CENTER FOR DRUG EVALUATION AND RESEARCH

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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:	April 9, 2009
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Subject:	Proprietary Name Review
Drug Name(s):	Ilaris (Canakinumab) Injection, 150 mg
Application Type/Number:	BLA 125319
Applicant/Applicant:	Novartis
OSE RCM #:	2009-289

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EXECUTIVE SUMMARY

This review is in response to a request from Novartis on January 13, 2009, for an assessment of the proposed proprietary name, Ilaris, regarding potential name confusion with other proprietary or established drug names in the usual practice settings.

DMEPA identified forty-two names as having potential orthographic and/or phonetic similarity to Ilaris. Additionally, the Applicant submitted an external risk assessment of the proprietary name, which identified two additional names. Thus, DMEPA analyzed forty-four names for their potential to cause confusion with Ilaris. Our Failure Mode Effects Analysis determined that the name similarity between Ilaris and the 44 names identified was unlikely to result in medication errors related to name confusion. This finding was consistent with and supported by the external risk assessment of the proprietary name submitted by the Applicant. Thus the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Ilaris, for this product.

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, 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 In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject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.

In addition, the proposed name must be reevaluated 90 days before approval of the BLA, even if the proposed product characteristics as stated in this review are not altered.

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from Novartis on January 13, 2009, for an assessment of the proposed proprietary name, Ilaris, regarding potential name confusion with other proprietary or established drug names in the usual practice settings. The Applicant submitted an external study in support of their proposed proprietary name. Novartis also submitted container labels and carton labeling for review, which will be reviewed under separate cover (OSE Review #2009-64).

1.2 PRODUCT INFORMATION

Ilaris (Canakinumab) is a recombinant human monoclonal anti-human interleukin -1Beta antibody being investigated for the treatment of Cryopyrin Associated Periodic Syndrome (CAPS) in adults and children aged 4 years and older. The recommended dose for a body weight >40 kg is 150 mg, and for a body weight $\geq$ 15 kg and $\leq$ 40 kg is 2 mg/kg, administered subcutaneously every 8 weeks. Ilaris is supplied as a 150 mg lyophilized powder. Reconstitution with 1 mL of preservative-free sterile water for injection is required prior to administration.

1.3 REGULATORY HISTORY

Ilaris (Canakinumab) is currently under review by the Division of Analgesics, Anesthetics, and Rheumatology Products under BLA 125319.

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. Sections 2.1, 2.2, and 2.3 identify specific information associated with the methodology for the proposed proprietary name, Ilaris.

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 Ilaris, the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (6 letters), upstrokes (two, capital letter 'I', and lowercase letter 'l'), down strokes (none), cross strokes (none), and dotted (one, lower case letter 'i'). Additionally, several letters in Ilaris may be vulnerable to ambiguity when scripted, including the capital letter 'I' may appear as capital letters 'P', 'S', 'D', 'J' or 'A'; lower case 'l' may look like lower case 'e', 'b', 'f', 'h', 'k' or 't'; lower case 'a' may look like lower case 'e', 'o' or 'c'; lower case letter 'r' may appear as lower case 'e', 'n', 's', 'v' or 'u'; lower case 'i' may appear as lower case 'e', 'j' or 'l'; and lower case 's' may appear as lower case 'a', 'c', 'n' or 'r'. As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Ilaris.

When searching to identify potential names that may sound similar to Ilaris, the DMEPA staff search for names with similar number of syllables (3), stresses (I-lar-is; i-LAR-is; i-lar-IS), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary such as 'Ilar-' may sound like 'Alar-', 'Elar-', 'Iler' and '-is' may sound like '-es'. The Applicant's intended pronunciation (i-LAR-is) was also taken into consideration, as it was included in the Proprietary Name Review Request. Moreover, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

2.2 FDA PRESCRIPTION ANALYSIS STUDIES

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, the following inpatient medication order, outpatient and verbal prescription was communicated during the FDA prescription studies.

Figure 1. Ilaris Study (conducted on March 31, 2009)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order #1: Ilaris 150mg inject under the skin x 1 dose	Ilaris 150 mg Inject under the skin x 1 dose
Inpatient Medication Order #2: 1) Ilaris 150 mg inject under the skin x 1 dose	

[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)

2.3 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

For this product, the Applicant submitted an external evaluation of the proposed proprietary name. The Division of Medication Error Prevention and Analysis 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 DMEPA'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.

