CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

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PROPRIETARY NAME REVIEW(S)

Department of Health and Human Services Public Health Service Food and Drug Administration Center for Drug Evaluation and Research Office of Surveillance and Epidemiology	
Date:	March 23, 2011
Application Type/Number:	NDA 22534
Through:	Irene Z. Chan, Pharm.D., BCPS, Acting Team Leader Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Charlene A. Baksh, Pharm.D., Ph.D., Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Docefrez (Docetaxel) for Injection, 20 mg per vial 80 mg per vial
Applicant/sponsor:	Sun Pharma Global FZE
OSE RCM #:	2011-312

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

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EXECUTIVE SUMMARY

This review summarizes DMEPA's evaluation of Sun Pharma Global FZE's proposed proprietary name, Docefrez, for Docetaxel for Injection. Our evaluation of the proposed proprietary name, Docefrez, did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of this review. Thus, DMEPA finds the proposed proprietary name Docefrez acceptable 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 proposed proprietary name, Docefrez, must be re-evaluated.

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

1 BACKGROUND

1.1 INTRODUCTION

This review re-evaluates the proposed proprietary name, Docefrez, regarding promotional concerns and potential name confusion with other proprietary or established drug names in the usual practice settings. A re-evaluation was needed due to approval of the NDA being delayed beyond one year of our last review of the name.

1.2 REGULATORY HISTORY

DMEPA previously reviewed this proposed proprietary name, Docefrez, under NDA 22534 (OSE Review #2009-982 dated August 11, 2009). We found the name conditionally acceptable at that time.

1.3 PRODUCT INFORMATION

Docefrez is a microtubule inhibitor indicated for the treatment of breast cancer, non-small cell lung cancer, hormone refractory prostate cancer (b) (4). For dosage information see Appendix B. Docefrez is a lyophilized powder that requires reconstitution with the supplied diluent and one further dilution (in 0.9% Sodium Chloride solution or 5% Dextrose solution) prior to administration via intravenous infusion. Docefrez will be supplied in cartons, each containing 1 vial of Docefrez and 1 vial of diluent. After reconstitution, if stored between 2˚C and 25˚C (36˚F and 77˚F), Docefrez is stable for 4 hours.

2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment for all proprietary names. Sections 2.1 and 2.2 identify specific information associated with the methodology for the proposed proprietary name, Docefrez.

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter 'D' 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]

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

To identify drug names that may look similar to Docefrez, 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 (8 letters), upstrokes (2, capital letter "D" and lower case letter 'f'), downstrokes (2, lower case 'f' and 'z'), cross strokes (two, lower case 'f' and 'z' when written with a cross stroke), and dotted (none). Additionally, several letters in Docefrez may be vulnerable to ambiguity when scripted (see Appendix C). As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Docefrez.

When searching to identify potential names that may sound similar to Docefrez, the DMEPA staff search for names with similar number of syllables (three), stresses (DO-ce-frez, do-CE-frez, or do-ce-FREZ), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary such as 'Do-' may sound like 'Da' and '-frez' may sound like 'freeze' or 'phrase'. The Applicant's intended pronunciation (dō-sə-'frāz) was also taken into consideration, as it was included in the Proprietary Name Review Request. However, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary (see Appendix C).

2.2 FDA Prescription Analysis Studies

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

Figure 1. Docefrez Prescription Study (conducted on February 24, 2011)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order: Docefrez 80mg IV over 1 hour x 1.	"Docefrez Dispense 1 vial Bring to clinic"
Outpatient Prescription: Docefrez 80mg #1 Bring to clinic	

3 RESULTS

The following sections represent the results from DMEPA's database searches, Expert Panel Discussion (EPD), Prescription studies, and the Safety Evaluator Risk Assessment. We also sought input from the Division of Drug Oncology Products (DDOP) regarding the proprietary name.

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

3.1 DATABASE AND INFORMATION SOURCES

The searches yielded a total of 23 names as having some similarity to the name Docefrez. Nine names, Aciphex, Claforan, Cleviprex, Clonidine, Decadron, Doculax, Doribax, Dovonex, and Ocuflox, were previously reviewed in OSE review 2009-982. Since the product characteristics of Docefrez have not changed since our previous review, these names were not re-reviewed. Thus, we reviewed 14 new names.

Twelve of the names were thought to look like Docefrez. These include Acephen, Acerflex, Acuflex, Busulfex, Claritin, Clorfed, Dacogen, Dandrex, Decavac, Doculace, Dolotic, and Zortress.

Two of the names were thought to sound similar to Docefrez. These include Tussicaps and Tussi-pres.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of February 18, 2011.

3.2 EXPERT PANEL DISCUSSION

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

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

3.3 FDA PRESCRIPTION ANALYSIS STUDIES

A total of 38 practitioners responded to the prescription analysis studies. All practitioner responses were evaluated, and it was found that no names were of currently marketed products.

Twenty-seven of the participants interpreted the name correctly as "Docefrez". In the written prescription studies, all the practitioners spelled the name correctly. Several practitioners misinterpreted the drug name in the verbal prescription study. Most of the verbal study responses were misspelled phonetic variations of the proposed name, Docefrez. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 SAFETY EVALUATOR SEARCHES

Independent searches by the primary Safety Evaluator resulted in one additional name that was thought to sound similar to Docefrez and represent a potential source of drug name confusion.

The name, Disophrol, was identified to have sound-alike similarities.

Thus, a total of 15 names were identified for their similarity to Docefrez from the combined searches: one identified by the primary safety evaluator, and 14 identified in section 3.1.

3.5 COMMENTS FROM THE DIVISION OF DRUG ONCOLOGY PRODUCTS (DDOP)

On February 25, 2011, DMEPA notified the Division of Drug Oncology Products (DDOP) via e-mail that we had no objections to the proposed proprietary name Docefrez. Per e-mail correspondence from DDOP on March 2, 2011, they indicated they have no issues with our assessment of the proposed proprietary name, Docefrez.

