoid sinus surgery. The application references Asmanex Twisthaler (mometasone furoate inhalation powder) as a listed drug that was previously approved for the treatment of asthma.

The sponsor submitted a Phase 3 clinical trial (RESOLVE II) to support the proposed indication. In review of this NDA, CDER/DPARP requests two clinical sites for inspections for the RESOLVE II Study based on enrollment of a relatively large number of study subjects and efficacy results from these sites.

Protocol P500-1113

This was a Phase 3, multicenter, randomized, single-blind, parallel-group study to evaluate the safety and efficacy of Mometasone Furoate Sinus Implant in adult patients with chronic sinusitis and recurrent sinus obstruction.

The primary objective of the study was to assess the safety and efficacy of the steroid-releasing S8 Sinus Implant when used in post-sinus surgery patients who present with recurrent sinus obstruction due to polyposis.

The study had co-primary efficacy endpoints that included change from baseline to Day 30 in Nasal Obstruction/Congestion score as determined by patients using a daily diary; and change from baseline to Day 90 in bilateral polyp grade as determined from video-endoscopies reviewed by an independent panel of 3 sinus surgeons who were masked to treatment assignment.

The study's main eligibility criteria included adult patients diagnosed with chronic rhinosinusitis (CRS) who underwent bilateral total ethmoidectomy at least 90 days prior to screening and had Nasal Obstruction/Congestion score of at least 2 (scale from 0 to 3), despite use of topical intranasal steroid irrigations or sprays for at least 14 days preceding scoring; who were indicated for repeat endoscopic

sinus surgery (ESS) based on pre-specified clinical symptoms and endoscopic evidence of bilateral sinus obstruction due to polypoid (minimum grade 2 on each side, as determined by an independent reviewer based on video-endoscopy review). Also, in the opinion of the physician, both S8 Sinus Implant and sham procedures were technically feasible bilaterally (able to pass 7 mm diameter implant into middle meatus on both sides).

Patients meeting eligibility were randomized in a 2:1 ratio to either a treatment or control group, respectively. Patients in the treatment group underwent an in-office bilateral placement of the S8 Sinus Implant in the ethmoid sinuses. Patients in the control group underwent an in-office bilateral sham procedure, consisting of advancement of a delivery system with the S8 Sinus Implant into the ethmoid sinuses followed by removal without deployment. Patients returned for 4 follow-up visits at Days 14, 30, 60, and 90. Follow-up assessment included real-time endoscopic grading and patient-reported outcomes using instantaneous daily diary and reflective paper questionnaires, documentation of concomitant medications, and elicitation of adverse events (AEs).

The study randomized 300 subjects from 34 clinical sites in the United States. The first subject enrolled on December 23, 2014 and the last subject completed the follow-up visit on August 29, 2016.

3. RESULTS (by site):

Name of CI, Address	Site #, Protocol #, and # of Subjects	Inspection Date	Classification
Stacey Silvers, M.D. Madison ENT & Facial Plastic Surgery 161 Madison Avenue, Suite 11W New York, New York 10016	Site #31 Protocol P500-1113 (RESOLVE II) Number of Subjects: 33	July 25-28, 2017	Pending Preliminary classification NAI
Andrew Gould, M.D. Advanced ENT and Allergy 4004 Dupont Circle, Suite 220 Louisville, Kentucky 40207	Site #03 Protocol P500-1113 (RESOLVE II) Number of Subjects: 20	June 15-19, 2017	NAI

Key to Compliance Classifications

NAI (No Action Indicated) = No deviation from regulations.

VAI (Voluntary Action Indicated) = Deviation(s) from regulations.

OAI (Official Action Indicated) = Significant deviations from regulations. Data unreliable.

Pending = Preliminary classification based on information in 483 or preliminary communication with the field; EIR has not been received from the field, and complete review of EIR is pending. Final classification occurs when the post-inspectional letter has been sent to the inspected entity.

Clinical Study Site Investigators

1. Stacey Silvers, M.D. (Site #31, New York, NY)

The site screened 54 subjects and enrolled 33 subjects for Study Protocol P500-1113. An audit of 33 enrolled subjects' records was conducted. All 33 enrolled subjects completed the study.

The inspection evaluated the following documents: source records, screening and enrollment logs, case report forms, electronic files, study drug accountability logs, study monitoring visits, and correspondence. Informed consent documents and sponsor-generated correspondence were also inspected. Source documents for enrolled subjects whose records were reviewed were verified against the case report forms and NDA subject line listings. There were no limitations during conduct of the clinical site inspection.

For the co-primary efficacy endpoint of change from baseline to Day 30 in Nasal Obstruction/ Congestion score as determined by patients using a daily diary, source document data for all 33 enrolled subjects were verified against the data listings and no discrepancies were noted. For the co-primary efficacy endpoint of change from baseline to Day 90 in bilateral polyp grade as determined from video-endoscopies reviewed by an independent panel of sinus surgeons, the source documents are not located at the site. The field investigator verified the endoscopic grading at baseline and at Day 90 determined by investigators in 12 out of 22 subjects who receive S8 Sinus Implant, which are comparable to the endoscopic grading assessed by independent review panel. For secondary efficacy endpoint of Reflective Nasal Obstruction/ Congestion Score, source document data were verified for 22 subjects at the site who received the S8 Sinus Implant and no discrepancies were noted. No under-reporting of adverse events or serious adverse events were noted.

