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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
Office of Medication Error Prevention and Risk Management**

Proprietary Name Review

Date: October 11, 2013

Reviewer: Morgan Walker, PharmD, MBA
Division of Medication Error Prevention and Analysis

Team Leader: Jamie Wilkins Parker, PharmD
Division of Medication Error Prevention and Analysis

Drug Name and Strength: Dyloject (Diclofenac Sodium) Injection
37.5 mg/mL in 1 mL (b) (4) vials

Application Type/Number: NDA 022396

Applicant/Sponsor: Hospira

OSE RCM #: 2013-1776

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

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1 INTRODUCTION

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

1.1 REGULATORY HISTORY

The original request was submitted to the Agency on December 22, 2009. The name was found acceptable on March 19, 2010. The Applicant received a CR on October 1, 2010. Thus, the Applicant resubmitted this request for proprietary name review on July 30, 2013 due to the elapsed time from the approval of the original request for proprietary name submission. None of the product characteristics have changed from the original submission.

1.2 PRODUCT INFORMATION

The following product information is provided in the July 30, 2013 proprietary name submission.

- Active Ingredient: Diclofenac Sodium
- Indication of Use: [REDACTED] (b) (4)
- Route of Administration: Intravenous [REDACTED] (b) (4)
- Dosage Form: Solution for injection
- Strength: 37.5 mg/1 mL
- Dose and Frequency: 37.5 mg administered by intravenous bolus injection [REDACTED] (b) (4) every 6 hours as needed for pain, not to exceed 150 mg per 24 hours
- How Supplied: 1 mL [REDACTED] (b) (4) vials in cartons of 25 vials
- Storage: USP Controlled Room Temperature

2 RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion OPDP determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Anesthesia, Analgesia, and Addiction Products concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) SEARCH

This name does not contain a USAN Stem¹.

2.2.2 Components of the Proposed Proprietary Name

The Applicant did not indicate in their submission that the proposed name, Dyloject, is has a derivation or intended meaning. This proprietary name is comprised of a single word that contains the suffix ‘ject’ which may imply injection as a route of administration. After considering the use of the product (route of administration is injection), DMEPA cannot envision a scenario that would contribute to a medication error as a result of the suffix, ‘ject’ being present in the name.

2.2.3 FDA Name Simulation Studies

Sixty-five practitioners participated in DMEPA’s prescription studies. The interpretations did not overlap with any currently marketed products nor did the misinterpretations sound or look similar to any currently marketed products or any products in the pipeline. There were 5 voice study participants who misinterpreted the string “Dylo” as “Dialo”. Twenty-two of the voice study participants misinterpreted the ‘y’ as an ‘i’. We have considered these variations in our look-alike and sound-alike searches and analysis (see Appendix B). Appendix C contains the results of the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines at Initial Review

In response to the OSE, August 28, 2013 e-mail, the Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.5 Failure Mode and Effects Analysis of Similar Names

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in the proposed proprietary name. These variations were used in the search for names similar to Dyloject. Table 1 lists the names with potential orthographic, phonetic, or spelling similarity to the proposed proprietary name, Dyloject identified by the primary reviewer, the Expert Panel Discussion (EPD), other review disciplines, and the FDA Prescription Simulation. The highlighted names are names previously reviewed in OSE Review #2009-2488. Our analysis of the remaining seven names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics. We determined none of the seven names will pose a risk for confusion as described in Appendix D.

¹ The August 21, 2013 search of the United States Adopted Name (USAN) stems.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, and (b) (4))					
Look Similar to Dyloject					
Dylaxol	FDA	(b) (4) ***	FDA	Dyclonine	FDA
(b) (4) ***	FDA	Dysport	FDA	Decaject	FDA
Redi-ject***	FDA	Depoject	FDA		
(b) (4) ***	FDA	Diclofenac	FDA		
Look and Sound Similar to Dyloject					
Lidoject-1	FDA	(b) (4) ***	FDA		
Diltzac	FDA				

2.2.6 Communication of DMEPA’s Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Anesthesia, Analgesia, and Addiction Products via e-mail on September 25, 2013. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Anesthesia, Analgesia, and Addiction Products on October 10, 2013, they stated no additional concerns with the proposed proprietary name, Dyloject.