After the Safety Evaluator has determined the overall risk associated with 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 the Division's risk assessment concurs or differs with the findings. When the proprietary name risk assessments differ, the Division of Medication Error Prevention and Analysis provides a detailed explanation of these differences.

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The searches yielded a total of thirty-five names as having some similarity to the name Ilaris.

Twenty-two of the names were thought to look like Ilaris. These include: Alaira, Aldara, Alinia, Alora, Aloxia, Alrex, Claravis, Clarex, Clarix, Elase, Elavil, Eurax, Flarex, Iberet-500, Idenix, Iletin, Ilosone, b(4)
Letairis, Luveris, Tilarin, and Uloric. Four of the names were thought to sound like Ilaris. These include: Alarin, Cylaris, Micardis, and Omnaris. The remaining nine names were thought to look and sound similar to Ilaris: Alera, Alertis, Cilaris, Claris. , Ilacen, Liatris, Soliris, and Trivaris.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of March 4, 2009.

3.2 EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMEPA staff (See Section 3.1 above) and noted no additional names thought to have orthographic or phonetic similarity to insert Ilaris.

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 FDA PRESCRIPTION ANALYSIS STUDIES

A total of twenty-nine practitioners responded with one of the responses overlapping with an existing name (Xolair), which will be included in the Safety Evaluator Assessment. Twenty of the participants interpreted the name correctly as "Ilaris," with correct interpretation occurring in both the inpatient written studies. The remainder of the written responses misinterpreted the drug name. In the verbal studies, all responses were misspelled phonetic variations of the proposed name, Ilaris. See Appendix B for the complete listing of interpretations from the verbal and written prescription studies.

3.4 EXTERNAL STUDY

In the proposed name risk assessment submitted by the Applicant, — identified and evaluated a total of four names thought to have some potential for confusion with the name Ilaris: Elavil, Flarex, Lasix and Alaris. Of the four names identified by — one name was identified as a company name (Alaris). Of the remaining three drug names, DMEPA also identified Elavil and Flarex during the database searches. The names Alaris and Lasix, will be added to the Safety Evaluator Assessment. b(4)

3.5 COMMENTS FROM THE DIVISION OF ANALGESICS, ANESTHETICS, AND RHEUMATOLOGY PRODUCTS (DAARP)

In response to the OSE Date, March 6, 2009 e-mail, (DAARP) did not forward any comments and/or concerns on the proposed name at the initial phase of the name review.

DMEPA notified the Division of Analgesics, Anesthetics, and Rheumatology Products via e-mail that we had no objections to the proposed proprietary name, Ilaris, on March 13, 2009. Per e-mail correspondence from the Division of Analgesics, Anesthetics, and Rheumatology Products on April 6, 2009, they indicated they concur with our assessment of the proposed proprietary name, Ilaris.

3.6 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator resulted in seven additional names which were thought to look or sound similar to Ilaris and represent a potential source of drug name confusion.

The names identified to have look-alike similarities are Aloxi, Clari, Clarus, Clorix, Harin, and Ibarin. The name, Alois, was identified to have look-alike and sound-alike similarities. Additionally, we note that attempts to identify the drug name Aloxia were unsuccessful. We assume that this name was misspelled during the search process (i.e. Aloxia for Aloxi). Thus, we evaluated a total of 44 names: one identified from the FDA Prescription Analysis Studies, two identified in the External Study, seven identified by the primary safety evaluator and 34 already identified in section 3.1 above.

4 DISCUSSION

Forty-four names were evaluated for their potential similarity to the proposed name, Ilaris. Eleven lacked orthographic and/or phonetic similarity and were not evaluated further (see Appendix C).

Failure mode and effect analysis (FMEA) was then applied to determine if the proposed proprietary name could potentially be confused with the remaining thirty-three names and lead to medication errors. This analysis determined that the name similarity between Ilaris was unlikely to result in medication errors with any of the 33 products for the reasons presented in Appendices D through N. This finding was consistent with and supported by an independent risk assessment of the proprietary name submitted by the Applicant.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Ilaris, is not 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, Ilaris, for this product at this time. Our assessment supports the findings of the External Study submitted by the Applicant. The Division of Analgesics, Anesthetics, and Rheumatology Products concurs with this assessment. Additionally, DDMAC does not object to the proposed name, Ilaris, from a promotional perspective.