In general, this clinical site appeared to be in compliance with Good Clinical Practices. Data submitted by this clinical site appear acceptable in support of this specific indication.

2. Andrew Gould, M.D. (Site #03, Louisville, Kentucky)

The site screened 29 subjects and enrolled 20 subjects for Study Protocol KRX-0502-306. An audit of all 20 enrolled subjects' records was conducted. Among the 20 enrolled subjects, 19 subjects completed the study and one subject discontinued from the study. The reason for discontinuation is due to subject's withdrawal after surgery.

The inspection evaluated the following documents: source records, screening and enrollment logs, case report forms, study drug accountability logs, study monitoring visits, and correspondence. Informed consent documents and sponsor-generated correspondence were also inspected. Source documents for enrolled subjects whose records were reviewed were verified against the case report forms and NDA subject line listings. There were no limitations during conduct of the clinical site inspection.

Source documents for the raw data used to assess the primary study endpoint were verifiable at the study site. No under-reporting of adverse events were noted.

In general, this clinical site appeared to be in compliance with Good Clinical Practices. A Form FDA 483 (Inspectional Observations) was not issued. Data submitted by this clinical site appear acceptable in support of this specific indication.

{See appended electronic signature page}

Min Lu, M.D., M.P.H.
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CONCURRENCE:

{See appended electronic signature page}

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

CONCURRENCE:

{See appended electronic signature page}

Kassa Ayalew, M.D.
Branch Chief, Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

cc:

Central Doc. Rm.
Review Division /Medical Team Leader/ Banu Karimi-Shah
Review Division/Medical Officer/ Miya Paterniti
Review Division /Project Manager/ Nina Ton
OSI/DCCE/ Division Director/Ni Khin
OSI/DCCE/Branch Chief/Kassa Ayalew
OSI/DCCE/Team Leader/ Susan Thompson
OSI/DCCE/Team Leader/Janice Pohlman
OSI/DCCE/GCP Reviewer/Min Lu
OSI/ GCP Program Analyst/Yolanda Patague

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/s/

MIN LU
08/30/2017

SUSAN D THOMPSON
08/30/2017

KASSA AYALEW
08/31/2017

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

Complete for all new NDAs, BLAs, Efficacy Supplements, and PLR Conversion Labeling Supplements

Application: NDA 209310

Application Type: New NDA

Drug Name(s)/Dosage Form(s): Mometasone Furoate Sinus Implant, 1350 mcg

Applicant: Intersect ENT, Inc.

Receipt Date: March 7, 2017

Goal Date: January 7, 2018

1. Regulatory History and Applicant's Main Proposals

Intersect ENT submitted a new drug application for mometasone furoate, a corticosteroid-eluting implant, indicated for (b) (4) polyps, in patients 18 years of age and older.

2. Review of the Prescribing Information

This review is based on the applicant's 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 of Prescribing Information (SRPI)" checklist (see Section 4 of this review).

3. Conclusions/Recommendations

SRPI format deficiencies were identified in the review of this PI. For a list of these deficiencies, see Section 4 of this review.

All SRPI format deficiencies of the PI will be conveyed to the applicant in the 74-day letter. The applicant will be asked to correct these deficiencies and resubmit the PI in Word format by June 2, 2017. The resubmitted PI will be used for further labeling review.

Selected Requirements of Prescribing Information

4. Selected Requirements of Prescribing Information

The Selected Requirement of Prescribing Information (SRPI) is a 41-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.

Highlights

See Appendix for a sample tool illustrating Highlights format.

HIGHLIGHTS GENERAL FORMAT

- YES** 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:** 10-point font*
- NO** 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:** The length of HL is longer than one-half page*
- NO** 3. A horizontal line must separate:
 - HL from the Table of Contents (TOC), **and**
 - TOC from the Full Prescribing Information (FPI).***Comment:** There is no horizontal line to separate Highlights from the Table of Contents and Table of Contents from the Full Prescribing Information*
- YES** 4. All headings in HL (from Recent Major Changes to Use in Specific Populations) must be **bolded** and presented in the center of a horizontal line. (Each horizontal line should extend over the entire width of the column.) The HL headings (from Recent Major Changes to Use in Specific Populations) should be in UPPER CASE letters. See Appendix for HL format.
Comment:
- YES** 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 for HL format.
Comment:
- YES** 6. Each summarized statement or topic in HL must reference the section(s) or subsection(s) of the 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:
- NO** 7. Headings in HL must be presented in the following order:

Selected Requirements of Prescribing Information

Heading	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 five labeling sections in the FPI: BOXED WARNING, INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, and WARNINGS AND PRECAUTIONS.

