

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
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PROPRIETARY NAME REVIEW(S)

**Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management**

Proprietary Name Review--Final

Date: October 28, 2011

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Drug Name(s): Intermezzo (Zolpidem Tartrate) Sublingual Tablets

Application Type/Number: NDA 022328

Applicant: Transcept Pharmaceuticals, Inc.

OSE RCM #: 2011-3888

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

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1 INTRODUCTION

This re-assessment of the proposed proprietary name, Intermezzo, is written in response to the request from Transcept Pharmaceuticals to evaluate the name Intermezzo from a promotional and safety perspective. Transcept Pharmaceuticals resubmitted a request for proprietary name evaluation because the proposed dose for women changed since our last review. DMEPA found the proposed name, Intermezzo, acceptable in OSE Review # 2011-560 dated May 25, 2011, OSE Review # 2009-222 dated June 17, 2009, OSE Review # 2008-1770 dated February 5, 2009, and OSE Review # 06-0129 dated November 2, 2006.

2 METHODS AND DISCUSSION

For re-assessments of proposed proprietary names, DMEPA searches a standard set of databases and information sources (see section 4) to identify names with orthographic and phonetic similarity to the proposed name that have been proposed or approved since the previous OSE proprietary name review. For this review we used the same search criteria described in OSE Review # 2011-560. The only change to the proposed product characteristics since the last proprietary name review was a change in the dosing for women. Previously all adults (men and women) were to receive 3.5 mg as needed for middle of the night awakenings. Now, the proposed dose is 1.75 mg as needed for women and the dose remains 3.5 mg as needed for men. Although this is a change in dosing regimen, the 1.75 mg dose, in addition to the 3.5 mg dose, was evaluated in our previous reviews because the dose for elderly, debilitated, or hepatically impaired patients is 1.75 mg. Thus, the change in dose for women would not change our evaluation of previously identified names. Therefore, we did not re-evaluate previous names of concern. The searches of the databases yielded one new name (b) (4) thought to look similar to Intermezzo and represent a potential source of drug name confusion.

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. Failure mode and effects analysis was applied to determine if the proposed proprietary name could potentially be confused with Intermezzo and lead to medication errors. This analysis determined that the name similarity between Intermezzo and the identified name was unlikely to result in medication error for the reasons presented in Appendix A.

Additionally, DMEPA searched the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. The Safety Evaluator did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of October 14, 2011.

OPDP re-reviewed the proposed name on October 20, 2011 and had no concerns regarding the proposed name from a promotional perspective.

3 CONCLUSIONS

The re-evaluation of the proposed proprietary name, Intermezzo, did not identify any vulnerabilities that would result in medication errors with the additional name noted in this review. Thus, DMEPA has no objection to the proprietary name, Intermezzo, 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 Neurology Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

If you have further questions or need clarifications, please contact Laurie Kelley, OSE project manager, at 301-796-5068.

4 REFERENCES

1. Duffy, F; OSE review 06-0129, Proprietary Name Review of Intermezzo; November 2, 2006.
2. Holmes, L; OSE review 2008-1770, Proprietary Name Review of Intermezzo; February 5, 2009.
3. Holmes, L; OSE review 2009-222, Proprietary Name Review of Intermezzo [pre-action]; June 17, 2009.
4. Holmes, L; OSE Review 2011-560, Proprietary Name Review of Intermezzo; May 25, 2011.
5. **Drugs@FDA** (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>)
Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved [brand name](#), [generic drugs](#), [therapeutic biological products](#), [prescription](#) and [over-the-counter](#) human drugs and [discontinued drugs](#) and “[Chemical Type 6](#)” approvals.
6. **USAN Stems** (<http://www.ama-assn.org/ama/pub/category/4782.html>)
USAN Stems List contains all the recognized USAN stems.
7. **Division of Medication Error Prevention and Analysis Proprietary Name Consultation Request**
Compiled list of proposed proprietary names submitted to the Division of Medication Error Prevention and Analysis for review. The list is generated on a weekly basis from the Access database/tracking system.