3 CONCLUSIONS

The proposed proprietary name is acceptable from both a promotional and safety perspective.

If you have further questions or need clarifications, please contact Vaishali Jarral, OSE project manager, at 301-796-4248.

3.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your July 30, 2013 submission are altered, the name must be resubmitted for review.

4 REFERENCES

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

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

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

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

3. Drug Facts and Comparisons, online version, St. Louis, MO

(<http://factsandcomparisons.com>)

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

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. *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. *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.

10. Access Medicine (www.accessmedicine.com)

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

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

USAN Stems List contains all the recognized USAN stems.

12. Red Book (www.thomsonhc.com/home/dispatch)

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

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

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

14. Medical Abbreviations (www.medilexicon.com)

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

15. CVS/Pharmacy (www.CVS.com)

This database contains commonly used over the counter products not usually identified in other databases.

16. Walgreens (www.walgreens.com)

This database contains commonly used over the counter products not usually identified in other databases.

17. Rx List (www.rxlist.com)

RxList is an online medical resource dedicated to offering detailed and current pharmaceutical information on brand and generic drugs.

18. Dogpile (www.dogpile.com)

Dogpile is a [Metasearch](#) engine that searches multiple search engines including Google, Yahoo! and Bing, and returns the most relevant results to the search.

19. Natural Standard (<http://www.naturalstandard.com>)

Natural Standard is a resource that aggregates and synthesizes data on complementary and alternative medicine.

APPENDICES

Appendix A

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

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, we consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.). DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.²

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

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

DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product. DMEPA considers the product characteristics associated with the proposed product throughout the risk assessment because the product characteristics of the 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.

² National Coordinating Council for Medication Error Reporting and Prevention. <http://www.nccmerp.org/about/MedErrors.html>. Last accessed 10/11/2007.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. DMEPA considers how these product characteristics may or may not be present in communicating a product name throughout the medication use system. Because drug name confusion can occur at any point in the medication use process, DMEPA considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.³

The DMEPA considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA compares the proposed proprietary name with the proprietary and established name of existing and proposed drug products and names currently under review at the FDA. DMEPA compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. DMEPA examines the phonetic similarity using patterns of speech. If provided, DMEPA will consider the Sponsor's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Sponsor has little control over how the name will be spoken in clinical practice. The orthographic appearance of the proposed name is evaluated using a number of different handwriting samples. DMEPA applies expertise gained from root-cause analysis of postmarketing medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g., "T" may look like "F," lower case 'a' looks like a lower case 'u,' etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details).

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

Table 1. Criteria Used to Identify Drug Names that Look- or Sound-Similar to a Proposed Proprietary Name.

Type of Similarity	Considerations when Searching the Databases		
	<i>Potential Causes of Drug Name Similarity</i>	<i>Attributes Examined to Identify Similar Drug Names</i>	<i>Potential Effects</i>
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> 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/Similar shape Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, DMEPA considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the

safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

DMEPA searches the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name. A standard description of the databases used in the searches is provided in the reference section of this review. To complement the process, the DMEPA uses a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, DMEPA reviews the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel. DMEPA also evaluates if there are characteristics included in the composition that may render the name unacceptable from a safety perspective (abbreviation, dosing interval, etc.).

2. Expert Panel Discussion

DMEPA gathers CDER professional opinions on the safety of the proposed product and discussed the proposed proprietary name (Expert Panel Discussion). The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Office of Prescription Drug Promotion (OPDP). We also consider input from other review disciplines (OND, ONDQA/OBP). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

The primary Safety Evaluator presents the pooled results of the database and information searches to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend additional names, additional searches by the primary Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

3. FDA Prescription Simulation Studies

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

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically

scanned and one prescription is delivered to a random sample of participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants record their interpretations of the orders which are recorded electronically.