Comment: There is no revision date

HIGHLIGHTS DETAILS

Highlights Heading

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

Comment:

Highlights Limitation Statement

- YES** 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:

Product Title in Highlights

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

Comment:

Initial U.S. Approval in Highlights

- YES** 11. Initial U.S. Approval 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:

Selected Requirements of Prescribing Information

- N/A** 13. The BW must have a title in UPPER CASE, following the word “**WARNING**” and other words to identify the subject of the warning. Even if there is more than one warning, the term “**WARNING**” and not “**WARNINGS**” should be used. For example: “**WARNING: SERIOUS INFECTIONS and ACUTE HEPATIC FAILURE**”. If there is more than one warning in the BW title, the word “and” in lower case can separate the warnings. The BW title 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 must be placed immediately beneath the BW title, and should be centered 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 title 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 five sections of the FPI: BOXED WARNING, INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, and WARNINGS AND PRECAUTIONS. Labeling sections for RMC must be listed in the same order in HL as they appear in the 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) --- 8/2015.”

Comment:

- N/A** 18. A changed section must be listed under the RMC heading for at least one year after the date of the labeling change and must be removed at the first printing subsequent to the one year period. (No listing should be one year older than the revision date.)

Comment:

Dosage Forms and Strengths in Highlights

- N/A** 19. For a product that has more than one dosage form (e.g., capsules, tablets, injection), bulleted headings should be used.

Comment:

Contraindications in Highlights

YES

Selected Requirements of Prescribing Information

20. All contraindications listed in the FPI must also be listed in HL. If there is more than one contraindication, each contraindication should be bulleted. If no contraindications are known, must include the word “None.”

Comment:

Adverse Reactions in Highlights

- YES** 21. 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 which should be a toll-free number) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.**”

Comment:

Patient Counseling Information Statement in Highlights

- YES** 22. 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:

- **See 17 for PATIENT COUNSELING INFORMATION**

If a product **has (or will have)** 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

- NO** 23. The revision date must be at the end of HL, and should be **bolded** and right justified (e.g., “**Revised: 8/2015**”).

Comment:

Selected Requirements of Prescribing Information

Contents: Table of Contents (TOC)

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

- NO** 24. The TOC should be in a two-column format.
***Comment:** TOC is not in a two-column format*
- YES** 25. 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** 26. The same title 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** 27. In the TOC, all section headings must be **bolded** and should be in UPPER CASE.
Comment:
- YES** 28. 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 (for, of, to) and articles (a, an, the), or conjunctions (or, and)].
Comment:
- YES** 29. The section and subsection headings in the TOC must match the section and subsection headings in the FPI.
Comment:
- YES** 30. If a section or subsection required by regulation [21 CFR 201.56(d)(1)] is omitted from the FPI, the numbering in the TOC must not change. The heading “**FULL PRESCRIBING INFORMATION: CONTENTS***” must be followed by an asterisk and the following statement must appear at the end of the 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

31. 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.

BOXED WARNING
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
6 ADVERSE REACTIONS
7 DRUG INTERACTIONS
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation (if not required to be in Pregnancy and Lactation Labeling Rule (PLLR) format, use "Labor and Delivery")
8.3 Females and Males of Reproductive Potential (if not required to be in PLLR format, use "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 (by guidance)
12.5 Pharmacogenomics (by guidance)
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
13.2 Animal Toxicology and/or Pharmacology
14 CLINICAL STUDIES
15 REFERENCES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

Comment:

YES

32. 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)*]."

Comment:

Selected Requirements of Prescribing Information

- N/A** 33. For each RMC listed in HL, the corresponding new or modified text in the FPI must be marked with a vertical line on the left edge.

Comment:

FULL PRESCRIBING INFORMATION DETAILS

FPI Heading

- YES** 34. The following heading “**FULL PRESCRIBING INFORMATION**” must be **bolded**, must appear at the beginning of the FPI, and should be in UPPER CASE.

Comment:

BOXED WARNING Section in the FPI

- N/A** 35. All text in the BW should be **bolded**.

Comment:

- N/A** 36. The BW must have a title in UPPER CASE, following the word “**WARNING**” and other words to identify the subject of the warning. (Even if there is more than one warning, the term, “**WARNING**” and not “**WARNINGS**” should be used.) For example: “**WARNING: SERIOUS INFECTIONS and ACUTE HEPATIC FAILURE**”. If there is more than one warning in the BW title, the word “and” in lower case can separate the warnings.

Comment:

CONTRAINDICATIONS Section in the FPI

- N/A** 37. If no Contraindications are known, this section must state “None.”

