CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 22-220

PROPRIETARY NAME REVIEW(S)

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:	May 29, 2008
To:	Wiley Chambers, M.D., Acting Director Division of Anti-Infective and Ophthalmology Products
Through:	Todd Bridges, RPh, Team Leader Denise Toyer, Pharm D, Deputy Director Carol Holquist, RPh, Director Division of Medication Error Prevention
From:	Diane C. Smith, PharmD, Safety Evaluator Division of Medication Error Prevention
Subject:	Proprietary Name, Label and Labeling Review
Drug Name(s):	Trivaris (Triamcinolone Acetonide) 8 mg/0.1 mL
Application Type/Number:	NDA 22-220
Applicant:	Allergan, Inc.
OSE RCM #:	2007-1001

NOTE: This review contains proprietary and confidential information that should not be released to the public.

CONTENTS

EXECUTIVE SUMMARY

The result of the Proprietary Name Risk Assessment found that the proposed name, Trivaris, has some similarity to other proprietary drug names, but the findings of the FMEA indicates that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors. Thus, we do not object to the use of the proprietary name Trivaris for this product.

The results of the Label and Labeling Risk Assessment found that the presentation of information and design of the proposed container labels and carton labeling appear to be vulnerable to confusion that could lead to medication errors. We believe the risks we have identified can be addressed and mitigated prior to drug approval, and provide recommendations in section 6.2 that aim at reducing the risk of medication errors.

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, we rescind this Risk Assessment finding, and recommend that the name be resubmitted for review. Additionally, if the product approval is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

1 BACKGROUND

1.1 INTRODUCTION

This review was written in response to a request from the Division of Anti-Infective and Ophthalmology Products for assessment of the proprietary name, Trivaris, regarding potential name confusion with other proprietary or established names. Container labels and carton labeling were also submitted and reviewed from a medication error perspective.

1.2 REGULATORY HISTORY

Trivaris is a 505(b)(2) application that provides for a preservative-free formulation of triamcinolone acetonide in a pre-filled syringe for intravitreal administration. The reference listed drug is Kenalog-40. Currently, Kenalog-40 (NDA# 14-901) and the other approved generic triamcinolone acetonide products, and Triesence (NDA# 22-223 and 22-048) are other triamcinolone acetonide products with differentiating product characteristics (see Appendix A for details).

Additionally, the Applicant submitted an independent name analysis conducted by _____ , for the name Trivaris, and the analysis was evaluated as part of this review. b(4)

1.3 PRODUCT INFORMATION

Trivaris is the proposed name for Triamcinolone Acetonide injectable suspension USP (8 mg/ 0.1 mL). Trivaris is a corticosteroid indicated for ophthalmic use in sympathetic ophthalmia, temporal arteritis, uveitis, and ocular inflammatory conditions unresponsive to topical corticosteroids. Additional proposed uses for Trivaris include Intramuscular Use and Intra-Articular or soft tissue use. The recommended intravitreal dose is 4 mg (0.05 mL), the dose for the other indications may vary from 2.5 mg to 100 mg depending on the specific disease entity being treated. Trivaris will be available as a 0.1 mL prefilled single dose syringe.

2 METHODS AND MATERIALS

This section consists of two sections which describe the methods and materials used by the medication error staff conducting a proprietary name risk assessment (see 2.1 Proprietary Name Risk Assessment) and label, labeling, and/or packaging risk assessment (see 2.2 Container, Carton Label, and Insert Label Risk Assessment). The primary focus for both of the assessments is to identify and remedy potential sources of medication error prior to drug approval. The Division of Medication Error Prevention 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. [1]

2.1 PROPRIETARY NAME RISK ASSESSMENT

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, Trivaris, and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, and ANDA products currently under review by the Agency.

For the proprietary name, Trivaris, the medication error staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Sections 2.1.1 for detail) and held an CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.2). We also conduct internal CDER prescription analysis studies (see 2.1.3), and, when provided, external prescription analysis studies results are considered and incorporated into the overall risk assessment (see detail 2.1.3).