4. Comments from Other Review Disciplines

DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

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

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

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, considers all aspects of the name that may be misleading or confusing, conducts a Failure Mode and Effects Analysis, and provides an overall decision on acceptability dependent on their risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.⁴ When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product

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

characteristics listed in Section 1.2 of this review. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

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

“Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting? And are there any components of the name that may function as a source of error beyond sound/look-alike?”

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

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

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

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

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

- a. OPDP finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with OPDP’s findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].
- b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].

- c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
- d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
- e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product but involve a naming characteristic that when incorporated into a proprietary name, may be confusing, misleading, cause or contribute to medication errors.

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

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

The threshold set for objection to the proposed proprietary name may seem low to the Applicant/Sponsor. However, the safety concerns set forth in criteria a through e above are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), the Joint Commission, and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names, confusing, or misleading names and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, the Agency and/or Sponsor can identify and rectify prior to approval to avoid patient harm.

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

past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency’s credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Sponsors’ have changed a product’s proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners’ vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval.

Appendix B: Letters and Letter Strings with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Dyloject	Scripted May Appear as	Spoken May Be Interpreted as
Capital ‘D’	G, O, T, B , P, R	B, T
Lower case ‘d’	cl, ci, a, l, el, v	b, t
Lower case ‘y’	f, j, p, u, v, x, z	e, i, j, u
Lower case ‘l’	b,e, s, A, P, I, t, c	
Lower case ‘o’	a, c, e, u	Oh
Lower case ‘j’	f, g, p, q, y, z	
Lower case ‘e’	a, i, l, o, u,p, c	Any vowel
Lower case ‘c’	a, e, i, l	z, k, s if followed by an e or i
Lower case ‘t’	f, i, l, r, x, A	d, f, p, pt, v
Letter strings associated with the proposed name, Dyloject		
lo	b	
ct	cl, d	
oj	y, g	
ec	ce, ee, ic, ie, ia, ea, ae, ai	

Appendix C: Prescription Simulation Samples and Results

Figure 1. Dyloject Study (Conducted on August 9, 2013)

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Medication Order:</u> <i>Dyloject 37.5mg (b)(4) X1</i></p>	<p>Dyloject UAD Bring to clinic Disp.: #1</p>
<p><u>Outpatient Prescription:</u> <i>Dyloject #1 UAD Bring to clinic</i></p>	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

192 People Received Study
 65 People Responded

Study Name: Dyloject

Total	24	23	18
INTERPRETATION	OUTPATIENT	VOICE	INPATIENT TOTAL
DIALOJECT	0	1	0 1
DIALOJET	0	4	0 4
DILOCHECK	0	1	0 1
DILOCHEK	0	1	0 1
DILOGET	0	3	0 3
DILOJECT	0	7	0 7
DILOJES	0	1	0 1
DILOJET	0	4	0 4

DYLOJECT	24	0	17	41
DYLOJECT 37.5 MG	0	0	1	1
DYLOJET	0	1	0	1

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

No.	Proprietary Name	Active Ingredient	Similarity to Dyloject	Failure preventions
1.	Dylaxol	Bisacodyl	Look alike	Ending lacks orthographic similarity.
2.	Gonal-f RFF Redi-ject***	Follitropin alfa for injection	Look alike	Lacks orthographic similarity
3.	(b) (4) ***	Epinephrine	Look alike	Approved and currently marketed as Auvi-Q
4.	(b) (4) **	Golimumab	Look alike	Lacks orthographic similarity
5.	Diclofenac	N/A	Look alike	Lacks orthographic similarity
6.	Dyclonine	N/A	Look alike	Lacks orthographic similarity
7.	Diltzac	Diltiazem hydrochloride	Look alike and sound alike	Lacks orthographic and phonetic similarity

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**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: July 29, 2010

To: Bob Rappaport, MD, Director
Division of Anesthesia and Analgesia Products

Through: Carlos Mena-Grillasca, RPh, Team Leader
Denise P. Toyer, PharmD, Deputy Director
Division of Medication Error Prevention and Analysis (DMEPA)

From: Walter Fava, R.Ph., MSED., Safety Evaluator
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name(s): Dyloject (Diclofenac Sodium) Injection
37.5 mg/mL vial

Application Type/Number: NDA 022396

Applicant: Javelin Pharmaceuticals Inc.

