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
Office of Medication Error Prevention and Risk Management

Proprietary Name Review

Date:	July 28, 2011
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Drug Name(s):	Ferriprox (Deferiprone) Tablets 500 mg
Application Type/Number:	NDA 021825
Applicant:	ApoPharma
OSE RCM #:	2011-1398

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

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Ferriprox (Deferiprone), from a safety and promotional perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively.

1.1 REGULATORY HISTORY

DMEPA initially reviewed the name Ferriprox in OSE Review 2006-169, dated January 30, 2007, and found the name unacceptable due to concerns that the name was misleading because the "Ferr" portion of the name may imply that Ferriprox is an iron supplement. The name was later resubmitted for reconsideration and re-evaluated in the September 3, 2009 OSE Review 2009-1153. The Applicant stated there would be a Risk Evaluation and Mitigation Strategy (REMS) with restricted distribution plan in place prior to marketing the product and this information was considered in our re-evaluation of the name. DMEPA found the name acceptable in OSE Review 2009-1153 based on this information. A Complete Response action was taken on November 30, 2009. The Applicant submitted a Class 2 resubmission and Request for Review of a Proprietary Name which were received on April 13, 2011 and April 29, 2011, respectively. No REMS was submitted during this cycle.

Ferriprox is currently marketed in multiple countries outside the United States. Additionally, Ferriprox is an Orphan Drug.

1.2 PRODUCT INFORMATION

Ferriprox is an iron chelator indicated for the treatment of patients with transfusional iron overload when current chelation therapy is inadequate. The recommended dosage is 25 mg/kg to 33 mg/kg body weight, orally, three times a day for a total daily dose of 75 mg/kg to (b) (4) mg/kg body weight. The recommended initial total daily dose of Ferriprox is 75 mg/kg body weight. The dose should be rounded to the nearest ½ tablet. Ferriprox is a scored tablet and breakable in half. It will be supplied in 100-count bottles.

Ferriprox has a boxed warning concerning agranulocytosis and neutropenia. The Agency has not yet determined whether a REMS and/or restricted distribution plan will be required for this product.

2 RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

DDMAC determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Hematology Products concurred with the findings of DDMAC's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) SEARCH

The United States Adopted Name (USAN) stem search conducted on July 15, 2011, identified that a USAN stem is not present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The proposed name Ferriprox is misleading due to the "Ferr" prefix in the name which may imply that Ferriprox is an iron supplement product when, in fact, it is a product used to treat iron overload. Although "fer-" and "ferr-" are not USAN stems, there are multiple prescription and non-prescription iron-containing products on the market that begin with these letters, for example, Ferrlecit, Fergon, Feratab, and Fer-In-Sol, to name a few. All of the aforementioned products are iron supplements. Additionally, there are two currently available iron chelators, Desferal (deferoxamine mesylate) and Exjade (deferasirox). Neither of these proprietary names begin with "Fer" or "Ferr". Because the name Ferriprox strongly suggests that the product is an iron supplement when in fact it is indicated as a treatment for iron overload, DMEPA believes that confusion can ensue regarding the product's suggested versus its actual indication.

2.2.3 FDA Adverse Event Reporting System (AERS) Selection of Cases

Ferriprox is currently marketed in countries throughout Europe, Asia, Africa, South America and elsewhere. Therefore, DMEPA searched the Adverse Event Reporting System (AERS) database on June 3, 2011 using the MedDRA High Level Group Terms "Medication Errors" and "Product Quality Issues", active ingredient "Deferiprone", trade name "Ferriprox", and verbatim "Ferr%" and "Defer%".

The reports were manually reviewed to determine if a medication error occurred. Duplicate reports were combined into cases. Cases that described a medication error were categorized by type of error. We reviewed the cases within each category to identify factors that contributed to the medication errors. If the root cause(s) were associated with name confusion involving Ferriprox, the cases were considered pertinent to this review. Those cases that did not describe a medication error or did not describe an error applicable to this review were excluded from further analysis.

The search yielded one foreign case from Greece (ISR #5523063) which described a chelation overdose involving Ferriprox and another agent. Thus, this case does not inform this review and will not be discussed further.

2.2.4 FDA Name Simulation Studies

Twenty-nine practitioners participated in DMEPA's prescription studies. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.5 Comments from Other Review Disciplines

In response to the OSE email dated May 12, 2011, the Division of Hematology Products (DHP) did not forward any comments or concerns relating to the proposed name at the initial phase of the name review.

2.2.6 Failure Mode and Effects Analysis of Similar Names

Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Ferriprox (see Appendix B). These names were identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD and Other Disciplines)

Look Similar		Sound Similar		Look and Sound Similar	
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Folplex	EPD Panel	None	None	Ferrex	EPD Panel
Ferro-Sequels	EPD Panel			Ferric PS	EPD Panel
Femogen	EPD Panel			Ferraplus	EPD Panel
Femara	EPD Panel			Feridex IV	EPD Panel
Femstat	EPD Panel				
Femcon	EPD Panel				
Fempatch	EPD Panel				
Femring	EPD Panel				
Femtrace	EPD Panel				
Propinox	EPD Panel				
Tussplex DM	EPD Panel				
Ferrlecit	EPD Panel				
Fertinex	EPD Panel				
Ferragen	EPD Panel				
(b) (4)	EPD Panel				
Firmagon	EPD Panel				
Feraplex	EPD Panel				
Ferroflex	EPD Panel				
Ferralet	Primary Safety Evaluator				
Ferralet Plus	Primary Safety Evaluator				
Ferralet 90	Primary Safety Evaluator				
Tussplex	Primary Safety Evaluator				

Our analysis of the 26 names contained in Table 1 considered the information obtained in the previous sections along with the product characteristics for the names indentified in Table 1 above. We determined the 26 names will not pose a risk for confusion as described in Appendices D and E.

DMEPA communicated these findings to the Division of Hematology Products via e-mail on July 14, 2011. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Hematology Products on July 20, 2011 they stated they had no issues with the proposed proprietary name, Ferriprox.

3 DISCUSSION

The Agency has not yet determined that this NDA will require a REMS and/or restricted distribution plan. Thus, DMEPA re-reviewed the names that were evaluated in our previous proprietary name reviews for Ferriprox (OSE Reviews 2006-169 and 2009-1153, dated January 30, 2007 and September 2009, respectively). We determined that if Ferriprox does not have a REMS or restricted distribution plan, those names do not pose a risk for confusion because they lack convincing orthographic or phonetic similarity to the name Ferriprox and/or have product characteristics that differentiate them from Ferriprox.

Although we did not identify any look-alike or sound-alike names of concern, we were concerned that the name could be misleading because of the "Fer(r)" prefix which may infer that this product is an iron supplement rather than a product that is used to treat iron overload. This misconception could lead to confusion in the marketplace given the fact that a REMS or restricted distribution program may not be in place when the product is marketed.

DMEPA held a teleconference with the Applicant on July 26, 2011, and communicated our concerns that the name could be misleading and confused as an iron supplement rather than treatment for iron overload. We requested the Applicant provide justification or supporting evidence that their proposed name would not lead to confusion if marketed.

On July 27, 2011, the Applicant submitted an amendment to the request for review of a proprietary name (see Appendix F). The amendment included justification in support of their proposed proprietary name, Ferriprox, with particular emphasis on their committment to a restricted distribution program through a single specialty pharmacy. Additionally, the Applicant believes that given the rarity of the condition for which the product is indicated, only a small number of specialists will be responsible for prescribing Ferriprox. These providers will be required to enroll in a registry per the Applicants own initiative regardless of whether a Risk Evaluation and Mitigation Strategy (REMS) is required for this product. Additionally, the Applicant has been supplying Ferriprox to patients through a treatment IND for over a decade. The Applicant believes that introduction of a different name may lead to more confusion because Ferriprox is already being used and has some recognition in the United States.

Restricted distribution programs that are not part of a REMS are not enforceable by the Agency and typically can be removed from the market at any time. However, there is precedence for this type of voluntary program with another iron chelation product,

Exjade, that shares some overlap in its adverse event profile with Ferriprox. Given the justification provided by the Applicant and the existing model in practice for this type of voluntary oversight program with iron chelation products, DMEPA believes that the risk for confusion is adequately addressed at this point in time. However, we reserve the right to re-examine the proprietary name if confusion in the marketplace is detected after marketing.

4 CONCLUSIONS

DMEPA concludes the proposed proprietary name is acceptable from both a promotional and safety perspective. However, if any of the proposed product characteristics and commitments made by the Applicant as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

The proposed proprietary name, Ferriprox, must be re-reviewed if NDA approval is delayed beyond 90 days.

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

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

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. ***Access Medicine*** *(www.accessmedicine.com)*

    Access Medicine® from McGraw-Hill contains full-text information from approximately 60 titles; it includes tables and references. Among the titles are: Harrison's Principles of Internal Medicine, Basic & Clinical Pharmacology, and Goodman and Gilman's The Pharmacologic Basis of Therapeutics.

13. ***USAN Stems (http://www.ama-assn.org/ama/pub/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml)***

    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 promotional and safety aspects of a proposed proprietary name. The promotional review of the proposed name is conducted by DDMAC. DDMAC evaluates proposed proprietary names to determine if they are overly fanciful, so as to misleadingly imply unique effectiveness or composition, as well as to assess whether they contribute to overstatement of product efficacy, minimization of risk, broadening of product indications, or making of unsubstantiated superiority claims. DDMAC provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, we consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.). 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]

Following the preliminary screening of the proposed proprietary name, DMEPA gathers to discuss their professional opinions on the safety of the proposed proprietary name. This meeting is commonly referred to the Center for Drug Evaluation and Research (CDER) Expert Panel discussion. DMEPA also considers other aspects of the name that may be misleading from a safety perspective. DMEPA staff conducts a prescription simulation studies using FDA health care professionals. When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name and misleading nature of the proposed proprietary name with a focus on the avoidance of medication errors.