4 DISCUSSION

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

4.1 PROMOTIONAL ASSESSMENT

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name. DMEPA concurred with the findings of DDMAC's promotional assessment of the proposed name.

4.2 SAFETY ASSESSMENT

We identified a total of 15 names as having some similarity to Docefrez. No other aspects of the name were determined to represent a potential source of confusion.

Five of the names were eliminated from further evaluation because they lacked convincing orthographic and/or phonetic similarity to the proposed proprietary name, Docefrez (see Appendix E).

Failure Mode and Effects Analysis (FMEA) was then applied to determine if the proposed proprietary name, Docefrez, could potentially be confused with the 10 remaining names and lead to medication errors. This analysis determined that the name similarity to Docefrez was unlikely to result in medication errors with any of the 10 products for the reasons presented in Appendices F and G.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Docefrez, is not vulnerable to name confusion that could lead to medication errors, nor is it considered promotional. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objections to the proprietary name, Docefrez, for this product at this time. The proposed proprietary name must be re-reviewed 90 days before the approval of the NDA.

If any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change. The Applicant will be notified via letter from DMEPA.

If you have further questions or need clarifications on this review, please contact the OSE Regulatory Project Manager, Sarah Simon, at 301-796-5205.

5.1 COMMENTS TO THE APPLICANT

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

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

6 REFERENCES

1. MICROMEDEX INTEGRATED INDEX (HTTP://CSI.MICROMEDEX.COM)

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

2. PHONETIC AND ORTHOGRAPHIC COMPUTER ANALYSIS (POCA)

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

3. DRUG FACTS AND COMPARISONS, ONLINE VERSION, ST. LOUIS, MO (HTTP://FACTSANDCOMPARISONS.COM)

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

4. 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)

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

8. U.S. PATENT AND TRADEMARK OFFICE (HTTP://WWW.USPTO.GOV)

Provides information regarding patent and trademarks.

9. CLINICAL PHARMACOLOGY ONLINE (WWW.CLINICALPHARMACOLOGY-IP.COM)

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

10. DATA PROVIDED BY THOMSON & THOMSON'S SAEGIS ™ ONLINE SERVICE, AVAILABLE AT (WWW.THOMSON-THOMSON.COM)

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

11. NATURAL MEDICINES COMPREHENSIVE DATABASES (WWW.NATURALDATABASE.COM)

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

12. STAT!REF (WWW.STATREF.COM)

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

13. USAN STEMS (HTTP://WWW.AMA-ASSN.ORG/AMA/PUB/CATEGORY/4782.HTML)

List contains all the recognized USAN stems.

14. RED BOOK PHARMACY'S FUNDAMENTAL REFERENCE

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

15. LEXI-COMP (WWW.LEXI.COM)

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

16. MEDICAL ABBREVIATIONS BOOK

Contains commonly used medical abbreviations and their definitions.

17. OSE Review #2009-982, Proprietary Name Review for Docefrez (Docetaxel) for Injection 20 mg and 80 mg per vial, Holmes, Loretta; August 11, 2009.

APPENDICES

Appendix A:

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

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

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases 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,

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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.

typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA staff considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.[5] DMEPA provides the product characteristics considered for this review in section one.

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

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 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

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

Look-alike			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. FDA PRESCRIPTION ANALYSIS STUDIES

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

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

4. COMMENTS FROM THE OND REVIEW DIVISION OR GENERIC DRUGS

DMEPA REQUESTS THE OFFICE OF NEW DRUGS (OND) OR OFFICE OF GENERIC DRUGS (OGD) REGULATORY DIVISION RESPONSIBLE FOR THE APPLICATION FOR THEIR COMMENTS OR CONCERNS WITH THE PROPOSED PROPRIETARY NAME AND ANY CLINICAL ISSUES THAT MAY IMPACT THE DMEPA REVIEW DURING THE INITIAL PHASE OF THE NAME REVIEW. ADDITIONALLY, WHEN APPLICABLE, AT THE SAME TIME DMEPA REQUESTS CONCURRENCE/NON-CONCURRENCE WITH DDMAC'S DECISION ON THE NAME. THE PRIMARY SAFETY EVALUATOR ADDRESSES ANY COMMENTS OR CONCERNS IN THE SAFETY EVALUATOR'S ASSESSMENT.

THE OND OR OGD REGULATORY DIVISION IS CONTACTED A SECOND TIME FOLLOWING OUR ANALYSIS OF THE PROPOSED PROPRIETARY NAME. AT THIS POINT, DMEPA CONVEYS THEIR DECISION TO ACCEPT OR REJECT THE NAME. THE OND OR OGD REGULATORY DIVISION IS REQUESTED TO CONCUR/NOT CONCUR WITH DMEPA'S FINAL DECISION.

5. SAFETY EVALUATOR RISK ASSESSMENT OF THE PROPOSED PROPRIETARY NAME

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[6] When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase. In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Section one. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

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

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

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

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: Docefrez Indications and Dosage

Indication	Dosage
Breast cancer: locally advanced or metastatic	60 mg to 100 mg/m^2 single agent
(b) (4)	
Non-small cell lung cancer, after platinum therapy failure	75 mg/m^2 single agent
(b) (4)	
Hormone refractory prostate cancer	75 mg/m^2 with 5 mg prednisone twice a day continuously
(b) (4)	
Premedication Regimen	Oral corticosteroids such as dexamethasone 16 mg per day (e.g., 8 mg twice a day) for 3 days starting 1 day before administration. Hormone refractory prostate cancer: oral dexamethasone 8 mg, at 12, 3, and 1 hours before treatment

