CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-180

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:	June 5, 2009
To:	Rafel Dwaine Rieves, MD, Acting Director Division of Medical Imaging and Hematology Products
Through:	Kellie Taylor, PharmD, Team Leader Denise P. Toyer, PharmD, Deputy Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Loretta Holmes, BSN, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Feraheme (Ferumoxytol Injection) 127.5 mg/4.25 mL, 255 mg/8.5 mL, and 510 mg/17 mL (30 mg/mL)
Application Type/Number:	NDA 22-180
Applicant:	AMAG Pharmaceuticals, Inc.
OSE RCM #:	2009-902

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EXECUTIVE SUMMARY

This re-assessment of the proprietary name is written in response to a notification that NDA 22-180 may be approved within 90 days. DMEPA found the proposed proprietary name, Feraheme, acceptable in OSE Review #2008-1522, dated December 17, 2008. Since that review, none of Feraheme's product characteristics have changed.

During this re-review we identified 72 new names for their similarity to Feraheme. The results of the Failure Mode Effects Analysis found that the proposed name, Feraheme, is not vulnerable to name confusion that could lead to medication errors with any of the 72 names. Thus, the Division of Medication Error Prevention and Analysis does not object to the use of the proprietary name, Feraheme, for this product.

DMEPA considers this a final review, however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Medical Imaging and Hematology Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

1 BACKGROUND

1.1 PRODUCT INFORMATION

Feraheme (Ferumoxytol Injection) is a superparamagnetic iron oxide coated with polyglucose sorbitol carboxymethylether. Feraheme is indicated for the treatment of iron deficiency anemia in adult patients with chronic kidney disease. The recommended dose is 510 mg intravenously, intially, followed by 510 mg intravenously 3 to 8 days later. Feraheme is administered undiluted at a rate of up to 1 mL per second. Feraheme contains 30 mg of elemental iron per mL and will be available in single use vials containing 510 mg per 17 mL, 255 mg per 8.5 mL, and 127.5 mg per 4.25 mL. The vials will be packaged in 1-count and 10-count cartons. Ferumoxytol Injection is to be stored at controlled room temperature, 20 to 25°C (68 to 77°F). Excursions permitted to 15° to 30°C (59° to 86°F).

DMEPA acknowledges that the Applicant has slightly modified the dose from [redacted] to "510 mg" since our previous review of the name. We do not consider this slight change in the dosing information as a change in product characteristics so we proceeded with our review on that premise. b(4)

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 re-assessment of a proprietary name 90 days prior to approval of an application. Section 2.1 identifies the specific search criteria associated with the proposed proprietary name, Feraheme.

2.1 SEARCH CRITERIA

We used the same search criteria used in OSE Review #2008-1522. Please refer to Section 2.1.1 of that review for the search criteria.

2.2 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

For this product, the Applicant submitted an independent risk assessment of the proposed proprietary name conducted by a consulting firm, Drug Safety Institute (DSI). 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 the Division of Medication Error Prevention and Analysis 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.

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 Sponsor. The Safety Evaluator then determines whether the Division of Medication Error Prevention and Analysis risk assessment concurs or differs with the findings. When the proprietary name risk assessments differ, we provide a detailed explanation of these differences.

The independent risk assessment is typically evaluated in our initial review of the proposed proprietary name. However, at the time of our initial review of this name, DMEPA was unaware that an independent risk assessment had been submitted by the Applicant. Thus, it will be evaluated in this review.

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The searches of the databases listed in Section 6 yielded a total of 12 new names as having some similarity to the name Feraheme.

Eleven of the names were thought to look like Feraheme. These include Ferranem, Ferragen, Ferralet, Fareston, Ferrlecit, Persantine, Ferraton, Fenahex, Furalan, [redacted],***, and Novaheme. The remaining name, Teramine, was thought to look and sound similar to Feraheme.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name as of May 29, 2009.

3.2 EXPERT PANEL DISCUSSION

The Expert Panel, as described in Appendix A, Section 2, 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 Feraheme.

