

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

201923Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME 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:	July 31, 2014
Application Type and Number:	NDA 201923
Product Name and Strength:	Iluvien (Fluocinolone acetonide) Intravitreal Implant, 0.19 mg
Product Type:	Single Ingredient
Rx or OTC:	Rx
Applicant/Sponsor Name:	Alimera Sciences
Submission Date:	July 15, 2014
Panorama #:	2014-25858
DMEPA Primary Reviewer:	Rachna Kapoor, PharmD
DMEPA Team Leader:	Yelena Maslov, PharmD

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Iluvien, from a safety and promotional perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively. The Applicant submitted an external name study from the (b) (4) for this proposed proprietary name.

1.1 REGULATORY HISTORY

The sponsor previously submitted this proposed proprietary name, Iluvien on July 15, 2010. The Division of Medication Error Prevention and Analysis (DMEPA) found the name, Iluvien acceptable in OSE Review #2010-1548, dated October 13, 2010.

The proposed proprietary name must be re-reviewed since the last approval of this NDA is more than 90 days. Thus, the sponsor re-submitted the name, Iluvien, for review on July 15, 2014.

1.2 PRODUCT INFORMATION

The following product information is provided in the July 15, 2014 proprietary name submission.

- Intended pronunciation: i loo' vee en
- Active Ingredient: fluocinolone acetonide
- Indication of Use: the treatment of (b) (4) diabetic macular edema
- Route of Administration: intravitreal
- Dosage Form: intravitreal insert
- Strength: 0.19 mg
- Dose and Frequency: insert into the posterior segment of the affected eye through a pars plana insertion. It is designed to release fluocinolone acetonide at an initial rate of 0.25 mcg/day. (b) (4)
- How Supplied: a sterile single use preloaded inserter with a 25-gauge needle, packaged in a tray sealed with a (b) (4) lid
- Storage: store at 15° – 30°C (59° – 86°F)

2 RESULTS

The following sections provide information obtained and considered in the overall evaluation of the proposed proprietary name.

2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Transplant and Ophthalmology Products (DTOP) concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the name.

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proprietary name¹.

2.2.2 Components of the Proposed Proprietary Name

The Applicant stated that there is no derivation or intended meaning for the proposed name, Iluvien in their submission. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 FDA Name Simulation Studies

Sixty-one practitioners responded to DMEPA's prescription studies. The interpretations did not overlap with any currently marketed products nor did the misinterpretations sound or look similar to any currently marketed products or any products in the pipeline. In the written outpatient study, 7 of 21 participants correctly interpreted the prescription. Common misinterpretations in the written outpatient study were substitution of 'F' for 'I', 'b' for 'lu', 'r' for 'v', 'r' for 'i', and 'e', 'ir', and 'i' for 'u'. In the written inpatient study, 14 of 20 participants correctly interpreted the prescription. Common misinterpretations in the written inpatient study were substitution of 'F' for 'I', 'a' for 'e', and 'w' for 'n'. In the voice study, none of the 20 participants correctly interpreted the prescription. Common misinterpretations in the voice study include: 'e' for 'i', 'a' for 'e', 'b' for 'v', and 'ill' for 'il'.

2.2.4 Comments from Other Review Disciplines at Initial Review

In response to the OSE, July 25, 2014 e-mail, the Division of Transplant and Ophthalmology Products (DTOP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Table 1 lists the number of names with the combined orthographic and phonetic score of $\geq 50\%$ retrieved from our POCA search organized as highly similar, moderately similar or low similarity for further evaluation. Table 1 also includes names identified from the FDA Prescription Simulation.

¹USAN stem search conducted on July 25, 2014.

Table 1. POCA Search Results	Number of Names
Highly similar name pair: combined match percentage score $\geq 70\%$	2
Moderately similar name pair: combined match percentage score $\geq 50\%$ to $\leq 69\%$	263
Low similarity name pair: combined match percentage score $\leq 49\%$	0

2.2.6 Safety Analysis of Names with Potential Orthographic, Spelling, and Phonetic Similarities

Our analysis of the two hundred sixty-five names contained in Table 1 determined two hundred sixty-five names will not pose a risk for confusion as described in Appendices C through H.

2.2.7 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Transplant and Ophthalmology Products (DTOP) via e-mail on July 30, 2014. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from DTOP on July 30, 2014, they stated no additional concerns with the proposed proprietary name, Iluvien.

3 CONCLUSIONS

The proposed proprietary name is acceptable from both a promotional and safety perspective.

If you have further questions or need clarifications, please contact Karen Townsend, OSE project manager, at 301-796-5413.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Iluvien, and have concluded that this name is acceptable.

If any of the proposed product characteristics as stated in your July 15, 2014 submission are altered, the name must be resubmitted for review.

4 REFERENCES

1. **USAN Stems** (<http://www.ama-assn.org/ama/pub/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/approved-stems.page>)

USAN Stems List contains all the recognized USAN stems.

2. **Phonetic and Orthographic Computer Analysis (POCA)**

POCA is a system that FDA designed. As part of the name similarity assessment, POCA is used to evaluate proposed names via a phonetic and orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists that operates in a similar fashion. POCA is publicly accessible.

Drugs@FDA

Drugs@FDA is an FDA Web site that contains most of the drug products approved in the United States since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present.

Drugs@FDA contains official information about FDA-approved *brand name* and *generic drugs*; *therapeutic biological products*, *prescription* and *over-the-counter* human drugs; and *discontinued drugs* (see Drugs @ FDA Glossary of Terms, available at http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther_biological).