Appendix C: Letters with possible orthographic or phonetic misinterpretation

Letters in name, Docefrez	Scripted may appear as	Spoken may be interpreted as
Capital 'D'	O, P, B, T	B, T
lower case 'd'	cl	
lower case 'o'	a, e, u	Any vowel
lower case 'c'	a, e, r	z, k, s
lower case 'e'	c, undotted i, l	Any vowel
lower case 'f'	p, t, x	wr
lower case 'r'	h, n, s, t, v	
lower case 'e'	c, undotted i, l	Any vowel
lower case 'z'	g, n, v, x, y	c, s, x

Appendix D: FDA Prescription Study Responses

Inpatient Medication Order	Outpatient Medication Order	Voice Prescription
Docefrez	Docefrez	Doxifan
Docefrez	Docefrez	Dosafrez
Docefrez	Docefrez	Dosefraz
Docefrez	Docefrez	Docefrez
Docefrez	Docefrez	Dosifrez
Docefrez	Docefrez	Docifrez
Docefrez	Docefrez	Docifrez
Docefrez	Docefrez	Dosafrez
Docefrez	Docefrez	Docefrez
Docefrez	Docefrez	Dosafraz
	Docefrez	Dosasfras
	Docefrez	Dosifres
	Docefrez	Dosafrez
	Docefrez	
	Docefrez	

Appendix E: Names Lacking Orthographic and/or Phonetic Similarity

Name	Similarity to Docefrez
Claritin	Look
Busulfex	Look
Dolotic	Look
Tussicaps	Sound
Zortress	Look

Appendix F: Products with no numerical overlap in strength, dose, or route of administration

Product name with potential for confusion	Similarity to Docefrez	Strength	Usual Dose
Docefrez (Docetaxel) Injection	**NA**	**20 mg and 80 mg vials**	**60 mg/m^2 to 100 mg/m^2 intravenously every 3 weeks**
Disophrol (Dexbrompheniramine maleate/ Pseudoephedrine sulfate) Tablet OTC product	Look	6 mg/120 mg	1 tablet orally every 12 hours
Acephen (Acetaminophen) Suppository OTC product	Look	120 mg, 325 mg, 650 mg	1 suppository rectally every 4 to 6 hours
Acerflex (Magnesium, Iron, Zinc, Manganese, Copper, Iodine, Molybdenum, Ascorbic Acid, Choline, Inositol, Calcium, Chromium, Selenium, Sodium, Potassium Chloride, Vitamin A, Vitamin D, Vitamin E, Phytonadione Thiamine, Riboflavin, Pyridoxine, Cyanocobalamin, Niacin, Folic Acid, Pantothenic Acid, Biotin, Phosphorus) Oral powder for suspension OTC product	Look	1 packet	Reconstitute 1 packet at a 1 to 5 dilution (e.g., 100 g Acerflex and 500 ml water) and take orally once daily
Acuflex (Acetaminophen/ Phenyltoloxamine Citrate) Tablet	Look	635 mg/55 mg	1 to 2 tablets orally every 4 hours
Clorfed (Chlorpheniramine maleate/ Pseudoephedrine hydrochloride) Tablet	Look	4 mg/60 mg	1 tablet orally every 12 hours

Product name with potential for confusion	Similarity to Docefrez	Strength	Usual Dose
Docefrez (Docetaxel) Injection	**NA**	**20 mg and 80 mg vials**	**60 mg/m^2 to 100 mg/m^2 intravenously every 3 weeks**
Dandrex (Selenium sulfide) Shampoo	Look	1%	Massage 5 to 10 mL of shampoo into wet scalp, leave on scalp 2-3 minutes, rinse thoroughly
Decavac (Diphtheria and tetanus toxoids) Suspension for Injection	Look	Diphtheria 2 Lf units and tetanus 5 Lf units	Patients previously not immunized should receive 2 primary doses of 0.5 mL each, given at an interval of 4 to 8 weeks; third (reinforcing) dose of 0.5 mL 6 to 12 months later
Doculace (Docusate sodium) Softgel Capsule	Look	50 mg, 100 mg	Dosage range: Adults, Adolescents, and Children >= 12 years: 50 mg to 300 mg orally daily in single or divided doses. Children 2 to < 12 years: 50 mg to 150 mg PO daily in single or divided doses
Tussi-press-B (Phenylephrine Hydrochloride, Brompheniramine Maleate, Dextromethorphan Hydrobromide) Oral Solution	Sound	10 mg/4mg/30mg per 5 mL	5 mL to 10 mL by mouth every 4 to 6 hours as needed

Appendix G: Potentially confusing name with orthographic and multiple differentiating product characteristics that decrease the risk of medication error

Proposed name	**Strength**	**Usual Dosage and Administration**
Docefrez (Docetaxel) Injection	**20 mg and 80 mg vials**	**60 mg/m^2 to 100 mg/m^2 intravenously every 3 weeks**
Failure: Name confusion	**Causes (can be multiple)**	**Prevention of Failure**
Dacogen (Decitabine) Injection **Strengths:** 50 mg/vial **Usual Dose and Administration:** (3-day regimen) 15 mg/m^2 IV over 3 hr every 8 hr for 3 days repeated every 6 wk for a minimum of 4 cycles (5-day regimen) 20 mg/m^2/day IV over 1 hr for 5 days repeated every 4 wk for a minimum of 4 cycles	**Orthographic Similarities:** Both names begin with "D". If Docefrez is written without a downstroke "z," then it would be similar to Dacogen having one downstroke. **Numerical Overlap in Dose:** The potential exists for a dose of Docefrez to overlap with a dose of Dacogen, being only 1-digit in difference (e.g. 135 mg vs. 35 mg), especially if the mg/m^2 dosing is not specified	Medication errors unlikely to occur due to orthographic difference and differences in frequencies and the dosing and procedure in which these medications are dispensed. *Rationale:* The letter "f" in Docefrez does not look similar to the letter "g" in Dacogen, which may help to differentiate the names. The frequency of administration for Dacogen is either every 8 hours or once daily, whereas Docefrez is administered every 3 weeks. The dosing for both Dacogen and Docefrez are based on mg/ m^2 dosing; however, the numeric multiples are very different. Also, chemotherapy orders are likely to be specified on a designated order sheet, which would define the body surface area used in dosage calculation, as well as the final calculated dose. This would allow for double-checks of the dose prior to drug preparation. Thus, the additional information that is likely to be specified on the order may help to differentiate the names.

