CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-202

PROPRIETARY NAME REVIEW(S)

Department of Health and Human Services

Public Health Service

Food and Drug Administration

Center for Drug Evaluation and Research

Office of Surveillance and Epidemiology

Date:	April 29, 2009
To:	Bob Rappaport, M.D., Director Division of Anesthesia, Analgesia and Rheumatology Products
Thru:	Denise Toyer, PharmD., Deputy Director Carol Holquist, R.Ph., Director Division of Medication Error Prevention and Analysis
From:	Melina Griffis, R.Ph, Acting Team Leader Division of Medication Error Prevention and Analysis
Subject:	Proprietary Name, Label and Labeling Review
Drug Name(s):	Zipsor (Diclofenac Potassium) Capsules 25 mg
Application Type/Number:	NDA 22-202
Applicant:	Xanodyne Pharmaceuticals, Inc.
OSE RCM #:	2008-463

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

CONTENTS

EXECUTIVE SUMMARY

DMEPA previously reviewed the proposed proprietary name; Zipsor, without objection. Since that review, none of Zipsor's product characteristics have changed. Upon re-review we identified 13 new names for their similarity to Zipsor. The results of the Failure Mode and Effects Analysis found that the proposed name, Zipsor, is not vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention and Analysis does not object to the use of the proprietary name, Zipsor, 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, the Applicant provided revised labels and labeling based on DMEPA recommendations in OSE review #2007-2024). DMEPA has provided one additional comment to communicate to the Applicant. We refer you to section 5 of this review.

1 BACKGROUND

1.1 INTRODUCTION

This re-assessment of the proprietary name is written in response to a notification that NDA 22-202 will be approved within 90 days. DMEPA found the proposed proprietary name, Zipsor acceptable in OSE review 2007-2024 dated June 12, 2008

1.2 PRODUCT INFORMATION

Zipsor is indicated for the treatment of mild to moderate pain and will be available in a 25 mg soft gelatin capsule. The recommended dosage is 25 mg given four times daily.

Zipsor capsules will be packaged in white HDPE bottles, containing 100 capsules and sealed with a heat induction seal, and a child resistant closure. The physician sample blister cards will contain a dual adhesive child resistant label applied to the back of each blister card.

2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a re-assessment of a proprietary name 90 days prior to approval of an NDA/BLA. Section 2.1 identifies the specific search criteria associated with the proposed proprietary name, Zipsor.

2.1 SEARCH CRITERIA

The DMEPA staff considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

For this review, particular consideration was given to drug names beginning with the letter 'Z' 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 Zipsor, the staff also consider the other orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (six letters), upstrokes (one, capital letter 'Z'), downstokes (one, lowercase 'p'), cross-strokes (none), and dotted letters ('i'). Additionally, several letters in Zipsor may be vulnerable to ambiguity when scripted, including the letter 'Z' may appear as 'L','C' of 'F'; lower case 'i' may appear as a lower case 'e' or 'o', lower case 'o' may appear as 'a'; and lower case 'r' may appear as 'v'. As such, the staff also considers these alternate appearances when identifying drug names that may look similar to Zipsor.

When searching to identify potential names that may sound similar to Zipsor, the staff search for names with similar number of syllables (two), stresses (ZIP-soar or zip-SOAR), and placement of vowel and consonant sounds. In addition, several letters in Zipsor may be subject to interpretation when spoken, including the letter 's' may be interpreted as 'z'; the letter 'o' may be interpreted as 'ou'; or the letter 'Z' may be interpreted as 'S'. The Sponsor's intended pronunciation of the proprietary name is ZIP-soar.

2.2 LABEL AND LABELING RISK ASSESSMENT

The label and labeling of a drug product are the primary means by which practitioners and patients (depending on configuration) interact with the pharmaceutical product. The container labels and carton labeling communicate critical information including proprietary and established name, strength, dosage form, container quantity, expiration, and so on. The insert labeling is intended to communicate to practitioners all information relevant to the approved uses of the drug, including the correct dosing and administration.