RxNorm

RxNorm contains the names of prescription and many OTC drugs available in the United States. RxNorm includes generic and branded:

- Clinical drugs – pharmaceutical products given to (or taken by) a patient with therapeutic or diagnostic intent
- Drug packs – packs that contain multiple drugs, or drugs designed to be administered in a specified sequence

Radiopharmaceuticals, contrast media, food, dietary supplements, and medical devices, such as bandages and crutches, are all out of scope for RxNorm (<http://www.nlm.nih.gov/research/umls/rxnorm/overview.html#>).

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment considers the promotional and safety aspects of a proposed proprietary name.

1. **Promotional Assessment:** For prescription drug products, the promotional review of the proposed name is conducted by OPDP. For over-the-counter (OTC) drug products, the promotional review of the proposed name is conducted by DNCE. OPDP or DNCE evaluates proposed proprietary names to determine if they are overly fanciful, so as to misleadingly imply unique effectiveness or composition, as well as to assess whether they contribute to overstatement of product efficacy, minimization of risk, broadening of product indications, or making of unsubstantiated superiority claims. OPDP or DNCE provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment:** The safety assessment is conducted by DMEPA, and includes the following:
 - a. **Preliminary Assessment:** We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.²

***Table 2- Prescreening Checklist for Proposed Proprietary Name**

	Affirmative answers to these questions indicate a potential area of concern.
Y/N	Does the name have obvious Similarities in Spelling and Pronunciation to other Names?
Y/N	Are there Manufacturing Characteristics in the Proprietary Name?
Y/N	Are there Medical and/or Coined Abbreviations in the Proprietary Name?
Y/N	Are there Inert or Inactive Ingredients referenced in the Proprietary Name?
Y/N	Does the Proprietary Name include combinations of Active Ingredients
Y/N	Is there a United States Adopted Name (USAN) Stem in the Proprietary Name?
Y/N	Is this the same Proprietary Name for Products containing Different Active Ingredients?
Y/N	Is this a Proprietary Name of a discontinued product?

² National Coordinating Council for Medication Error Reporting and Prevention.
<http://www.nccmerp.org/about/MedErrors.html>. Last accessed 10/11/2007.

- b. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@fda, CernerRxNorm, and names in the review pipeline using a 50% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:
- Highly similar pair: combined match percentage score $\geq 70\%$.
 - Moderately similar pair: combined match percentage score $\geq 50\%$ to $\leq 69\%$.
 - Low similarity: combined match percentage score $\leq 49\%$.

Using the criteria outlined in the check list (Table 3-5) that corresponds to each of the three categories (highly similar pair, moderately similar pair, and low similarity), DMEPA evaluates the name pairs to determine the acceptability or non-acceptability of a proposed proprietary name. Based on our root cause analysis of post marketing experience errors, we find the expression of strength and dose, which is often located in close proximity to the drug name itself on prescriptions and medication orders, is an important factor in mitigating or potentiating confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion is limited (e.g., route, frequency, dosage form, etc.).

- For highly similar names, there is little that can mitigate a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are likely to be rejected by FDA. (See Table 3)
- Moderately similar names with overlapping or similar strengths or doses represent an area for concern for FDA. The dosage and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics (e.g., route, frequency, dosage form, etc.) to mitigate confusion may be limited when the strength or dose overlaps. FDA will review these names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4)
- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist (See Table 5).

- c. FDA Prescription Simulation Studies: DMEPA staff also conducts a prescription simulation studies using FDA health care professionals.

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants record their interpretations of the orders which are recorded electronically.

- d. Comments from Other Review Disciplines: DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name.

Table 3. Highly Similar Name Pair Checklist (i.e., combined Orthographic and Phonetic score is $\geq 70\%$).

Answer the questions in the checklist below. Affirmative answers to these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion, provided that the pair do not share a common strength or dose (see Step 1 of the Moderately Similar Checklist).			
<u>Orthographic Checklist</u>		<u>Phonetic Checklist</u>	
Y/N	Do the names begin with different first letters? <i>Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.</i>	Y/N	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar* when scripted? <i>*FDA considers the length of names different if the names differ by two or more letters.</i>	Y/N	Do the names have different syllabic stresses?
Y/N	Considering variations in scripting of some letters (such as <i>z</i> and <i>f</i>), is there a different number or placement of upstroke/downstroke letters present in the names?	Y/N	Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?
Y/N	Is there different number or placement of cross-stroke or dotted letters present in the names?	Y/N	Across a range of dialects, are the names consistently pronounced differently?
Y/N	Do the infixes of the name appear dissimilar when scripted?		
Y/N	Do the suffixes of the names appear dissimilar when scripted?		

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is $\geq 50\%$ to $\leq 69\%$).

<p>Step 1</p>	<p>Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths have a higher potential for confusion and should be evaluated further (see Step 2).</p> <p>For single strength products, also consider circumstances where the strength may not be expressed.</p> <p>For any combination drug products, consider whether the strength or dose may be expressed using only one of the components.</p> <p>To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion:</p> <ul style="list-style-type: none"> ○ Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa. ○ Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. ○ Similar sounding doses: 15 mg is similar in sound to 50 mg
<p>Step 2</p>	<p>Answer the questions in the checklist below. Affirmative answers to these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion between moderately similar names with overlapping or similar strengths or doses.</p>

<p>Orthographic Checklist (Y/N to each question)</p> <ul style="list-style-type: none"> • Do the names begin with different first letters? <p>Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.</p> <ul style="list-style-type: none"> • Are the lengths of the names dissimilar* when scripted? <p>*FDA considers the length of names different if the names differ by two or more letters.</p> <ul style="list-style-type: none"> • Considering variations in scripting of some letters (such as <i>z</i> and <i>f</i>), is there a different number or placement of upstroke/downstroke letters present in the names? • Is there different number or placement of cross-stroke or dotted letters present in the names? • Do the infixes of the name appear dissimilar when scripted? • Do the suffixes of the names appear dissimilar when scripted? 	<p>Phonetic Checklist (Y/N to each question)</p> <ul style="list-style-type: none"> • Do the names have different number of syllables? • Do the names have different syllabic stresses? • Do the syllables have different phonologic processes, such as vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?
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Table 5: Low Similarity Name Pair Checklist (i.e., combined score is $\leq 49\%$).