OSE RCM #: 2010-639

1 INTRODUCTION

This re-assessment of the proposed proprietary name responds to the anticipated approval of this NDA within 90 days from the date of this review. The Division of Medication Error Prevention and Analysis (DMEPA) found the proposed proprietary name, Dyloject, acceptable in OSE Review # 2009-2488, dated March 19, 2010. The Division of Anesthesia and Analgesia Products did not have any concerns with the proposed name, Dyloject, and the Division of Drug Marketing, Advertising and Communication (DDMAC) found the name acceptable from a promotional perspective on January 07, 2010.

2 METHODS AND RESULTS

For the proposed proprietary name, DMEPA staff searched a standard set of databases and information sources (see section 4) to identify names with orthographic and/or phonetic similarity to the proposed name that have been approved since the previous proprietary name review. We used the same search criteria previously used in OSE Review #2009-2488. Since none of the proposed product characteristics were altered we did not re-evaluate previous names of concern. Additionally, DMEPA searches the United States Adopted Names (USAN) stem list to determine if the name contains any USAN stems as of the last USAN updates. 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.

The searches of the databases referenced in Section 4 did not yield any new names thought to look or sound similar to Dyloject and represent a potential source of drug name confusion.

DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, Dyloject, as of July 27, 2010.

3 CONCLUSIONS AND RECOMMENDATIONS

The proprietary name risk assessment findings indicate that the proposed name, Dyloject, is not vulnerable to name confusion that could lead to medication errors nor is the name considered promotional. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Dyloject, 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 Anesthesia and Analgesia Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

4 REFERENCES

1. OSE review # 2009-2488 dated March 9, 2010; Proprietary Name Review of Dyloject; Walter Fava, Safety Evaluator.

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.

4. *CDER Proposed Names List*

Compiled list of proposed proprietary names submitted to the Division of Medication Error Prevention and Analysis (DMEPA) for review. The list is updated weekly and maintained by DMEPA.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22396	ORIG-1	HOSPIRA INC	diclofenac sodium injection

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

/s/

WALTER L FAVA
07/29/2010

CARLOS M MENA-GRILLASCA
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07/29/2010



**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: March 19, 2010

To: Bob Rappaport, MD, Director
Division of Anesthesia, Analgesia, and Rheumatology Products

Through: Carlos M Mena-Grillasca, R.Ph., Team Leader
Denise Toyer, PharmD, Deputy Director
Carol Holquist, R.Ph., Director
Division of Medication Error Prevention and Analysis (DMEPA)

From: Walter Fava, R.Ph., MSED., Safety Evaluator
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name(s): Dyloject (Diclofenac Sodium) Injection
37.5 mg/mL in 1 mL (b) (4) vials

Application Type/Number: NDA 022396

Applicant/Applicant: Javelin Pharmaceuticals, Inc.

OSE RCM #: 2009-2488

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

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EXECUTIVE SUMMARY

Dyloject is the proposed proprietary name for Diclofenac Sodium 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, Dyloject, conditionally 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 Division of Anesthesia, Analgesia, and Rheumatology Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

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 Javelin Pharmaceuticals Inc., dated December 22, 2009, for an assessment of the proposed proprietary name, Dyloject, regarding potential name confusion with other proprietary or established drug names in the usual practice settings. DMEPA will assess labels and labeling in a separate forthcoming review.

1.2 PRODUCT INFORMATION

Dyloject is a non-steroidal anti-inflammatory (b) (4). It is administered (b) (4) intravenously (b) (4) with a bolus dose of 37.5 mg (b) (4) every 6 hours as need for pain, not to exceed 150 mg per 24 hours. Dyloject will be supplied in 1 mL (b) (4) vials in cartons of 25 vials. Each vial will have a 37.5 mg/mL concentration.