Appendix A: FMEA Table

Proposed name: Intermezzo (Zolpidem Tartrate) Sublingual Tablets	Strength(s): 1.75 mg and 3.5 mg	Usual dose: 1 tablet as needed when a middle-of-the-night awakening is followed by difficulty returning to sleep
Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Causes (could be multiple)	Prevention of Failure Mode
(b) (4)		

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/s/

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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: May 25, 2011

Application Type/Number: NDA 022328

Through: Irene Z. Chan, PharmD, BCPS, Team Leader
Carol A. Holquist, RPh, Director
Division of Medication Error Prevention and Analysis (DMEPA)

From: Loretta Holmes, BSN, PharmD, Safety Evaluator
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name and Strength: Intermezzo (Zolpidem Tartrate Sublingual Tablets)
1.75 mg and 3.5 mg

Applicant: Transcept Pharmaceuticals, Inc.

OSE RCM #: 2011-560

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EXECUTIVE SUMMARY

This review summarizes DMEPA's evaluation of the proposed proprietary name, Intermezzo, for Transcept Pharmaceuticals' Zolpidem Tartrate Sublingual Tablets.

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, Intermezzo, acceptable for this product. We consider this a final review, however, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change. DMEPA will notify the Applicant of this decision via letter.

1 BACKGROUND

1.1 INTRODUCTION

This review responds to a March 1, 2011 request from Transcept Pharmaceutical, Inc. for assessment of the proposed proprietary name, Intermezzo, regarding potential name confusion with other proprietary or established drug names in the usual practice settings and promotional concerns. Additionally, the container labels, carton labeling and insert labeling were evaluated for their potential contribution to medication errors under separate cover (OSE Review 2011-220/2011-221, dated April 15, 2011).

1.2 REGULATORY HISTORY

The proposed name, Intermezzo, was previously reviewed in [OSE Review 06-0129, dated January 11, 2007; OSE Review 2008-1770, dated February 5, 2009; and OSE Review 2009-222, dated June 25, 2009]. DMEPA found the proposed name, Intermezzo, acceptable in all of the aforementioned reviews.

This is a 505(b)(2) application and the Reference Listed Drug (RLD) is Ambien (Zolpidem Tartrate) tablets (NDA 019908).

1.3 PRODUCT INFORMATION

Intermezzo (Zolpidem Tartrate Sublingual Tablet) is a non-benzodiazepine hypnotic of the imidazopyridine class. It is indicated for use as needed for the treatment of insomnia when a middle-of-the-night awakening is followed by difficulty returning to sleep. Intermezzo should only be taken if the patient has four hours of bedtime remaining before being active again.

The recommended dosage in adults is 3.5 mg taken as needed when a middle-of-the-night awakening is followed by difficulty returning to sleep. For elderly or debilitated patients, the recommended dosage is 1.75 mg. Intermezzo is a Schedule IV controlled substance. Intermezzo will be available in 1.75 mg and 3.5 mg strength tablets and supplied in cartons containing 30 unit-dose pouches. The recommended storage temperature is between 20°C to 25°C (68°F to 77°F).

The product characteristics of Intermezzo have not changed since our previous review of the name.

2 METHODS AND MATERIALS

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

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter ‘I’ 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}

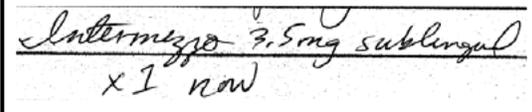
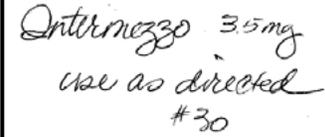
To identify drug names that may look similar to Intermezzo, the DMEPA Safety Evaluators also consider the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (ten letters), upstrokes (two, capital ‘I’ and lower case ‘t’), potential downstrokes (two, lower case ‘z’), cross strokes (three, actual and potential, lower case ‘t’, ‘z’ and ‘z’), and dotted letters (none). Additionally, several letters in Intermezzo may be vulnerable to ambiguity when scripted (see Appendix B). As a result, the DMEPA Safety Evaluators also consider these alternate appearances when identifying drug names that may look similar to Intermezzo.

When searching to identify potential names that may sound similar to Intermezzo, the DMEPA Safety Evaluators search for names with similar number of syllables (four), stresses (IN-ter-mez-zo, in-TER-mez-zo, in-ter-MEZ-zo, or in-ter-mez-ZO), and placement of vowel and consonant sounds. Additionally, the DMEPA Safety Evaluators consider that pronunciation of parts of the name can vary (see Appendix B). The Applicant’s intended pronunciation of the name is “in ter mét zoh”. However, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

2.2 FDA PRESCRIPTION ANALYSIS STUDIES

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

Figure 1. Intermezzo Prescription Studies (conducted on March 11, 2011)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
<p><u>Inpatient Medication Order:</u></p> 	“Intermezzo 3.5 mg times 1 stat”
<p><u>Outpatient Prescription:</u></p> 	

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 RESULTS

The following sections describe DMEPA's findings from the database searches, CDER Expert Panel Discussion, and FDA prescription analysis studies.