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 (see detail 2.1.5). The overall risk assessment is based on the findings of a Failure Modes and Effects Analysis (FMEA) of the proprietary name, and is focused on the avoidance of medication errors. FMEA is a systematic tool for evaluating a process and identifying where and how it might fail. [2] FMEA is used to analyze whether the drug names identified with look- or sound-alike similarity to the proposed name could cause confusion that subsequently leads to medication errors in the clinical setting. We use the clinical expertise of the medication error staff to anticipate the conditions of the clinical setting that the product is likely to be used in 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. As such, the staff considers the product characteristics associated with the proposed drug throughout the risk assessment, since 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 drug name include, but are not limited to established name of the proposed product, the proposed indication, 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

---

[1] National Coordinating Council for Medication Error Reporting and Prevention. http://www.nccmerp.org/aboutMedErrors.html. Last accessed 10/11/2007.

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

occur at any point in the medication use process, we 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.[3]

2.1.1 Search Criteria

The medication error staff considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix B.

For this review, particular consideration was given to drug names beginning with the letter 'T' 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.[4][5]

To identify drug names that may look similar to Trivaris, the Staff also consider the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (8 letters), upstrokes (one capital letter 'T'), downstokes (none), cross-strokes (none), and dotted letters (two, letter 'i'). Additionally, several letters in Trivaris may be vulnerable to ambiguity when scripted, including the letter 'T' may appear as 'I', 'L', 'Z' or 'F'; lower case 'ri' may appear as a lower case 'u'; lower case 'v' may appear as 'u' or 'r'; lower case 'a' may appear as 'c', 'e' or 'o'; lower case 'i' may appear as 'e' and lower case 's' may appear as 'n'. As such, the Staff also considers these alternate appearances when identifying drug names that may look similar to Trivaris.

When searching to identify potential names that may sound similar to Trivaris, the medication error staff search for names with similar number of syllables (3), stresses (TRI-Va-ris, Tri-VA-ris or Tri-va-RIS), and placement of vowel and consonant sounds. In addition, several letters in Trivaris may be subject to interpretation when spoken, including the vowel 'i' may be interpreted as letter 'y'; 'var' may be interpreted as 'ver' or 'bare', the letters 'is' may be interpreted as 'ish'. The Applicant's intended pronunciation of the proprietary name could not be expressly taken into consideration, as this was not provided with the proposed name submission.

The Staff also consider the product characteristics associated with the proposed drug throughout the identification of similar drug names, since the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting For this review, the medication error staff were provided with the following information about the proposed product: the proposed proprietary name (Trivaris), the established name (Triamcinolone acetonide), proposed indication (ophthalmic use in sympathatetic ophthalmia, temporal arteritis, uveitis, and ocular inflammatory conditions unresponsive to topical corticosteroids), strength (8 mg/0.1 mL), dose (4 mg [0.05 mL] for ophthalmology and 2.5 mg to 100 mg for other indications) , frequency of administration (as needed), route (intravitreally, intramuscular, intra-articular or soft tissue) and dosage form of the product (injectable suspension). Appendix A provides a more detailed listing of the product characteristics the Medication Error Staff general take into consideration.

Lastly, the medication error staff also consider the potential for the proposed 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. As such, these broader safety implications of the name are considered and evaluated

---

[3] Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

[4] Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at http://www.ismp.org/Tools/confuseddrugnames.pdf

[5] Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artifical Inteligence in Medicine (2005)

throughout this assessment and the medication error staff provide additional comments related to the safety of the proposed name or product based on their professional experience with medication errors.

2.1.1.1 Database and Information Sources

The proposed proprietary name, Trivaris, was provided to the medication error staff of the Division of medication error staff to conduct a search 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 Trivaris using the criteria outlined in 2.1.1. A standard description of the databases used in the searches is provided in Section 7. To complement the process, the medication error staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (COPA), 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 medication error staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The findings of the individual Safety Evaluators were then pooled and presented to the Expert Panel.