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. DMEPA considers the product characteristics associated with the proposed product throughout the risk assessment because the product characteristics of the

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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.

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. DMEPA considers how these product characteristics may or may not be present in communicating a product name throughout the medication use system. Because drug name confusion can occur at any point in the medication use process, DMEPA 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.[2] The product characteristics considered for this review appears in Appendix B1 of this review.

The DMEPA considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA compares the proposed proprietary name with the proprietary and established name of existing and proposed drug products and names currently under review at the FDA. DMEPA 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. DMEPA examines the phonetic similarity using patterns of speech. If provided, DMEPA will consider the Sponsor's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Sponsor has little control over how the name will be spoken in clinical practice. The orthographic appearance of the proposed name is evaluated using a number of different handwriting samples. DMEPA applies expertise gained from root-cause analysis of postmarketing 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).

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*
	Similar spelling	Identical prefix	• Names may appear similar

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

Look-alike		Identical infix Identical suffix Length of the name Overlapping product characteristics	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/Similar shape Upstrokes Down strokes Cross-strokes 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, DMEPA 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 searches 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. A standard description of the databases used in the searches is provided in the reference section of this review. To complement the process, the DMEPA uses 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, DMEPA reviews 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. DMEPA also evaluates if there are characteristics included in the composition that may render the name unacceptable from a safety perspective (abbreviation, dosing interval, etc.).

2. Expert Panel Discussion

DMEPA gathers gather CDER professional opinions on the safety of the proposed product and discussed the proposed proprietary name (Expert Panel Discussion). 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). We also consider input from other review disciplines (OND, ONDQA/OBP). 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 database and information searches to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend additional 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 Simulation 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 participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants record their interpretations of the orders which are recorded electronically.

4. Comments from Other Review Disciplines

DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary

name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with DDMAC's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

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

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

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, considers all aspects of the name that may be misleading or confusing, conducts a Failure Mode and Effects Analysis, and provides an overall decision on acceptability dependent on their 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.[3] 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 Appendix B1 of this review. 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***

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

practice setting? And Are there any components of the name that may function as a source of error beyond sound/look-alike"

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 or because of some other component of the name. 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.

Moreover, 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 Overall 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 but involve a naming characteristic that when incorporated into a proprietary name, may be confusing, misleading, cause or contribute to medication errors.

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 generally recommends that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for 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 Sponsor 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/Sponsor. However, the safety concerns set forth in criteria a through e above are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), the Joint Commission, and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names, confusing, or misleading 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 preventable source of medication error that, in many instances, the Agency and/or Sponsor can identify and rectify prior to approval to avoid patient harm.

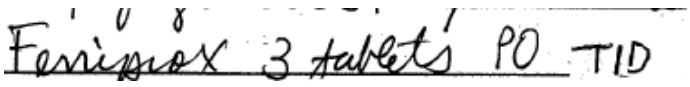
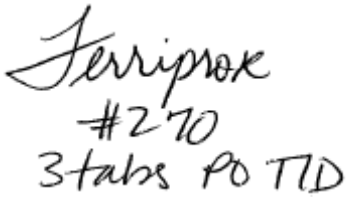
Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Sponsors have undertaken higher-leverage strategies, such as drug name changes, 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 approving the error-prone proprietary name. Moreover, even after Sponsors' 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.

Appendix B: Letters with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, NAME	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'F'	P, T	PF, Ph
lower case 'f'	p, t	
lower case 'e'	a, i, l, p	Any Vowel
lower case 'r'	s, n, e, ,v	
lower case 'r'	s, n, e, ,v	
"rr"	m, ss	
lower case 'i'	e	Any Vowel
lower case 'p'	yn, ys, g, j, l, q	b
lower case 'r'	s, n, e, ,v	
lower case 'o'	a, c, e, u	Any Vowel
lower case 'x'	a, d, skinny f, k, n, p, r, t, v, y	ks, kz, s, z

Appendix C: Prescription Simulation Samples and Results

Figure 1. Ferriprox Study (Conducted on May 24, 2011)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order: 	"Ferriprox Take three tablets by mouth three times a day Dispense a quantity of 270"
Outpatient Prescription: 	

FDA Prescription Simulation Responses.

Inpatient Medication Order	Outpatient Prescription	Voice Prescription
FENIPROX	FERRIPRO	SERAPROX
FERRIPROX	FERRIPROX	SEROPROX
FERRIPROX	FERRIPROX	FERRAPROX
FERRIPROX	FERRIPROX	SERAPROX
FERRIPROX	FERRIPROX	THERAPROX
FERRIPROX	TERRIPROX	FERAPROX
FERRIPROX	FERRIPROX	SERAPROX
FENIPROX	FERRIPROX	FARAPOD
FENIPROX		SARAPROX
		SEREPROX
		SARAPROX

Appendix D: Proprietary names not likely to be confused or not used in usual practice settings for the reasons described**.**

	Proprietary Name	Similarity to Ferriprox	Failure preventions
1	Ferrlecit (Sodium ferric Gluconate) Injection	Look	This name was evaluated in a previous review of Ferriprox (OSE Review 2009-1153) and it was determined the name did not pose a risk for confusion.
2	Fertinex (Urofollitropin) for Injection	Look	This name was evaluated in a previous review of Ferriprox (OSE Review 2009-1153) and it was determined the name did not pose a risk for confusion.

	Proprietary Name	Similarity to Ferriprox	Failure preventions
3	Ferragen (Ferrous Fumarate, Intrinsic Factor, Ascorbic Acid, and Cyanocobalamin) Capsules	Look	This name was evaluated in a previous review of Ferriprox (OSE Review 2009-1153) and it was determined the name did not pose a risk for confusion.
4	(b) (4)		
5	Ferrex 150 (Polysaccharide Iron Complex) Capsules	Look	This name was evaluated in a previous review of Ferriprox (OSE Review 2009-1153) and it was determined the name did not pose a risk for confusion.
6	Ferraplus 90 (Ascorbic Acid, Vitamin B-12, Docusate Sodium, Folic Acid, and Carbonyl Iron) Tablets	Look	This name was evaluated in a previous review of Ferriprox (OSE Review 2009-1153) and it was determined the name did not pose a risk for confusion.
7	Feridex IV (Ferumoxides) Injection	Look	This name was evaluated in a previous review of Ferriprox (OSE Review 2009-1153) and it was determined the name did not pose a risk for confusion.
8	Firmagon (Degarelix) for Injection	Look	This name was evaluated in a previous review of Ferriprox (OSE Review 2009-1153) and it was determined the name did not pose a risk for confusion.
9	Feraplex	Look	Foreign name (Puerto Rico) that lacks convincing orthographic or phonetic similarity to Ferriprox
10	Folplex 2.2 Cyanocobalamin (Vitamin B12), Folic Acid, Pyridoxine (Vitamin B6) Tablets	Look	Name lacks convincing orthographic or phonetic similarity to Ferriprox
11	Ferro-Sequels (Ferrous Fumarate)	Look	Name lacks convincing orthographic or phonetic similarity to Ferriprox
12	Femara (Letrozole)	Look	Name lacks convincing orthographic or phonetic similarity to Ferriprox

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

	Proprietary Name	Similarity to Ferriprox	Failure preventions
13	Femcon Fe (Ethinyl Estradiol, Norethindrone) Tablets	Look	Name lacks convincing orthographic or phonetic similarity to Ferriprox
14	Fempatch (Estradiol) Transdermal Patch	Look	Name lacks convincing orthographic or phonetic similarity to Ferriprox
15	Femring (Estradiol Acetate) Vaginal Insert	Look	Name lacks convincing orthographic or phonetic similarity to Ferriprox
16	Femstat (Butaconazole Nitrate) Vaginal Cream Vaginal Suppositories	Look	Name lacks convincing orthographic or phonetic similarity to Ferriprox
17	Femtrace (Estradiol Acetate) Tablets	Look	Name lacks convincing orthographic or phonetic similarity to Ferriprox
18	Propinox	Look	Name lacks convincing orthographic or phonetic similarity to Ferriprox
19	Ferric PS	Look	Name lacks convincing orthographic or phonetic similarity to Ferriprox
20	Ferralet	Look	These U.S. product names were found in SAEGIS. They are classified as "antitussives in combinations"; no other product characteristic information available. Year of last recorded sales was 1997.[4] Could not find these names in Facts and Comparisons Online, Clinical Pharmacy Online, or Lexicomp Online.
21	Ferralet Plus	Look	
22	Tussplex (Hydrocodone, Phenylephrine HCl, and Pyrilamine Maleate) Syrup	Look	This is a discontinued product and there are no generic equivalent products available. The year of last recorded sales was 2009.[7]

[4]Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at (www.thomson-thomson.com). Accessed on July 5, 2011.