Comment:

ADVERSE REACTIONS Section in the FPI

- YES** 38. When clinical trials adverse reactions data are included (typically in the “Clinical Trials Experience” subsection), the following verbatim statement (or appropriate modification) should precede the presentation of adverse reactions from clinical trials:

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

“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:

Selected Requirements of Prescribing Information

PATIENT COUNSELING INFORMATION Section in the FPI

NO 40. Must reference any FDA-approved patient labeling in Section 17 (PATIENT COUNSELING INFORMATION). The reference statement should appear at the beginning of Section 17 and include the type(s) of FDA-approved patient labeling (e.g., Patient Information, Instructions for Use, or Medication Guide). Recommended language for the reference statement should include one of the following five verbatim statements that is most applicable:

- Advise the patient to read the FDA-approved patient labeling (Patient Information).
- Advise the patient to read the FDA-approved patient labeling (Instructions for Use).
- Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).
- Advise the patient to read the FDA-approved patient labeling (Medication Guide).
- Advise the patient to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

Comment: *This statement is included: Advise the patient to read the Patient Card*

N/A 41. FDA-approved patient labeling (e.g., Patient Information, Instructions for Use, or Medication Guide) 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: Highlights and Table of Contents Format

HIGHLIGHTS OF PRESCRIBING INFORMATION

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

PROPRIETARY NAME (non-proprietary name) dosage form, route of administration, controlled substance symbol
Initial U.S. Approval: YYYY

WARNING: TITLE OF WARNING

See full prescribing information for complete boxed warning.

- Text (4)
- Text (5.x)

RECENT MAJOR CHANGES

Section Title, Subsection Title (x.x) M/201Y
Section Title, Subsection Title (x.x) M/201Y

INDICATIONS AND USAGE

PROPRIETARY NAME is a (insert FDA established pharmacologic class text phrase) indicated for ... (1)

Limitations of Use: Text (1)

DOSAGE AND ADMINISTRATION

- Text (2.x)
- Text (2.x)

DOSAGE FORMS AND STRENGTHS

Dosage form(s); strength(s) (3)

CONTRAINDICATIONS

- Text (4)
- Text (4)

WARNINGS AND PRECAUTIONS

- Text (5.x)
- Text (5.x)

ADVERSE REACTIONS

Most common adverse reactions (incidence > x%) are text (6.x)

To report **SUSPECTED ADVERSE REACTIONS**, contact name of manufacturer at toll-free phone # or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Text (7.x)
- Text (7.x)

USE IN SPECIFIC POPULATIONS

- Text (8.x)
- Text (8.x)

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

Revised: M/201Y

FULL PRESCRIBING INFORMATION: CONTENTS*

WARNING: TITLE OF WARNING

1 INDICATIONS AND USAGE

2 DOSAGE AND ADMINISTRATION

2.1 Subsection Title

2.2 Subsection Title

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

5.1 Subsection Title

5.2 Subsection Title

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

6.2 Immunogenicity

6.2 or 6.3 Postmarketing Experience

7 DRUG INTERACTIONS

7.1 Subsection Title

7.2 Subsection Title

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

8.2 Lactation (if not required to be in PLLR format use Labor and Delivery)

8.3 Females and Males of Reproductive Potential (if not required to be in PLLR format use Nursing Mothers)

8.4 Pediatric Use

8.5 Geriatric Use

8.6 Subpopulation X

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 Subsection Title

14.2 Subsection Title

15 REFERENCES

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

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

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

/s/

PHUONG N TON
05/19/2017

LADAN JAFARI
05/19/2017

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		
NDA # 209310 BLA#	NDA Supplement #: S- BLA Supplement #: S-	Efficacy Supplement Category: <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)
Proprietary Name: Sinuva (under review) Established/Proper Name: Mometasone Furoate Dosage Form: Sinus implant Strengths: 1350 mcg Route of Administration: Intranasal		
Applicant: Intersect ENT, Inc. Agent for Applicant (if applicable):		
Date of Application: March 7, 2017 Date of Receipt: March 7, 2017 Date clock started after Unacceptable for Filing (UN):		
PDUFA Goal Date: January 7, 2018		Action Goal Date (if different): January 5, 2018
Filing Date: May 6, 2017		Date of Filing Meeting: April 27, 2017
Chemical Classification (original NDAs only) : <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 checked="" type="checkbox"/> Type 3- New Dosage Form; New Dosage Form and New Combination <input type="checkbox"/> Type 4- New Combination <input type="checkbox"/> Type 5- New Formulation or New Manufacturer <input type="checkbox"/> Type 7- Drug Already Marketed without Approved NDA <input type="checkbox"/> Type 8- Partial Rx to OTC Switch <input type="checkbox"/> Type 9-New Indication or Claim (will <u>not</u> be marketed as a separate NDA after approval) <input type="checkbox"/> Type 10-New Indication or Claim (will be marketed as a separate NDA after approval)		
Proposed indication(s)/Proposed change(s): Treatment of (b) (4) polyps, in patients ≥ 18 years of age who have had ethmoid sinus surgery		
Type of Original NDA: AND (if applicable) Type of NDA Supplement:		<input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> 505(b)(2) <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)
<i>If 505(b)(2)NDA/NDA Supplement: Draft the “505(b)(2) Assessment” review found at:</i> http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/UCM027499		
Type of BLA <i>If 351(k), notify the OND Therapeutic Biologics and Biosimilars Team</i>		<input type="checkbox"/> 351(a) <input type="checkbox"/> 351(k)