2.1.2 CDER Expert Panel Discussion

An Expert Panel Discussion is held by the Division of Medication Error Prevention to gather CDER professional opinions on the safety of the product and the proprietary name, Trivaris. Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed. This group is composed of the Division Medication Error Prevention Staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC).

The pooled results of the medication error staff were presented 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 Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

2.1.3 CDER 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 Trivaris 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 a total of 123 healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The results are used by the Safety Evaluator to identify any orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of Trivaris in handwriting and verbal communication of the name, two requisition orders were written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These requisition orders are optically scanned and one requisition order was delivered to a random sample of 123 participating health professionals via e-mail. In addition, a verbal requisition 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 requisition orders, the participants send their interpretations of the orders via e-mail to the medication error staff.

Figure 1. Trivaris Study (conducted on May 18, 2007)

HANDWRITTEN REQUISTION	VERBAL REQUISITION
Requisition Sample #1: Trivaris 4mg syringe	Trivaris 4 mg syringe
Requisition Sample #2: Trivaris 4mg	

2.1.4 External Proprietary Name Risk Assessment

For this product, the Applicant submitted an independent risk assessment of the proposed proprietary name conducted by [redacted] The Division of Medication Error Prevention conducts an independent analysis and evaluation of the data provided, and responds to the overall findings of the assessment. When the external proprietary name risk assessment identifies potentially confusing names that were not captured in the medication error staff's database searches or in the Expert Panel Discussion, these names are included in the Safety Evaluator's Risk Assessment and analyzed independently by the Safety Evaluator to determine if the potentially confusing name could lead to medication errors in usual practice settings.

b(4)

After the Safety Evaluator has determined the overall risk assessment of the proposed name, the Safety Evaluator compares the findings of their overall risk assessment with the findings of the proprietary name risk assessment submitted by the Applicant. The Safety Evaluator then determines whether our risk assessment concurs or differs with the findings. When the proprietary name risk assessments differ, we provide a detailed explanation of these differences.

2.1.5 Safety Evaluator Risk Assessment of the Proposed Proprietary Name

Based on the criteria set forth in Section 2.1.1, the Safety Evaluator Risk Assessment applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Modes and Effects Analysis and provide an overall risk 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 name, we seek to evaluate the potential for a proposed name to be confused with another drug name as a result of the name confusion and 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 look- or sound-alike drug names prior to approval,

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

where actions to overcome these issues are easier and more effective then remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is not yet marketed, the Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Appendix B. 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 evaluation, and studies, and identifies potential failure modes by asking: "Is the name Trivaris convincing 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 Trivaris 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 posses similarity that would cause confusion at any point in the medication use system and the name is eliminated from further review.

In the second stage of the Risk Assessment, all potential failure modes are evaluated 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 ultimately not be a source of medication errors in the usual practice setting, the name is eliminated 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 that an alternate proprietary name be used. In rare instances, the FMEA findings may provide other risk-reduction strategies, such as product reformulation to avoid an overlap in strength or an alternate modifier designation may be recommended as a means of reducing the risk of medication errors resulting from drug name confusion.

We will object to the use of proposed proprietary name when the one or more of the following conditions are identified in the Safety Evaluator's Risk Assessment:

1. 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 trade name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. We identify 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)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains an USAN stem, particularly in a manner that is contradictory to the USAN Council's definition.

5. Medication Error Staff identify a potential source of medication error within the proposed proprietary name. 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 another drug product.

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

If none of these conditions are met, then we will not object to the use of the proprietary name. If any of these conditions are met, then we will object to the use of the proprietary 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 1 through 5 are supported either by FDA Regulation or by external healthcare authorities, including The Institute of Medicine, The World Health Organization, The Joint Commission, and The Institute for Safe Medication Practices, have examined medication errors resulting from look- or sound-alike drug names and called for Regulatory Authorities to address the issue prior to approval.

Furthermore, we contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, can be identified and remedied prior to approval to avoid patient harm.