Appendix E: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

	Proposed name: Ferriprox (Deferiprone) Tablets	**Strength: 500 mg**	**Usual dose: 500 mg to 3,000 mg orally three times per day (tablet is scored and can be split to obtain 250 mg dosage increments)**
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
23	Tussplex DM (Chlorpheniramine Maleate, Dextromethorphan HBr and Phenylephrine HCl) Syrup Strength: 2 mg/15 mg/5 mg per 5 mL Dose: 2.5 mL to 10 mL (½ teaspoonful to 2 teaspoonsful) every 6 hours as needed	Orthographic: The beginning letters "F" vs. "T" may look similar when scripted. Both names contain the downstroke letter "p" in a similar position. The ending letters "ex" vs. "ox" may look similar when scripted. Route of administration: Oral	Orthographic: The second position letters "e" vs. "u" do not look similar. Tussplex contains the upstroke letter "l" vs. Ferriprox which has no upstroke letters. Frequency of administration: Three times per day vs. every 6 hours as needed Dose: 25 mg/kg to 33 mg/kg (500 mg to 3,000 mg) vs. 2.5 mL to 10 mL (½ teaspoonful to 2 teaspoonsful) Status: Tussplex DM has been discontinued. The year of last recorded sales was 2009.[5]

[5]Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at (www.thomson-thomson.com). Accessed on July 5, 2011.

	Proposed name: Ferriprox (Deferiprone) Tablets	**Strength: 500 mg**	**Usual dose: 500 mg to 3,000 mg orally three times per day (tablet is scored and can be split to obtain 250 mg dosage increments)**
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
24	Femogen (Esterified Estrogens) Strength: 0.625 mg, 1.25 mg, and 2.5 mg Dose: 0.625 mg to 10 mg orally once daily or three times per day	Orthographic: Both names begin with the letters "Fe". The letters "rr" may look similar to the letter "m". The downstroke letters "p" vs. "g" may look similar when scripted. Route of administration: Oral Frequency of administration: Once daily	Orthographic: The ending letters "rox" vs. "en" do not look similar. Ferriprox appears longer in length because it contains nine letters vs. Femogen which has seven letters. Strength: 500 mg vs. 0.625 mg, 1.25 mg, and 2.5 mg Dose: 25 mg/kg to 33 mg/kg (500 mg to 3,000 mg) vs. 0.625 mg to 10 mg Status: Femogen was Withdrawn FR effective 1989.
25	Ferroflex-150 (Ascorbic Acid 60 mg, Cyanocobalamin 25 mcg, Ferrous Asparto Glycinate 50 mg, Folic Acid 1mg, Polysaccharide-Iron Complex 100 mg, Succinic Acid 50 mg, Threonic Acid 0.8 mg) Capsules Dose: One tablet orally once daily	Orthographic: Both names begin with the letters "Ferr". The letters "p" vs. "f" may look similar when scripted. The ending letters "ox" vs. "ex" may look similar. Dose: One tablet Route of administration: Oral Dosage form: Tablets	Orthographic: Ferroflex contains the upstroke letter "l" in the seventh position vs. Ferriprox which does not have an upstroke letter in that position. Frequency of administration: Three times per day vs. once daily Status: Ferroflex-150 has been discontinued.

	Proposed name: Ferriprox (Deferiprone) Tablets	**Strength: 500 mg**	**Usual dose: 500 mg to 3,000 mg orally three times per day (tablet is scored and can be split to obtain 250 mg dosage increments)**
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
26	Ferralet 90 (Carbonyl iron, Ferrous Gluconate 90 mg, Folic Acid, Cyanocobalamin 12 mcg, Ascorbic Acid 120 mg, Docusate Sodium 50 mg) Tablet Dose: One tablet orally once daily	Orthographic: Both names begin with the letters "Ferr". The ending letters "ox" vs. "et" may look similar when scripted. Dose: One tablet Route of administration: Oral Dosage form: Tablets	Orthographic: Ferriprox contains the downstroke letter "p" whereas Ferralet has no downstroke letters. Ferralet contains the upstroke letter "l" whereas Ferriprox has no upstroke letters. Frequency of administration: Three times per day vs. once daily

Appendix F: ApoPharma amendment to the proprietary name request (submitted on July 27, 2011)

BEST AVAILABLE COPY

ApoPharma
Innovative Drug Division of Apotex Inc.

July 27, 2011

Ann Farrell, M.D.
Acting Director
Division of Hematology Products
Center for Drug Evaluation and Research
U.S. Food and Drug Administration
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266
UNITED STATES OF AMERICA

Submitted via the Electronic Submissions Gateway

Re: Deferiprone 500 mg film-coated tablets (NDA 21-825)
Amendment to the Request for Review of a Proprietary Name submitted on 29 April 2011

Attn: Dr. Mara Miller, Regulatory Project Manager

Dear Dr. Farrell:

Further to the teleconference between ApoPharma and the Division of Medication Errors Prevention and Analysis (DMEPA) on 26 July 2011, ApoPharma hereby submits through its US agent, CATO Research Ltd., an amendment to its request for review of a proprietary name, dated 29 April 2011.

ApoPharma provides the following justification in support of the submission of 29 April 2011:

1) Should Ferriprox be approved in the United States, given the rarity of the condition for which the product is being indicated it will be prescribed by a relatively small number of specialists, usually hematologists, responsible for the treatment of iron-overloaded patients. The company intends to have Ferriprox distributed through a centralized pharmacy program, with a registry of health care providers prescribing it and of patients treated with this medicine. The company is also proposing to have a medication guide distributed to health care providers and to patients prior to the first delivery of the medication, detailing its indication, benefits and risks to thoroughly familiarize them with the characteristics of the product. It is considered that these measures will educate physicians and patients on the safe use of Ferriprox and will markedly reduce the risk of prescribing errors.

2) ApoPharma believes that there will be little or no risk of a dispensing error at the pharmacy level. The company is committed to a model in which post-approval distribution of Ferriprox will take place exclusively through a single specialty pharmacy

APOPHARMA INC., 200 Barmac Drive, Toronto, Ontario M9L 2Z7
Tel: 416-749-9300; Fax: 416-401-3869

Appendix F: ApoPharma amendment to the proprietary name request (submitted on July 27, 2011), cont'd

which will be certified annually by ApoPharma. The pharmacy will utilize mail services to deliver the product primarily to patients' homes and in certain cases to other healthcare settings. This restricted source of dispensing, combined with education of the limited number of pharmacists involved, will minimize the risk of dispensing errors at the pharmacy. A list of products distributed by the specialty pharmacy is presented in Attachment 1, none of which contain the syllable "fer". The only product dispensed through this pharmacy that is targeted at modifying iron levels will be Ferriprox.

3) From a practical perspective, erroneous dispensing of Ferriprox for an iron supplement is also extremely remote, not only because of the controlled, one pharmacy dispensing, but also because of the strength of the tablets. Except for a few neutraceuticals, which are not dispensed in the centralized pharmacy to be used for Ferriprox, we know of no 500 mg iron supplements. In addition, it would be unusual for more than one dose of an iron supplement to be taken in a day, whereas Ferriprox is almost universally prescribed to be taken three times per day.

4) One element of the patients' registry initiative will be education of patients, prior to treatment, on the risks associated with the use of Ferriprox. This enhanced familiarity with the prescribed product is anticipated to help patients recognize and flag any other products erroneously prescribed or dispensed in place of Ferriprox.

5) The name Ferriprox is approved in over 60 countries worldwide and has been in use for over 10 years in many of these jurisdictions. Specialists who will be prescribing Ferriprox will be familiar with its name through medical literature and international conferences. In addition, ApoPharma has been providing Ferriprox to patients in the United States through a treatment IND for over a decade. Those patients and their hematologists are already familiar with the name Ferriprox through the investigational label. The inclusion of a different name may introduce some level of confusion that is unwarranted if there is no *bona fide* risk of confusing Ferriprox with other products containing the 'fer' syllable. In addition, the name Ferriprox is already recognized in the US medical literature as the proprietary name for deferiprone, as demonstrated by a number of references during the past few years (please refer to Attachment 2).

6) An extensive pharmacovigilance program in place in European and other markets, where Ferriprox has been approved for up to 11 years, has not identified reports of prescription errors confusing Ferriprox with other medicinal products, including any other drug containing the syllable 'fer' in its proprietary name. While that does not prove the complete absence of such errors, it does suggest that misprescribing is not a significant risk, particularly given the higher number of transfusionally iron-overloaded patients in Europe alone compared with the estimated number of patients in the US that will be treated with Ferriprox.

In summary, we believe that the restrictions being placed on the prescribing and dispensing of Ferriprox, combined with the education of the specialists and patients involved and the practical considerations that further minimize the risk of any inadvertent prescribing or dispensing of

Appendix F: ApoPharma amendment to the proprietary name request (submitted on July 27, 2011), cont'd

Ferriprox for an iron supplement or *vice versa*, together with the successful use of the name throughout Europe and elsewhere, provide sufficient evidence to enable maintenance of the Ferriprox name. In the absence of reasonable expectation of a risk of confusion, beyond that afforded by sharing a prefix similar to that of some iron supplements, we trust that the FDA will agree with the merit of approving this name and thus facilitating the provision of Ferriprox to the patient community as early as possible after completion of a successful FDA review.

The 2009 New Drug Application of Ferriprox as first line therapy included a REMS. In the resubmission of Ferriprox as a second line agent, and with the extensive proposed controls, particularly with the proposed registry, we believe that such a program may not be necessary. However, ApoPharma will act accordingly if the FDA considers the need to be compelling.

A name validation survey of pharmacists and physicians to test the use of the proprietary name Ferriprox in the United States is not available. ApoPharma considers that a sufficient number of precautions have already been proposed, as described above, but would carefully take into account any further advice from DMEPA, while remaining aware that the PDUFA goal date for NDA 21-825 is 14 October 2011.