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, 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 resubmitted for evaluation.

5.1 COMMENTS TO THE DIVISION

We are willing to meet with the Division for further discussion, if needed. Please copy DMEPA on any communication to the Applicant with regard to this review. If you have further questions or need clarifications, please contact Chris Wheeler, project manager, at 301-796-0151.

5.2 COMMENTS TO THE APPLICANT

5.2.1 Proprietary Name

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

Ilaris will be re-reviewed 90 days prior to the approval of the BLA. If we find the name unacceptable following the re-review, we will notify you.

APPEARS THIS WAY ON ORIGINAL

6 REFERENCES

1. Micromedex Integrated Index (http://csi.micromedex.com)

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

2. Phonetic and Orthographic Computer Analysis (POCA)

POCA is a database which was created for the Division of Medication Error Prevention and Analysis, FDA. 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.

3. Drug Facts and Comparisons, online version, St. Louis, MO (http://factsandcomparisons.com)

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

4. AMF Decision Support System [DSS]

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

5. 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.

6. 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.

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

The FDA Orange Book provides a compilation of approved drug products with therapeutic equivalence evaluations.

8. U.S. Patent and Trademark Office (http://www.uspto.gov)

USPTO provides information regarding patent and trademarks.

9. Clinical Pharmacology Online (www.clinicalpharmacology-ip.com)

Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. It also provides a keyword search engine.

10. 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.

11. Natural Medicines Comprehensive Databases (www.naturaldatabase.com)

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

12. Stat!Ref (www.statref.com)

Stat!Ref contains full-text information from approximately 30 texts; it 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.

13. USAN Stems (http://www.ama-assn.org/ama/pub/category/4782.html)

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

15. Lexi-Comp (www.lexi.com)

Lexi-Comp is a web-based searchable version of the Drug Information Handbook.

16. Medical Abbreviations Book

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 staff 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 staff also conducts 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

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

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 proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff 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 staff considers 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 staff considers 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 in spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examines 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 staff applies 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 staff compares 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.

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

[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	• 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-stokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-	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

Lastly, the DMEPA staff also considers 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 staff conducts 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 staff 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 staff 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) staff 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/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 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 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 is 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 posses 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

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

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).

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.

Appendix B: FDA Prescription Study Responses.

Inpatient Medication Order #1	Inpatient Medication Order #2	Verbal Prescription
Ilaris	Ilaris	Allaris
Ilaris	Ilaris	Alaris
Ilaris	Ilaris	Xolair
Ilaris	Ilaris	Allera
Ilaris	Ilaris	Olaris
Ilaris	Ilaris	Celeris
	Ilaris	Alleres
	Ilaris	
	Ilaris	
	Ilaris	
	Ellaris	
	Ilaris	
	Ilaris	
	Ilaris	
	Ilaris	
	Cllaus	

Appendix C: Proprietary names that lack convincing orthographic and/or phonetic similarities

Proprietary Name	Similarity to Haris
Aldara	Look
Aletris	Look and Sound
Elavil	Look
Eurax	Look
Iberet-500	Look
Iletin	Look
Letairis	Look
Liatris	Look and Sound
Micardis	Sound
Lasix	Look
Luveris	Look

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Appendix D: Product not identified as drug

Proprietary Name	Similarity to Haris	Reason
Idenix	Look	Applicant name
Claris	Look and Sound	Trademarked Company Name-manufacturer of dermatological products(products not identified)
Alaris	Look and Sound	Healthcare Company name

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Appendix E: Proprietary names that are internationally registered

Proprietary Name	Similarity to Haris	Active Ingredient	Country
Alarin	Sound	Loratadine	Turkey
Alois	Look and Sound	Memantine	Brazil
Clari	Look	Clarithromycin	Singapore
Clarus	Look	Bromhexine Isotretinoin	Brazil Canada

Clorix	Look	Moclobemide	South Africa
Ibarin	Look	Fluconazole	Chile
Ilacen	Look and Sound	Diflunisal	Spain
Harin	Look	Pentoxifylline	Korea
Clarex	Look	Phenylephrine, Boric Acid	Mexico
Clarix	Look	Oxymetazoline	Venezuela

Appendix F: Discontinued products with no available generics

Proprietary Name	Active Ingredient	Similarity to Haris
Elase	Chloramphenicol; Desoxyribonuclease; Fibrinolysin	Look

Appendix G: Proprietary names with Preassigned NDA number, but NDA not submitted to Agency.