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

/s/

CHARLENE A BAKSH
03/23/2011

IRENE Z CHAN
03/23/2011

CAROL A HOLQUIST
03/25/2011

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:	February 23, 2010
To:	Robert Justice, MD, Director Division of Drug Oncology Products
Through:	Kristina C. Arnwine, PharmD, Team Leader Denise P. Toyer, PharmD, Deputy Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Loretta Holmes, BSN, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name:	Docefrez (Docetaxel) for Injection 20 mg per vial and 80 mg per vial
Application Type/Number:	NDA 022534
Applicant:	Sun Pharma Global FZE
OSE RCM #:	2009-1428

CONTENTS

1 INTRODUCTION

This review is written in response to the anticipated approval of this NDA within 90 days from the date of this review. On May 26, 2009, DDMAC reviewed the proposed name and had no concerns regarding the proposed name from a promotional perspective and did not offer any additional comments relating to the proposed name. The review division nor ONDQA expressed any concerns with the proposed name, Docefrez, during our initial review. DMEPA found the proposed name, Docefrez, acceptable in OSE Review 2009-982, dated August 11, 2009.

2 METHODS

Since completion of our initial review, ONDQA has expressed concerns with the proposed proprietary name. Some of these concerns appeared to be related to the promotional aspect of the name, thus, these concerns were forwarded to DDMAC for their input. See the comments from ONDQA below:

> ONDQA's Concerns
> *"Up till now, there was no issue brought forward over this name. However, new concerns have emerged with the name. Specifically, does the character string "frez" supply or provide some advantage to the manufacture of this freeze-dried product? Will this open a door for other "frez" type suffixes? In that this is not the finished product to be administered (it must be diluted), what does "frez" supply or imply regarding errors and other issues related to the final form. "Frez" is implies something cold or frozen. Can anyone bet me that someone won't throw this product in a freezer?"*

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources (see section 6) to identify names with orthographic and phonetic similarity to the proposed name that have been approved since the previous OSE proprietary name review. We used the same search criteria used in OSE Review 2009-982 for the proposed proprietary name, Docefrez. Additionally, we searched for names that ended with the suffix "-frez".

DMEPA searches the USAN stem list to determine if the name contains any USAN stems as of the last USAN update. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proposed proprietary name, and focuses on the avoidance of medication errors.

3 RESULTS

The searches of the databases did not yield any new names thought to look or sound similar to Docefrez and represent a potential source of drug name confusion. We did not find any names that use the suffix "-frez".

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name as of January 29, 2010.

Below is DDMAC's response to ONDQA's concerns with the proposed name:

> DDMAC's Response
> *"...we don't feel that the suffix "frez" suggests any promotional advantage or superiority over other freeze dried products. In terms of ONDQA's other concerns, they seem to be safety related (proper handling, etc.), and are therefore not within DDMAC's jurisdiction."*

4 DISCUSSION

DMEPA considered the comments from ONDQA and DDMAC's response in our re-evaluation of the proposed name. ONDQA's concerns center around questions that concern the following:

1) The "frez" portion of the name may provide some advantage to the manufacturer of this "freeze-dried" product.
2) The door may be opened for the proliferation of other "-frez" type suffixes.
3) The safety implications of having "frez" in the name which may imply that the product can be frozen.

Each of these concerns is addressed below.

1) According to DDMAC, the suffix "frez" does not suggest any promotional advantage or superiority over other freeze dried products. DMEPA concurs with DDMAC's assessment.
2) We acknowledge ONDQA's concern about the proliferation of the suffix "-frez". However, the "-frez" portion of the name is not a USAN stem or a standard method of identifying products that are "freeze-dried". Additionally, in our database searches, we did not identify any names that contain the suffix "-frez". With regards to the proliferation of proprietary names containing the suffix "-frez", DMEPA would review all proposed names for future NDA and ANDA applications and would evaluate names that contain the suffix "-frez" for orthographic and/or phonetic similarity to approved/pending proprietary and established names. If applicable, we also review the appropriateness of the suffix. Thus, we do not believe proliferation of the suffix "-frez" is a concern at this time.
3) Although the Applicant states the "frez" portion of the name is derived from the fact that the product is "freeze-dried", this term is not mentioned in the insert labeling. The Applicant refers to the product as being a lyophilized powder, therefore, there is no evidence that healthcare practitioners will relate "freeze-dried" to the proposed name. Since the storage conditions are adequately displayed on the labels and labeling and drug storage conditions are not typically conveyed in proprietary names, it is unlikely that healthcare practitioners will interpret the "frez" portion of the name to mean that the product should be kept in a freezer

5 CONCLUSIONS AND RECOMMENDATIONS

Our re-review of the proposed name, Docefrez, did not identify any additional names thought to look or sound similar to the proposed name since our last review. Additionally, our evaluation did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of this review. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Docefrez, 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 Drug Oncology Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

6 REFERENCES

1. OSE Review 2009-982 Docefrez Proprietary Name Review; Holmes, Loretta

2. **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.