The following documents accompany this submission:

- Form FDA 356h – Application to Market a New Drug, Biologic or an Antibiotic Drug for Human Use
- A copy of the statement from ApoPharma transferring regulatory contact for this NDA to CATO Research.

The correspondence, information and data in this submission are confidential and should not be disclosed without the written consent of ApoPharma Inc. The submission has been scanned using Microsoft Forefront Client Security and is free from viruses.

For all regulatory communications regarding this application, please contact Ms. Lynda Sutton, US agent, by phone at 1 (919) 361-2286, by fax at 1 (919) 361-2290 or by e-mail at lsutton@cato.com. Alternatively, you may contact the undersigned by phone at 1 (416) 401-7296, by fax at 1 (416) 401-3869 or by e-mail at jconnell@apotex.com

Sincerely,

John Connelly, PhD
Vice President, Regulatory Affairs
ApoPharma Inc.

Attachments
cc: L. Sutton, Chief Regulatory Officer, CATO Research

Appendix F: ApoPharma amendment to the proprietary name request (submitted on July 27, 2011), cont'd

Attachment 1: List of products distributed by the specialty pharmacy

Rituxan
Gammagard
Octagam
Gamunex
Carimune
Venogolublin
Iveegam
Prolastin
Hepagam B
Koate
Humate
Stimate
(b) (4)
Recombinate
Refacto
Benefix
Advate

Appendix F: ApoPharma amendment to the proprietary name request (submitted on July 27, 2011), cont'd

Attachment 2: Publications with "Ferriprox" Reference

Cell functions impaired by frataxin deficiency are restored by drug-mediated iron relocation. Kakhlon et al. Blood, 2008

COPYRIGHT MATERIAL

Fatal agranulocytosis after deferiprone therapy in a child with diamond-blackfan anemia. Henter JI and Karlen J, Blood 2007

COPYRIGHT MATERIAL

Action of chelators in iron-loaded cardiac cells: accessibility to intracellular labile iron and functional consequences. Glickstein et al., Blood, 2006

COPYRIGHT MATERIAL

Oral chelators deferasirox and deferiprone for transfusional iron overload in thalassemia major: new data, new questions. Neufeld, Blood, 2006

COPYRIGHT MATERIAL

Role of deferiprone in chelation therapy for transfusional iron overload. Hoffbrand et al., Blood, 2004

COPYRIGHT MATERIAL

The Iron Disorders Institute Guide to Anemia
By Cheryl Garrison (Book). Publisher: Cumberland House. 2009 (2nd edition)

COPYRIGHT MATERIAL

Appendix F: ApoPharma amendment to the proprietary name request (submitted on July 27, 2011), cont'd

Iron-Chelating Therapy for Transfusional Iron Overload.
Garry M. Brittenham, NEJM, 2011

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

/s/

IRENE Z CHAN on behalf of LORETTA HOLMES
07/28/2011

IRENE Z CHAN
07/28/2011

CAROL A HOLQUIST
07/28/2011

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:	September 3, 2009
To:	Rafel Dwaine Rieves, M.D., Acting Director Division of Medical Imaging and Hematology Products
Through:	Kristina C. Arnwine, PharmD, Team Leader Denise P. Toyer, PharmD, Deputy Director Carol A. Holquist, RPh, 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:	Ferriprox (Deferiprone) Tablets 500 mg
Application Type/Number:	NDA 21-825
Applicant:	ApoPharma, Inc.
OSE RCM #:	2009-1153

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CONTENTS

EXECUTIVE SUMMARY

This re-assessment of the proprietary name is written in response to a request for reconsideration of the proposed proprietary name, Ferriprox, NDA 21-825. DMEPA did not recommend the use of the proposed name because the name included the prefix "Ferr" which was thought to be misleading because most products that contain this prefix are iron supplements. The concern for including this prefix was that the product might be mistaken for an iron supplement rather than an iron chelator.

The Applicant has provided persuasive information that has reversed our decision on the non-acceptability of the proposed name. Specifically the Applicant indicates the product will have a REMS and be distributed from a single specialty pharmacy. Additionally, the Applicant states that the name has been used globally for 10 years without confusion.

(b) (4)

Thus, DMEPA re-reviewed the proposed name based on these changes in the product characteristics.

Based on the aforementioned information and the Proprietary Name Risk Assessment findings, we have no objection to the use of the proposed name, Ferriprox, 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 INTRODUCTION

This review is written in response to a request from ApoPharma, Inc. on June 15, 2009, for reconsideration of the proposed proprietary name, Ferriprox.

1.2 REGULATORY HISTORY

DMEPA previously reviewed the proposed proprietary name, Ferriprox, in OSE Review 2006-169, dated January 30, 2007 when the application was in the IND phase of development. We objected to the use of the name at that time because we considered the name misleading due to the use of the prefix "Ferr". It was thought that the prefix "Ferr" may imply that Ferriprox is an iron supplement product rather than a product used to treat iron overload. Our comments concerning the name were forwarded to the Applicant on March 24, 2009 in response to their request for a proprietary name review at the time the NDA was submitted. In response, the Applicant submitted a request for reconsideration of the proposed name. (b) (4)

1.3 PRODUCT INFORMATION

Ferriprox is the proposed name for Deferiprone. Ferriprox is an iron chelator indicated for the treatment of iron overload in patients with transfusion-dependent thalessemia and for the treatment of iron overload in patients with other transfusion-dependent anemias for whom the use of other iron chelators has been considered inappropriate. The recommended dosage is 25 mg/kg to 33 mg/kg body weight, orally, three times per day for a total daily dose of 75 mg/kg to (b) (4) mg/kg body weight. The dose should be rounded to the nearest half-tablet. Ferriprox has a boxed warning concerning neutropenia and agranulocytosis. Weekly monitoring of the patient's absolute neutrophil count is recommended. Ferriprox will have a REMS and the product will likely be distributed exclusively through a single specialty pharmacy that will be utilizing mail services to deliver the product primarily to patient's homes and in certain cases to other healthcare settings. All products will ship directly from the manufacturer to the specialty pharmacy distributor in the U.S. The product will be dispensed on a named-patient basis based on a prescription submitted from the patient's physician.

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. Since prescription studies were conducted during the previous reviews, they were not repeated during this review. Section 2.1 identifies the specific search criteria associated with the proposed proprietary name, Ferriprox.

2.1 SEARCH CRITERIA

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.[1,2]

To identify drug names that may look similar to Ferriprox, 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 (9 letters), upstrokes (one, capital letter 'F'), downstrokes (one, lower case 'p'), cross strokes (two, capital letter 'F' and lower case 'x'), and dotted letters (one, lower case 'i'). Additionally, several letters in Ferriprox may be vulnerable to ambiguity when scripted, including the capital letter 'F' which may appear as capital letters 'L', 'P' or 'T'; lower case 'e' may look like lower case 'a', undotted 'i', 'l' or 'o'; lower case 'r' may look like lower case 'n', 's' or 'v'; lower case letter 'i' may appear as lower case 'c', 'e', 'l' or 'r'; lower case 'p' may appear as lower case 'f', 'g' or 'q'; lower case 'o' may appear as lower case 'a', 'e' or 'u'; lower case 'x' may appear as lower case 'k', 't', 'y' or 'z'. As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Ferriprox.

When searching to identify potential names that may sound similar to Ferriprox, the DMEPA staff search for names with similar number of syllables (three), stresses (FER-ri-prox, fer-RI-prox or fer-ri-PROX), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary such as insert using the following example, 'Fer' may sound like 'Pher' or 'Fair'. The Applicant provided their intended pronunciation of the proprietary name (Feh' ri prox) in the proposed

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[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)

name submission and, therefore, it was taken into consideration. However, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

2.2 SAFETY EVALUATOR RISK ASSESSMENT

DMEPA reviewed the rationale submitted by the Applicant in support of the proposed proprietary name, Ferriprox (see Appendix B). (b) (4) DMEPA re-evaluated the name from a safety perspective due to the revised product characteristics.

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The searches of the databases listed in Section 6 yielded a total of 20 names as having some similarity to the name Ferriprox.

Sixteen of the names were thought to look like Ferriprox. These include Ferabex, Feridex IV, Ferndex, (b) (4) Ferrimin 150, Ferritol, Ferrlecit, Ferrocite, Ferromin, Paraflex, Fertinex, Firmagon, Paregoric, Peridex, Permapen, and Prevpac. One of the names, Loprox, was thought to sound like Ferriprox. The remaining three names, FerriPlus, Ferrex 150, and FerraPlus were thought to look and sound similar to Ferriprox

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name as of August 20, 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 Ferriprox.

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 SAFETY EVALUATOR RISK ASSESSMENT

3.3.1 DMEPA's Response to Applicant's Rationale for Proprietary Name Reconsideration

DMEPA reviewed the Applicant's rationale for reconsideration of the proposed proprietary name, Ferriprox. The information provided by the Applicant addresses our concerns that the name could be misleading. The information currently available (such as, the product will have a REMS and restricted distribution) was not available when we initially reviewed the name.

3.3.2 Safety Review

Independent searches by the primary Safety Evaluator resulted in four additional names, Ferragen, Ferrotrin, Periflex, and Trisenox which were thought to look similar to Ferriprox and represent a potential source of drug name confusion.