In most circumstances, these names are viewed as sufficiently different to minimize confusion. Exceptions to this would occur in circumstances where there are data that suggest a name with low similarity might be vulnerable to confusion with your proposed name (for example, misinterpretation of the proposed name as a marketed product in a prescription simulation study). In such instances, FDA would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

Appendix B: Prescription Simulation Samples and Results

Figure 1. Iluvien Study (Conducted on July 24, 2014)

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Medication Order:</u></p> <p><i>Iluvien insert intravitreally in affected eye one time</i></p>	<p>Iluvien Bring to clinic Dispense: #1</p>
<p><u>Outpatient Prescription:</u></p> <p><i>Iluvien Bring to clinic #1</i></p>	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

Study Name: Iluvien

As of Date 7/29/2014

263 People Received Study

61 People Responded

Total	21	20	20	
INTERPRETATION	OUTPATIENT	VOICE	INPATIENT	TOTAL
ELLUVIAN	0	1	0	1
ELUBIAN	0	1	0	1
ELUBIEN	0	1	0	1
ELUVIAN	0	10	0	10
ELUVIEN	0	1	0	1
ELUVION	0	1	0	1
FLUVIAN	0	0	1	1
FLUVIEN	0	0	1	1
FLUVIENT	1	0	0	1
IBRIEN	1	0	0	1
ILERVIEN	1	0	0	1
ILEVIEN	1	0	0	1
ILIRVIEN	1	0	0	1
ILIVIEN	1	0	0	1
ILIVIREN	2	0	0	2
ILLUDIAN	0	1	0	1
ILLUVIAN	0	2	0	2
ILLUVIEN	0	1	0	1
ILURIEN	3	0	0	3

ILURREN	1	0	0	1
ILUVIAN	0	1	0	1
ILUVIEN	7	0	14	21
ILUVIEW	0	0	4	4
ILUVIREN	1	0	0	1
SLURREN	1	0	0	1

Appendix C: Highly Similar Names (i.e., combined POCA score is $\geq 70\%$)

No.	Proposed name: Iluvien Strength: 0.19 mg Usual Dose: Insert into the posterior segment of the affected eye through a pars plana insertion	POCA Score (%)	Orthographic and/or phonetic differences in the names sufficient to prevent confusion	Prevention of Failure Mode
1.	(b) (4)***	72	This name was denied in OSE RCM#2010-535 (ANDA 090721) (b) (4) The name approved under this ANDA is Falmina on March 28, 2012.	N/A
2.	(b) (4)			

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Appendix D: Moderately Similar Names (i.e., combined POCA score is $\geq 50\%$ to $\leq 69\%$) with no overlap or numerical similarity in Strength and/or Dose

No.	Proposed Name	POCA Score (%)
1.	Ilosone	66
2.	Ilotycin	62
3.	Isovue-M 200, Isovue-M-200, Isovue-M 300, Isovue-M-300	60, 60, 60, 60
4.	Aluvea	60
5.	Iclusig	57
6.	Iletin I, Iletin NPH	56, 54
7.	Ibudone	54
8.	Insulin	52
9.	Iophen	52

Appendix E: Moderately Similar Names (i.e., combined POCA score is $\geq 50\%$ to $\leq 69\%$) with overlap or numerical similarity in Strength and/or Dose

No.	Proposed name: Iluvien Strength: 0.19 mg Usual Dose: Insert into the posterior segment of the affected eye through a pars plana insertion	POCA Score (%)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
1.	(b) (4)		
2.	Ilopan	64	The infix of this name pair has sufficient orthographic differences. The number of syllables in both names is different. The last syllable in both names gives the names a distinctly different sound when spoken.
3.	Alophen	62	The infix of this name pair has sufficient orthographic differences. The number of syllables in both names is different. The last syllable in both names gives the names a distinctly different sound when spoken.
4.	(b) (4)		
5.	Milophene	60	The prefix and suffix of this name pair have sufficient orthographic differences. The number of syllables in both names is different. The first and last syllables in both names give the names a distinctly different sound when spoken.

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No.	Proposed name: Iluvien Strength: 0.19 mg Usual Dose: Insert into the posterior segment of the affected eye through a pars plana insertion	POCA Score (%)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
6.	Ilozyme	58	<p>The infix and suffix of this name pair have sufficient orthographic differences.</p> <p>The number of syllables in both names is different. The last syllable in both names gives the names a distinctly different sound when spoken.</p>
7.	Ibuprin	57	<p>The infix of this name pair has sufficient orthographic differences.</p> <p>All the syllables in both names give the names a distinctly different sound when spoken.</p>
8.	Isovate	56	<p>The infix and suffix of this name pair have sufficient orthographic differences.</p> <p>All the syllables in both names give the names a distinctly different sound when spoken.</p>
9.	Luveris	54	<p>The prefix and suffix of this name pair have sufficient orthographic differences.</p> <p>The number of syllables in both names is different. The second and last syllables in both names give the names a distinctly different sound when spoken.</p>
10.	Inulin	54	<p>The infix of this name pair has sufficient orthographic differences.</p> <p>The number of syllables in both names is different. The second and last syllables in both names give the names a distinctly different sound when spoken.</p>
11.	Iofen	54	<p>The infix of this name pair has sufficient orthographic differences.</p> <p>All the syllables in both names give the names a distinctly different sound when spoken.</p>
12.	Ibifon 600	52	<p>The infix of this name pair has sufficient orthographic differences.</p> <p>All the syllables in both names give the names a distinctly different sound when spoken.</p>