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 EXTERNAL PROPRIETARY NAME ASSESSMENT

In the proposed name risk assessment submitted by the Applicant, Drug Safety Institute identified and evaluated a total of 64 drug names thought to have some potential for confusion with the name Feraheme.

Of the 64 names identified in the DSI study, two names, Femara and Theraflu, were thought by practitioners to sound similar to Feraheme. Three names, Fer-In-Sol, Flexeril, and Hemabate were thought by practitioners to look similar to Feraheme and five names, Femhrt, Fergon, Ferrex 150, Ferrlecit, and Ferrous Sulfate were thought to look and sound similar to Feraheme. The remaining 54 names were identified by DSI's Computerized Orthographic and Phonetic Analysis (COPA) as having some similarity (phonetic or orthographic) to Feraheme (see Appendix B).

Of the 64 names, DMEPA identified the following 3 names with our current searches, Ferragen, Ferralet, and Ferrlecit.

3.4 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator did not identify any additional names which were thought to look or sound similar to Feraheme and represent a potential source of drug name confusion.

Seven names, Femhrt, Feratab, Femara, Ferrimin, Pherazine, Sarafem, and Serophene that were identified by DSI were identified in our previous Feraheme proprietary name review. None of Feraheme's product characteristics have significantly changed since the previous review. Therefore, the original assessment of those names is maintained and they will not be re-evaluated in this review. Please see OSE Review #2008-1522 for a detailed analysis of those names.

4 DISCUSSION

Sixty-six new names were evaluated for their potential similarity to the proposed name, Feraheme. Fifty names 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 name could potentially be confused with the remaining 16 names and lead to medication errors. This analysis determined that the name similarity between Feraheme was unlikely to result in medication errors with any of the 16 products for the reasons presented in Appendices D through I.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Feraheme, 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, Feraheme, for this product at this time. Additionally, DDMAC does not object to the proposed name, Feraheme, from a promotional perspective.

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Medical Imaging and Hematology Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

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, Rudolph's 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. [1]

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.

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

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[1] 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. [2] 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.[3] 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.

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

[3] 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-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

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. 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.[4] 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:

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

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

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

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

a. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].

b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].

c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.

d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.

e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

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

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

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

predictable and a preventable source of medication error that, in many instances, the Agency and/or Applicant can identify and rectify prior to approval to avoid patient harm.

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

Appendix B: Names identified in the DSI COPA analysis and not categorized as look and/or sound alike names

Name	Name
CHEMET	PHENAHIST
DERMAZENE	PHERAZINE
ELPHEMET	PROCRIT
ERVAHIST	SARAFEM
FABRAZYME	SER-A-GEN
FELDENE	SERATHIDE
FEMAGENE	SEROPHENE
FEMAZOLE	TETRA-HY
FERANCEE	THERA
FERAPLEX	THERA-HEMATINIC
FERATAB	THERA-M
FERATE	THERABID
FERATE-C	THERAC
FERIDEX	THERACYS
FERNDEX	THERAGEN
FEROWEET	THERAHIST
FERRA-CAP	THERAMINE
FERRA-TD	THERANEED
FERRACOMP	THERAPHON
FERRAGEN	THERASEAL
FERRALET	THERAVEE
FERRALYN	THERAVIM
FERRETS	THERAVIM-M
FERRIMIN	THEREMS
FERRIMIN 150	THEREMS-H
FORANE	THEREMS-M
PERMAPEN	VERAMYST

Appendix C: Names Lacking Orthographic and/or Phonetic Similarity.