(b) (4) DMEPA re-reviewed the four names identified in our previous Ferriprox proprietary name review. Those names are:

(b) (4) Ferrum Phos, Ferroplex, and Ferropro. We found (b) (4) does not impact our previous look-alike/sound-alike evaluation of those names. See OSE Review 2006-169 for a detailed analysis of those names.

The name, FerriPlus, was identified to have look-alike and sound-alike similarities. However, we note that attempts to identify the drug name FerriPlus were unsuccessful. We determined the name was misspelled during the search process (i.e., FerriPlus for FerraPlus). Thus, we evaluated FerraPlus (already identified in section 3.1 above).

4 DISCUSSION

The Applicant requested resubmission of the proposed name. The Applicant has provided persuasive information that has reversed our decision on the non-acceptability of the proposed name. Specifically the Applicant indicates the product will have a REMS and be distributed from a single specialty pharmacy. Additionally, the Applicant states that the name has been used globally for 10 years without confusion.

(b) (4) DMEPA re-reviewed the proposed name based on these changes in the product characteristics. DDMAC nor the Division of Medical Imaging and Hematology Products had concerns with the proposed name. Twenty-three names were identified and evaluated for their potential similarity to the proposed name, Ferriprox. Three names lacked orthographic and/or phonetic similarity and were not evaluated further (see Appendix D).

Failure mode and effect analysis (FMEA) was then applied to determine if the proposed name could potentially be confused with the remaining 20 names and lead to medication errors. This analysis determined that the name similarity between Ferriprox was unlikely to result in medication errors with any of the 20 products for the reasons presented in Appendices E through J.

5 CONCLUSIONS AND RECOMMENDATIONS

DMEPA considered data submitted by the Applicant in support of the proposed proprietary name, Ferriprox, and re-evaluated previously reviewed names (b) (4) Our findings indicate that the proposed name, Ferriprox, is not vulnerable to name confusion that could lead to medication errors nor is it considered promotional. Thus, we reverse the original decision to object to the name and have no objection to the proprietary name, Ferriprox, for this product at this time.

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.

5.1 COMMENTS TO THE APPLICANT

We have reconsidered our initial determination of the proposed proprietary name, Ferriprox, and based on the information you have provided in support of the proposed proprietary name have concluded that it is acceptable.

6 REFERENCES

1. OSE Review 2006-169 Ferriprox Proprietary Name Review

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

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

3. 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.

4. 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.

5. AMF Decision Support System [DSS]

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

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

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

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

Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved brand name, generic drugs, therapeutic biological products, prescription and over-the-counter human drugs and discontinued drugs and "Chemical Type 6" approvals.

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

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

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

USPTO provides information regarding patent and trademarks.

10. 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.

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

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

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

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

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

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.

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

USAN Stems List contains all the recognized USAN stems.

15. Red Book Pharmacy's Fundamental Reference

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

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

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

17. 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.

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

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

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

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

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

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.

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.[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.

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

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 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: Rationale for reconsideration of the proposed proprietary name, Ferriprox

This request is being made in response to the FDA's letter dated 24 March 2009 in which ApoPharma' s request for the proprietary name Ferriprox was rejected. Deferiprone is the United States Adopted Name (USAN) for 3-hydroxy-1,2-dimethylpyridin-4-one, and is an orally active iron chelator. The captioned product is the subject of NDA 21-825, which includes proposed labels and labeling. The proposed indication is for the treatment of iron overload in patients with transfusion-dependent thalassemia and for the treatment of iron overload associated with other transfusion-dependent anemias in patients for whom the use of other iron chelators has been considered inappropriate.

DMEPA has noted that there are some prescription and non-prescription iron containing products with the prefix 'Fer' or "fen", most of which are iron supplements. In addition, although the two currently available iron chelators Desferal (deferoxamine mesylate) and Exjade (deferasirox) do not have the prefix 'Fer' or 'ferr', the proprietary name Desferal does contain the syllable 'fer'.

ApoPharma' s justification for the reconsideration of the proprietary name Ferriprox is as follows:

1) Ferriprox will be prescribed by specialists, usually hematologists, who are responsible for the treatment of iron overloaded patients. It is unlikely that a specialist focusing on the treatment of iron overload will erroneously prescribe an iron supplement to the patient instead of prescribing Ferriprox. Iron supplements are not prescribed for patients with iron overload. They are needed for patients with iron deficiency anemia or those at risk such as during pregnancy, nursing, periods of rapid growth in children, and following blood loss due to ulcers, wounds, surgery, etc. These conditions are often treated by general practitioners. In addition, all brand name iron supplements in the United States contain the warning "Do not use if you have high levels of iron in your blood". It is common knowledge among thalassemia patients that they have high levels of iron, so they would take extra care in avoiding iron supplementation.

2) It is believed that there is little or no risk of a dispensing error at the pharmacy level. ApoPharma Inc. is well advanced into its planning for post-approval distribution and is committed to a model in which Ferriprox will be distributed exclusively through a single specialty pharmacy that will utilize mail services to deliver the product primarily to patients' homes and in certain cases to other healthcare settings. This restricted source of dispensing, combined with an education of the limited pharmacists involved, will greatly minimize the risk of dispensing errors at the pharmacy. A list of products distributed by the specialty pharmacy is presented in Attachment 1; the only iron-related product at this pharmacy is Ferriprox. Since deferiprone is an orphan drug, a small number of prescriptions are expected to be dispensed for Ferriprox. In addition, there will also be a significant price difference between Ferriprox and iron supplement products which would provide a secondary level of pharmacist awareness that Ferriprox is not to be dispensed for iron supplementation.

3) The name Ferriprox is approved in over 60 countries worldwide and has been in use for 10 years in many of these jurisdictions. Specialists who will be prescribing Ferriprox will be familiar with its name through medical literature, international conferences and compassionate use. The inclusion of a different name may introduce some level of unnecessary confusion, if there is no bonafide risk of confusing Ferriprox with other products containing the Fer syllable. Similarly, there would be an added cost for the name change, considering the relatively small number of prescriptions anticipated for the US market.

4) There is now an extensive Pharmacovigilance program in place throughout Europe where Ferriprox was approved in 1999. Yet, we are not aware of any reports of prescription errors between Desferal and Ferriprox from Europe or any other international jurisdiction where Ferriprox has been available for nearly a decade. Neither are we aware of reports of prescription errors between Ferriprox and another drug bearing the prefix 'Fer' in its proprietary name. While that does not necessarily mean there have been no errors, it does suggest this is not a significant risk, particularly since there are more than 10 times the number of patients in Europe alone than there are in the US and in that jurisdiction, between 30 and 50 % of thalassemia patients are estimated to be receiving Ferriprox.

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

Name	Similarity to Ferriprox
Prevpac	Look
Loprox	Sound
Ferrex 150	Look and Sound

Appendix D: **Unapproved Proprietary Name**

Proprietary Name	Similarity to Ferriprox	Status and Date
(b) (4)		

Appendix E: **Discontinued Products**

Proprietary Name	Similarity to Ferriprox	Comments
Ferndex (Dextroamphetamine Sulfate) Tablets	Look	The ANDA for this product was withdrawn in 1993. It is unlikely this product would be prescribed by name.
Fertinex (Urofollitropin) For Injection	Look	This product was discontinued in 2003. There are no generic equivalents available.

Appendix F: Non-drug product

Proprietary Name	Similarity to Ferriprox	Comments
Periflex (family name) Periflex Advanced Periflex Junior Periflex Infant	Look	This is a dietary supplement used for the management of phenylketonuria. It is a powder.

Appendix G: Drug names not found in commonly referenced databases (See Section 6, References 2 through 17)

Name	Similarity to Ferriprox
Ferabex	Look
Ferritol	Look

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

Product name with potential for confusion	Similarity to Ferriprox	Strength:	Usual Dose
Ferriprox	**NA**	**500 mg**	**25 mg/kg to 33 mg/kg (500 mg to 3000 mg) orally three times per day**
Firmagon (Degarelix) For Injection	Look	80 mg and 120 mg vials	240 mg subcutaneously once, then 80 mg subcutaneously every 28 days

Appendix I: Single strength products with multiple differentiating product characteristics

Product name with potential for confusion	Similarity to Ferriprox	Strength	Usual Dose (if applicable)	Differentiating Product Characteristics (Ferriprox vs. Product)
Ferriprox	**NA**	**500 mg Tablets**	**25 mg/kg to 33 mg/kg (500 mg to 3000 mg) orally three times per day**	**NA**
Paregoric (Opium) Oral Liquid Schedule C-III Controlled Substance	Look	2 mg/5 mL (0.4 mg/mL)	5 mL to 10 mL once daily to four times per day	*Dose*: 500 mg to 3000 mg vs. 2 mg (5 mL) to 4 mg (10 mL) *Dosage form*: Tablet vs. oral liquid *Status*: Non-controlled substance vs. Schedule C-III controlled substance.
Ferrlecit (Sodium Ferric Gluconate) Injection	Look	62.5 mg/5 mL (12.5 mg/mL)	125 mg intravenously at every hemodialysis for 8 doses	*Dose*: 500 mg to 3000 mg vs. 125 mg *Dosage Form*: Tablet vs. injection *Route of Administration*: Oral vs. intravenous
Trisenox (Arsenic Trioxide) Injection	Look	10 mg/10 mL (1 mg/mL)	0.15 mg/kg via intravenous infusion once daily	*Dose*: 500 mg to 3000 mg vs. 0.15 mg/kg *Dosage Form*: Tablet vs. injection *Route of Administration*: Oral vs. intravenous
Peridex (Chlorhexidine Gluconate) Oral Rinse	Look	0.12%	½ ounce oral rinse twice daily for 30 seconds	*Dose*: 500 mg to 3000 mg vs. ½ ounce/1 tablespoonful/15 mL
Permapen (Penicillin G Benzathine) Injection	Look	1,200,000 units per 2 mL prefilled syringe	300,000 units to 2,400,000 units intramuscularly once or every 7 days for 3 doses (depending on indication)	*Dose*: 500 mg to 3000 mg vs. 300,000 units to 2,400,000 units *Dosage Form*: Tablet vs. injection *Route of Administration*: Oral vs. intramuscular
Feridex IV (Ferumoxides) Injection	Look	56 mg iron/5 mL (11.2 mg iron/mL)	0.56 mg iron/kg	*Dose*: 500 mg to 3000 mg vs. 0.56 mg iron/kg *Dosage Form*: Tablet vs. injection *Route of Administration*: Oral vs. intravenous