Given the critical role that the label and labeling has in the safe use of drug products, it is not surprising that 33 percent of medication errors reported to the USP-ISMP Medication Error Reporting Program may be attributed to the packaging and labeling of drug products, including 30 percent of fatal errors[3] to identify potential errors with all medications similarly packaged, labeled or prescribed. The Division uses FMEA and the principles of human factors to identify potential sources of error with the proposed product labels and insert labeling, and provide recommendations that aim at reducing the risk of medication errors.

On December 16, 2008 the Applicant submitted the following labels for our review:

- Blister Card Carton and Container Labels: (Appendix F)
- Carton Labeling: (Appendix G)

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

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

[3] Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006. p275.

3 RESULTS

3.1 PROPRIETARY NAME RISK ASSESSMENT

3.1.1 Database and Information Sources

The searches yielded a total number of 15 names as having some similarity to the name Zipsor.

Fourteen names were thought to look like Zipsor, which include: Zipra, Ziproc, Zipan, Lipitor, Insulin Lispro, Lipsoyn, Zipos, Ziprol, Zepan, Zymar, Zanosar, Zemplar, Zofran and Lipram. The remaining name, Zocor was thought to sound similar to Zipsor.

Additionally, the Division of Medication Error Prevention and Analysis did not identify any United States Adopted Names (USAN) stems in the name Zipsor, as of the last date searched on March 31, 2009.

3.1.2 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 Zipsor.

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

3.1.3 Safety Evaluator Risk Assessment

Independent searches by the primary Safety Evaluator resulted in one additional name which was thought to sound similar to Zipsor (Simcor) and represent a potential source of drug name confusion.

Three (Zipan, Lipitor and Zocor) of the 16 names identified in the database searches were previously reviewed in the initial Zipsor proprietary name review (OSE # 2007-2024). Zipsor has not undergone any product characteristic changes since the previous review therefore these names did not undergo further analysis in this review.

One name, Insulin Lispro, was determined to lack orthographic similarity to Zipsor, therefore was not analyzed further (see Appendix B).

Twelve names were analyzed to determine if drug names could be confused with Zipsor and if the drug name confusion could likely result in a medication error.

Failure mode and effect analysis (FMEA) was then applied to determine if the proposed name could potentially be confused with any of the 12 names and lead to medication errors. This analysis determined that the name similarity between Zipsor and the identified names was unlikely to result in medication errors with any of the 12 products identified for the reason presented in Appendices C through D.

3.2 LABEL AND LABELING

All previous recommendations from OSE review # 2007-2024 have been implemented.

The dosage form has been revised to read 'Liquid Filled Capsules'.

4 DISCUSSION

4.1 PROPRIETARY NAME RISK ASSESSMENT

Thirteen new names were evaluated for their potential similarity to the proposed name, Zipsor. The FMEA indicates that the proposed name is not likely to result in name confusion that could lead to medication errors.

4.2 LABEL AND LABELING RISK ASSESSMENT

All label and labeling recommendations have been implemented with one exception. The Applicant has revised the dosage form statement to read 'Liquid Filled Capsules'. In consultation with Dr. Al Hakim, the reviewing chemist for this product, 'Liquid Filled Capsules' is not considered an appropriate designation of the dosage form for this product. It was determined that 'Capsule' is the appropriate dosage form designation for this product and all labels and labeling should be revised to reflect this.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Zipsor, is not vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Zipsor, for this product at this time. Additionally, DDMAC does not object to the proposed name, Zipsor from a promotional perspective.

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

Please forward the following comment to the Applicant:

We note that you have revised your container labels and carton labeling to read 'Liquid Filled Capsule', however, based on input from the Chemistry, Manufacturing and Control review team this dosage form designation is not appropriate for this product. All container labels and carton labeling should be revised to reflect 'Capsule' as the appropriate dosage form for Zipsor.

6 REFERENCES

1. ***OSE reviews 2007-2024 dated June 12, 2008.***

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

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

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

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

exists which operates in a similar fashion. This is a database which was created for the Division of Medication Error Prevention and Analysis, FDA.

4. ***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.