2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment for all proprietary names. Sections 2.1, 2.2, 2.3, and 2.4 identifies specific information associated with the methodology for the proposed proprietary name, Dyloject.

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.

To identify drug names that may look similar to ‘Dyloject’, 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 (eight letters), upstrokes (3, capital letter ‘D’, lower case letters ‘l’ and ‘t’), downstrokes (two, lower case letters ‘y’ and ‘j’), cross strokes (1, lower case letter ‘t’), and dotted letters (one, lower case ‘j’). Additionally, several letters in Dyloject may be vulnerable to ambiguity when scripted (see Appendix B). As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Dyloject.

When searching to identify potential names that may sound similar to Dyloject, the DMEPA staff searches for names with similar number of syllables (Three), stresses (DY-lo-ject, dy-LO-ject, or dy-lo-JECT), and placement of vowel and consonant sounds. The Applicant’s intended pronunciation was not provided in the Request for Proprietary Name Review. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary. Furthermore, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

2.2 FDA PRESCRIPTION ANALYSIS STUDIES

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

Figure 1. Dyloject Study (conducted on January 11 and January 15, 2010)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
<p data-bbox="264 1220 854 1251"><u>Inpatient Medication Order January 11, 2010:</u></p> <p data-bbox="342 1262 935 1314"><i>Dyloject Injekt 37.5mg</i> (b) (4)</p>	<p data-bbox="1040 1220 1370 1287">Dyloject 37.5 mg (b) (4) every 6 hours</p>
<p data-bbox="264 1350 854 1381"><u>Inpatient Medication Order January 15, 2010:</u></p> <p data-bbox="280 1392 1016 1459"><i>Dyloject 37.5mg</i> (b) (4)</p>	

2.3 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

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

After the Safety Evaluator has determined the overall risk associated with the proposed name, the Safety Evaluator compares the findings of their overall risk assessment with the findings of the proprietary name risk assessment submitted by the Applicant. The Safety Evaluator then determines whether the Division's risk assessment concurs or differs with the findings. When the proprietary name risk assessments differ, the Division of Medication Error Prevention and Analysis provides a detailed explanation of these differences.

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The searches yielded a total of 12 names as having some similarity to the name Dyloject.

Nine of the names were thought to look like Dyloject. These include (b) (4) Azilect, Dyazide, Dysport, Dylix, Dyclone, Dyflex-G, Dyfilin-GG, and Glofil. The three remaining names, (b) (4)***, Dyna-hex, and Dyloject, were thought to look and sound similar to Dyloject.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of January 22, 2010.

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 Dyloject.

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 60 practitioners responded but none of the responses overlapped with any existing or proposed drug names. Thirty-two of the participants interpreted the name correctly as "Dyloject," with correct interpretation occurring in both inpatient written studies (n=32) and no correct responses were submitted for the verbal study. All of the verbal responses and the remainder of the written responses misinterpreted the drug name. In the verbal studies, all responses were misspelled phonetic variations of the proposed name, Dyloject. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 EXTERNAL STUDY

In the proposed name risk assessment submitted by the Applicant, (b) (4) identified and evaluated a total of 67 drug names (Becomject, Benoject, Bilopque, Biloric, Cyclogen, Digex, Digitek, Dilacor, Dilaudid, Dilex-G, Dilor, Dilor-400, Dilor-G, Dilotab, Diocto, Diocto C, Diocto-K, Dionex, Dologesic, Dyflex, Dyflex-200, Dyflex-G, Dylix, Monoject, Niloric, Cyanoject, Depoject-40,

Depoject-80, Depotest, Diflucan, Dilocaine, Flexoject, Lidoject-1, Dilaudid HP, Dilomine, Dramoject, Phenoject, Abboject, Arthroject, Caverject, Cytotec, Decaject, Delatest, Diovan, Dolorac, Dolorex, Dolotic, Duricef, Dyazide, Dyclone, Dycomene, Estroject, Hylorel, Mylocel, Phiso hex, Prilosec, Testoject, Vasotec, Xeloda, Zelapar, Zocor, Zolofl, Zyllo, Zylet, Zylloprim, Zyrtec, and Zyvox) that were thought to have some look-alike and/or sound-alike qualities and potential for confusion with Dyloject.