No.	Proposed name: Iluvien Strength: 0.19 mg Usual Dose: Insert into the posterior segment of the affected eye through a pars plana insertion	POCA Score (%)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
13.	Ilevro	50	<p>The suffix of this name pair has sufficient orthographic differences.</p> <p>The number of syllables in both names is different. The second and last syllables in both names give the names a distinctly different sound when spoken.</p>
14.	Idarubicin	50	<p>The infix of this name pair has sufficient orthographic differences.</p> <p>All the syllables in both names give the names a distinctly different sound when spoken.</p>
15.	Iveegam En	50	<p>The infix of this name pair has sufficient orthographic differences.</p> <p>The number of syllables in both names is different. The first and last syllables in both names give the names a distinctly different sound when spoken.</p>

Appendix F: Low Similarity Names (i.e., combined POCA score is $\leq 49\%$)

No.	Name	POCA Score (%)
1.	None	

Appendix G: Names not likely to be confused or not used in usual practice settings for the reasons described.

No.	Name	POCA Score (%)	Failure preventions
1.	Aleudrin	64	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
2.	Inoven	63	International product marketed in United Kingdom.
3.	Aluzine	62	International product marketed in United Kingdom.
4.	(b) (4)***	60	This name was denied in OSE RCM#2012-2380 and 2012-2381 (ANDA 076681) (b) (4). The name approved under this ANDA is Falmina on March 28, 2012.
5.	(b) (4)***	60	This application ANDA (b) (4) was withdrawn on (b) (4).
6.	Iduridin	60	International product marketed in United Kingdom, Norway and Italy.
7.	(b) (4)***	58	This name was denied in OSE RCM#2009-1995 (IND (b) (4) and NDA (b) (4)) (b) (4). This name reconsideration was denied in OSE RCM#2010-1041 (NDA (b) (4)). This application NDA (b) (4) is in complete response since (b) (4).
8.	(b) (4)***	56	This name was not reviewed. The name approved under this application NDA 021911 was Banzel on November 14, 2008.
9.	Isclufen	56	International product marketed in United Kingdom.
10.	(b) (4)***, (b) (4)***	56, 56	DMETS did not recommend this name in ODS Consult#2007-1914 (b) (4). The name approved under this NDA 020140 was Fusilev on March 7, 2008.
11.	Vilofane	56	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.

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No.	Name	POCA Score (%)	Failure preventions
12.	Ibumetin	54	International product marketed in Netherlands, Finland, Austria, Denmark, Norway and Sweden.
13.	Ilex Skin	54	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
14.	Isisfen	54	International product marketed in United Kingdom.
15.	Iver-On	54	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
16.	(b) (4)***	52	This name was denied in OSE RCM#2010-2149 and 2010-2150 (ANDA (b) (4)) (b) (4) Another name for this application has not yet been submitted.
17.	Incurin	52	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
18.	(b) (4)***	51	This name was an alternate name and was not reviewed. The name approved under this application NDA 018066 was Unisom on October 18, 1978.
19.	(b) (4)***	51	Name entered by safety evaluator in POCA database. Unable to find product characteristics in commonly used drug databases.
20.	Exuviance	50	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
21.	Ibuleve	50	International product marketed in Singapore and South Africa.
22.	Iridium	50	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.

*** This document contains proprietary and confidential information that should not be released to the public.

Appendix H: Names not likely to be confused due to notable orthographic and phonetic differences.

No.	Name	POCA Score (%)
1.	Levlen	66
2.	(b) (4) ***	64
3.	HALAVEN	63
4.	LUMIGAN	62
5.	Lutein	62
6.	(b) (4) ***	60
7.	(b) (4) ***	60
8.	Olivine	60
9.	Tildiem	60
10.	Tri Levlen	60
11.	Volumen ***	60
12.	Alidrin	59
13.	(b) (4) ***	59
14.	LONITEN	59
15.	LUFYLLIN	59
16.	Lufyllin-400	59
17.	Silybin	59
18.	Aleve-D	58
19.	ELMIRON	58
20.	Levsin	58
21.	LEVULAN	58
22.	Lidifen	58
23.	(b) (4) ***	58
24.	Siltussin	58
25.	Tildren	58
26.	VUSION	58

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No.	Name	POCA Score (%)
27.	ALUPENT	57
28.	(b) (4)***	57
29.	Hylutin	57
30.	LOGEN	57
31.	(b) (4)***	57
32.	RELAFEN	57
33.	SILPHEN	57
34.	Tilarin	57
35.	(b) (4)	56
36.	Aloquin	56
37.	Aluline	56
38.	ELESTRIN	56
39.	EULEXIN	56
40.	(b) (4)	56
41.	HALCION	56
42.	(b) (4)***	56
43.	LOPURIN	56
44.	Lugacin	56
45.	Malvin	56
46.	Pileran	56
47.	Tylophen	56
48.	Tylosin	56
49.	Zileuton	56
50.	Albutein	55
51.	ELIXICON	55
52.	FOLLUTEIN	55
53.	(b) (4)***	54

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No.	Name	POCA Score (%)
54.	ALEVE PM	54
55.	Allfen	54
56.	Alpain	54
57.	Alphen	54
58.	Aluminum	54
59.	C10-36 OLEFIN	54
60.	C24-28 Olefin	54
61.	C30-45 OLEFIN	54
62.	ELAVIL	54
63.	ELOCON	54
64.	ELOXATIN	54
65.	Flavone	54
66.	FLOVENT	54
67.	(b) (4)***	54
68.	Fluzone	54
69.	HELICIN	54
70.	Lavoclen	54
71.	Lotussin	54
72.	Luden's	54
73.	Ludent	54
74.	Lumen C	54
75.	Lumicain	54
76.	(b) (4)***	54
77.	Nelova 1/50 M	54
78.	PRELUDIN	54
79.	TALACEN	54
80.	(b) (4)***	54