Additionally, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to remedy post-approval. Educational efforts and so on are low-leverage strategies that have proven to have limited effectiveness at alleviating the medication errors involving drug name confusion. Higher-leverage strategies, such as drug name changes, have been undertaken 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 the approving the error-prone proprietary name. Moreover, even after Applicant's have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioner's vocabulary, and as such, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, we believe 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 limitations of the process).

If we object to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the FMEA process is used to identify strategies to reduce the risk of medication errors. We are likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for us to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name, and so we may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

2.2 LABEL AND LABELING RISK ASSESSMENT

The label and labeling of a drug product are the primary means by which practitioners and patients (depending on configuration) interact with the pharmaceutical product. The container labels and carton labeling communicate critical information including proprietary and established name, strength, form, container quantity, expiration, and so on. The insert labeling is intended to communicate to practitioners all information relevant to the approved uses of the drug, including the correct dosing and administration.

Given the critical role that the label and labeling has in the safe use of drug products, it is not surprising that 33 percent of medication errors reported to the USP-ISMP Medication Error Reporting Program may be attributed to the packaging and labeling of drug products, including 30 percent of fatal errors.[7]

Because the Medication Error Prevention staff analyze reported misuse of drugs, we are able to use this experience to identify potential errors with all medication similarly packaged, labeled or prescribed. Our Division uses FMEA and the principles of human factors to identify potential sources of error with the proposed product labels and insert labeling, and provided recommendations that aim at reducing the risk of medication errors.

The Division of Medication Error Prevention reviewed the following labels and labeling submitted by the Applicant on August 15, 2007 (see Appendix I, J and K for images):

- Syringe Label
- Blister Labeling
- Carton Labeling
- Prescribing Information (no image)

Additionally, the Applicant submitted a mock-up of the proposed syringe for review and comment.

3 RESULTS

3.1 PROPRIETARY NAME RISK ASSESSMENT

3.1.1 Database and Information Sources

The Division of Medication Error Prevention conducted a search of the internet, several standard published databases and information sources (see Section 7 References) for existing drug names which sound-alike or look-alike to Trivaris to a degree where potential confusion between drug names could occur and result in medication errors in the usual clinical practice settings. In total, 21 names were identified as having some similarity to the name Trivaris: Trivarion, Travance, Trizivar [redacted], Lavoris, Invirase, Univasc, Trivastin, Rhinaris, Tarceva, Truvada, Triavil, Trivanex, Omnaris, Tribulus, Trivass. [redacted], Trivora, Trizivir, Luveris and Letairis. b(4)

Thirteen of the 21 names that were thought to look like Trivaris, these names include: Trivarion, Travance, Trizivar, [redacted], Lavoris, Invirase, Univasc, Trivastin, Rhinaris, Tarceva, Truvada, Triavil and Trivanex. Two names were thought to sound like Trivaris (Omnaris and Tribulus). The remaining six additional names (Trivass, [redacted], Trivora, Trizivir, Luveris and Letaris) were thought to look and sound similar to Trivaris. b(4)

The proposed proprietary name, Trivaris, does not contain a USAN stem as of the last date searched, February 27, 2008.

[7] Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006. p275.

3.1.2 Expert Panel Discussion

The Expert Panel reviewed the pool of names identified by our staff (see section 3.1.1), and noted an additional two names, Trexima and Triesence, as having an orthographic similarity to Trivaris. The panel commented that the name, Trivaris, is also a consultant corporation in Burlington, Ontario.

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

3.1.3 CDER Prescription Analysis Studies

A total of 39 practitioners responded, but none of the responses overlapped with any existing or proposed drug names. About two-thirds of the participants (n=29) interpreted the name correctly as "Trivaris" with correct interpretation occurring more frequently in the written studies. The remainder of the responses misinterpreted the drug name. The majority of misinterpretations occurred in the phonetic prescription study, with the vowel letter 'e' reported as 'a'. Additionally, one respondent misinterpreted the letter 'v' as the letter 'm'. In the written prescription studies, the letter 'a' was misinterpreted as an 'o' by one respondent, and the 'a' was misinterpreted as 'e' by one respondent. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.1.4 External Name Studies