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

   USAN Stems List contains all the recognized USAN stems.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22534	ORIG-1	SUN PHARMA GLOBAL FZE	DOCEFREZ INJECTION (20/80 MG/VIAL)

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/s/

LORETTA HOLMES
02/23/2010

KRISTINA C ARNWINE
02/23/2010

DENISE P TOYER
02/23/2010

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:	August 11, 2009
To:	Robert Justice, MD, Director Division of Drug Oncology 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:	Docefrez (Docetaxel) for Injection 20 mg and 80 mg per vial
Application Type/Number:	NDA 22-534
Applicant:	Sun Pharma Global FZE
OSE RCM #:	2009-982

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

CONTENTS

EXECUTIVE SUMMARY

Docefrez is the proposed proprietary name for Docetaxel for Injection. This proposed name was evaluated from a safety and promotional perspective based on the product characteristics provided by the Applicant. We sought input from pertinent disciplines involved with the review of this application and considered it accordingly. Our evaluation did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of this review. Thus, DMEPA finds the proposed proprietary name, Docefrez, conditionally acceptable for this product. The proposed proprietary name must be re-reviewed 90 days before approval of the NDA.

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

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from Sun Pharma Global FZE on May 13, 2009, for an assessment of the proposed proprietary name, Docefrez, regarding potential name confusion with other proprietary or established drug names in the usual practice settings. Additionally, the container labels, carton and insert labeling are being evaluated for their potential contribution to medication errors under separate cover OSE Review 2009-983 (Label and Labeling Review).

1.2 REGULATORY HISTORY

This NDA for Docefrez is a 505(b)(2) application and the reference listed drug is Taxotere (Docetaxel) Injection Concentrate (NDA 20-449). The active drug and diluent formulation of Docefrez differ from that of Taxotere Injection Concentrate. Additionally, the method of preparation differs between the two products. However, the products share the same indications of use (except Docefrez does not have the treatment of squamous cell carcinoma of the head and neck indication), dosing, route of administration, and frequency of administration.

1.3 PRODUCT INFORMATION

Docefrez is the proposed proprietary name for Docetaxel for Injection. Docefrez is a microtubule inhibitor indicated for the treatment of breast cancer, non-small cell lung cancer, hormone refractory prostate cancer (b) (4). For dosage information see Appendix A. Docefrez is a lyophilized powder that requires reconstitution with the supplied diluent and one further dilution (in 0.9% Sodium Chloride solution or 5% Dextrose solution) prior to administration via intravenous infusion. In order to minimize patient exposure to the plasticizer DEHP (di-2-ethylhexyl phthalate), which may be leached from PVC infusion bags or sets, the final Docefrez dilution for infusion should be stored in bottles (glass, polypropylene) or plastic bags (polypropylene, polyolefin) and administered through polyethylene-lined administration sets. Docefrez infusion solution, if stored between 2˚C and 25˚C (36˚F and 77˚F) is stable for 4 hours. Fully prepared Docefrez infusion solution (in either 0.9% Sodium Chloride solution or 5% Dextrose solution) should be used within 4 hours (including the 1 hour intravenous administration).

Docefrez will be supplied in cartons, each containing a blister pack containing 1 vial of Docefrez and 1 vial of diluent and should be stored between 2˚C to 8˚C.

2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment for all

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

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter 'D' 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 Docefrez, 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 (8 letters), upstrokes (2, capital letter "D" and lower case letter 'f'), downstrokes (2, lower case 'f' and 'z'), cross strokes (two, lower case 'f' and 'z' when written with a cross stroke), and dotted (none). Additionally, several letters in Docefrez may be vulnerable to ambiguity when scripted, including the capital letter 'D' may appear as capital letters 'O' or 'P'; lower case 'o' may look like lower case 'a', 'e' or 'u'; lower case 'c' may look like lower case 'a', 'e' or 'r'; lower case letter 'e' may appear as lower case 'c', undotted 'i'or 'l'; lower case 'f' may appear as lower case 'p', 't' or 'x'; lower case 'r' may appear as lower case 'h', 'n', 's, 't', or 'v'; and lower case 'z' may appear as lower case 'g', 'n', 'v', 'x' or 'y'. As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Docefrez.

When searching to identify potential names that may sound similar to Docefrez, the DMEPA staff search for names with similar number of syllables (three), stresses (DO-ce-frez, do-CE-frez, or do-ce-FREZ), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary such as 'Do-' may sound like 'Da' and '-frez' may sound like 'freeze' or 'phrase'. The Applicant provided their intended pronunciation of the proprietary name (dō-sə-'frāz) in the proposed 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.

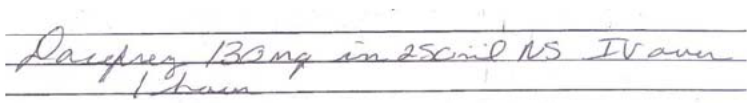
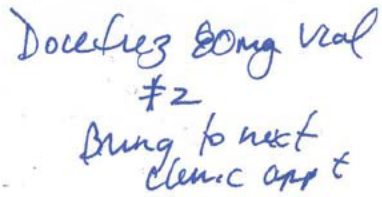
2.2 FDA PRESCRIPTION ANALYSIS STUDIES

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

[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)

Figure 1. Docefrez Prescription Study (conducted on June 2, 2009)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order: 	"Docefrez, one hundred and thirty milligrams in two hundred and fifty milliliters of normal saline, IV over one hour"
Outpatient Prescription: 	

3 RESULTS

3.1 Database and Information Sources

The searches yielded a total of 24 names as having some similarity to the name Docefrez.

Eighteen of the names were thought to look like Docefrez. These include Duricef, Doceplex, Dovonex, Rocephin, Ducolax, Aciphex, Cleviprex, Doribax, Decofed Syrup, Docef, Decadron, Claforan, Clarifoam EF, Clofarex, Desferal, Entereg, Demadex, and Ocuflox. Six of the names were thought to look and sound similar to Docefrez. These include Doxepin, Docefrez, Docetaxel, Doxapram, Dacex, and Dacef.

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

3.2 Expert Panel Discussion

The Expert Panel reviewed the pool of names identified by DMEPA staff (See Section 3.1.1. above) and noted no additional names thought to have orthographic or phonetic similarity to insert Docefrez.