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No.	Name	POCA Score (%)
81.	Ala-Quin	53
82.	Aliclen	53
83.	DELFIN	53
84.	Evoxin	53
85.	Salicin	53
86.	Selepen	53
87.	(b) (4)***	53
88.	ACLOVATE	52
89.	(b) (4)***	52
90.	Alferon N	52
91.	alfuzosin	52
92.	Aliskiren	52
93.	Allethrin	52
94.	(b) (4)***	52
95.	ALPHALIN	52
96.	(b) (4)***	52
97.	ALYACEN 1/35	52
98.	ALYACEN 7/7/7	52
99.	Alyacen 7/7/7***	52
100.	ALYACEN 777	52
101.	Baltussin	52
102.	Biloptin	52
103.	DIOVAN	52
104.	Dologen	52
105.	Eldoquin	52
106.	Eluant	52
107.	Eribulin	52

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No.	Name	POCA Score (%)
108.	Estivin	52
109.	Everone	52
110.	FELDENE	52
111.	Finevin	52
112.	GALZIN	52
113.	LEUKERAN	52
114.	LEVAQUIN	52
115.	(b) (4)***	52
116.	Leventa	52
117.	LEVOPHED	52
118.	LIDOPEN	52
119.	LITHANE	52
120.	Lorsin	52
121.	(b) (4)***	52
122.	(b) (4)***	52
123.	LUPRON	52
124.	LYGEN	52
125.	MALATHION	52
126.	Melamin	52
127.	Mollifene	52
128.	Nelgen	52
129.	Paroven	52
130.	(b) (4)***	52
131.	Pilagan	52
132.	Ri-Tussin	52
133.	SALURON	52
134.	Silafed	52

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No.	Name	POCA Score (%)
135.	SILVADENE	52
136.	TELDRLIN	52
137.	(b) (4)***	52
138.	Toluene	52
139.	Urimin	52
140.	Valuphed	52
141.	Vitussin	52
142.	(b) (4)***	52
143.	Aclacin	51
144.	Alloin	51
145.	Calabren	51
146.	CILOXAN	51
147.	Elantan	51
148.	Eldisine	51
149.	(b) (4)***	51
150.	ELIXOMIN	51
151.	(b) (4)***	51
152.	Folacin	51
153.	Leucine	51
154.	Levacet	51
155.	MILONTIN	51
156.	Pullulan	51
157.	Silicon	51
158.	Uridon	51
159.	Uritin	51
160.	(b) (4)***	51
161.	Alanine	50

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No.	Name	POCA Score (%)
162.	ALAVERT	50
163.	Allerfrin	50
164.	Almodan	50
165.	Alocane	50
166.	Altafrin	50
167.	Alverine	50
168.	Azlocillin	50
169.	BELDIN	50
170.	Cala-Gen	50
171.	(b) (4) ***	50
172.	Elliona ***	50
173.	(b) (4) ***	50
174.	(b) (4) ***	50
175.	Eraldin	50
176.	Euglucon	50
177.	(b) (4) ***	50
178.	Flunixin	50
179.	Fluogen	50
180.	LARIN 1.5/30	50
181.	LARIN 1/20	50
182.	(b) (4) ***	50
183.	(b) (4) ***	50
184.	(b) (4) ***	50
185.	Lecithin	50
186.	Levius	50
187.	LEVOLET	50
188.	LIPOFEN	50

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No.	Name	POCA Score (%)
189.	Livial	50
190.	Mylagen	50
191.	Nylidrin	50
192.	ORVATEN	50
193.	Otrivin	50
194.	Pilopine	50
195.	Relcofen	50
196.	(b) (4)***	50
197.	Salacyn	50
198.	SALAGEN	50
199.	Siltane	50
200.	Sloprin	50
201.	Solian	50
202.	SOLODYN	50
203.	(b) (4)***	50
204.	Tellurium	50
205.	Tilidine	50
206.	Trilaurin	50
207.	Uni-Ann	50
208.	Urotoin	50
209.	VELIVET	50
210.	VELOSULIN	50
211.	Vivarin	50
212.	Wal-itin	50

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/s/

RACHNA KAPOOR
07/31/2014

YELENA L MASLOV
08/01/2014

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date: October 13, 2010

Application Type/Number: NDA 201923

Through: Kristina A. Toliver, PharmD, Team Leader
Denise P. Toyer, PharmD, Deputy Director
Division of Medication Error Prevention and Analysis (DMEPA)

From: Loretta Holmes, BSN, PharmD, Safety Evaluator
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name: Iluvien (Fluocinolone Acetonide Intravitreal Insert)
0.19 mg

Applicant: Novartis Pharmaceuticals Corporation

OSE RCM #: 2010-1548

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EXECUTIVE SUMMARY

This review summarizes DMEPA's proprietary name risk assessment of Iluvien (Fluocinolone Acetonide Intravitreal Insert) 0.19 mg. Our evaluation did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of this review. Thus, DMEPA finds the proposed proprietary name, Iluvien, acceptable for this product. The proposed proprietary name must be re-reviewed if approval of the NDA is more than 90 days from the signature date of this review.

Additionally, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

1 BACKGROUND

1.1 INTRODUCTION

This review responds to a July 15, 2010 request from Alimera Sciences, Inc. for an assessment of the proposed proprietary name, Iluvien, regarding potential name confusion with other proprietary or established drug names in the usual practice settings.

The container labels, carton and insert labeling are being evaluated for their potential contribution to medication errors under separate cover (OSE Review 2010-1549).

1.2 REGULATORY HISTORY

DMEPA found the proposed proprietary name, Iluvien, acceptable in OSE Review 2010-105, dated June 15, 2010 when the application was an IND. The NDA for Iluvien was submitted on July 15, 2010 and will receive priority review.