Name	Similarity to Feraheme
Ferralet	Look
Ferrlecit	Look
Persantine	Look
Chemet	DSI COPA
Dermazene	DSI COPA
Elphemet	DSI COPA
Ervahist	DSI COPA
Fabrazyme	DSI COPA
Feldene	DSI COPA
Femazole	DSI COPA
Fer-In-Sol	Look (DSI)
Ferancee	DSI COPA
Feraplex	DSI COPA
Ferate	DSI COPA
Ferate-C	DSI COPA
Fergon	Look and Sound (DSI)
Feridex	DSI COPA
Ferndex	DSI COPA
Feroweet	DSI COPA
Ferra-Cap	DSI COPA
Ferra-TD	DSI COPA
Ferracomp	DSI COPA
Ferralyn	DSI COPA
Ferrets	DSI COPA
Ferrex 150	DSI COPA
Ferrimin 150	Look and Sound (DSI)
Ferrous Sulfate	Look and Sound (DSI)
Flexeril	Look (DSI)
Forane	DSI COPA
Hemabate	Look (DSI)
Permapen	DSI COPA
Procrit	DSI COPA
Serathide	DSI COPA
Tetra-Hy	DSI COPA
Thera	DSI COPA
Thera-Hematinic	DSI COPA
Thera-M	DSI COPA
Therabid	DSI COPA
Therac	DSI COPA
Theracys	DSI COPA
Theraflu	Sound (DSI)
Theraneed	DSI COPA
Theraphon	DSI COPA
Theraseal	DSI COPA
Theravee	DSI COPA

Name	Similarity to Feraheme
Theravim-M	DSI COPA
Therems	DSI COPA
Therems-H	DSI COPA
Therems-M	DSI COPA
Veramyst	DSI COPA

Appendix D: Proprietary or Established Names used only in Foreign Countries

Proprietary Name	Similarity to Feraheme	Country	Description
Fenahex	Look	Phillipines	(Tamoxifen)
Ferranem	Look	Chile	(Cyanocobalamin//Folic Acid/Ferrous Sulfate)
Ferraton	Look	Ecuador	(Ferrous Fumarate)
Femagene	DSI COPA	South Africa	(Feminine Hygiene Product Line)

Appendix E: Drug products that are discontinued and no generic equivalent is available

Proprietary Name	Similarity to Feraheme	Status and Date
Furalan (Nitrofurantoin) Tablets	Look	According to Drugs@FDA, this product has been discontinued and there are no therapeutic equivalents available.
Teramine (Phentermine) Tablets and Capsules	Look	Per telephone conversation with the company (Legere Pharmaceuticals), they no longer market this product. Unable to determine if generic equivalent products are available since information about this product is very limited.
Ferragen (Ferrous Fumarate, Intrinsic Factor, Ascorbic Acid, and Cyanocobalamin) Capsules	Look	Obtained conflicting information about this product. Per SAEGIS, the manufacturer was Pecos and the last recorded sales were in 2004[5]. Per Micromedex, the manufacturer is Contract Pharmaceuticals who per telephone conversation stated the product has not been manufactured since 2001.
Phenahist [Phenahist-TR] (Phenylpropanolamine, Phenylephrine, Chlorpheniramine, Hyoscyamine, Atropine, and Scopolamine) Tablets	DSI COPA	Phenahist was listed in the DSI COPA results, however, the product information stated in the DSI comparative safety analysis is for Phenahist-TR. Per Micromedex, Phenahist is a foreign product (Hong Kong) which contains different active ingredients. Phenahist-TR was discontinued in 2000.
Ser-A-Gen (Hydralazine, Hydrochlorothiazide, Reserpine) Tablets	DSI COPA	This ANDA application was withdrawn in 1994. There are no generic equivalents.
Therahist (Chlorpheniramine, Dextromethorphan, and Phenylpropanolamine) Oral Liquid	DSI COPA	Last recorded sales of this product were in 2003[6].

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

Appendix F: Drug names not found in commonly referenced databases (See Section 6, References 1 through 16)

Name	Similarity to Feraheme	Comments
Theragen (Capsaicin) 0.025% Cream	DSI COPA	Conflicting information available. Per SAEGIS, Harmony Laboratories is the manufacturer and last recorded sales were in 2008[7]. Per Micromedex, the manufacturer is Reese Pharmaceuticals. Unable to find this product name on either manufacturer's website. This product could not be found in standard drug information databases such as Red Book, Facts and Comparisons online, Lexicomp online or Clinical Pharmacology online.
Theravim (vitamin preparation)	DSI COPA	This product could not be found in standard drug information databases such as Red Book, Facts and Comparisons online, Lexicomp online or Clinical Pharmacology online. Limited product information in Micromedex.