In the proposed name risk assessment submitted by the Applicant, the [redacted] identified and evaluated a total of seventy-two drug names thought to have some potential for confusion with the name Trivaris. Sixty-seven (67) of the seventy-two (72) names were not previously identified in the Medication Error Prevention Staff searches, the Expert Panel Discussion, or FDA prescription studies. These sixty-seven names were listed in either the Computerized Orthographic and Phonologic Analysis (COPA) or the DSI Internal Expert Panel Discussion, however DSI did not specifically list whether they share look-alike and/or sound-alike characteristics with Trivaris. The remaining five names listed look-alike (Cialis, Trivora 21-day, Trivora 28-day and Trizivir) or sound-alike characteristics (Trazodone). b(4)

3.1.5 Safety Evaluator Risk Assessment

Independent searches by the primary Safety Evaluator did not identify any additional names thought to look or sound similar to Trivaris and represent a potential source of drug name confusion. As such, a total of ninety (90) names were analyzed to determine if the drug names could be confused with Trivaris and if the drug name confusion would likely result in a medication error.

All of the identified names were determined to have some orthographic and/or phonetic similarity to Trivaris, and thus determined to present some risk for confusion. Failure mode and effects analysis was then applied to determine if the proposed name, Trivaris, could potentially be confused with any of the ninety names and lead to medication error.

This analysis determined that the name similarity between Trivaris and the identified names was unlikely to result in medication errors for all ninety product names. Sixty-five names were not considered further because they lacked convincing orthographic and/or phonetic similarities with Trivaris (Appendix D). Ten products have been discontinued or withdrawn from the market and have no generic equivalents available (Appendix E). Three names are used for products marketed in foreign countries, and thus determined by FMEA to pose minimal risk for error in the usual practice setting (see Appendix F). For nine of the names FMEA determined that medication errors were unlikely because the products do not overlap in strength or dosage with Trivaris and have minimal orthographic and/or phonetic similarity to Trivaris (Appendix G). One name (Trivastin) was found in the U.S. Patent and Trademark Office

database. However, this product was abandoned by the Applicant and no product information was found in common drug references (Appendix H). Two names [redacted], are proposed names proprietary names for other products which have not been approved or were approved under a different proprietary name, and thus were determined by FMEA to pose minimal risk of error in the usual practice setting (Appendix H). b(4)

3.2 LABEL AND LABELING RISK ASSESSMENT

[redacted] b(4)

2 Page(s) Withheld

1 Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

5 CONCLUSIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Trivaris, has some similarity to other proprietary names, but the findings of the FMEA indicates that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors. This finding was consistent with and supported by an independent risk assessment of the proprietary name submitted by the Applicant. As such, the Division of Medication Error Prevention has no objection to the use of the name, Trivaris, for this product. Additionally, DDMAC does not object to the proposed name, Trivaris, from a promotional perspective.

The Label and Labeling Risk Assessment found [redacted] We believe the risks we have identified can be addressed and mitigated prior to drug approval, and provides recommendations in Section 6 that aim at reducing the risk of medication errors. b(4)

However, if **any** of the proposed product characteristics as stated in this review are altered prior to approval of the product, we rescind this Risk Assessment finding, and recommends that the name be resubmitted for review. If 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. Additionally, if the product approval is delayed beyond 90 day from the date of this review, the proposed name must be resubmitted for evaluation.

6 RECOMMENDATIONS

6.1 COMMENTS TO THE DIVISION

6.1.1 Proprietary name

The Division of Medication Error Prevention has no objections to the use of the proprietary name Trivaris for this product. However, if **any** of the proposed product characteristics as state in this review are altered prior to approval of the product, we rescind this Risk Assessment finding, and recommend that the name be resubmitted for review. If the approval is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

Based upon our assessment of the labels and labeling, the Division of Medication Error Prevention has identified areas of needed improvement. We have provided recommendations in section 6.2 and request this information be forwarded to the Applicant