3.1 DATABASE AND INFORMATION SOURCES

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

Eleven of the 12 names were thought to look like Intermezzo. These include [REDACTED] ^{(b) (4)}, Isentress, Integrelin, Infergen, Inflamase, Influenza (Virus Vaccine), Infanrix, Terlipressin, Trinessa, Etravirine, and Intuniv. One name, Intrezor, was thought to sound like Intermezzo.

Additionally, DMEPA Safety Evaluators did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name as of May 17, 2011.

3.2 CDER EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMEPA Safety Evaluators (see Section 3.1 above) and noted no additional names thought to have orthographic or phonetic similarity to insert PROPRIETARY NAME.

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 37 practitioners responded. Twenty-four of the practitioners interpreted the name correctly as "Intermezzo". None of the responses overlapped with any existing or proposed drug names. In the verbal prescription study, four practitioners interpreted the beginning letter as "E". See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 COMMENTS FROM THE DIVISION OF NEUROLOGY PRODUCTS (DNP)

3.4.1 Initial Phase of Review

In response to the email sent to the Division of Neurology Products (DNP) on March 10, 2011, DNP stated "we have no issues with the trade name proposal and see no emerging issues with the name..."

3.4.2 Midpoint of Review

On May 6, 2011, DMEPA notified DNP via e-mail that we had no objections to the proposed proprietary name, Intermezzo. Per e-mail correspondence from DNP on May 6, 2011, the Division stated "It's acceptable".

3.5 SAFETY EVALUATOR SEARCHES

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

Thus, we evaluated a total of 12 names. All of these names were identified in Database and Information Sources (Section 3.1).

4 DISCUSSION

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.

4.1 PROMOTIONAL ASSESSMENT

DDMAC evaluated the name, Intermezzo, from a promotional perspective and determined the name was acceptable. The Division of Neurology Products and the Division of Medication Error Prevention and Analysis concurred with this assessment.

4.2 SAFETY ASSESSMENT

In total, 12 names were identified as potential sources of name confusion with the proposed proprietary name, Intermezzo. DMEPA did not identify other aspects of the name that could function as a source of error. Nine of the 12 names were eliminated for the following reasons: eight names lack orthographic and/or phonetic similarity to Intermezzo and one name was evaluated in one of our previous reviews of Intermezzo and the product characteristics have not changed (see Appendices B and C).

Failure mode and effects analysis (FMEA) was then applied to determine if the proposed name could potentially be confused with the remaining three names and lead to medication errors.

This analysis determined that the name similarity between Intermezzo and these three products is unlikely to result in medication errors for the reasons presented in Appendix D.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Intermezzo, 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, Intermezzo, for this product at this time.

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

If you have further questions or need clarifications, please contact Laurie Kelley, OSE Project Manager, at 301-796-5068.

5.1 COMMENTS FOR THE PROPRIETARY NAME LETTER

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

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

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.

6 REFERENCES

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Provides information regarding patent and trademarks.

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

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

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

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

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

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

13. **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.

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.³

For the proposed proprietary name, DMEPA Safety Evaluators 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 Safety Evaluators also conduct internal CDER prescription analysis studies. When provided, DMEPA considers external prescription analysis study results and incorporate into the overall risk assessment.

³ 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.⁴ DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its Safety Evaluators 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 Safety Evaluators consider 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 Safety Evaluators consider the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.⁵ DMEPA provides the product characteristics considered for this review in section one.

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA Safety Evaluators also examine the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly and 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 Safety Evaluators apply 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 Safety Evaluators compare 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.

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

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

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 Safety Evaluators also consider 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 Safety Evaluators conduct 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 Safety Evaluators 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 Safety Evaluators 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) Safety Evaluators and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

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

3. FDA Prescription Analysis Studies

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

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

4. Comments from the OND review Division or Generic drugs

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

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

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

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

identifying where and how it might fail.⁶ When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

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

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

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

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

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)].