Appendix G: Name previously proposed for this product

Name	Similarity to Feraheme	Comments
[redacted]	Look	DDMAC objected to the use of this name and the review division agreed.

b(4)

Appendix H: Name of an abandoned trademark

Name	Similarity to Feraheme	Comments
Novaheme	Look	This trademark was abandoned in 1998. Information obtained from USPTO website[8].

[6] Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at (www.thomson-thomson.com). Accessed on May 31, 2009.

[7] Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at (www.thomson-thomson.com). Accessed on May 31, 2009.

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

Appendix I: Products with no numerical overlap in strength, dose and route of administration

Product name with potential for confusion	Similarity to Feraheme	Strength	Usual Dose
Feraheme (Ferumoxytol Injection)	**NA**	**127.5 mg/4.25 mL 255 mg/8.5 mL 510 mg/17 mL (30 mg/mL)**	**Usual dose: An initial dose of 510 mg intravenously followed by a second 510 mg dose intravenously 3 to 8 days later**
Fareston (Toremifene Citrate) Tablets	Look	60 mg	60 mg orally once daily
Theramine (Amino Acids, Glutamine, and Arginine) Capsules	DSI COPA	Not applicable	1 or 2 capsules orally one to four times per day

[8] U.S. Patent and Trademark Office (http://www.uspto.gov). Accessed May 29, 2009.

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

/s/

Loretta Holmes
6/5/2009 04:18:56 PM
DRUG SAFETY OFFICE REVIEWER

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6/9/2009 06:08:56 AM
DRUG SAFETY OFFICE REVIEWER

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:	December 17, 2008
To:	Rafel Dwaine Rieves, MD, Acting Director Division of Medical Imaging and Hematology Products
Thru:	Kristina C. Arnwine, PharmD, Acting Team Leader Denise P. Toyer, PharmD, Deputy Director Carol A. Holquist, RPh, Director Division of Medication Error Prevention and Analysis
From:	Loretta Holmes, BSN, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis
Subject:	Proprietary Name Review
Drug Name:	Feraheme (Ferumoxytol Injection) 127.5 mg/4.25 mL, 255 mg/8.5 mL, and 510 mg/17 mL (30 mg/mL)
Application Type/Number:	NDA 22-180
Applicant:	AMAG Pharmaceuticals, Inc.
OSE RCM #:	2008-1522

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

Contents

EXECUTIVE SUMMARY

The results of the Proprietary Name Risk Assessment found that the proposed name, Feraheme, is not vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention and Analysis has no objection to the use of the proprietary name, Feraheme, for this product at this time.

However, if any of the proposed product characteristics considered in this evaluation are altered prior to approval of the product, we rescind this Risk Assessment finding, and the name must be resubmitted for review. This name must be re-evaluated 90 days prior to approval of the NDA.

1 BACKGROUND

1.1 INTRODUCTION

This review was written in response to a request from the Division of Medical Imaging and Hematology Products for assessment of the proposed proprietary name, Feraheme, regarding potential name confusion with other proprietary or established drug names.

1.2 REGULATORY HISTORY

The Applicant initially submitted the proposed proprietary names [redacted] (primary) and [redacted] (alternate) for our review and comment. During the initial steps in the proprietary name review process for this product, the Division of Drug Marketing, Advertising, and Communications (DDMAC) objected to the proposed name [redacted] and had no objections to the proposed name, [redacted], from a promotional perspective. However, in a September 9, 2008 labeling meeting, the Division expressed promotional concerns with the proposed proprietary name, [redacted], and requested another review of the name by DDMAC. Upon re-review of the name, DDMAC concurred that the name is misleading and overstates the efficacy of the drug. Therefore, DMEPA did not proceed with a safety review of the proposed names [redacted]. Subsequently, the Applicant submitted the names Feraheme (primary) and [redacted] (alternate) for review and comment. DMEPA notes that these names were submitted late in the review cycle and, thus, were not able to be reviewed before the action date. The application received a complete response action on October 17, 2008. b(4)

This NDA also has a risk management plan (RiskMAP) that was evaluated in OSE Review 2008-559, dated September 23, 2008. Additionally, the labels and labeling are being evaluated in a separate review (OSE Review 2008-569).