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

3.3 FDA Prescription Analysis Studies

A total of 21 practitioners responded but none of the responses overlapped with any existing or proposed drug names. Twelve of the participants interpreted the name correctly as "Docefrez" with correct interpretation occurring only in the outpatient written studies (n=12). The remainder of the written responses misinterpreted the drug name. In the verbal studies, all responses were misspelled phonetic variations of the proposed name, Docefrez. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 COMMENTS FROM THE DIVISION OF DRUG ONCOLOGY PRODUCTS (DDOP)

In response to the OSE May 26, 2009 e-mail, DDOP did not have any comments and/or concerns on the proposed name at the initial phase of the name review.

DMEPA notified DDOP via e-mail that we had no objections to the proposed proprietary name, Docefrez, on July 29, 2009. DDOP has not yet responded to that e-mail.

3.5 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator resulted in 6 additional names which were thought to look or sound similar to Docefrez and represent a potential source of drug name confusion.

Five names were identified to have look-alike similarities and they are: Paraflex, (b) (4) ***, Codeprex, Duraprep, and Doculax. One name, Dosaflex, was identified to have look-alike and sound-alike similarities.

We note one name was misspelled on the EPD master sheet (i.e., D**u**colax for D**o**culax). Thus, we evaluated Doculax (identified by the Safety Evaluator). Additionally, we recognized the "-frez" portion of the name could be written and/or pronounced as "freeze" and took this into consideration when evaluating the name. We contacted the Office of New Drugs and ONDQA on whether or not "freeze" could be considered a finished dosage form and whether or not they would have objection to it being contained in the proprietary name.

4 DISCUSSION

DDMAC did not have concerns with the proposed proprietary name from a promotional perspective. The Division of Drug Oncology Products and ONDQA were consulted on whether they had any concerns with the "-frez" portion of the name. Neither expressed concerns with the proposed name.

In addition to questioning the "-frez" portion of the name, DMEPA identified and evaluated twenty-nine names for their potential similarity to the proposed name, Docefrez. Three names lacked orthographic and/or phonetic similarity and were not evaluated further (see Appendix D). Additionally, the names Docefrez and Docetaxel were identified by the EPD panel as look-alike and sound-alike names but were not evaluated further because they are identical to the proposed proprietary name and established name, respectively, for this NDA.

Failure Mode and Effects Analysis (FMEA) was then applied to determine if the potential name could potentially be confused with the remaining 24 names and lead to medication errors. This analysis determined that the name similarity between Docefrez was unlikely to result in medication errors with any of the 24 products for the reasons presented in Appendices E through J.

5 CONCLUSIONS AND RECOMMENDATIONS

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

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMEPA rescinds this Risk Assessment finding and the name must be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. If the approval of this application is delayed beyond 90 days

from the signature date of this review, the proposed name must be resubmitted for evaluation. If you have further questions or need clarifications, please contact Sandra Griffith, project manager, at 301-796-2445.

5.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Docefrez, and have concluded that it is acceptable. Docefrez will be re-reviewed 90 days prior to the approval of the NDA. If we find the name unacceptable following the re-review, we will notify you.

6 REFERENCES

1. 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.

2. 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.

3. AMF Decision Support System [DSS]

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

4. 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.

5. 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.

6. 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.

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

USPTO provides information regarding patent and trademarks.

8. 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.

9. 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.

10. 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.

11. 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.

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

USAN Stems List contains all the recognized USAN stems.

13. Red Book Pharmacy's Fundamental Reference

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

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

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

15. Medical Abbreviations Book

Medical Abbreviations Book contains commonly used medical abbreviations and their definitions.

APPENDICES

Appendix A: Docefrez Indications and Dosage

Indication	**Dosage**
Breast cancer: locally advanced or metastatic	60 mg to 100 mg/m^2 single agent
(b) (4)	
Non-small cell lung cancer, after platinum therapy failure	75 mg/m^2 single agent
(b) (4)	
Hormone refractory prostate cancer	75 mg/m^2 with 5 mg prednisone twice a day continuously
(b) (4)	
Premedication Regimen	Oral corticosteroids such as dexamethasone 16 mg per day (e.g., 8 mg twice a day) for 3 days starting 1 day before administration. Hormone refractory prostate cancer: oral dexamethasone 8 mg, at 12, 3, and 1 hours before treatment

Appendix B:

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

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

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

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail. [4] DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

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

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

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly in spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examines the orthographic appearance of the proposed

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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.

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. FDA Prescription Analysis Studies

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

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

4. Comments from the OND review Division or Generic drugs

DMEPA requests the Office of New Drugs (OND) or Office of Generic Drugs (OGD) Regulatory Division responsible for the application for their comments or concerns with the proposed proprietary name and any clinical issues that may impact the DMEPA review during the initial phase of the name

review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with DDMAC's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

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

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[6] When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

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

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

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

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

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

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

The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not ultimately be a source of medication errors in the usual practice setting, the primary Safety Evaluator

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

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 C: FDA Prescription Study Responses.

Inpatient Medication Order	Outpatient Medication Order	Voice Prescription
Dacefrez	Docefrez	Dosafrez
Darefrez	Docefrez	Dusofres
Darefrez	Docefrez	
Dareprez	Docefrez	
Dareprez	Docefrez	
Darfrey	Docefrez	
Darghrez	Docefrez	
	Docefrez	
	Docefrez	
	Docefrez	
	Docetrez	
	Docetrez	

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

Name	Similarity to Docefrez
Dovonex	Look
Entereg	Look
Doxepin	Look and Sound

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

Proprietary Name	Similarity to Docefrez	Country	Description
Doceplex	Look and Sound	Mexico Central America Dominican Republic Venezuela	This appears to be the name for slightly different products in the various countries. All of the products are some type of multivitamin poduct.
Dacef	Look and Sound	South Africa	(Cefadroxil)
Docef	Look and Sound	Mexico	This product was an oral cephalosporin (established name not available). Per SAEGIS, the last recorded sales of this product were in 2006[7], so it appears this product is no longer marketed.