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

- 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 proposed name "Intermezzo"	When scripted may appear as:	When spoken may be interpreted as:
Capital 'I'	E, F, J	Any vowel
lower case 'n'	m, u, x, r, h, s	dn, gn, kn, mn, pn
lower case 't'	r, f, x, A	d
lower case 'e'	a, i, l, p	Any vowel
lower case 'r'	s, n, e, v	
lower case 'm'	m, nn, n, v, w, wi, vi, onc, z	
lower case 'e'	a, i, l, p	Any vowel
lower case 'z'	c, e, g, n, m, q, r, s, v	c, s, x
lower case 'z'	c, e, g, n, m, q, r, s, v	c, s, x
lower case 'o'	a, c, e, u	Any vowel, oh
'Inter'		'Enter'

Appendix C: FDA Prescription Study Responses

Inpatient Medication Order	Outpatient Medication Order	Voice Prescription
Intermezzo	Intermexxo	Entermezol
Inermezzo	Intermezzo	Entermezzal
Intermezzo	Intermezzo	entermizol
Intermezzo	Intermezzo	Enternizol
Intermezzo	Intermezzo	Intermezal
Intermezzo	Intermezzo	Intermezol
Intermezzo	Intermezzo	Intermezzo
Intermezzo	Intermezzo	Intermezzo
Intermezzo	Intermezzo	Intermezzo
Intermezzo	Intermezzo	Intermisal
intermezzo	Intermezzo	Intermisal
Intermizzo		Intermizal
intermizzo		intermizol

Appendix C: Name Evaluated in a Previous Review of Intermezzo

Name
Infergen

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

Name	Similarity to Intermezzo
Integrelin	Look
Infanrix	Look
Terlipressin	Look
Etravirine	Look
Intuniv	Look
Isentress	Look
Trinessa	Look
Intezor	Sound

Appendix I: Products with multiple differentiating product characteristics and/or orthographic/phonetic differences

Product name with potential for confusion	Similarity to Intermezzo	Strength	Signa	Differentiating Product Characteristics (Intermezzo vs. Product)
Intermezzo	N/A	1.75 mg and 3.5 mg	1.75 mg or 3.5 mg as needed when a middle-of-the-night awakening is followed by difficulty returning to sleep	N/A
(b) (4)				
Inflamase Forte Inflamase Mild (Prednisolone Sodium Phosphate) Ophthalmic Solution	Look	Forte: 0.9% Mild: 0.11%	One drop or two drops into the affected eye(s) every hour; every 2 hours; every 4 hours, three times per day; or four times per day	<p>The letter “r” precedes the letter “m” in Intermezzo whereas the letter “a” precedes the letter “m” in Inflamase. The double letters “zz” in Intermezzo help to differentiate the names.</p> <p><u>Route of administration:</u> Oral vs. ocular</p> <p><u>Frequency of administration:</u> Once daily as needed vs. three or more times per day</p> <p><u>Strength:</u> 1.75 mg or 3.5 mg vs. 0.9% or 0.11%</p> <p><u>Dosage form:</u> Tablets vs. ophthalmic solution</p> <p><u>Status:</u> Inflamase Forte and Inflamase Mild have been discontinued; the year of last recorded sales was (b) (4) respectively.</p>

Product name with potential for confusion	Similarity to Intermezzo	Strength	Signa	Differentiating Product Characteristics (Intermezzo vs. Product)
Intermezzo	N/A	1.75 mg and 3.5 mg	1.75 mg or 3.5 mg as needed when a middle-of-the-night awakening is followed by difficulty returning to sleep	N/A
Influenza (Virus Vaccine) Multiple Brands: Afluria, Agriflu, Fluarix, Fluvirin, Fluzone and others	Look	Not applicable	0.25 mL (Afluria and Fluzone, pediatric dose) or 0.5 mL intramuscularly once yearly	The infix letters “rme” vs. “uen” do not look similar. The double letters “zz” in Intermezzo help to differentiate the names. <u>Dose:</u> 1.75 mg or 3.5 mg vs. 0.25 mL or 0.5 mL <u>Route of administration:</u> Oral vs. Intramuscular <u>Frequency of administration:</u> Once daily vs. once yearly

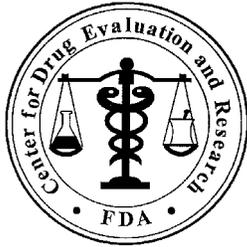
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/s/