1.3 PRODUCT INFORMATION

Feraheme (Ferumoxytol Injection) is a superparamagnetic iron oxide nanoparticle coated with polyglucose sorbitol carboxymethylether and is formulated with mannitol. Feraheme is indicated for the treatment of iron deficiency anemia in patients with chronic kidney disease. It is administered intravenously at doses up to 510 mg as a rapid injection at a rate of up to 1 mL/sec. A second dose up to 510 mg may be administered [redacted] to 8 days after the first dose. Ferumoxytol Injection contains 30 mg of elemental iron/mL and will be available in single use vials containing 510 mg/17 mL, 255 mg/8.5 mL, and 127.5 mg/4.25 mL. The vials will be packaged in 1-count and 10-count cartons. Ferumoxytol Injection is to be stored at controlled room temperature, 20 to 25°C (68 to 77°F). Excursions permitted to 15° to 30°C (59° to 86°F). b(4)

2 METHODS AND MATERIALS

This section describes the methods and materials used by the Division of Medication Error Prevention and Analysis medication error staff conducting a proprietary name risk assessment (see 2.1 Proprietary Name Risk Assessment). The primary focus for the assessment is to identify and remedy potential sources of medication error prior to drug approval. The Division of Medication Error Prevention and Analysis 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, Feraheme, and the proprietary and established names of drug products existing in the marketplace and those pending IND, BLA, NDA, and ANDA products currently under review by CDER.

For the proprietary name, Feraheme, the medication error staff of the Division of Medication Error Prevention and Analysis 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 a CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.1.2). The Division of Medication Error Prevention and Analysis also conducts internal FDA prescription analysis studies (see 2.1.2) and, when provided, external prescription analysis studies results are considered and incorporated 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 (see detail 2.1.3). 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. The Division of Medication Error Prevention and Analysis uses 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

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[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.

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, the Division of Medication Error Prevention and Analysis 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.[3]

2.1.1 Search Criteria

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

For this review, particular consideration was given to drug names beginning with the letter 'F' 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 Feraheme, 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 (2, capital letter 'F' and lowercase 'h'), downstrokes (none), cross-strokes (none), and dotted letters (none). Additionally, several letters in Feraheme may be vulnerable to ambiguity when scripted, including the letter 'F' which may appear as 'P', 'S', or 'T'; lowercase 'e' appear as a lowercase undotted 'i' or 'l'; lowercase 'r' appear as lowercase 'n', 's', or 'v'; lowercase 'a' appear as lowercase 'ce', 'ci', 'e', or 'o'; lowercase 'h' appear as a lowercase 'b', 'k' or 'n'; lowercase 'm' appear as lowercase 'n'. As such, the Staff also consider these alternate appearances when identifying drug names that may look similar to Feraheme.

When searching to identify potential names that may sound similar to Feraheme, the medication error staff search for names with similar number of syllables (three), stresses (FER-a-heme, fer-A-heme, or fer-a-HEME), and placement of vowel and consonant sounds. In addition, several letters in Feraheme may be subject to interpretation when spoken, including the letters "Fer" which may be interpreted as "Fair", "Pher" or "Ther" and "heme" which may be interpreted as "hime". 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 considers 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 (Feraheme), the established name (Ferumoxytol Injection), proposed indication of use (iron deficiency anemia in patients with chronic kidney disease), strength (127.5 mg, 255 mg, and 510 mg), dose (up to 510 mg), frequency of administration (once, may repeat a second dose in ~to 8 days), route of administration (intravenous), and dosage form of the product (injection). Appendix A provides a more detailed listing of the product characteristics the medication error staff generally take into consideration. b(4)

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

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[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)

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 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 Databases and Information Sources

The proposed proprietary name, Feraheme, was provided to the 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 Feraheme 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 (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 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.

2.1.1.2 CDER Expert Panel Discussion

An Expert Panel Discussion is held by the Division of Medication Error Prevention and Analysis to gather CDER professional opinions on the safety of the product and the proprietary name, Feraheme. Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed. This group is composed of the Division of Medication Error Prevention and Analysis 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.