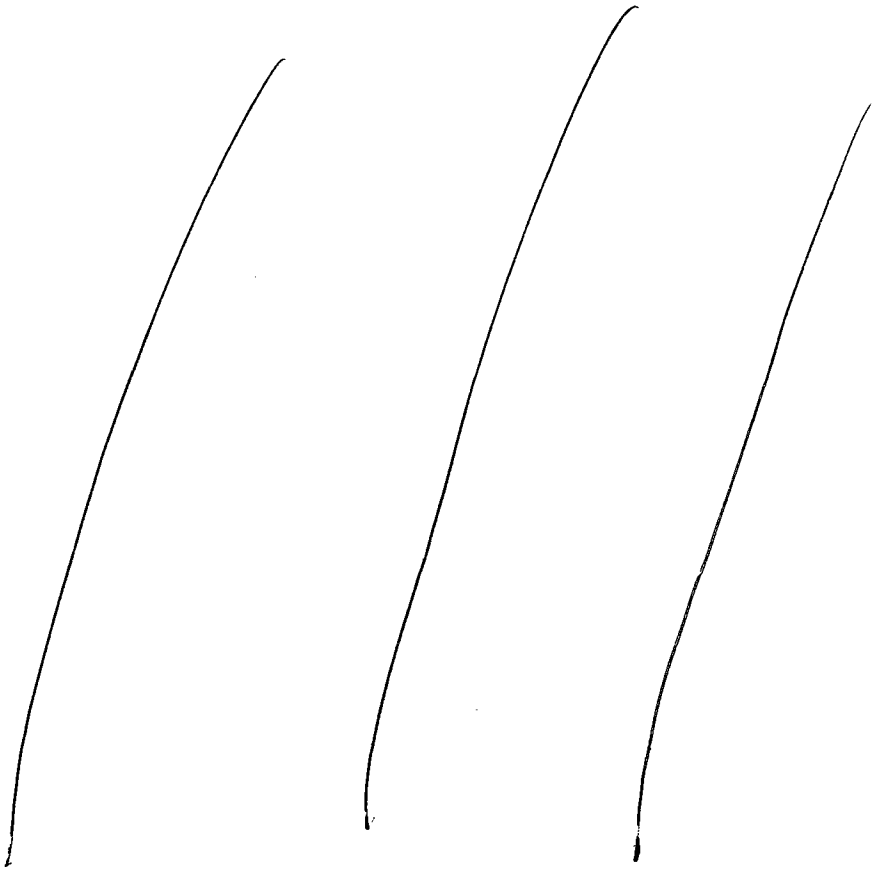
We would be willing to meet with the Division for further discussion, if needed. We would appreciate feedback of the final outcome of this review. Please copy us on any communication to the applicant with regard to this review. If you have any further questions or need clarifications, please contact Cherye Milburn, OSE Project Manager, at 301-796-2084.

6.2 COMMENTS TO THE APPLICANT

6.2.1 Proprietary Name

The Division of Medication Error Prevention has no objections to the use of the proprietary name, Trivaris, for this product. If **any** of the proposed product characteristics stated in this review are altered prior to approval of this product, we rescind this Risk Assessment finding, and recommend that the name be resubmitted for evaluation. If product approval is delayed beyond 90 days from the date of the review, the proposed name will be re-evaluated.

6.2.2 Labels and Labeling



b(4)

1 Page(s) Withheld

/ Trade Secret / Confidential (b4)

Draft Labeling (b4)

Draft Labeling (b5)

Deliberative Process (b5)

7 REFERENCES

1. Adverse Events Reporting System (AERS)

AERS is a database application in CDER FDA that contains adverse event reports for approved drugs and therapeutic biologics. These reports are submitted to the FDA mostly from the manufactures that have approved products in the U.S. The main utility of a spontaneous reporting system that captures reports from health care professionals and consumers, such as AERS, is to identify potential postmarketing safety issues. There are inherent limitations to the voluntary or spontaneous reporting system, such as underreporting and duplicate reporting; for any given report, there is no certainty that the reported suspect product(s) caused the reported adverse event(s); and raw counts from AERS cannot be used to calculate incidence rates or estimates of drug risk for a particular product or used for comparing risk between products.