Four of the 67 names, four names, Dyazide, Dyllox, Dyclone, and Dyflex-G, were previously identified in DMEPA Staff searches and the Expert Panel Discussion.

3.5 COMMENTS FROM THE DIVISION OF ANESTHESIA, ANALGESIA, AND RHEUMATOLOGY PRODUCTS (DAARP)

3.5.1 Initial Phase of Review

On January 7, 2010, DMEPA notified the Division of Anesthesia, Analgesia, and Rheumatology Products, via e-mail that we received a request for a proprietary name review of the proposed name, Dyloject and asked if they had any concerns with the name. On February 23, 2010, DAARP responded via e-mail correspondence that they had no issues with the proposed name, Dyloject.

3.5.2 Midpoint of Review

DMEPA notified the Division of Anesthesia, Analgesia, and Rheumatology Products, via e-mail that we had no objections to the proposed proprietary name; Dyloject, on February 25, 2010. As of the signature date of this review, DAARP did not provide any additional comments or concerns with our assessment of the proposed proprietary name, Dyloject.

3.6 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator resulted in identification of one additional name, Lidoject-2, which was thought to look or sound similar to Dyloject and represent a potential source of drug name confusion. We noted that one of the names identified in EPD, is the same product as the test name only marketed in the United Kingdom, and therefore was not further evaluated. As such, a total of 75 names were identified for their orthographic and/or phonetic similarity with Dyloject.

4 DISCUSSION

4.1 PROMOTIONAL REVIEW

DDMAC did not identify any concerns with the proposed name from a promotional perspective. DAARP and DMEPA concurred with this assessment.

4.2 SAFETY REVIEW

DAARP did not express concerns with the proposed name. DMEPA identified a total of seventy five names having some similarity to the proposed name. Upon evaluation of the 75 names, sixty-six names were eliminated because they lacked orthographic and/or phonetic similarity (see Appendix D). We did not identify any other aspects of the name that would function as a source of error.

Failure mode and effect analysis (FMEA) was then applied to determine if the proposed name could potentially be confused with the remaining 9 names and lead to medication errors. This analysis determined that the name similarity between Dyloject was unlikely to result in medication errors with any of the 9 products for the reasons presented in Appendices E through G. This finding was consistent with and supported by an independent risk assessment of the proprietary name submitted by the Applicant.

5 CONCLUSIONS AND RECOMMENDATIONS

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

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.

5.1 COMMENTS TO THE DIVISION

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 Anesthesia, Analgesia, and Rheumatology Products, should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

We are willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Cheryle Milburn, Project Manager, at 301-796-2084.

5.2 COMMENTS TO THE APPLICANT

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

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

If **any** of the proposed product characteristics are altered prior to approval of this NDA, the proprietary name should be resubmitted for review.

6 REFERENCES

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

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

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

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

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

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

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

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

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

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

6. ***Drugs@FDA*** (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>)

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

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

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

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

USPTO provides information regarding patent and trademarks.

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

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

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

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

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

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

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

Stat!Ref contains full-text information from approximately 30 texts; it includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology, and Dictionary of Medical Acronyms Abbreviations.

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

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

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

APPENDICES

Appendix A:

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.¹

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity and hold a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name. 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.

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

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.² DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

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

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA staff considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.³ DMEPA provides the product characteristics considered for this review in section one.

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly 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.

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

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

Table 1. Criteria used to identify drug names that look- or sound-similar to a proposed proprietary name.