Review Classification: <i>The application will be a priority review if:</i> <ul style="list-style-type: none"> 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) The product is a Qualified Infectious Disease Product (QIDP) A Tropical Disease Priority Review Voucher was submitted A Pediatric Rare Disease Priority Review Voucher was submitted 		<input checked="" type="checkbox"/> Standard <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		
Resubmission after withdrawal? <input type="checkbox"/>		Resubmission after refuse to file? <input type="checkbox"/>		
Part 3 Combination Product? <input checked="" type="checkbox"/> <i>If yes, contact the Office of Combination Products (OCP) and copy them on all Inter-Center consults</i>		<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 checked="" 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)		
<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: <ul style="list-style-type: none"> <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) 		
Collaborative Review Division (if OTC product):				
List referenced IND Number(s): 116042				
Goal Dates/Product Names/Classification Properties	YES	NO	NA	Comment
PDUFA/BsUFA and Action Goal dates correct in the electronic archive? <i>If no, ask the document room staff to correct them immediately. These are the dates used for calculating inspection dates.</i>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
Are the established/proper and applicant names correct in electronic archive? <i>If no, ask the document room staff to make the corrections. Also, ask the document room staff to add the established/proper name to the supporting IND(s) if not already entered into electronic archive.</i>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		

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> http://inside.fda.gov:9003/CDER/OfficeofBusinessProcessSupport/ucm163969.htm <i>If no, ask the document room staff to make the appropriate entries.</i>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Application Integrity Policy	YES	NO	NA	Comment
Is the application affected by the Application Integrity Policy (AIP)? <i>Check the AIP list at:</i> http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm <i>If yes, explain in comment column.</i>	<input type="checkbox"/>	<input checked="" type="checkbox"/>		
If affected by AIP, has OC been notified of the submission? If yes, date notified:	<input type="checkbox"/>	<input type="checkbox"/>		
User Fees	YES	NO	NA	Comment
Is Form 3397 (User Fee Cover Sheet)/Form 3792 (Biosimilar User Fee Cover Sheet) included with authorized signature?	<input checked="" type="checkbox"/>	<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 from receipt. Review stops. Contact the User Fee Staff. If appropriate, send UN letter.</i>	Payment for this application (<i>check daily email from UserFeeAR@fda.hhs.gov:</i>): <input type="checkbox"/> Paid <input type="checkbox"/> Exempt (orphan, government) <input checked="" 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. Contact the User Fee Staff. If appropriate, send UN letter.</i>	Payment of other user fees: <input checked="" type="checkbox"/> 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> http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079320.pdf	Has the user fee bundling policy been appropriately applied? <i>If no, or you are not sure, consult the User Fee Staff.</i> <input checked="" type="checkbox"/> 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? (<i>Check the 356h form, cover letter, and annotated labeling</i>). If yes, answer the bulleted questions below:	<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"/>		

<ul style="list-style-type: none"> 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"/>																		
<ul style="list-style-type: none"> 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)]? <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>	<input type="checkbox"/>	<input checked="" type="checkbox"/>																		
<ul style="list-style-type: none"> Is there unexpired exclusivity on another listed drug product containing the same active moiety (e.g., 5-year, 3-year, orphan, or pediatric exclusivity)? <p>Check the Electronic Orange Book at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm</p> <p>If yes, please list below:</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> </td><td> </td><td> </td><td> </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													<input type="checkbox"/>	<input checked="" type="checkbox"/>		
Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration																	
<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 and GAIN exclusivity will extend both of the timeframes in this provision by 6 months and five years, respectively. 21 CFR 314.108(b)(2). Unexpired orphan or 3-year exclusivity may block the approval but not the submission of a 505(b)(2) application.</i></p>																				
<ul style="list-style-type: none"> If FDA has approved one or more pharmaceutically equivalent (PE) products in one or more NDAs before the submission date of the original 505(b)(2) application, did the applicant identify one such product as a listed drug (or an additional listed drug) relied upon and provide an appropriate patent certification or statement [see 21 CFR 314.50(i)(1)(i)(C) and 314.54]? <p>Check the Electronic Orange Book at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm</p> <p>If no, include template language in the 74-day letter.</p> <p>Failure to identify a PE is an approvability issue but not a filing issue [see 21 CFR 314.125(b)(19)]</p> <p>Note: Pharmaceutical equivalents are drug products in identical dosage forms and route(s) 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; <u>and</u> (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.</p>	<input checked="" type="checkbox"/>	<input type="checkbox"/>																		

Exclusivity	YES	NO	NA	Comment
Does another product (same active moiety) have orphan exclusivity for the same indication? <i>Check the Orphan Drug Designations and Approvals list at: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm</i>	<input type="checkbox"/>	<input checked="" type="checkbox"/>		
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)(14)]? <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"/>	
NDAs/NDA efficacy supplements only: Has the applicant requested 5-year or 3-year Waxman-Hatch exclusivity? If yes, # years requested: 3 <i>Note: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.</i>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
NDAs only: Is the proposed product a single enantiomer of a racemic drug previously approved for a different therapeutic use?	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	
If yes , did the applicant: (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)? <i>If yes, contact the Orange Book Staff (CDER-Orange Book Staff).</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
BLAs only: Has the applicant requested 12-year exclusivity under section 351(k)(7) of the PHS Act? <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>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	