5. ***AMF Decision Support System [DSS]***

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

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

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

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

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

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

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

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

Provides information regarding patent and trademarks.

10. ***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.

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

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

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

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

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

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.

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

List contains all the recognized USAN stems.

15. ***Red Book Pharmacy's Fundamental Reference***

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

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

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

17. ***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. [4]

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

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

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail. [5] 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.

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

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

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.[6] 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.

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

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

Type of similarity	**Considerations when searching the databases**		
	Potential causes of drug name similarity	*Attributes examined to identify similar drug names*	*Potential Effects*
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstrokes Down strokes Cross-stokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

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

1. Database and Information Sources

DMEPA staff conducts searches of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name using the criteria outlined in Section 2.1.

Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the DMEPA staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel.

2. CDER Expert Panel Discussion

DMEPA conducts an Expert Panel Discussion to gather CDER professional opinions on the safety of the proposed product and the proposed proprietary name. The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

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

3. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[7] 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:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Name	Similarity to Zipsor
Insulin Lispro	Look

Appendix C: Proprietary Names of Products Marketed in a Foreign Country

Product Name	Country
Zipos (cefuroxime)	Portugal
Zipra (ziprasidone	Mexico
Ziprol (pantoprazole)	Brazil
Zepan (diazepam)	Mexico
Ziproc (clozapine)	Philippines

Appendix D: Products with no overlap in strength or usual dosage and contain multiple differentiating product characteristics

Product name with potential for confusion	Strength	Usual Dose (if applicable)
Zipsor (diclofenac potassium)	25 mg	One tablet every 6 hours as needed for pain
Simcor (niacin/simvastatin)	500 mg/20 mg, 750 mg/20 mg and 1000 mg/20 mg	500mg/20 mg to 2000/40 mg once daily
Zemplar (paricalcitrol)	0.0002 mg/mL 0.0005 mg/mL 1 mcg, 2 mcg, and 4 mcg capsules	0.04 mcg/kg to 0.1 mcg/kg (2.8 – 7 mcg) administered as a bolus dose no more frequently than every other day at any time during dialysis 1 to 4 mcg given up to 3 times weekly
Zanosar (streptozocin)	1 gm/vial	500 mg/m^2 of body surface area for five consecutive days every six weeks or 1000 mg/m^2 of body surface area at weekly intervals for the first two courses (weeks)
Liposyn (safflower and soybean oil)	5 gm/mL, 10 gm/mL and 10 gm/mL	Should be administered intravenous as part of a total nutrition program via peripheral vein or central venous catheter
Lipram (amylase, protease, and lipase)	4500 units, CR5, PN10, PN16, PN20 and UL20	Dose individualized based on patient needs
Zofran (ondansetron)	4 mg and 8 mg tablets, 4 mg ODT and 4mg/5 mL oral solution 2 mg/mL Injection	4 mg to 8 mg given up to 3 times daily single 32-mg dose or three 0.15-mg/kg doses

Appendix E: Products with single strength availability but have differentiating product characteristics

Product name with potential for confusion	Strength	Usual Dose	Differentiating Product Characteristics
Zipsor (diclofenac potassium)	25 mg	One tablet every 6 hours as needed for pain	• Route of Administration: Oral • Dosage Form: Capsule • Dose: 1 tablet • Frequency: every 2 hours and four times a day
Zymar (gatifloxacin)	0.3 % Opthalmic Drops	One drop every 2 hrs for 1-2 days then one drop four times daily	• Route of Administration (oral vs. ophthalmic) • Dosage Form (capsule vs. ophthalmic solution)
Zanosar (streptozocin)	1 gm/vial	500 mg/m^2 of body surface area for five consecutive days every six weeks or 1000 mg/m^2 of body surface area at weekly intervals for the first two courses (weeks)	• Route of Administration (oral vs. intravenous) • Dosage Form (capsule vs. powder for injection) • Dose (1 drop vs. xx mg) • Frequency (every 2 hours and four times a day vs. daily for 5 days)

Appendix F: Blister Carton and Container Labels

(b) (4)

Appendix G: Retail Container Label

(b) (4)

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