Type of similarity	Considerations when searching the databases		
	<i>Potential causes of drug name similarity</i>	<i>Attributes examined to identify similar drug names</i>	<i>Potential Effects</i>
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> 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-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> 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.⁴ When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

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

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

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

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names possess 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:

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

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

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

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

- a. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC’s findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].
- b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
- c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
- d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
- e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

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

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

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

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

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

Appendix B: Letters with Possible Orthographic or Phonetic misinterpretation

Letters in Name, Dyloject	Scripted may appear as	Spoken may be interpreted as
Capital ‘D’	‘O’, ‘P’	‘T’, ‘B’
Lower case ‘y’	‘g’, ‘p’, ‘j’	‘i’, ‘e’, ‘u’, ‘a’, ‘o’
Lower case ‘l’	‘i’, ‘t’, ‘e’	--
Lower case ‘o’	Any vowel	Any vowel
Lower case ‘j’	‘g’, ‘y’, ‘p’	‘g’, ‘ch’
Lower case ‘e’	Any vowel	Any vowel
Lower case ‘c’	Any vowel	‘ck’, ‘k’, ‘s’
Lower case ‘t’	‘l’, ‘x’	‘d’

Appendix C: FDA Prescription Study Responses.

Inpatient Medication Order #1 (January 11, 2010)	Inpatient Medication Order #2 (January 15, 2010)	Voice Prescription (January 11, 2010)
Dyloject	Dyloject	Dialaject
Dyloject	Dyloject	Dilaject
Dyloject	Dyloject	Dilaject
Dyloject	Dyloject	Dilaject
Dyloject	Dyloject	Dialaject
Dyloject	Dyloject	Dilojet
Dyloject	Dyloject	Dialazac
Dyloric	Dyloject	Dialeject
Dylojick	Dylojict	Dialajet
Dyloject	Dylojict	Delijet
Dyloject	Dyloject	Dilaject
Dylo???	Dylojict	Dilaject
Dyloject	Dyloject	Dylaject
Dylojext	Dyloject	Dilagect
Dyloject	Dylojict	Dialaject
Dyloject	Dyloject	Dial-a-ject
Dyloject	Dyloject	Dialinject
Dyloject	Dyloject	Dial-a-ject
	Dyloject	Dilaject
	Dylojict	
	Dyloject	
	Dyloject	
	Dyloject	

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

Name	Name	Name	Name
Abboject	Dilocaine	Dyclone	Xeloda
Arthrotec	Dilor	Dycomene	Zelapar
Becomject	Dilor-400	Dyflex	Zocor
Benoject	Dilor-G	Dyflex-200	Zoloft
Bilopaque	Dilotab	Dyflex-G	Zyflo
Biloric	Diocto	Dylix	Zylet
Caverject	Diocto C	Estroject	Zyloprim
Cyclogen	Diocto-K	Flexoject	Zyrtec
Cytotec	Dionex	Hylorel	Zyvox
Delatest	Diovan	Monoject	(b) (4)
Diflucan	Dologesic	Mylocel	Dyfilin-GG
Digex	Dolorac	Niloric	Glofil
Digitek	Dolorex	Phenoject	Dyna-hex
Dilacor	Dolotic	Phisohex	Depotest
Dilaudid	Dramoject	Prilosec	Cyanoject
Dilaudid HP	Duricef	Testoject	
Dilex-G	Dyazide	Vasotec	

Appendix E: Proprietary names with orthographic and/or phonetic similarity to Dyloject with ‘Not Approvable’ status

Proprietary Name	Similarity to Dyloject	Status
(b) (4) ***	Look and Sound	DMEPA objected to name in 2002 (RCM #02-0197) ANDA (b) (4). Trademark abandoned in 2003.