1.3 PRODUCT INFORMATION

Iluvien is the proposed proprietary name for Fluocinolone Acetonide Intravitreal Insert. Iluvien is a synthetic corticosteroid indicated for the treatment of diabetic macular edema. Iluvien is for intravitreal use only. It is inserted into the posterior segment of the affected eye through a pars plana insertion. (b) (4)

Iluvien contains 0.19 mg of Fluocinolone Acetonide and is designed to release Fluocinolone Acetonide at an initial rate of 0.25 mcg per day. Iluvien will be supplied in a single use preloaded inserter with a 25-gauge needle, packaged in a tray. Iluvien should be stored at 15-30°C (59-86°F)

2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment for all proprietary names. Section 2.1 identifies specific information associated with the methodology for the proposed proprietary name, Iluvien.

DMEPA did not repeat the FDA Prescription Analysis Studies for this name review because it has been less than one year since the studies were conducted and they were analyzed in our previous proprietary name review of Iluvien (OSE Review 2010-105). Additionally, Iluvien was not submitted to the Expert Panel Discussion for review because our previous review of the name was completed just one month prior to the Applicant's request for proprietary name review under the NDA. However, the primary Safety Evaluator conducted an independent search of the databases (see Section 6). We also note the Applicant submitted an independent name assessment (conducted by (b) (4).) of Iluvien. This independent name assessment was evaluated in our previous review of Iluvien.

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter ‘I’ when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.^{1,2}

To identify drug names that may look similar to Iluvien, the primary DMEPA Safety Evaluator also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (seven letters), upstrokes (one, lower case “l”), downstrokes (none), cross strokes (none), and dotted letters (one, lower case “i”). Additionally, several letters in Iluvien may be vulnerable to ambiguity when scripted (see Appendix B). As a result, the DMEPA Safety Evaluator also considers these alternate appearances when identifying drug names that may look similar to Iluvien.

When searching to identify potential names that may sound similar to Iluvien, the DMEPA Safety Evaluator searches for names with similar number of syllables (four), stresses (I-lu-vi-en, i-LU-vi-en, i-lu-VI-en, or i-lu-vi-EN), and placement of vowel and consonant sounds. Additionally, the DMEPA Safety Evaluator considers that pronunciation of parts of the name can vary (see Appendix B). The Applicant’s intended pronunciation of the name is “i loo’ vee en”. However, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

This Safety Evaluator did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name as of September 13, 2010.

3.2 COMMENTS ON PROMOTIONAL PERSPECTIVE OF THE NAME

DDMAC had no concerns regarding the proposed name from a promotional perspective and did not offer any additional comments relating to the proposed name.

3.3 COMMENTS FROM THE DIVISION OF ANTI-INFECTIVE AND OPHTHALMOLOGY PRODUCTS (DAIOP)

3.3.1 Initial Phase of Review

DAIOP did not forward any comments or concerns regarding the proposed name at the initial phase of the name review in OSE Review 2010-105, dated June 15, 2010. Therefore, DMEPA did not send an initial phase email during this review cycle.

3.3.2 Midpoint of Review

On October 5, 2010, DMEPA notified DAIOP via e-mail that we had no objections to the proposed proprietary name, Iluvien. Per e-mail correspondence from the DAIOP on October 7, 2010, the Division stated “Clinical has no objection to the name. I cannot imagine another discipline having a problem either.”

¹ Institute for Safe Medication Practices. Confused Drug Name List (1996-2006). Available at <http://www.ismp.org/Tools/confuseddrugnames.pdf>

² Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

3.4 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator resulted in identification of six names which were thought to look similar to Iluvien and represent a potential source of drug name confusion. The names identified to have look-alike similarities are (b) (4) ***, (b) (4) ***, Fluviron, Fluzone, Fluist, and Elmiron. Additionally, the 27 names identified in our previous review of Iluvien were re-reviewed to determine if there were new concerns with potential look-alike or sound-alike similarities to Iluvien due to a change in their product characteristics (see Appendix C for a listing of those names). Thus, we evaluated a total of 33 names for their potential similarity to Iluvien.

4 DISCUSSION

This proposed name was evaluated from a safety and promotional perspective based on the product characteristics provided by the Applicant. We sought input from pertinent disciplines involved with the review of this application and considered it accordingly.

4.1 PROMOTIONAL ASSESSMENT

DDMAC evaluated the name Iluvien from a promotional perspective and determined the name was acceptable. The Division of Anti-infective and Ophthalmology Products and the Division of Medication Error Prevention and Analysis concurred with this assessment.

4.2 SAFETY ASSESSMENT

In total, 33 names were evaluated (27 from OSE Review 2010-105 and six new names) as potential sources of name confusion with the proposed proprietary name, Iluvien. DMEPA did not identify other aspects of the name that could function as a source of error. Twenty-seven of the 33 names were not evaluated further. We identified these 27 names in our previous review of Iluvien. Their product characteristics have not changed (see Appendix C).

Failure mode and effects analysis (FMEA) was then applied to determine if the proposed name could potentially be confused with the remaining six names and lead to medication errors.

This analysis determined that the name similarity between Iluvien and these six products is unlikely to result in medication errors for the reasons presented in Appendix D.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Iluvien, is not promotional nor is it vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Iluvien, for this product at this time.

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of this product NDA, DMEPA rescinds this Risk Assessment finding and the name must be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. If the approval of this application is delayed beyond 90 days from the signature date of this review, the proposed name must be re-evaluated. If you have further questions or need clarifications, please contact Brantley Dorch, OSE Project Manager, at 301-796-0150.

5.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Iluvien, and have concluded that it is acceptable.