LORETTA HOLMES
05/25/2011

IRENE Z CHAN
05/25/2011

CAROL A HOLQUIST
05/25/2011



**Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology**

Date: June 17, 2009

To: Russell Katz, MD, Director
Division of Neurology Products

Through: Kristina C. Arnwine, PharmD, Team Leader
Denise P. Toyer, PharmD, Deputy Director
Division of Medication Error Prevention and Analysis (DMEPA)

From: Loretta Holmes, BSN, PharmD, Safety Evaluator
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name(s): Intermezzo (Zolpidem Tartrate) Sublingual Tablet
1.75 mg and 3.5 mg

Application Type/Number: NDA 22-328

Applicant/Applicant: Transcept Pharmaceuticals, Inc.

OSE RCM #: 2009-222

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EXECUTIVE SUMMARY

This re-assessment of the proprietary name is written in response to a notification that NDA 22-328 may be approved within 90 days. DMEPA found the proposed proprietary name, Intermezzo, acceptable in OSE Review #2008-1770, dated February 5, 2009. Since that review, none of Intermezzo's product characteristics have changed.

During this re-review we did not identify any new names. 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 Neurology products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

1 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a re-assessment of a proprietary name 90 days prior to approval of an application. We used the same search criteria used in OSE Review #2008-1770 for the proposed proprietary name, Intermezzo. Please refer to Section 2.1.1 of that review for the search criteria.

2 RESULTS

2.1 DATABASE AND INFORMATION SOURCES

The searches of the databases listed in Section 4 did not yield any new names as having some similarity to the name Intermezzo.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of June 4, 2009.

2.2 EXPERT PANEL DISCUSSION

The Expert Panel, as described in Appendix A, Section 2, noted there were no additional names thought to have orthographic or phonetic similarity to Intermezzo. However, the Expert Panel had the following comments concerning the proposed proprietary name Intermezzo:

- Intermezzo is also trademarked as a hair preparation.
- Intermezzo has an active patent for perfumes and cosmetics and dental implants.
- Check for look-alike names beginning with the letter "O".

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

2.3 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator (which included searching for look-alike names beginning with the letter "O") did not identify any additional names which were thought to look or sound similar to Intermezzo and represent a potential source of drug name confusion.

In our previous review of this name, the primary Safety Evaluator identified multiple non-pharmaceutical trademarks for the name "Intermezzo". Those trademarks were re-evaluated and they are still not thought to represent a potential source of drug name confusion.

3 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Intermezzo, 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, Intermezzo, for this product at this time. Additionally, DDMAC does not object to the proposed name, Intermezzo, 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 Neurology Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

4 REFERENCES

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

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

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

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

3. *AMF Decision Support System [DSS]*

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

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

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

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

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

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

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

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

USPTO provides information regarding patent and trademarks.

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

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

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

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

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

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

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

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

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

USAN Stems List contains all the recognized USAN stems.

13. *Red Book Pharmacy's Fundamental Reference*

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

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

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

15. *Medical Abbreviations Book*

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

APPENDICES

Appendix A:

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

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

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

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

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

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

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.

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	<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. 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.

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

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

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

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

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).

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/s/

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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: February 5, 2009

To: Russell Katz, MD, Director
Division of Neurology Products

Thru: Kristina C. Arnwine, PharmD, Team Leader
Denise P. Toyer, PharmD, Deputy Director
Carol A. Holquist, RPh, Director
Division of Medication Error Prevention and Analysis

From: Loretta Holmes, BSN, PharmD, Safety Evaluator
Division of Medication Error Prevention and Analysis

Subject: Proprietary Name Review

Drug Name: Intermezzo (Zolpidem Tartrate) Sublingual Tablet
1.75 mg and 3.5 mg

Application Type/Number: NDA 22-328

Applicant: Transcept Pharmaceuticals, Inc.

OSE RCM #: 2008-1770

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

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EXECUTIVE SUMMARY

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

If any of the proposed product characteristics as stated in this review are altered prior to approval of the product; the Division of Medication Error Prevention and Analysis rescinds this Risk Assessment finding, and recommends that the name, labels, and labeling be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. Additionally, if the product approval is delayed beyond 90 day from the date of this review, the proposed name must be resubmitted for evaluation.