Appendix J: Potential confusing name with numerical similarity or overlap in strength or dose

Proprietary Name: Ferriprox	**Strength: 500 mg Tablets**	**Usual Dose: 25 mg/kg to 33 mg/kg (500 mg to 3000 mg) orally three times per day**
Failure Mode: Name confusion	**Causes (could be multiple)**	**Rationale**
Ferrimin 150 (Ferrous Fumarate) Tablets *Strength*: 150 mg *Dose*: 150 mg three times per day OTC Product	Orthographic similarity: Beginning letters ("Ferri") Both products are available in a single strength so the strength can be omitted from a prescription and the dose prescribed by the number of tablets to be taken (e.g., 1 tablet) The products have an overlapping frequency of administration (three times per day).	Medication errors unlikely to occur due to orthographic differences between the names in addition to different methods of product distribution and access. *Rationale:* The ending letters of the names look different ("prox" vs. "min"). The downstroke of the "p" in Ferriprox may also help to differentiate the names. Ferrimin 150 is an OTC product so it does not require a prescription whereas Ferriprox requires a prescription and will likely be distributed by a single specialty pharmacy that maintains a patient and physician Ferriprox registry.
Ferrocite (Ferrous Fumarate) Tablets *Strength*: 324 mg *Dose*: 324 mg three times per day	Orthographic similarity: Beginning letters ("Ferr") Both products are available in a single strength so the strength can be omitted from a prescription and the dose prescribed by the number of tablets to be taken (e.g., 1 tablet) The products have an overlapping frequency of administration (three times per day).	Medication errors unlikely to occur due to orthographic differences between the names in addition to different methods of product distribution. *Rationale:* The ending letters of the names look different ("iprox" vs. "ocite"). The downstroke of the "p" in Ferriprox may also help to differentiate the names. Ferriprox will likely be distributed by a single specialty pharmacy that maintains a patient and physician Ferriprox registry whereas Ferrocite is distributed through normal pharmacy distribution channels.
Ferromin [Iron (soy protein amino acid chelate)] Tablets *Strength*: 25 mg *Dose*: 25 mg (unable to find the frequency of administration for this product) OTC Product	Orthographic similarity: Beginning letters ("Ferr") Both products are available in a single strength so the strength can be omitted from a prescription and the dose prescribed by the number of tablets to be taken (e.g., 1 tablet)	Medication errors unlikely to occur due to orthographic differences between the names in addition to different methods of product distribution and access. *Rationale:* The ending letters of the names look different ("iprox" vs. "omin"). The downstroke of the "p" in Ferriprox may also help to differentiate the names. Ferromin is an OTC product so it does not require a prescription whereas Ferriprox requires a prescription and will likely be distributed by a single specialty pharmacy that maintains a patient and physician Ferriprox registry.

Proprietary Name: Ferriprox	**Strength: 500 mg Tablets**	**Usual Dose: 25 mg/kg to 33 mg/kg (500 mg to 3000 mg) orally three times per day**
Failure Mode: Name confusion	**Causes (could be multiple)**	**Rationale**
Ferragen (Ferrous Fumarate 200 mg, Intrinsic Factor 100 mg, Ascorbic Acid 250 mg, and Cyanocobalamin 0.01 mg) Capsules *Strength*: Not Applicable *Dose*: Unable to find dosage information for this product	Orthographic similarity: Beginning letters ("Ferr") Both products are available in a single strength so the strength can be omitted from a prescription and the dose prescribed by the number of tablets to be taken (e.g., 1 tablet)	Medication errors unlikely to occur due to orthographic differences between the names in addition to different methods of product distribution. *Rationale:* The ending letters of the names look different ("iprox" vs. "agen"). Ferriprox will likely be distributed by a single specialty pharmacy that maintains a patient and physician Ferriprox registry whereas Ferragen is distributed through normal pharmacy distribution channels.
Ferrotrin (Ascorbic Acid 29 mg, Folic Acid 192 mcg, Vitamin B-12 6 mcg, Ferrous Fumarate 42 mg, and Liver-Stomach Complex 100 mg) Capsules *Strength:* Not Applicable *Dose*: 1 capsule or more orally once daily OTC Product	Orthographic similarity: Beginning letters ("Ferr") Both products are available in a single strength so the strength can be omitted from a prescription and the dose prescribed by the number of tablets to be taken (e.g., 1 tablet)	Medication errors unlikely to occur due to orthographic differences between the names in addition to differing product characteristics. *Rationale:* The ending letters of the names look different ("iprox" vs. "otrin"). The products differ in frequency of administration (three times per day vs. once daily). Ferrotrin is an OTC product so it does not require a prescription whereas Ferriprox requires a prescription and will likely be distributed by a single specialty pharmacy that maintains a patient and physician Ferriprox registry.

Proprietary Name: Ferriprox	**Strength: 500 mg Tablets**	**Usual Dose: 25 mg/kg to 33 mg/kg (500 mg to 3000 mg) orally three times per day**
Failure Mode: Name confusion	**Causes (could be multiple)**	**Rationale**
FerraPlus 90 (Ascorbic Acid 120 mg, B-12 12 mcg, Docusate Sodium 50 mg, Folic Acid 1 mg, and Carbonyl iron 90 mg) Tablets *Strength*: Not Applicable *Dose*: 1 tablet orally once daily	Orthographic similarity: Beginning letters ("Ferr) and downstroke letter ("p") Phonetic similarity: ("Ferri" vs. "Ferra") Both products are available in a single strength so the strength can be omitted from a prescription and the dose prescribed by the number of tablets to be taken (e.g., 1 tablet)	Medication errors unlikely to occur due to orthographic differences between the names in addition to different methods of product distribution. *Rationale:* The ending letters of the names look different ("rox" vs. "lus"). The upstroke letter "l" in Ferraplus may help to differentiate the names. The ending syllables ("-prox" vs. "-plus") sound different. The products differ in frequency of administration (three times per day vs. once daily). Ferriprox will likely be distributed by a single specialty pharmacy that maintains a patient and physician Ferriprox registry whereas FerraPlus 90 is distributed through normal pharmacy distribution channels.
Paraflex (Chlorzoxazone) Tablets 250 mg **Paraflex was discontinued in 1997, however, there are generic products available**	Orthographic similarity: Beginning letters ("Fer" vs. "Par") and ("p" vs. "f") and ("ox vs. "ex") Both products are available in a single strength so the strength can be omitted from a prescription and the dose prescribed by the number of tablets to be taken (e.g., 1 tablet) The products have an overlapping frequency of administration (three times per day)	Medication errors unlikely to occur due to orthographic differences between the names in addition to differing product characteristics. *Rationale:* The upstroke letter "l" in Paraflex may help to differentiate the names. The middle letters ("ri" vs. "a") look different. Ferriprox contains more letters than Paraflex (nine vs. eight) and appears longer in length when scripted. The products differ in frequency of administration (three times per day vs. once daily). Ferriprox will likely be distributed by a single specialty pharmacy that maintains a patient and physician Ferriprox registry whereas Paraflex is distributed through normal pharmacy distribution channels.

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/s/

LORETTA HOLMES
09/03/2009

CAROL A HOLQUIST
09/04/2009

CONSULTATION RESPONSE

DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY
(DMETS; WO22, Mailstop 4447)

DATE RECEIVED: August 31, 2006 **DATE OF DOCUMENT:** August 17, 2006	**DESIRED COMPLETION DATE:** February 16, 2007	**OSE REVIEW #:** 2006-169

TO: George Q. Mills, MD
Director, Division of Medical Imaging and Hematology Products
HFD-160

THROUGH: Linda Y. Kim-Jung, PharmD, Team Leader
Denise P. Toyer, PharmD, Deputy Director
Carol A. Holquist, RPh, Director
Division of Medication Errors and Technical Support

FROM: Loretta Holmes, PharmD, Safety Evaluator
Division of Medication Errors and Technical Support

PRODUCT NAME: **Ferriprox**
(Deferiprone) Film-Coated Tablets, 500 mg
(b) (4)

IND#: 45,724

SPONSOR: ApoPharma Incorporated

RECOMMENDATIONS:

1. DMETS did not identify any look-alike or sound-alike name concerns with the proposed proprietary name, Ferriprox. However, DMETS does not recommend the use of the name, Ferriprox, because it may be misleading. The name may imply that Ferriprox is an iron supplement product instead of a product used to treat iron overload (see Section II).

2. DMETS recommends implementation of the label and labeling revisions outlined in Section III of this review to minimize potential errors with the use of this product.