6 REFERENCES

1. Abdus-Samad, Jibril. OSE Review 2010-105: Proprietary Name Review of Iluvien. June 15, 2010.

2. *Micromedex Integrated Index* (<http://csi.micromedex.com>)

Contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.

3. *Phonetic and Orthographic Computer Analysis (POCA)*

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion. This is a database which was created for the Division of Medication Error Prevention and Analysis, FDA.

4. *Drug Facts and Comparisons, online version, St. Louis, MO* (<http://factsandcomparisons.com>)

Drug Facts and Comparisons is a compendium organized by therapeutic course; contains monographs on prescription and OTC drugs, with charts comparing similar products.

5. *FDA Document Archiving, Reporting & Regulatory Tracking System [DARRTS]*

DARRTS is a government database used to organize Applicant and Sponsor submissions as well as to store and organize assignments, reviews, and communications from the review divisions.

6. *Division of Medication Errors Prevention and Analysis proprietary name consultation requests*

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

7. *Drugs@FDA* (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>)

Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present.

Drugs@FDA contains official information about FDA approved [brand name](#), [generic drugs](#), [therapeutic biological products](#), [prescription](#) and [over-the-counter](#) human drugs and [discontinued drugs](#) and “[Chemical Type 6](#)” approvals.

8. *Electronic online version of the FDA Orange Book* (<http://www.fda.gov/cder/ob/default.htm>)

Provides a compilation of approved drug products with therapeutic equivalence evaluations.

9. *U.S. Patent and Trademark Office* (<http://www.uspto.gov>)

Provides information regarding patent and trademarks.

10. *Clinical Pharmacology Online* (www.clinicalpharmacology-ip.com)

Contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. Provides a keyword search engine.

11. *Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at* (www.thomson-thomson.com)

The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and trade names that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

12. *Natural Medicines Comprehensive Databases* (www.naturaldatabase.com)

Contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.

13. *Stat!Ref* (www.statref.com)

Contains full-text information from approximately 30 texts. Includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolph's Pediatrics, Basic Clinical Pharmacology and Dictionary of Medical Acronyms Abbreviations.

14. *USAN Stems* (<http://www.ama-assn.org/ama/pub/category/4782.html>)

List contains all the recognized USAN stems.

15. *Red Book Pharmacy's Fundamental Reference*

Contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.

16. *Lexi-Comp* (www.lexi.com)

A web-based searchable version of the Drug Information Handbook.

17. *Medical Abbreviations Book*

Contains commonly used medical abbreviations and their definitions.

APPENDICES

Appendix A:

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.³

For the proposed proprietary name, DMEPA Safety Evaluators search a standard set of databases and information sources to identify names with orthographic and phonetic similarity and hold a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name. DMEPA Safety Evaluators also conduct internal CDER prescription analysis studies. When provided, DMEPA considers external prescription analysis study results and incorporate into the overall risk assessment.

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and focuses on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.⁴ DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the

³ National Coordinating Council for Medication Error Reporting and Prevention. <http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

⁴ Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its Safety Evaluators to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. Accordingly, the DMEPA Safety Evaluators consider the product characteristics associated with the proposed drug throughout the risk assessment because the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA Safety Evaluators consider the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.⁵ DMEPA provides the product characteristics considered for this review in section one.

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA Safety Evaluators also examine the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly and even dissimilarly spelled drug name pairs to appear very similar to one another. The similar appearance of drug names when scripted has led to medication errors. The DMEPA Safety Evaluators apply expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g., “T” may look like “F,” lower case ‘a’ looks like a lower case ‘u,’ etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details). In addition, the DMEPA Safety Evaluators compare the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. If provided, DMEPA will consider the Applicant’s intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Applicant has little control over how the name will be spoken in clinical practice.

⁵ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

Table 1. Criteria used to identify drug names that look- or sound-similar to a proposed proprietary name.

Type of similarity	Considerations when searching the databases		
	Potential causes of drug name similarity	Attributes examined to identify similar drug names	Potential Effects
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	<ul style="list-style-type: none"> Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, the DMEPA Safety Evaluators also consider the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

DMEPA Safety Evaluators conduct searches of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA Safety Evaluators use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the DMEPA Safety Evaluators review the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel.

2. CDER Expert Panel Discussion

DMEPA conducts an Expert Panel Discussion to gather CDER professional opinions on the safety of the proposed product and the proposed proprietary name. The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) Safety Evaluators and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

The primary Safety Evaluator presents the pooled results of the DMEPA staff to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of names, additional searches by the primary Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

3. FDA Prescription Analysis Studies

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of the 123 participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants send their interpretations of the orders via e-mail to DMEPA.

4. Comments from the OND review Division or Generic drugs

DMEPA requests the Office of New Drugs (OND) or Office of Generic Drugs (OGD) Regulatory Division responsible for the application for their comments or concerns with the proposed proprietary name and any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with DDMAC's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND or OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to concur/not concur with DMEPA's final decision.

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.⁶ When applying FMEA to assess the risk of a proposed proprietary

⁶ Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Section one. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, Expert Panel Discussion, and prescription studies, external studies, and identifies potential failure modes by asking:

“Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?”

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names possess similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

In the second stage of the Risk Assessment, the primary Safety Evaluator evaluates all potential failure modes to determine the likely *effect* of the drug name confusion, by asking:

“Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?”

The answer to this question is a central component of the Safety Evaluator’s overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not ultimately be a source of medication errors in the usual practice setting, the primary Safety Evaluator eliminates the name from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend the use of an alternate proprietary name.

DMEPA will object to the use of proposed proprietary name when the primary Safety Evaluator identifies one or more of the following conditions in the Risk Assessment:

- a. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC’s findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].
- b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
- c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.