Proprietary Name	Similarity to Haris
	Look

Appendix H: Proposed secondary name not used because primary name approved for drug product.

Proprietary Name	Similarity to Haris	Approved Name
—	Look	—

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Appendix I: Abandoned Trade names

Proprietary Name	Similarity to Haris	Status
Cilaris	Look and Sound	Abandoned trademarks as of (June 19, 2007 -Canada) Trademark changed to Cylaris (February 17, 2009)- discussed in Appendix L

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Appendix J: Products not approved by the Agency or withdrawn from Agency prior to approval

Proprietary Name	Similarity to Ilaris	Status
—	Look	Withdrawn from Pending December 19, 1997

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Appendix K: Products with no numerical overlap in strength and usual dose

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Ilaris (Canakinumab) Injection		150 mg (lyophilized powder)	Treatment of Cryopyrin-Associated Periodic Syndrome (CAPS): Body Weight(BW) >40 kg: 150 mg Body Weight(BW)≥15 kg and ≤40 kg: 2 mg/kg Administered every 8 weeks
Alora (Estradiol Transdermal System)	Look	0.025 mg/24 hr, 0.05 mg/24 hr 0.075 mg/24 hr, 0.1 mg/24 hr,	Apply one patch to skin twice weekly.
Aloxi (Palonosetron)	Sound	Capsules: 0.5 mg Injection: 0.25 mg Base/5 mL; 0.075 mg Base/1.5 mL	Take one capsule 1 hour prior to chemo Administer 0.25 mg IV over 30 seconds, 30 minutes prior to chemo Administer 0.075 mg IV over 10 seconds before induction of anesthesia

Appendix L: Single strength products with multiple differentiating product characteristics

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Differentiating product characteristics
Ilaris (Canakinumab) Injection		**150 mg (lyophilized powder)**	**Treatment of Cryopyrin Associated Periodic Syndrome (CAPS)** **Body Weight(BW) ≥40 kg: 150 mg** **Body Weight(BW) ≥15 kg and <40 kg: 2 mg/kg** **Administered every 8 weeks**	
Alera (Hydroquinone)	Look and Sound	Topical: 4% emulsion	Hyperpigmented skin: Apply to affected area and rub in well twice daily	**Dosage form:** Injection vs. Emulsion **Route of Administration:** Subcutaneous vs. Topical **Frequency of Administration:** Every 8 weeks vs. Twice daily **Dose:** 150 mg for BW>40 kg or 30 mg to 80 mg for BW ≥15 kg and ≤40 kg vs. Apply sparingly **Storage Conditions:** Pharmacy Refrigerator vs. Pharmacy Shelf
Omnaris (Ciclesonide)	Sound	**Intranasal Spray:** 50 mcg/actuation	Perennial or Seasonal Allergic Rhinitis: Administer 2 sprays in each nostril per day	**Dosage form:** Injection vs. Nasal spray **Route of Administration:** Subcutaneous vs. Intranasal **Frequency of Administration:** Every 8 weeks vs. once daily **Dose:** 150 mg for BW>40 kg or 30 mg to 80 mg for BW ≥15 kg and ≤40 kg vs. 2 Sprays **Storage Conditions:** Pharmacy Refrigerator vs. Pharmacy Shelf
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