Format and Content				
<p><i>Do not check mixed submission if the only electronic component is the content of labeling (COL).</i></p>	<input type="checkbox"/> All paper (except for COL) <input checked="" type="checkbox"/> All electronic <input type="checkbox"/> Mixed (paper/electronic) <input checked="" type="checkbox"/> CTD <input type="checkbox"/> Non-CTD <input type="checkbox"/> Mixed (CTD/non-CTD)			
<p>If mixed (paper/electronic) submission, which parts of the application are submitted in electronic format?</p>				
Overall Format/Content	YES	NO	NA	Comment
<p>If electronic submission, does it follow the eCTD guidance?¹ If not, explain (e.g., waiver granted).</p>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<p>Index: Does the submission contain an accurate comprehensive index?</p>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
<p>Is the submission complete as required under 21 CFR 314.50 (<i>NDA</i>s/<i>NDA</i> efficacy supplements) or under 21 CFR 601.2 (<i>BLA</i>s/<i>BLA</i> efficacy supplements) including:</p> <p><input checked="" type="checkbox"/> legible <input checked="" type="checkbox"/> English (or translated into English) <input checked="" type="checkbox"/> pagination <input checked="" type="checkbox"/> navigable hyperlinks (electronic submissions only)</p> <p>If no, explain.</p>	<input type="checkbox"/>	<input type="checkbox"/>		
<p>BLAs only: Companion application received if a shared or divided manufacturing arrangement?</p> <p>If yes, BLA #</p>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Forms and Certifications				
<p><i>Electronic forms and certifications with electronic signatures (scanned, digital, or electronic – similar to DARRTS, e.g., /s/) are acceptable. Otherwise, paper forms and certifications with hand-written signatures must be included. Forms include: user fee cover sheet (3397/3792), application form (356h), patent information (3542a), financial disclosure (3454/3455), and clinical trials (3674); Certifications include: debarment certification, patent certification(s), field copy certification, and pediatric certification.</i></p>				
Application Form	YES	NO	NA	Comment
<p>Is form FDA 356h included with authorized signature per 21 CFR 314.50(a)?</p> <p><i>If foreign applicant, a U.S. agent must sign the form [see 21 CFR 314.50(a)(5)].</i></p>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
<p>Are all establishments and their registration numbers listed on the form/attached to the form?</p>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

¹ <http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm333969.pdf>

Patent Information (NDAs/NDA efficacy supplements only)	YES	NO	NA	Comment
Is patent information submitted on form FDA 3542a per 21 CFR 314.53(c)?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Financial Disclosure	YES	NO	NA	Comment
Are financial disclosure forms FDA 3454 and/or 3455 included with authorized signature per 21 CFR 54.4(a)(1) and (3)? <i>Forms must be signed by the APPLICANT, not an Agent [see 21 CFR 54.2(g)].</i> <i>Note: Financial disclosure is required for bioequivalence studies that are the basis for approval.</i>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
Clinical Trials Database	YES	NO	NA	Comment
Is form FDA 3674 included with authorized signature? <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>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
Debarment Certification	YES	NO	NA	Comment
Is a correctly worded Debarment Certification included with authorized signature? <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&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>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Field Copy Certification (NDAs/NDA efficacy supplements only)	YES	NO	NA	Comment
For paper submissions only: Is a Field Copy Certification (that it is a true copy of the CMC technical section) included? <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>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	

Controlled Substance/Product with Abuse Potential	YES	NO	NA	Comment
<p><u>For NMEs:</u> Is an Abuse Liability Assessment, including a proposal for scheduling, submitted per 21 CFR 314.50(d)(5)(vii)?</p> <p><i>If yes, date consult sent to the Controlled Substance Staff:</i></p> <p><u>For non-NMEs:</u> <i>Date of consult sent to Controlled Substance Staff:</i></p>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
Pediatrics	YES	NO	NA	Comment
<p><u>PREA</u></p> <p>Does the application trigger PREA?</p> <p><i>If yes, notify PeRC@fda.hhs.gov to schedule required PeRC meeting²</i></p> <p><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 & deferral requests, pediatric plans, and pediatric assessment studies must be reviewed by PeRC prior to approval of the application/supplement.</i></p>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
<p>If the application triggers PREA, is there an agreed Initial Pediatric Study Plan (iPSP)?</p> <p><i>If no, may be an RTF issue - contact DPMH for advice.</i></p>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<p>If required by the agreed iPSP, are the pediatric studies outlined in the agreed iPSP completed and included in the application?</p> <p><i>If no, may be an RTF issue - contact DPMH for advice.</i></p>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	
<p><u>BPCA:</u></p> <p>Is this submission a complete response to a pediatric Written Request?</p> <p><i>If yes, notify Pediatric Exclusivity Board RPM (pediatric exclusivity determination is required³</i></p>	<input type="checkbox"/>	<input checked="" type="checkbox"/>		