- d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
- e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

In the event that DMEPA objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMEPA will provide a contingency objection based on the date of approval. Whichever product, the Agency approves first has the right to use the proprietary name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

The threshold set for objection to the proposed proprietary name may seem low to the Applicant. However, the safety concerns set forth in criteria a through e are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), Joint Commission on Accreditation of Hospitals (JCOAH), and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and a preventable source of medication error that, in many instances, the Agency and/or Applicant can identify and rectify prior to approval to avoid patient harm.

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Applicants have undertaken higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Applicant and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Applicants' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval. (See Section 4 for limitations of the process).

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in proposed name “Iluvien”	When scripted may appear as:	When spoken may be interpreted as:
Capital ‘I’	l, T, number 1	any vowel
lowercase ‘l’	b, e, i	
lowercase ‘u’	a, n, o, r	any vowel
lowercase ‘v’	n, r, u	b, f
lowercase ‘i’	a, c, e, l	any vowel
lowercase ‘e’	a, i, l, o	any vowel
lowercase ‘n’	m, r, s, u	m
‘lu’		‘loo’, ‘lew’
‘vien’		‘vion’, ‘vian’, ‘bien’

Appendix C: Names identified in our previous review of Iluvien. Since the Iluvien product characteristics and the product characteristics of the listed names remain the same, these names will not be re-reviewed because our previous analysis determined that name confusion was unlikely to occur between these names and Iluvien.

Name	Similarity to Iluvien
Inovelon	Look
Levlen	Look
Ibuprofen	Sound
Lumigan	Sound
Luvox	Look and Sound
Enjuvia	Look and Sound
Ibuprin	Look and Sound
Invanz	Look and Sound
Luveris	Look and Sound
Iletin	Look
Innovar	Look

Name	Similarity to Iluvien
Flovent	Look
Ilosone	Look
Intuniv	Look
Thrive	Look
Ambien	Look and Sound
Elavil	Look and Sound
Alinia	Look
Devrom	Look
Ellence	Look
Ibren	Look
Ilaris	Look
Imuran	Look
Alavert	Sound
Allfen	Sound
Aviane	Sound
Ilopan	Look and Sound

Appendix D: Products with multiple differentiating product characteristics

Product name with potential for confusion	Similarity to Iluvien	Strength	Usual Dose (if applicable)	Differentiating Product Characteristics (Iluvien vs. Product)
Iluvien (Fluocinolone Acetonide) Intravitreal Insert	N/A	0.19 mg	Insert into posterior segment of the affected eye. (b) (4)	N/A

(b) (4)



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Product name with potential for confusion	Similarity to Iluvien	Strength	Usual Dose (if applicable)	Differentiating Product Characteristics (Iluvien vs. Product)
Iluvien (Fluocinolone Acetonide) Intravitreal Insert	N/A	0.19 mg	Insert into posterior segment of the affected eye. (b) (4)	N/A
(b) (4)				
Fluvirin (Influenza virus vaccine) Injection	Look	No strength. Ingredients vary from year to year	0.5 mL intramuscularly once, may repeat yearly	<i>Route of administration:</i> Intravitreal vs. intramuscular <i>Dose:</i> 1 insert vs. 0.5 mL <i>Dosage form:</i> Intravitreal insert vs. tablets

*** This document contains proprietary and confidential information that should not be released to the public.***

Product name with potential for confusion	Similarity to Iluvien	Strength	Usual Dose (if applicable)	Differentiating Product Characteristics (Iluvien vs. Product)
Iluvien (Fluocinolone Acetonide) Intravitreal Insert	N/A	0.19 mg	Insert into posterior segment of the affected eye. (b) (4) 	N/A
Leven (21-day) Leven (28-day) (Ethinyl Estradiol and Levonorgestrel) Tablets <i>Leven has been discontinued, however, generics are available</i>	Look	0.03 mg/0.15 mg	1 tablet once daily	<i>Route of administration:</i> Intravitreal vs. oral <i>Frequency of administration:</i> Once, (b) (4) vs. once daily <i>Dosage form:</i> Intravitreal insert vs. tablets

Product name with potential for confusion	Similarity to Iluvien	Strength	Usual Dose (if applicable)	Differentiating Product Characteristics (Iluvien vs. Product)
Iluvien (Fluocinolone Acetonide) Intravitreal Insert	N/A	0.19 mg	Insert into posterior segment of the affected eye. ^(b) ₍₄₎	N/A
Fluzone Fluzone High Dose (Influenza virus vaccine) Injection	Look	No strength. Ingredients vary from year to year.	<p>Fluzone: Age 6 months to 35 months: 0.25 mL intramuscularly once</p> <p>Age 3 years to 8 years: 0.5 mL intramuscularly once; repeat the dose at least one month later for those being vaccinated for the first time or were vaccinated for the first time last season with only one dose</p> <p>Age 9 years and older: 0.5 mL intramuscularly once</p> <p>Fluzone High Dose: Elderly: 0.5 mL intramuscularly once</p> <p>Influenza vaccine may be repeated yearly</p>	<p><i>Dose:</i> One insert vs. 0.25 mL or 0.5 mL</p> <p><i>Route of administration:</i> Intravitreal vs. intramuscular</p> <p><i>Dosage form:</i> Intravitreal insert vs. injection</p>

Product name with potential for confusion	Similarity to Iluvien	Strength	Usual Dose (if applicable)	Differentiating Product Characteristics (Iluvien vs. Product)
Iluvien (Fluocinolone Acetonide) Intravitreal Insert	N/A	0.19 mg	Insert into posterior segment of the affected eye. (b) (4)	N/A
Elmiron (Pentosan Polysulfate Sodium) Capsules	Look	100 mg	1 capsule three times per day	<i>Route of administration:</i> Intravitreal vs. oral <i>Frequency of administration:</i> Once, (b) (4) vs. three times per day <i>Dosage form:</i> Intravitreal insert vs. capsules

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/s/

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