1 BACKGROUND

1.1 INTRODUCTION

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

Additionally, the container labels, carton and insert labeling are being evaluated for their potential contribution to medication errors under separate cover in OSE Review 2008-1770 (Label and Labeling Review).

1.2 REGULATORY HISTORY

The Division of Medication Error Prevention and Analysis previously reviewed the proposed proprietary name, Intermezzo, in OSE Review 06-0129, dated January 11, 2007 and had no objections to the use of the name at that time.

This is a 505(b)(2) application and the Reference Listed Drug (RLD) is Ambien (Zolpidem Tartrate) Tablets (NDA 19-908).

DMEPA notes that in a letter from the Division to the Applicant, dated December 11, 2008, CMC had the following comments concerning the established name (b) (4)

1.3 PRODUCT INFORMATION

Intermezzo (Zolpidem Tartrate) Sublingual Tablet is a non-benzodiazepine hypnotic of the imidazopyridine class. It is indicated for use as needed for the treatment of insomnia when a middle-of-the-night awakening is followed by difficulty returning to sleep. Patients should take it right before they are ready to return to sleep and are able to stay in bed 4 hours before being active again. The recommended dose for adults is 3.5 mg sublingually once daily as needed; for elderly or debilitated patients, 1.75 mg once daily as needed; and for patients with hepatic insufficiency, an initial dose of 1.75 mg once daily as needed. The total daily dose of Intermezzo should not exceed 3.5 mg. It should not be administered with or immediately after a meal. Intermezzo is a Schedule Four controlled substance. It will be available in 1.75 mg and 3.5 mg strengths (b) (4)

2 METHODS AND MATERIALS

This section describes the methods and materials used by the Division of Medication Error Prevention and Analysis staff conducting a proprietary name risk assessment (see 2.1 Proprietary Name Risk Assessment). The primary focus of the assessment is to identify and remedy potential sources of medication error prior to drug approval. The Division of Medication Error Prevention and Analysis defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.¹

2.1 PROPRIETARY NAME RISK ASSESSMENT

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, *Intermezzo*, and the proprietary and established names of drug products existing in the marketplace and those pending IND, BLA, NDA, and ANDA products currently under review by CDER.

For the proprietary name, *Intermezzo*, the Division of Medication Error Prevention and Analysis staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Sections 2.1.1 for detail) and held a CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.1.2).

The Division of Medication Error Prevention and Analysis normally conducts internal CDER prescription analysis studies and, when provided, external prescription analysis studies results are considered and incorporated into the overall risk assessment. However, because this name was previously evaluated, CDER prescription analysis studies were not repeated and a re-analysis of the external prescription analysis was not conducted upon this re-review of *Intermezzo*.

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name (see detail 2.1.2). The overall risk assessment is based on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and is focused on the avoidance of medication errors. FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.² FMEA is used to analyze whether the drug names identified with look- or sound-alike similarity to the proposed name could cause confusion that subsequently leads to medication errors in the clinical setting. The Division of Medication Error Prevention and Analysis uses the clinical expertise of the DMEPA staff to anticipate the conditions of the clinical setting that the product is likely to be used in based on the characteristics of the proposed product.

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

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

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

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

2.1.1 Search Criteria

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

For this review, particular consideration was given to drug names beginning with the letter ‘I’ when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.^{4,5}

To identify drug names that may look similar to Intermezzo, the staff also consider the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (10 letters), upstrokes (2, capital letter ‘I’ and lowercase ‘t’), downstrokes (2, lowercase ‘z’ and ‘z’), cross-strokes (one, lowercase ‘t’), and dotted letters (none). Additionally, several letters in Intermezzo may be vulnerable to ambiguity when scripted, including the letter ‘I’ which may appear as ‘F’, ‘J’ or ‘T’; lowercase ‘n’ appear as a lowercase ‘r’, ‘s’ or ‘v’; lowercase ‘t’ appear as lowercase ‘f’, ‘l’ (if the letter ‘t’ is uncrossed), ‘r’, or ‘x’; lowercase ‘e’ appear as lowercase ‘l’ or undotted ‘i’; lowercase ‘r’ appear as lowercase ‘n’, ‘s’, or ‘v’; lowercase ‘m’ appear as lowercase ‘n’; lowercase ‘z’ appear as lowercase undotted ‘j’, ‘x’, or ‘y’; and lowercase ‘o’ appear as lowercase ‘a’, ‘e’, or ‘u’. As such, the staff also consider these alternate appearances when identifying drug names that may look similar to Intermezzo.