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

3

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

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Proprietary Name	YES	NO	NA	Comment
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>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
REMS	YES	NO	NA	Comment
Is a REMS submitted? <i>If yes, send consult to OSE/DRISK and notify OC/OSL/DSC/PMSB via the CDER OSI RMP mailbox</i>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	
Prescription Labeling	<input type="checkbox"/> Not applicable			
Check all types of labeling submitted.	<input checked="" type="checkbox"/> Package Insert (Prescribing Information)(PI) <input type="checkbox"/> Patient Package Insert (PPI) <input type="checkbox"/> Instructions for Use (IFU) <input type="checkbox"/> Medication Guide (MedGuide) <input checked="" type="checkbox"/> Carton labeling <input checked="" type="checkbox"/> Immediate container labels <input type="checkbox"/> Diluent labeling <input checked="" type="checkbox"/> Other (specify) Patient Information			
	YES	NO	NA	Comment
Is Electronic Content of Labeling (COL) submitted in SPL format? <i>If no, request applicant to submit SPL before the filing date.</i>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
Is the PI submitted in Physician Labeling Rule (PLR) format? ⁴	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
If PI not submitted in PLR format , was a waiver or deferral requested before the application was received or in the submission? If requested before application was submitted , what is the status of the request? <i>If no waiver or deferral, request applicant to submit labeling in PLR format before the filing date.</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
For applications submitted on or after June 30, 2015: Is the PI submitted in Pregnancy and Lactation Labeling Rule (PLLR) format? Has a review of the available pregnancy, lactation, and females and males of reproductive potential data (if applicable) been included?	<input type="checkbox"/> <input type="checkbox"/>	<input checked="" type="checkbox"/> <input checked="" type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>	We are requesting it in the 74-day letter.
For applications submitted on or after June 30, 2015: If PI not submitted in PLLR format , was a waiver or deferral requested before the application was received or in the submission? If requested before application was submitted , what is the status of the request? <i>If no waiver or deferral, request applicant to submit labeling in PLLR format before the filing date.</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

⁴ <http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/LabelingDevelopmentTeam/ucm025576.htm>

Has all labeling [(PI, patient labeling (PPI, MedGuide, IFU), carton and immediate container labeling)] been consulted to OPDP?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Has PI and patient labeling (PPI, MedGuide, IFU) been consulted to OSE/DRISK? (<i>send WORD version if available</i>)	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Patient labeling consult is not needed
Has all labeling [PI, patient labeling (PPI, MedGuide, IFU) carton and immediate container labeling, PI, PPI been consulted/sent to OSE/DMEPA and appropriate CMC review office in OPQ (OBP or ONDP)?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
OTC Labeling	<input checked="" type="checkbox"/> Not Applicable			
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 <input type="checkbox"/> Other (specify)			
	YES	NO	NA	Comment
Is electronic content of labeling (COL) submitted?	<input checked="" 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 checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Other Consults	YES	NO	NA	Comment
Are additional consults needed? (e.g., IFU to CDRH; QT study report to QT Interdisciplinary Review Team)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<i>If yes, specify consult(s) and date(s) sent: CDRH Engineering Consult sent 3/22/2017</i>				
Meeting Minutes/SPAs	YES	NO	NA	Comment
End-of Phase 2 meeting(s)? Date(s): October 2, 2014 (IND 116042)	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
Pre-NDA/Pre-BLA/Pre-Supplement meeting(s)? Date(s):	<input type="checkbox"/>	<input checked="" type="checkbox"/>		
Any Special Protocol Assessments (SPAs)? Date(s):	<input type="checkbox"/>	<input checked="" type="checkbox"/>		

ATTACHMENT

MEMO OF FILING MEETING

DATE: April 27, 2017

BACKGROUND: Intersect ENT submitted a new drug application for mometasone furoate, a corticosteroid-eluting implant, indicated for the treatment of (b) (4) polyps, in patients 18 years of age and older.

REVIEW TEAM:

Discipline/Organization	Names		Present at filing meeting? (Y or N)
Regulatory Project Management	RPM:	Nina Ton	Y
	CPMS/TL:	Ladan Jafari	N
Cross-Discipline Team Leader (CDTL)			
Division Director/Deputy	Badrul Chowdhury Lydia Gilbert-McClain		Y Y
Office Director/Deputy			
Clinical	Reviewer:	Miya Paterniti	Y
	TL:	Banu Karimi-Shah	Y
Social Scientist Review (for OTC products)	Reviewer:		
	TL:		
OTC Labeling Review (for OTC products)	Reviewer:		
	TL:		
Clinical Microbiology (for antimicrobial products)	Reviewer:		
	TL:		
Clinical Pharmacology	Reviewer:	Yunzhao Ren	Y
	TL:	Bavna Saluja	Y
• Genomics	Reviewer:		
• Pharmacometrics	Reviewer:		
Biostatistics	Reviewer:	Kate Meaker	Y
	TL:	Shanti Gomatam	Y