2. Micromedex Integrated Index (http://weblern/)

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

3. Phonetic and Orthographic Computer Analysis (COPA)

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, FDA.

4. Drug Facts and Comparisons, online version, St. Louis, MO (http://weblern/)

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

5. AMF Decision Support System [DSS]

DSS is a government database used to track individual submissions and assignments in review divisions.

6. Division of Medication Error Prevention name consultation requests

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention 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 and generic drugs and therapeutic biological products; prescription and over-the-counter human drugs and therapeutic biologicals, 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. ***WWW location*** *http://www.uspto.gov.*

Provides information regarding patent and trademarks.

10. ***Clinical Pharmacology Online*** *(http://weblern/)*

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 tradenames that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

12. ***Natural Medicines Comprehensive Databases*** *(http://weblern/)*

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

13. ***Stat!Ref*** *(http://weblern/)*

Contains full-text information from approximately 30 texts. Includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs 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.pharmacist.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: Product Characteristics for Approved Triamcinolone Acetonide Products

Product Characteristics	Kenalog-40 Injection	Triesence	Trivaris
Indications	Allergic states, Dermatologic diseases, Endocrine disorders, Gastrointestinal diseases, Neoplastic diseases, Hematologic disorders, Nervous system, Renal diseases, Respiratory diseases, Rheumatic disorders, miscellaneous	Ophthalmic diseases: sympathetic ophthalmia, temporal arteritis, uvetitis, and ocular inflammatory unresponsive to topical steroids. Visualization during vitrectomy.	Ophthalmic Use Intramuscular Use Intra-Articular or soft tissue Use
Route of administration	Intramuscular Intra-Articular or soft tissue administration	Intravitreally	Intravitreally, Intramuscular, Intra-Articular or soft tissue
Strength	40 mg/mL	40 mg/mL	8 mg/0.1mL
Dose	2.5 mg to 100 mg	4 mg for Ophthalmic conditions 1 to 20 mg for visualization during vitrectomy	4 mg for Ophthalmic Use: 2.5 mg to 100 mg for Intramuscular and/or Intra-Articular or soft tissue Use:
Packaging configuration	1 mL vial, 5 mL vial, and 10 mL vial	1 mL vial	[redacted] Prefilled syringe without needle

b(4)

APPENDIX B:

The Medication Error Staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. The Division of Medication Error Prevention also compare 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. The Medication Error Staff 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* dissimilarly spelled drug name pairs to appear very similar to one another and the similar appearance of drug names when scripted has lead to medication errors. The Medication Error Staff apply their expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (i.e. "T" may look like "F," lower case 'a' looks like a lower case 'u,' etc), along with other orthographic attributes that determine the overall appearance of the drug name when scripted (see detail in Table 1 below). Additionally, since verbal communication of medication names is common in clinical settings, the Medication Error Staff compare the pronunciation of the proposed proprietary name with the pronunciation of other drug names. If provided, the Division of Medication Error Prevention will consider the Applicant's intended pronunciation of the proprietary name. However, because the Applicant has little control over how the name will be spoken in practice, we also consider a variety of pronunciations that could occur in the English language.

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	• 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 Downstrokes Cross-stokes	• Names may look similar when scripted, and lead to drug name confusion in written communication

		Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	
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	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Appendix C:

CDER Prescription Study Responses

Outpatient Prescription	Voice Prescription	Inpatient Medication Order
Trivaris	Triveris	Trivaris
Trivaris	Trivaris	Trivaris
Trivaris	Triveris	trivaris
Trivaris	Triveris	Trivaris
Trivaris	Triveris	Trivaris
Trivoris	Trivaris	Trivaris
Trivaris	Trivaris	Trivaris
Trivaris	Triveris	Trivaris
Trivaris	Trivaris	Trivaris
Trivaris	Trivaris	Trivaris
Triveres	Triveris	Travaris
Trivaris	Trivaris	Trivaris
Trivaris	Trimeris	Trivaris

Appendix D: Names lacking convincing look-alike and/or sound-alike similarities with Trivaris