2.1.2 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 Feraheme 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 Feraheme in handwriting and verbal communication of the name, inpatient medication orders and outpatient prescriptions (outpatient prescriptions were not used in the Feraheme prescription studies) are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These prescriptions are optically scanned and one prescription is delivered to a random sample of 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 the medication error staff.

Figure 1. Feraheme Prescription Study (conducted on November 4, 2008)

HANDWRITTEN PRESCRIPITON AND MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order (A): Feraheme 510 mg IVP x 1 dose	"Feraheme, 510 mg IV push X 1 dose"
Inpatient Medication Order (B): Feraheme 510 mg IVP x 1 dose	

2.1.3 Safety Evaluator Risk Assessment of the Proposed Proprietary Name

Based on the criteria set forth in Section 2.1.1, the Safety Evaluator 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, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform a 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 A. 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 Feraheme 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 Feraheme to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names possess similarity that would cause confusion at any point in the medication use system and the name is eliminated from further review.

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

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.

The Division of Medication Error Prevention and Analysis will object to the use of proposed proprietary name when 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. The Division of Medication Error Prevention and Analysis 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)].
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 and another drug product.

In the event that the Division of Medication Error Prevention and Analysis object 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 Sponsor/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, World Health Organization, Joint Commission, and 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, the Division of Medication Error Prevention and Analysis 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 Sponsor, 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 Sponsor'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 (e.g. new form introduced like Lamisil) (see limitations of the process in Section 4).

If the Division of Medication Error Prevention and Analysis objects 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. The Division of Medication Error Prevention and Analysis is likely to recommend that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for the Division of Medication Error Prevention and Analysis 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 Sponsor with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

3 RESULTS

3.1 PROPRIETARY NAME RISK ASSESSMENT

3.1.1 Database and Information Sources

The search identified 16 names as having some similarity to the name Feraheme.

Twelve of the 16 names were thought to look like Feraheme, which include: Feraken, [redacted], Focalin, Femhrt, Feratab, Fernisone, Femara, Terazosin, Flumadine, Ferabex, [redacted]**, and Perandren. Two names, Ferrimin and Pherazine, were thought to sound like Feraheme. Two names, Sarafem and Serophene, were thought to look and sound similar to Feraheme. b(4)

The Division of Medication Error Prevention and Analysis did not identify any USAN stems in the name Feraheme as of October 24, 2008.

3.1.2 Expert Panel Discussion

The Expert Panel reviewed the pool of names identified by the Division of Medication Error Prevention and Analysis staff (see section 3.1.1. above), and did not note any additional names thought to have orthographic or phonetic similarity to Feraheme and have the potential for confusion.

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

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 FDA Prescription Analysis Studies

A total of 29 practitioners responded, but none of the responses overlapped with any existing or proposed drug names. About 59% of the participants (n=17) interpreted the name correctly as "Feraheme" with correct interpretation occurring more frequently in the inpatient written study (A). The remainder of the respondents (n=12) misinterpreted the drug name. The majority of misinterpretations occurred in the verbal study with various misinterpretations such as "Eferraheme", "Feroheme", and "Isparaheem". See Appendix B for the complete listing of interpretations from the verbal and written prescription studies.

3.1.4 Safety Evaluator Risk Assessment of Proposed Proprietary Name

Independent searches by the primary Safety Evaluator identified two additional names, [redacted] ** and Tarabine, thought to look similar to Feraheme and represent a potential source of drug name confusion. As such, a total of 18 names were analyzed to determine if the drug names could be confused with Feraheme and if the drug name confusion would likely result in a medication error. b(4)

Failure modes and effects analysis was then applied to determine if the proposed name, Feraheme, could potentially be confused with any of the 18 names and lead to medication errors. This analysis determined that the name similarity between Feraheme and the identified names was unlikely to result in medication errors for all 18 products for reasons described/outlined in Appendices C through H.

4 DISCUSSION

4.1 PROPRIETARY NAME RISK ASSESSMENT

We evaluated 18 names for their potential similarity to Feraheme. The results of the Proprietary Name Risk Assessment found that the proposed name is not vulnerable to name confusion that could lead to medication errors.