Appendix F: Proposed names within the Agency

Proprietary Name	Similarity to Docefrez	Comments
		(b) (4)

Appendix G: Drug products that are discontinued

Proprietary Name	Similarity to Docefrez	Status and Date
Codeprex Pennkinetic (Codeine Polistirex 20 mg and Chlorpheniramine Polystirex 4 mg per 5 mL) Extended-release Oral Suspension	Look	This product was withdrawn by the Commissioner in March 2009. There are no generic equivalents available.

[7]Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at (www.thomson-thomson.com). Accessed on July 16, 2009.

Proprietary Name	Similarity to Docefrez	Status and Date
Dosaflex (Calcium Sennosides) 8.8 mg/5 mL Syrup	Look and Sound	Per SAEGIS, the last recorded sales of this product were in 1999[8]. Product information is limited. This was an OTC product and there are similar products currently available.

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

Product name with potential for confusion	Similarity to Docefrez	Strength	Usual Dose
Docefrez	**NA**	**20 mg and 80 mg vials**	**60 mg/m^2 to 100 mg/m^2 intravenously every 3 weeks**
Rocephin (Ceftriaxone Sodium) Powder for Injection Duplex container (drug chamber plus diluent chamber) *Rocephin is not currently marketed in all the specified strengths, however, generics are available in all the strengths specified*	Look	250 mg, 500 mg, 1 gm, 2 gm, and 10 gm vials	1 gm to 2 gm intravenously or intramuscularly once daily
Cleviprex (Clevidipine Butyrate) Injection	Look	25 mg/50 mL and 50 mg/100 mL (0.5 mg/mL)	1 mg/hr to 16 mg/hr via continuous intravenous infusion
Doribax (Doripenem) Powder for Solution	Look	500 mg vials	500 mg intravenously every 8 hours
Dacex family tradename: Dacex DM (syrup) Dacex PE (tablet) Dextromethorphan Hydrobromide, Guaifenesin, and Phenylephrine Hydrochloride	Look	Dacex DM: 25 mg/175 mg/12.5 mg per 5 mL Dacex PE: 30 mg/600 mg/10 mg	Dacex DM: 1.25 mL to 5 mL orally every 6 hours Dacex PE: 1 to 2 tablets orally every 12 hours

[8] Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at (www.thomson-thomson.com). Accessed on June 30, 2009.

Product name with potential for confusion	Similarity to Docefrez	Strength	Usual Dose
Docefrez	**NA**	**20 mg and 80 mg vials**	**60 mg/m^2 to 100 mg/m^2 intravenously every 3 weeks**
Claforan (Cefotaxime Sodium) Powder for Injection	Look	500 mg, 1 gm, 2 gm, 10 gm, 1 gm/50 mL, and 2 gm/50 mL	Dosage range: Adults: 1 gm to 2 gm intravenously or intramuscularly every 12 hours to every 4 hours Children: 50 mg/kg/day to 180 mg/kg/day in 4 to 6 divided doses
Clarifoam EF (Sodium Sulfacetamide and Sulfur) Aerosol Foam	Look	10%/5%	One application topically once daily/twice daily/three times per day
Desferal (Desferoxamine Mesylate) Powder for Injection	Look	500 mg and 2 gm vials	Intramuscular: 1 gm once, then 500 mg every 4 hours for 2 doses; 500 mg to 1 g/day Intravenous: 15 mg/kg/hr for first 1gm then if subsequent doses are needed, infuse at a rate not to excees 125 mg/hr Subcutaneous: 1 to 2 g/day over 8 to 24 hours with continuous infusion pump
Ocuflox (Ofloxacin) Ophthalmic Solution	Look	0.3%	Dosage range: 1 or 2 drops instilled into the affected eye(s) every 30 minutes to four times per day
Paraflex (Chloroxazone) Tablets	Look	250 mg	250 mg to 750 mg orally three times per day/four times per day
Duraprep (Iodine Povacrylex and Isopropyl Alcohol) Solution OTC product	Look	0.7%/74%	One application topically once

<u>Appendix I:</u> Products with overlap in strength, dose or achievable dose with multiple differentiating product characteristics

Product name with potential for confusion	**Similarity to Docefrez**	**Strength**	**Usual Dose (if applicable)**	**Differentiating Product Characteristics (Docefrez vs. Product)**
Docefrez	**NA**	**20 mg and 80 mg vials**	**60 mg/m^2 to 100 mg/m^2 intravenously every 3 weeks**	**NA**
Doculax (Docusate Sodium) Capsules OTC product	Look	100 mg	100 mg to 300 mg once daily	*Route of Administration*: Intravenous vs. oral *Frequency of Administration*: Once every 3 weeks vs. once daily *Dosage form*: For Injection vs. capsule *Method of dose determination*: calculated based on body surface area (BSA) vs. standard dose *Status*: prescription vs. OTC
Aciphex (Rabeprazole Sodium) Delayed-release Tablets	Look	20 mg	20 mg	*Route of Administration*: Intravenous vs. oral *Frequency of Administration*: Once every 3 weeks vs. once daily *Dosage form*: For Injection vs. tablet *Method of dose determination*: calculated based on BSA vs. standard dose
Demadex (Torsemide) Tablets	Look	5 mg, 10 mg, 20 mg, and 100 mg	5 mg to 200 mg	*Route of Administration*: Intravenous vs. oral *Frequency of Administration*: Once every 3 weeks vs. once daily *Dosage form*: For Injection vs. tablet *Method of dose determination*: calculated based on body surface area (BSA) vs. standard dose