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Cylaris Weight Loss Supplement: (Vitamin B6, Folic Acid, Vitamin B12, Selenium, Chromium, Caffeine Anhydrous, Cissus Quadrangularis, Soy)	Sound	Caplet	Weight Loss: One caplet twice daily before meals	**Route of Administration:** Subcutaneous vs. Oral **Frequency of Administration:** Every 8 weeks vs. Twice daily **Dosage Form:** Injection vs Caplet **Dose:** 150 mg for BW>40 kg or 30 mg to 80 mg for BW ≥15 kg and ≤40 kg vs. 1 caplet
Alrex (Loteprednol etabonate)	Look	Ophthalmic suspension: 0.2 %	Ophthalmic inflammatory conditions: Instill 1 to 2 drops into conjunctival sac of affected eye four times daily	**Dosage form:** Injection vs. Ophthalmic suspension **Route of Administration:** Subcutaneous vs. Intraocular **Frequency of Administration:** Every 8 weeks vs. four times daily **Dose:** 150 mg for BW>40 kg or 30 mg to 80 mg for BW ≥15 kg and ≤40 kg vs. One to two drops **Storage Conditions:** Pharmacy Refrigerator vs. Pharmacy Shelf
Flarex (Fluorometholone acetate)	Look	Ophthalmic suspension: 0.1 %	Ophthalmic inflammatory conditions: Instill 1 to 2 drops into the conjunctival sac four times daily.	**Dosage form:** Injection vs. Ophthalmic suspension **Route of Administration:** Subcutaneous vs. Intraocular **Frequency of Administration:** Every 8 weeks vs. four times daily **Dose:** 150 mg for BW>40 kg or 30 mg to 80 mg for BW ≥15 kg and ≤40 kg vs. One to two drops
Trivaris (Triamcinolone acetonide)	Look and Sound	Injection: 8 mg/0.1 mL	Inflammatory conditions Dosing: Variable Intravitreal: 4 mg Intramuscular: 60 mg Intraarticular: 2.5 mg to 15 mg	**Route of Administration:** Subcutaneous vs. Intravitreal; Intramuscular; Intraarticular **Frequency of Administration:** Every 8 weeks vs. Variable (2.5 mg to 60 mg) **Dose:** 150 mg for BW>40 kg or 30 mg to 80 mg for BW ≥15 kg and ≤40 kg vs. 2.5 mg to 100 mg per day

Appendix M: Products with potential numerical overlap or similarity in strength and/or dose but with multiple differentiating product characteristics

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Differentiating product characteristics
Ilaris (Canakinumab) Injection		**150 mg (lyophilized powder)**	**Treatment of Cryopyrin Associated Periodic Syndrome (CAPS):** **Body Weight(BW) >40 kg: 150 mg** **Body Weight(BW) ≥15 kg and ≤40 kg: 2 mg/kg** **Administered every 8 weeks**	
Alinia (Nitazoxanide)	Look	Tablets: 500 mg Oral Suspension: 100 mg per 5 mL	Diarrhea: Age dependent: (1 to 3 years): 100 mg every 12 hours; (4 to 11 years): 200 mg every 12 hours; (>12 years): 500 mg every 12 hours	**Route of Administration:** Subcutaneous vs. Oral **Frequency of Administration:** Every 8 weeks vs. Twice daily **Dose:** 150 mg for BW>40 kg or 30 mg to 80 mg for BW ≥15 kg and ≤40 kg vs. Age dependent: (1 to 3 years): 100 mg; (4 to 11 years): 200 mg; (>12 years): 500 mg **Storage Conditions:** Pharmacy Refrigerator vs. Pharmacy Shelf
Claravis (Isotretinoin)	Look	Capsules: 10 mg, 20 mg, 30 mg, 40 mg	Recalcitrant nodular acne: 0.5 mg to 1 mg/kg/day in 2 divided doses daily	**Route of Administration:** Subcutaneous vs. Oral **Frequency of Administration:** Every 8 weeks vs. Twice daily **Dose:** 150 mg for BW>40 kg or 30 mg to 80 mg for BW ≥15 kg and ≤40 kg vs. 0.5 mg to 1 mg/kg/day in 2 divided doses daily **Storage Conditions:** Pharmacy Refrigerator vs. Pharmacy Shelf
Ilosone (Erythromycin Estolate)	Look	Suspension: 125 mg base/5 mL ; 250 mg base/5 mL	Treatment of bacterial infections: Variable dosing: 250 mg- 4 gm in divided doses daily	**Route of Administration:** Subcutaneous vs. Oral **Frequency of Administration:** Every 8 weeks vs. Daily divided doses **Dose:** 150 mg for BW>40 kg or 30 mg to 80 mg for BW ≥15 kg and ≤40 kg vs. 250 mg to 4 gm