The findings of the Proprietary Name Risk Assessment are based upon current understanding of factors that contribute to medication errors involving name confusion. Although we believe the findings of the Risk Assessment to be robust, our findings do have limitations. First, because our assessment involves a limited number of practitioners, it is possible that the analysis did not identify a potentially confusing name. Also, there is some possibility that our Risk Assessment failed to consider a circumstance in which confusion could arise. However, we believe that these limitations are sufficiently minimized by the use of an Expert Panel and the CDER Prescription Studies that involved 123 CDER practitioners.

However, our risk assessment also faces limitations beyond the control of the Agency. First, our risk assessment is based on current health care practices and drug product characteristics, future changes to either could increase the vulnerability of the proposed name to confusion. Since these changes cannot be predicted for or accounted by the current Proprietary Name Risk Assessment process, such changes limit our findings. To help counterbalance this impact, we recommend that the proprietary name be re-submitted for review if approval of the product is delayed beyond 90 days.

5 CONCLUSIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Feraheme, is not vulnerable to name confusion that could lead to medication errors. As such, the Division of Medication Error Prevention and Analysis does not object to the use of the proprietary name, Feraheme, for this product. Additionally, DDMAC does not object to the proposed name, Feraheme, from a promotional perspective.

If **any** of the proposed product characteristics as stated in this review are altered prior to approval of the product; the Division of Medication Error Prevention and Analysis rescinds this Risk Assessment finding, and recommends that the name, labels, and labeling 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. Since this application received a complete response on October 17, 2008, this name must be re-evaluated upon the Applicant's complete response to the deficiencies and 90 days prior to approval of the NDA.

6 RECOMMENDATIONS

6.1 COMMENTS TO THE DIVISION

The Proprietary Name Risk Assessment findings indicate that the proposed name, Feraheme, is not vulnerable to name confusion that could lead to medication errors. As such, DMEPA does not object to the use of the proprietary name, Feraheme, for this product.

We would appreciate feedback on the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. Please copy the Division of Medication Error Prevention and Analysis on any correspondence to the Applicant pertaining to this issue. If you have further questions or need clarifications, please contact Janet Anderson, OSE Project Manager, at 301-796-0675.

6.2 COMMENTS TO THE APPLICANT

6.2.1 Proprietary Name

We have completed our review of the proposed proprietary name, Feraheme, and have concluded that it is acceptable. If **any** of the proposed product characteristics are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

7 REFERENCES

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

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

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

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

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

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

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)*

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

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

Provides information regarding patent and trademarks.

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

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

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)

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)

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.

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

List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

Contains commonly used medical abbreviations and their definitions.

APPENDICES

Appendix A:

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 and Analysis 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 (e.g. "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 and Analysis will consider the Sponsor's intended pronunciation of the proprietary name. However, because

the Sponsor 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 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-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

		characteristics	

Appendix B:

Prescription Study Responses

Inpatient Medication Order (A)	Voice Prescription	Inpatient Medication Order (B)
feraheme	Eferraheme	Ferahime
Feraheme	Feraheme	Feraheme
Feraheme	Feraheme	Feraheme
Feraheme	Feroheme	Ferahime
Feraheme	Ferraheme	Firahime
Feraheme	Ferrohem	
Feraheme	Isparaheem	
Feraheme	Sparaheme	
Feraheme		
Feraheme		
Feraheme		
Feraheme		
Feraheme (must be an iron product)		
Ferahime		
Ferahime		
Teraheme		

Appendix C: Name that lack convincing look-alike and/or sound-alike similarities to Feraheme