3. DDMAC finds the proprietary name, Ferriprox, acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Sam Chan, Project Manager, at 301-796-2283.

Division of Medication Errors and Technical Support (DMETS)
Office of Surveillance and Epidemiology
White Oak Bldg #22, Mailstop 4447
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: September 15, 2006

IND#: 45,724

NAME OF DRUG: Ferriprox
(Deferiprone) Film-Coated Tablets, 500 mg
(b) (4)

IND HOLDER: ApoPharma Incorporated

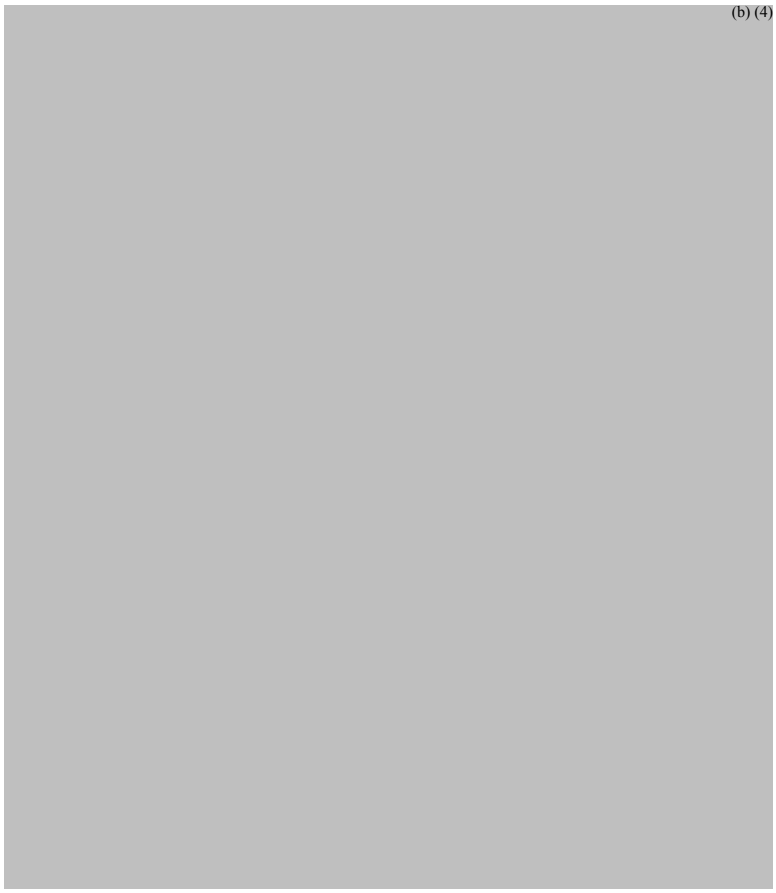
NOTE: This review contains proprietary and confidential information that should not be released to the public.

I. INTRODUCTION:

This consult was written in response to a request from the Division of Medical Imaging and Hematology Products (HFD-160), for assessment of the proprietary name, Ferriprox, regarding potential name confusion with other proprietary or established drug names. Container labels, carton and insert labeling were provided for review and comment.

PRODUCT INFORMATION

Ferriprox (deferiprone) is an iron chelator with the following indications: treatment of iron overload in patients with excessive body iron stores due to chronic transfusion therapy; and prevention of iron-induced cardiac disease in patients with iron overload. The recommended dosage is 25 mg/kg to 33 mg/kg of body weight orally three times a day, for a total daily dose of 75 mg/kg to (b) (4) mg/kg body weight. The recommended initial total daily dose of Ferriprox is 75 mg/kg body weight. After starting Ferriprox therapy, it is recommended that serum ferritin concentrations, or other indicators of body iron load, be monitored every two to three months to assess the long-term effectiveness of the chelation regimen in controlling the body iron load. Dose adjustments should be tailored to the individual patient's response and therapeutic goals (maintenance or reduction of body iron burden). The dose should be rounded to the nearest half-tablet, (b) (4) (see the dosage tables on page 3). Doses above (b) (4) mg/kg are not recommended because of the limited experience with those doses. Ferriprox will be supplied as 500 mg tablets (100-count container) (b) (4) (b) (4) Currently, Ferriprox is available commercially as an immediate-release tablet and is approved in 49 countries, including countries of the European Union, Asia, Middle East, South America and Australia.



Ferriprox Dosing Tables (taken from the package insert)

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts[1,2] as well as several FDA databases[3,4] for existing drug names which sound-alike or look-alike to Ferriprox to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted[5]. The Saegis[6] Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

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[1] MICROMEDEX Integrated Index, 2006, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

[2] Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

[3] AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-06, and the electronic online version of the FDA Orange Book.

[4] Phonetic and Orthographic Computer Analysis (POCA)

[5] WWW location http://www.uspto.gov/tmdb/index.html.

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

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Ferriprox. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC finds the proprietary name, Ferriprox, acceptable from a promotional perspective.

2. The Expert Panel identified four proprietary names that were thought to have the potential for confusion with Ferriprox. These products are listed in Table 1 (below and on page 5), along with the dosage forms available and usual dosage.

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
Ferriprox	Deferiprone Tablets: 500 mg Oral solution: 100 mg/mL (250 mL and 500 mL bottles)	Treatment of iron overload in patients with excessive body stores due to chronic transfusion therapy; prevention of iron-induced cardiac disease in patients with iron overload: 25 mg/kg to 33 mg/kg body weight, orally three times per day for a total daily dose of 75 mg/kg to 100 mg/kg body weight.	N/A
			(b) (4)

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
Ferriprox	Deferiprone Tablets: 500 mg Oral solution: 100 mg/mL (250 mL and 500 mL bottles)	Treatment of iron overload in patients with excessive body stores due to chronic transfusion therapy; prevention of iron-induced cardiac disease in patients with iron overload: 25 mg/kg to 33 mg/kg body weight, orally three times per day for a total daily dose of 75 mg/kg to 100 mg/kg body weight.	N/A
Ferrum Phosphoricum (Also called by the name *Ferrum Phos*) (There are multiple products with this name available from various manufacturers. One such product is made by Hyland, see below.)	Ferrum Phosphoricum (iron phosphae) Tablets The following strengths have been identified: 6X, 30X, and 30c	Dosage range: 4 tablets every 2 hours to 3 to 6 tablets 3 to 4 times per day (dose varies by product).	LA
Ferrum Phosphoricum (Hyland)	Ferrum phosphoricum (iron phosphate) 30X Tablets	Homeopathic remedy used to "help the lungs distribute oxygen throughout the body; is useful for inflammations such as sore throat and stuffy nose as well as nosebleeds and muscular strains": *Adults*: Dissolve 4 tablets under tongue four times per day. *Children*: 2 tablets under tongue four times per day. In acute cases, take 4 tablets every hour until relieved or as directed by a licensed practitioner.	
Ferroplex (Foreign product available in Central America, Brazil, and the Philippines)	Iron combination product (Additional product information not available)	Dosing information not available.	LA
Ferropro (Foreign product available in Thailand)	Ferrous fumarate, vitamins, and calcium phosphate (Additional product information not available)	Iron deficiency anemia. (Dosing information not available.)	LA

* Frequently used, not all-inclusive.
** L/A (look-alike), S/A (sound-alike)
***Name pending approval. Not FOI releasable.**

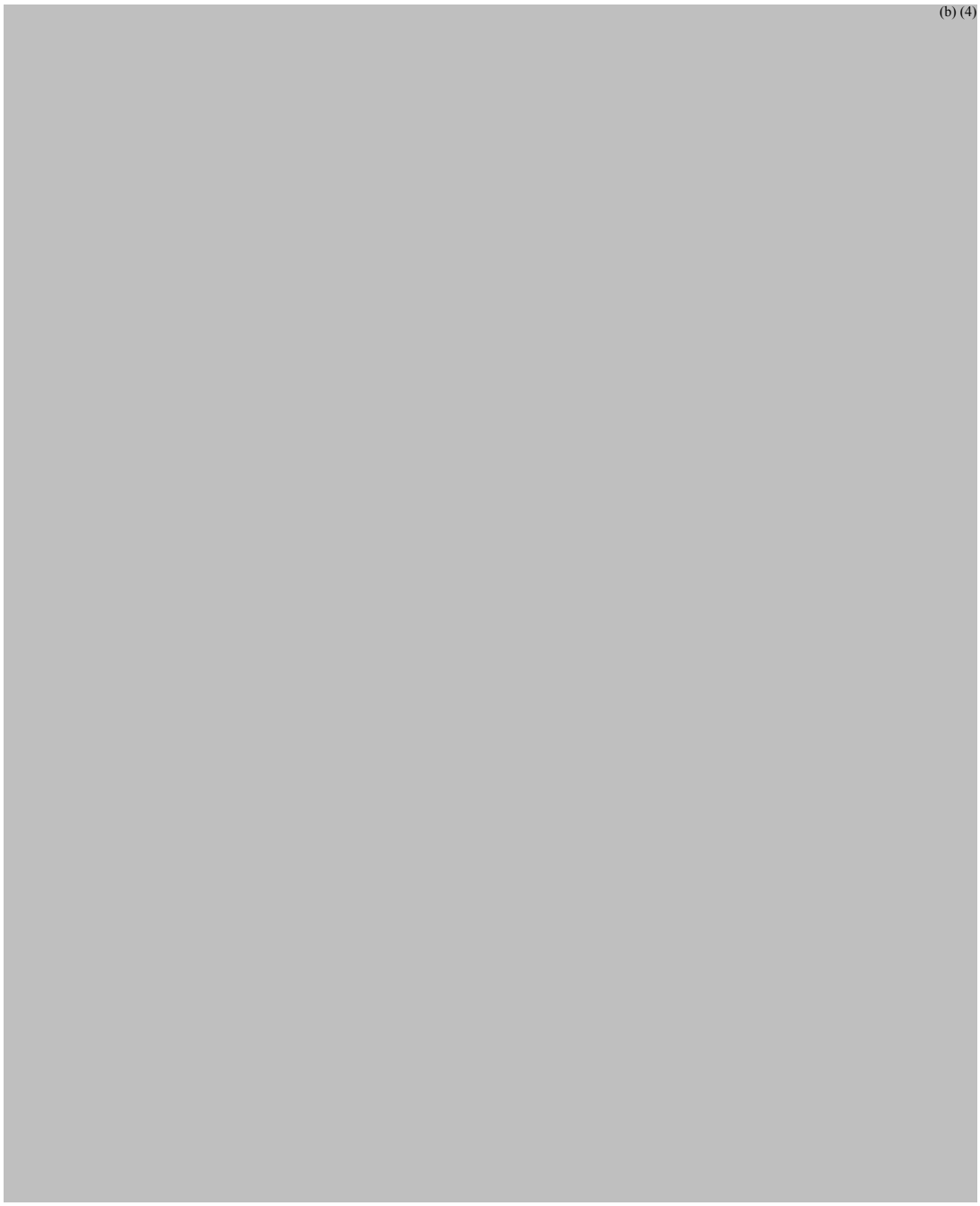
small sample size. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Ferriprox.