(Febuxostat)	Look	Tablet: 40 mg, 80 mg	Chronic management of hyperuricemia in patients with gout : One tablet daily	**Route of Administration:** Subcutaneous vs. Oral **Frequency of Administration:** Every 8 weeks vs. Daily **Dose:** 150 mg for BW>40 kg or 30 mg to 80 mg for BW ≥15 kg and ≤40 kg vs. One tablet **Storage Conditions:** Pharmacy Refrigerator vs. Pharmacy Shelf

Appendix N: Potential confusing name with numerical similarity in strength and dose or attainable dose

Proposed name: **Ilaris (Canakinumab) Injection**	**Strength:** **150 mg (lyophilized powder)**	**Usual dose:** **Treatment of Cryopyrin-Associated Periodic Syndrome (CAPS)** **Body Weight(BW) >40 kg: 150 mg** **Body Weight(BW) ≥15 kg and ≤40 kg: 2 mg/kg** **Administered every 8 weeks**
Failure Mode: Name confusion	**Causes (could be multiple)**	**Effects**
Soliris (Eculizumab) Injection **300 mg/30 mL vial** *Indication/Dose*: Paroxysmal Nocturnal Hemoglobinuria(PNH) 600 mg IV every 7 days for 4 weeks; then 900 mg IV every 14 days	Orthographic similarity (capital letter "I" vs. "S") and ("-ris" ending) Phonetic similarity ("laris" vs. "liris") The products are indicated for the treatment of rare medical conditions. The products must be stored under refrigerated conditions.	Medication errors unlikely to occur due to restricted distribution of Soliris and Ilaris. *Rationale*: Soliris is distributed through an applicant sponsored program entitled OneSource. The program provides PNH patients with a Nurse Case Manager, who is a registered nurse with healthcare and insurance experience, and is responsible for assisting patients with obtaining Soliris. There are authorized distributors for Soliris, that distribute to specialty pharmacies. When an order for Soliris is needed, the Applicant coordinates a drop shipment to the treatment facility. For Ilaris, the product will be stored at only one location of each of three specialty mail-order providers and will be shipped directly to a patient's home upon order by a physician. For the first dose administration, typically the physician will ask to have the product shipped directly to the physician's office in order to assist the patient with the first

		dose. Through the use of specialty pharmacies and mail order, the distribution and dispensing of both products will be closely monitored and controlled. Medication errors are unlikely to occur due to the restricted distribution.
Xolair (Omalizumab) Injection 150 mg lyophilized powder *Indication/Dose*: Moderate to severe asthma 150 mg to 375 mg subcutaneously every 2 to 4 weeks	Phonetic similarity ("lar" vs. "lair") The products are supplied as 150 mg lyophilized powders. The products are administered through subcutaneous injections The products must be stored under refrigerated conditions. The products overlap in dose. (150 mg; 30 mg to 80 mg vs. 150 mg to 375 mg)	Medication errors unlikely to occur due to administration restrictions for Xolair and restricted distribution for both Ilaris and Xolair. *Rationale*: The distribution of Xolair is managed through four specialty pharmacies. A patient's doctor will submit a statement of medical necessity (SMN) to the pharmacy. (A SMN, a written or typed document, will further mitigate the risk of error caused by phonetic similarity.) Before the start of treatment, patients must authorize shipment to their doctor's office. The administration restrictions of Xolair are due to the risk of severe allergic reactions (anaphylaxis) upon administration. Included in the Medication Guide, is a statement of warning, which advises for the administration of Xolair, at the patient's doctor's office. A similar warning is included in the package insert, as well as a black-box warning which further advises of the need for patients to be observed closely for an appropriate period of time after Xolair administration. The distribution plan for Ilaris details the availability of the product at only one location of each of three specialty mail-order providers. Ilaris will be shipped directly to a patient's home upon order by a physician. For the first dose administration, typically the physician will ask to have the product shipped directly to the physician's office in order to assist the patient with the first dose. Through the use of specialty pharmacies and mail order, the distribution and dispensing of Ilaris will be closely monitored and controlled.