Proprietary Name	Similarity to Trivaris	Proprietary Name	Similarity to Trivaris	Proprietary Name	Similarity to Trivaris	Proprietary Name	Similarity to Trivaris
Emtriva	COPA	Temaril	COPA	Triacin-C	COPA	Trifedrine	COPA
Ivarest	COPA	Tearisol	COPA	Triactin	COPA	TriHIBit	COPA
Nutrivir	COPA	Travasol	COPA	Triam-M	COPA	Trilafon	COPA
Octrivin	COPA	Travasorb	COPA	Trianide	COPA	Trileptal	COPA
Premarin	COPA	Travert	COPA	Triaprin	COPA	Trimazide	COPA
Prevacid	COPA	Trazodone	COPA	Tri-Aqua	COPA	Trimox	COPA
Rhinaris	Look-alike	Trexima	Look	Triacort	COPA	Trimpex	COPA
Trinovin	COPA	Triac	COPA	Triban	COPA	Trimtabs	COPA
Triostat	COPA	Triacet	COPA	Tricor	COPA	Trinate	COPA
Tri-Otic	COPA	Triad	COPA	Trihist	COPA	Tri-Nefrin	COPA
Trioxazin	COPA	Triavil	Look	Tridal	COPA	Trinotic	COPA
Tri-Pain	COPA	Tribulus	Sound	Triderm	COPA		
Tripedia	COPA	Tri-Vitamin	COPA	Tridesilon	COPA		
Triphasil	COPA	Trizivir	Look/Sound	Trivarion	COPA		
Trisenox	COPA	Omnaris	Sound	Tri-Vi-Sol	COPA		
Tristatin	COPA	Travance	Look	Tri-Vit	COPA		
Tritan	COPA	Triesence	Look	Tridil	COPA		

Appendix E: Products withdrawn from the market with no generic equivalents available.

Proprietary Name	Similarity to Trivaris
Triclos	COPA
Trigesic	COPA
Trinalin	COPA
Trimahist	COPA
Tritane	COPA
Trivora (21-day)	Look/Sound
Trixaicin	COPA
Trovan	COPA
Trovan IV	COPA
Travase	COPA

Appendix F: Proprietary Names used only in Foreign Countries

Proprietary Name	Similarity to Trivaris	Country
Trizivar	Look	South Africa
Trivanex	Look	Thailand
Trivass	Sound	Central America

Appendix G: Products with no numerical overlap in strength and dose.

Trivaris name (triamcinolone acetonide)		**8 mg/ 0.1 mL**	**Usual Dose: 4 mg in each eye as needed**
Product name with potential for confusion	**Similarity to Proposed Proprietary Name**	**Strength**	**Usual Dose (if applicable)**
Travatan	Look	0.04%	1 drop into each eye once daily in the evening
Trivora (28-day) (Ethinyl Estradiol/Levonorgestrel	Look/Sound	Triphasic oral contraceptive	1 tablet daily
Truvada	Look	200 mg and 300 mg	1 tablet by mouth daily
Vivarin	COPA	200 mg	1 tablet by mouth daily
Lavoris	Look	N/A	Rinse or gargle for 30 seconds
Invirase	Look	200 mg and 500 mg	1000 mg by mouth twice daily
Univasc	Look	7.5 mg and 15 mg	1 (7.5 mg) tablet daily
Letairis	Look/Sound	5 mg and 10 mg	5 mg by mouth daily
Luveris	Look/Sound	75 units	75 IU subcutaneously daily

Appendix H: Proposed proprietary names for products not approved or approved with another name.

Proprietary Name	**Similarity to Trivaris**
Trivastin (USPTO)	Look
—	Look
—	Sound

b(4)

3 Page(s) Withheld

_____ Trade Secret / Confidential (b4)

✓ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

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

/s/

Diane Smith
5/29/2008 03:08:06 PM
CSO

Todd Bridges
5/29/2008 04:14:35 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
5/29/2008 04:25:18 PM
DRUG SAFETY OFFICE REVIEWER