Appendix F: Proposed Proprietary Names Objected to by DMEPA

Proprietary Name	Similarity to Dyloject	Status
(b) (4) ***	Look and Sound	DMEPA objected to name in February 2010, response pending

Appendix G: Products with phonetic and/or orthographic similarity to Dyloject but with no overlap in strength and dose

Product name with potential for confusion	Similarity to Dyloject	Strength/Dosage form	Usual Dose
Dyloject (diclofenac sodium)		37.5 mg/mL injection	37.5 mg intravenously (b) (4) every 6 hours as needed for pain
Azilect (rasagiline)	Look	0.5 mg and 1 mg tablets	0.5 mg by mouth once a day
Dysport (abobotulinumtoxinA)	Look	300 units per vial and 500 units per vial injection	<u>Cervical Dystonia:</u> 500 units injected intramuscularly in divided doses in affected muscles every 3 months <u>Glabellar Lines:</u> 50 units injected intramuscularly in 10 unit doses to each affected muscle every 3 months
Depoject-40 (methylprednisolone acetate) Depoject-80 (methylprednisolone acetate) (Discontinued product available generically)	Look and Sound	40 mg/mL injection 80 mg/mL injection	<u>Adrenogenital syndrome:</u> 40 mg injected intramuscularly every 2 weeks <u>Rheumatoid arthritis:</u> 40mg to 120 mg injected intramuscularly once a week <u>Dermatologic lesions:</u> 40 mg to 120 mg injected intramuscularly for one to four weeks every 5 to 10 days <u>Asthma and allergic rhinitis:</u> 40 mg to 120 mg injected intramuscularly x1 dose <u>Intra-articular and soft tissue:</u> 4 mg to 80 mg injected intra-articularly x1 dose (depending on the joint size) <u>Intralesional:</u> 20 mg to 60 mg injected intralesionally x1 dose
Decaject (dexamethasone sodium phosphate)	Look and Sound	4 mg/mL injection	0.5 mg to 24 mg injected intramuscularly or intravenously one time

Appendix G: Potentially confusing names to Dyloject which are unlikely to cause medication errors

Failure Mode: Name confusion	Causes (could be multiple)	Rationale that minimizes the risk of a medication error
Dyloject (diclofenac sodium) Injection 37.5 mg/mL		Usual dose: 37.5 mg (b) (4) intravenous every 6 hours as needed for pain
Lidoject-1 (lidocaine 1%) Injection Lidoject-2 (lidocaine 2%) Injection	<p>Orthographic similarities include:</p> <p>Both names contain 8 letters, and have 7 of the same letters with identical 4 ending letters, 'ject'.</p> <p>Phonetic similarities include:</p> <p>Both names contain 3 syllables. The first two syllables of the names, 'Dylo' vs 'Lido', are comprised of the similar letters in a different sequence and have similar phonetic pronunciation of the second ('y' vs 'i') and fourth ('o') letters.</p> <p>Overlapping product characteristics include:</p> <p>Dosage form: Injectable</p> <p>Route of Administration: (b) (4) Intravenous vs Intramuscular or Intradermal or Intravenous</p>	<p>Despite orthographic and phonetic similarities, it is unlikely that these name pairs will result in medication errors.</p> <p><i>Rationale:</i></p> <p>The beginning letters, 'Dy' in Dyloject vs 'Li' in Lidoject appear different when scripted. Although a lower case letter 'd' may look similar to the letter 'L' when scripted, the downstroke of the 'y' in Dyloject appears different from the corresponding letter 'i' in Lidoject. The letter string, 'ylo' in Dyloject also appears different from the corresponding letterstring, 'ido' in Lidoject when scripted.</p> <p>Phonetically, if practitioners thought an order for Dyloject was Lidoject, they would need to clarify the product strength being ordered since Lidoject is available in two concentrations (1% and 2%) which do not overlap with Dyloject (37.5 mg/mL). This would also apply in the converse scenario if a verbal order for Lidoject was interpreted as Dyloject.</p> <p>Additionally, Lidoject-1 and Lidoject-2 are discontinued products, and although available generically, Drug Usage Data did not retrieve any prescribing data over the last five years for the proprietary name 'Lidoject'.</p>

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22396	ORIG-1	JAVELIN PHARMACEUTICA LS INC	diclofenac sodium injection

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

/s/

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