Nonclinical (Pharmacology/Toxicology)	Reviewer:	Luqi Pei	Y
	TL:	Carol Galvis	Y
Statistics (carcinogenicity)	Reviewer:		
	TL:		
Product Quality (CMC) Review Team:	ATL:	Craig Bertha	Y
	RBPM:	Florence Aisida	Y
• Drug Substance	Reviewer:	Monica Cooper	Y
• Drug Product	Reviewer:	Monica Cooper	
• Process	Reviewer:	Joanne Wang	N
• Microbiology	Reviewer:	Jason God	Y
• Facility	Reviewer:	Daniel DeCiero	N
• Biopharmaceutics	Reviewer:	Hansong Chen	N
• Immunogenicity	Reviewer:		
• Labeling (BLAs only)	Reviewer:		
• Other (e.g., Branch Chiefs, EA Reviewer)			
OMP/OMPI/DMPP (MedGuide, PPI, IFU)	Reviewer:		
	TL:		
OMP/OPDP (PI, PPI, MedGuide, IFU, carton and immediate container labeling)	Reviewer:	Kyle Snyder	N
	TL:		
OSE/DMEPA (proprietary name, carton/container labeling)	Reviewer:	Lissa Owens	Y
	TL:	Sarah Vee	N
OSE/DRISK (REMS)	Reviewer:		
	TL:		
OC/OSI/DSC/PMSB (REMS)	Reviewer:		
	TL:		

Bioresearch Monitoring (OSI)	Reviewer:	Min Lu	Y
	TL:		
Controlled Substance Staff (CSS)	Reviewer:		
	TL:		
Other reviewers/disciplines			
CDRH	Reviewer:	Joyce Lin	Y
	TL:		
Other attendees			

FILING MEETING DISCUSSION:

GENERAL <ul style="list-style-type: none"> 505(b)(2) filing issues: <ul style="list-style-type: none"> Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? Did the applicant provide a scientific “bridge” demonstrating the relationship between the proposed product and the referenced product(s)/published literature? <p>Describe the scientific bridge (e.g., information to demonstrate sufficient similarity between the proposed product and the listed drug(s) such as BA/BE studies or to justify reliance on information described in published literature):</p>		<input type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO <p>PK study Comparative bioavailability data</p>
<ul style="list-style-type: none"> Per reviewers, are all parts in English or English translation? <p>If no, explain:</p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	
<ul style="list-style-type: none"> Electronic Submission comments <p>List comments:</p>	<input type="checkbox"/> Not Applicable <input type="checkbox"/> No comments	

CLINICAL Comments:	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input checked="" type="checkbox"/> Review issues for 74-day letter
<ul style="list-style-type: none"> Clinical study site(s) inspections(s) needed? <p>If no, explain:</p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> Advisory Committee Meeting needed? <p>Comments:</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"> <i>this drug/biologic is not the first in its class</i> <i>the clinical study design was acceptable</i> <i>the application did not raise significant safety or efficacy issues</i> <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> 	<input type="checkbox"/> YES Date if known: <input checked="" type="checkbox"/> NO <input type="checkbox"/> To be determined Reason:
<ul style="list-style-type: none"> 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? <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
CONTROLLED SUBSTANCE STAFF <ul style="list-style-type: none"> Abuse Liability/Potential <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
CLINICAL MICROBIOLOGY Comments:	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter

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

<u>Facility/Microbiology Review (BLAs only)</u> Comments:	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<u>CMC Labeling Review (BLAs only)</u> Comments:	<input type="checkbox"/> Review issues for 74-day letter
APPLICATIONS IN THE PROGRAM (PDUFA V) (NME NDAs/Original BLAs) <ul style="list-style-type: none"> • 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? • If so, were the late submission components all submitted within 30 days? 	<input checked="" type="checkbox"/> N/A <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> • What late submission components, if any, arrived after 30 days? 	
<ul style="list-style-type: none"> • Was the application otherwise complete upon submission, including those applications where there were no agreements regarding late submission components? 	<input type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> • Is a comprehensive and readily located list of all clinical sites included or referenced in the application? 	<input type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> • Is a comprehensive and readily located list of all manufacturing facilities included or referenced in the application? 	<input type="checkbox"/> YES <input type="checkbox"/> NO

REGULATORY PROJECT MANAGEMENT	
Signatory Authority: Lydia Gilbert-McClain Date of Mid-Cycle Meeting (for NME NDAs/BLAs in “the Program” PDUFA V): 21st Century Review Milestones (see attached) (listing review milestones in this document is optional): Comments:	
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 type="checkbox"/> No review issues have been identified for the 74-day letter. <input checked="" type="checkbox"/> Review issues have been identified for the 74-day letter. <u>Review Classification:</u> <input checked="" type="checkbox"/> Standard Review <input type="checkbox"/> Priority Review
ACTION ITEMS	
<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 checked="" 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 ADRA's completed: April 2016

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

/s/

PHUONG N TON
05/19/2017

LADAN JAFARI
05/19/2017