Upon further review, the foreign names Ferroplex (iron combination product in Brazil, Central America, and the Philippines) and Ferropro (iron combination product in Thailand) were not reviewed further because they are foreign names that are not exact matches and there is a lack of product information available for an assessment of the names.

The remaining names of concern are discussed in detail below.

1. Look-alike and/or Sound-alike Name Concerns

a. (b) (4)



(b) (4)

[redacted]

b. Ferrum Phos was identified as a name with similar appearance to Ferriprox. Ferrum Phos is the shortened form of the name Ferrum Phosphoricum (iron phosphate), an over-the-counter (OTC) homeopathic remedy that is useful for: "helping the lungs distribute oxygen throughout the body; inflammations such as sore throat and stuffy nose; as well as nosebleeds and muscular strains". There are multiple products available with this name from various manufacturers. One such product is Ferrum Phosphoricum 30X tablets. The recommended dose is (adults) 4 tablets dissolved under the tongue four times per day and (children) 2 tablets dissolved under the tongue four times per day.

The orthographic similarities are due to the fact that both names begin with identical letters ("Ferr"). Additionally, the names may look similar if Ferrum Phos is written as one word or with both words placed in close proximity to one another. Furthermore the letters "pho" in Ferrum Phos may look similar to the letters "pro" in Ferriprox when the upstroke on the letter 'h" is not prominent when scripted. However, the middle letters ("um" vs. "i") and the ending letters ("s" vs. "x") do not look similar. These products differ in indication of use (sore throat, stuffy nose, etc. vs. iron overload), and strength (6X, 30X, and 30c vs. 500 mg and 100 mg/mL) which may help to differentiate the products. Additionally, the method of access for these two products is different (OTC vs. prescription) so it is unlikely that a prescription would be written for Ferrum Phos since it is a homeopathic remedy available over-the-counter.

Despite some orthographic similarities between the names, the different product characteristics will minimize the potential to confuse Ferrum Phos with Ferriprox.

Ferrumphos
Ferriprox

2. Proprietary Name Conveys Iron Content

DMETS believes that the name, "Ferriprox", may be misleading to practitioners and patients by leading them to assume that Ferrriprox is an iron "supplement" drug product. DMETS is concerned that the beginning letters of Ferriprox ("Ferr") may infer that this product contains iron and is to be used for iron replacement instead of iron overload. Although "fer-" and "ferr-" are not USAN stems, there are multiple prescription and non-pescription iron-containing products on the market that begin with these letters, for example, Ferrlecit, Fergon, Feratab, and Fer-In-Sol, to name a few. All of the aforementioned products are iron supplements. Additionally, DMETS conducted a

search of the Orange Book for products that contain the prefix "fer" or "ferr" and are not used for iron supplementation. We found one product, Feridex I.V. (ferumoxides) that is currently available that met those criteria. Feridex I.V. is classified as a radiological/contrast media product. The other products identified in the search have been discontinued: Fernisone (prednisone), Fernisolone-P (prednisolone), Ferrous Citrate Fe-59, Ferriseltz (ferric ammonium citrate), Ferndex (dextroamphetamine), and Fertinex (urofollitropin). Additionally, we identified two currently available iron chelators, Desferal (deferoxamine mesylate) and Exjade (deferasirox). Neither of these proprietary names contain the beginning "Fer" or "Ferr" letters. Because the name Ferriprox strongly suggests that the product is an iron supplement when in fact it is indicated as a treatment for iron overload, DMETS believes that confusion can ensue regarding the product's suggested versus its actual indication. Therefore, DMETS does not recommend the use of the proposed proprietary name, Ferriprox, because it may mislead practitioners into believeing that it is an iron supplement drug product rather than a drug which is used to treat iron overload.

IV. COMMENTS TO THE SPONSOR:

DMETS believes that the name, "Ferriprox", may be misleading to practitioners and patients by leading them to assume that Ferriprox is an iron "supplement" drug product. DMETS is concerned that the beginning letters of Ferriprox ("Ferr") may infer that this product contains iron and is to be used for iron replacement instead of iron overload. Although "fer-" and "ferr-" are not USAN stems, there are multiple prescription and non-pescription iron-containing products on the market that begin with these letters, for example, Ferrlecit, Fergon, Feratab, and Fer-In-Sol, to name a few. All of the aforementioned products are iron supplements. Additionally, DMETS conducted a search of the Orange Book for products that contain the prefix "fer" or "ferr" and are not used for iron supplementation. We found one product, Feridex I.V. (ferumoxides) that is currently available that met those criteria. Feridex I.V. is classified as a radiological/contrast media product. The other products identified in the search have been discontinued: Fernisone (prednisone), Fernisolone-P (prednisolone), Ferrous Citrate Fe-59, Ferriseltz (ferric ammonium citrate), Ferndex (dextroamphetamine), and Fertinex (urofollitropin). Additionally, we identified two currently available iron chelators, Desferal (deferoxamine mesylate) and Exjade (deferasirox). Neither of these proprietary names contain the beginning "Fer" or "Ferr" letters. Because the name Ferriprox strongly suggests that the product is an iron supplement when in fact it is indicated as a treatment for iron overload, DMETS believes that confusion can ensue regarding the product's suggested versus its actual indication. Therefore, DMETS does not recommend the use of the proposed proprietary name, Ferriprox, because it may mislead practitioners into believeing that it is an iron supplement drug product rather than a drug which is used to treat iron overload.

In the review of the container labels, carton and insert labeling of Ferriprox, DMETS has focused on safety issues relating to possible medication errors. DMETS has identified the following areas of improvement to minimize potential user error.

A. CONTAINER LABELS (500 mg tablets, 100-count [redacted] (b) (4) [redacted])

1. Please ensure that the established name is at least one-half the size of the proprietary name, in accordance with 21 CFR 201.10(g)(2). Add the dosage form, "tablets", to the established name. Delete the words "Film-coated" as part of the established name and finished dosae form. This statement is a descriptor and can appear below the strength

(see the example in recommendation number 2, below).

2. Reposition the statement of strength so that it appears below the finished dosage form (see example below) and increase its size to provide more prominence.

Example:

Ferriprox
Deferiprone Tablets
500 mg
(Film-coated Tablets)

3. (b) (4)

4. Insert the wording "Usual Dosage" prior to the statement "(b) (4) ". Consider revising the "(b) (4)" statement to: "See the package leaflet for full prescribing information" or similar verbiage.

5. Currently, the sponsor's trade logo and manufacturer information are more prominent than other important information such as the proprietary name, established name, and strength. Decrease the size of the manufacturers name or remove the blue background in order to decrease it's prominence.

(b) (4)

(b) (4)

(b) (4)

C. INSERT LABELING

In the DOSAGE AND ADMINISTRATION section of the package insert labeling, one of the sentences states: (b) (4) (b) (4) (see the sample on page 11, taken from the package insert labeling). Please clarify the sentence to read: (b) (4) so that "mg/kg" is placed next to each numerical dose specification. This may help to minimize any potential for confusion about the dose.

2 DOSAGE AND ADMINISTRATION

(b) (4)

Appendix A. Prescription Study Results for Ferriprox

Requisition A	**Requisition B**	**Verbal**
Fempiop	Fampix	Feraprop
Femprox	Fempax	Feraprox
Fenuprox	Fempaz	Feraprox
Ferreprox	Femprix	Ferprox
Ferreprox	Femprox	Pheraprox
Ferriprop	Femprox	Seraprop
Ferriprop	Femprox	Veraprox
Ferriprox	FERRIPOX	
feruprox	Ferriprix	
Feruprox	Ferriprox	
Fumprox	Ferriprox	
Fumprox	Ferriprox	
Furiprep	Ferriprox	
Furiprox	Ferriprox	
	Ferriprox	
	Finpox	

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Loretta Holmes
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Denise Toyer
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Carol Holquist
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