Name	Similarity to Feraheme
Focalin	Look
Terazosin	Look

Feratab	Look

Appendix D: Foreign Name

Name	Similarity to Feraheme	Country
Feraken	Look	Mexico

Appendix E: Discontinued Products

Name	Similarity to Feraheme	Comments
Ferabex	Look	Withdrawn by the Commissioner in 1971. Unable to find product characteristic information to determine if generics are available. It is unlikely this name would be used on a prescription.
Perandren	Look	Products (ointment and injection) withdrawn by the Commissioner in 1971 and 1986, respectively. Limited product information available. Unable to determine if generic products are available. It is unlikely this tradename would be used on a prescription.
Pherazine	Sound	Family tradename for a line of generic cough and cold products containing codeine and other ingredients. Products appear to have been discontinued in 1995. It is unlikely this tradename would be used on a prescription.
Ferrimin	Sound	This appears to be a discontinued product. Product information is limited and could only be found on the internet at www.drug3k.com. It's unlikely this name would be used on a prescription.
Fernisone	Look	This was a generic product that was withdrawn in 1992. There are other generic products available. It is unlikely that this name would be used on a prescription. The established name (prednisone) would more likely be used instead.

Appendix F: Pending names within the Agency

Name	Similarity to Feraheme	Comments
[redacted]	Look	This is an alternate proposed tradename that was not reviewed because DMEPA found the primary name (Firazyr) acceptable. The product received a not approvable action in April 2008.
[redacted]	Look	This product received a not approvable action in 1973.
[redacted]	Look	DMEPA objected to the use of this proposed primary tradename. We had no objections to the secondary name. The product received a not approvable action in 2006.

b(4)

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

Product name with potential for confusion	Similarity to Feraheme	Strength	Usual Dose (if applicable)
Proposed name: Feraheme (Ferumoxytol Injection)	**NA**	**30 mg/mL (127.5 mg/4.25 mL, 255 mg/8.5 mL, and 510 mg/17 mL vials)**	**Usual dose: Doses up to 510 mg intravenously once, may repeat a second dose in [redacted] to 8 days**
Femhrt (Ethinyl Estradiol and Norethindrone Acetate) Tablets	Look	2.5 mcg/0.5 mg and 5 mcg/1 mg	One tablet orally once daily
Sarafem (Fluoxetine Hydrochloride) Tablets and Capsules	Look	10 mg, 15 mg, and 20 mg	20 mg to 80 mg orally once daily during menstrual cycle or start 14 days before menstrual cycle and continue through first day of menses.
Femara (Letrozole) Tablets	Look	2.5 mg	2.5 mg orally once daily

b(4)

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

Appendix H: Single strength products with multiple differentiating product characteristics

Product name with potential for confusion	**Similarity to Proposed Proprietary Name**	**Strength**	**Usual Dose (if applicable)**	**Other differentiating product characteristics**
Proposed name: **Feraheme** **(Ferumoxytol Injection)**	N/A	**30 mg/mL** **127.5 mg/4.25 mL** **255 mg/8.5 mL** **510 mg/17 mL** **vials**	**Doses up to 510 mg intravenously once, may repeat a second dose in 4 to 8 days**	N/A
Serophene (Clomiphene Citrate) Tablets	Look and Sound	50 mg	50 mg to 100 mg orally once daily for 5 days	*Route of administration*: (oral vs. intravenous) *Dosage form*: (tablets vs. injection) *Frequency of administration*: (once daily for 5 days vs. once, may repeat dose in 4 to 8 days)
Tarabine (Cytarabine) Injection	Look	20 mg/mL	100 mg/m^2/day intravenous continuous infusion on days 1 through 7; 100 mg/m^2 intravenously every 12 hours days 1 through 7; 5 mg/m^2 to 75 mg/m^2 intrathecally once daily for 4 days or every 4 days.	*Method of dose determination*: [Tarabine dose is based on body surface area (the BSA is likely to be specified on the order) vs. Feraheme dose which is based on calculated iron replacement need] *Context of use*: Tarabine is a chemotherapeutic agent that will likely be ordered under a heading that identifies it as chemotherapy or ordered on a special chemotherapy order sheet vs. Feraheme which would not.
Flumadine (Rimantadine Hydrochloride) Tablets	Look	100 mg	100 mg orally once daily; 100 mg orally twice daily	*Route of administration*: (oral vs. intravenous) *Dosage form*: (tablets vs. injection) *Frequency of administration*: (once or twice daily vs. once, may repeat dose in 4 to 8 days)

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