Product name with potential for confusion	**Similarity to Docefrez**	**Strength**	**Usual Dose (if applicable)**	**Differentiating Product Characteristics (Docefrez vs. Product)**
Docefrez	**NA**	**20 mg and 80 mg vials**	**60 mg/m^2 to 100 mg/m^2 intravenously every 3 weeks**	**NA**
Duricef (Cefadroxil) Tablets Capsules Powder for Oral Suspension Duricef is no longer marketed, however, generics are available.	Look	Tablets: 1 g Capsules: 500 mg Oral Suspension (after reconstitution): 125 mg/5 mL 250 mg/5 mL 500 mg/5 mL	Adults: 1 g or 2 g orally per day in single or divided doses. Children: 30 mg/kg/day orally	*Route of Administration*: Intravenous vs. oral *Frequency of Administration*: Once every 3 weeks vs. once daily/twice daily *Dosage form*: For Injection vs. tablet/capsule/powder for oral suspension
Decofed (Pseudoephedrine) Syrup *Strength*: 30 mg/5 mL OTC prduct	Look	30 mg/5 mL	30 mg (5 mL) to 60 mg (10 mL) every 4 hours	*Route of Administration*: Intravenous vs. oral *Frequency of Administration*: Once every 3 weeks vs. every 4 hours *Dosage form*: For Injection vs. syrup *Method of dose determination*: calculated based on body surface area (BSA) vs. standard dose *Status*: Prescription vs. OTC

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

Proprietary Name: **Docefrez**	**Strength** **20 mg and 80 mg vials**	**Usual Dose:** **60 mg/m^2 to 100 mg/m^2 intravenously every 3 weeks**
Failure Mode: Name confusion	**Causes** **(could be multiple)**	**Effects**
Clofarex [this is a synonym for Clofarabine (established name)] Injection *Strength*: 20 mg/20 mL (1 mg/mL) *Dose*: 52 mg/m^2 intravenously once daily for five days, every 2 to 6 weeks	Orthographic similarity: In lowercase ("d" vs. "cl") and ("frez" vs. "farex") The potential exists for the dose of Docefrez and Clofarex to overlap (eg., 90 mg when dosing Clofarex in a person with a BSA of 1.73 and Docefrez in a person with a BSA of 1.5 at 60 mg/m^2)	Medication errors unlikely to occur due to orthographic differences between the names in addition to differing product characteristics. *Rationale:* There are 4 letters that precede the letter "f" in Docefrez whereas there are 3 in Cloforex which makes the beginning portion of Docefrez appear longer in length than the beginning portion of Clofarex. This may help to differentiate the names. The products differ in frequency of administration (once every 3 weeks vs. once daily for five days, every 2 to 6 weeks) which may also help to differentiate the names.
Decadron (Dexamethasone) (Dexamethasone Sodium Phosphate) Decadron has been discontinued (last recorded sales were in 2006[9]), however, generics are available in multiple dosage forms (oral, injection, ophthalmic solution) and from multiple manufacturers. The injection is listed since it is the dosage form of concern. *Strength*: Injection: 4 mg/mL and 10 mg/mL *Dose*: Dose is individualized. Intravenous and Intramuscular: Initially,	Orthographic similarity: ("Doce" vs. "Deca") and ("ron" vs. "rez") The potential exists for a dose of Docefrez to overlap with an intravenous dose of Decadron (e.g., 80 mg)	Medication errors unlikely to occur due to orthographic differences between the names in addition to differing context of use. *Rationale:* The letter "f" in Docefrez does not look similar to the letter "d" in Decadron which may help to differentiate the names. A dose of Decadron 80 mg (or similar) intravenously would be considered very high and only used for specific indications (e.g., treatment of shock). It is likely that the indication for such a high dose would be verified before dispensing should an order for Docefrez be confused as Decadron. On the other hand, an order for Docefrez would likely be written on a special "chemotherapy" order sheet or under a similar titled heading on an order sheet. Furthermore, the dosing of Docefrez is based on body surface area which is likely to be specified on the order along with the final calculated dose which would allow for double checks of the dose prior to drug preparation. Thus, the additional information that is likely to be specified on a Docefrez order may help to differentiate the names.

[9] Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at (www.thomson-thomson.com). Accessed July 30, 2009.

Proprietary Name: **Docefrez**	**Strength** **20 mg and 80 mg vials**	**Usual Dose:** **60 mg/m^2 to 100 mg/m^2 intravenously every 3 weeks**
Failure Mode: Name confusion	**Causes** **(could be multiple)**	**Effects**
0.5 mg to 9 mg per day depending on the disease being treated. For the treatment of unresponsive shock, high doses are suggested (e.g., 1 mg/kg as a single intravenous injection)		
Doxapram (Doxapram is an established name) Injection *Strength*: 400 mg/20 mL vial (20 mg/mL) *Dosage range*: Intravenous injection: 0.5 mg/kg to 1.5 mg/kg intravenously Intravenous infusion: 1 mg/min to 5 mg/min; 1 mg/kg/hr to 3 mg/kg/hr	Orthographic similarity: (The beginning letters "Do") and ("frez" vs. "pram") The potential exists for doses of Docefrez and Doxapram to overlap (e.g., 80 mg, 90 mg, 100 mg)	Medication errors unlikely to occur due to orthographic differences between the names in addition to differing context of use. *Rationale:* The middle letters of the names ("ce" vs. "xa") look different. Doxapram is indicated for use as a respiratory stimulant due to drug induced postanesthesia respiratory depression, drug induced CNS depression, or COPD associated with acute hypercapnia so it is more likely to be administered in a surgical, post-surgical, or intensive care type setting. Docefrez is less likely to be administered in these settings. Thus, the very different and specific indications of use for the products may help to differentiate the names. Additionally, Docefrez would likely be written on a special "chemotherapy" order sheet or under a similar titled heading on an order sheet. The dosing of Docefrez is based on body surface area which is likely to be specified on the order along with the final calculated dose which would allow for double checks of the dose prior to drug preparation. Thus, the additional information that is likely to be specified on a Docefrez order may help to differentiate the names.

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