When searching to identify potential names that may sound similar to Intermezzo, the DMEPA staff search for names with similar number of syllables (four), stresses (IN-ter-mez-zo, in-TER-mez-zo, in-ter-MEZ-zo, or in-ter-mez-ZO), and placement of vowel and consonant sounds. In addition, several letters in Intermezzo may be subject to interpretation when spoken, including the letters “Inter” which may be interpreted as “Enter” or “Inder”. The Applicant’s intended pronunciation of the proprietary name could not be expressly taken into consideration, as this was not provided with the proposed name submission.

The staff also considers the product characteristics associated with the proposed drug throughout the identification of similar drug names, since the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting. For this review, the DMEPA staff were provided with the following information about the proposed product: the proposed proprietary name (Intermezzo), the established name (Zolpidem Tartrate Sublingual Lozenge), proposed indication of use (insomnia), strength (1.75 mg and 3.5 mg), dose (1.75 mg or 3.5 mg), frequency of administration (once daily, as needed), route of administration (sublingual), and dosage form of the product (lozenge).

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

⁴ Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at <http://www.ismp.org/Tools/confuseddrugnames.pdf>

⁵ Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

Appendix A provides a more detailed listing of the product characteristics the DMEPA staff generally take into consideration.

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

2.1.1.1 Databases and Information Sources

The proposed proprietary name, Intermezzo, was provided to the DMEPA staff to conduct a search of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to Intermezzo using the criteria outlined in 2.1.1. A standard description of the databases used in the searches is provided in Section 7. To complement the process, the 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 findings of the individual Safety Evaluators were then pooled and presented to the Expert Panel.

2.1.1.2 CDER Expert Panel Discussion

An Expert Panel Discussion is held by the Division of Medication Error Prevention and Analysis to gather CDER professional opinions on the safety of the product and the proprietary name, Intermezzo. Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed. This group is composed of the Division of Medication Error Prevention and Analysis staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC).

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

2.1.2 Safety Evaluator Risk Assessment of the Proposed Proprietary Name

Based on the criteria set forth in Section 2.1.1, the Safety Evaluator applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Modes and Effects Analysis and provide an overall risk of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.⁶ When applying FMEA to assess the risk of a proposed proprietary name, we seek to evaluate the potential for a proposed name to be confused with another drug name as a result of the name confusion and cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to look- or sound-alike drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

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

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

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, expert panel evaluation, and studies, and identifies potential failure modes by asking: “Is the name Intermezzo 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 Intermezzo to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names possess similarity that would cause confusion at any point in the medication use system and the name is eliminated from further review.

In the second stage of the Risk Assessment, all potential failure modes are evaluated to determine the likely effect of the drug name confusion, by asking “Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?” The answer to this question is a central component of the Safety Evaluator’s overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would ultimately not be a source of medication errors in the usual practice setting, the name is eliminated from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend that an alternate proprietary name be used. In rare instances, the FMEA findings may provide other risk-reduction strategies, such as product reformulation to avoid an overlap in strength or an alternate modifier designation may be recommended as a means of reducing the risk of medication errors resulting from drug name confusion.

The Division of Medication Error Prevention and Analysis will object to the use of proposed proprietary name when one or more of the following conditions are identified in the Safety Evaluator’s Risk Assessment:

1. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the review Division concurs with DDMAC’s findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a trade name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. The Division of Medication Error Prevention and Analysis identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(c)(5)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains an USAN stem, particularly in a manner that is contradictory to the USAN Council’s definition.
5. DMEPA staff identify a potential source of medication error within the proposed proprietary name. The proprietary name may be misleading, or inadvertently introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

In the event that the Division of Medication Error Prevention and Analysis objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, we will provide a contingency objection based on the date of approval: whichever product is awarded approval first has the right to use the name, while we will recommend that the second product to reach approval seek an alternative name.

If none of these conditions are met, then we will not object to the use of the proprietary name. If any of these conditions are met, then we will object to the use of the proprietary name. The threshold set for objection to the proposed proprietary name may seem low to the Sponsor/Applicant; however, the safety concerns set forth in criteria 1 through 5 are supported either by FDA Regulation or by external healthcare authorities, including the Institute of Medicine, World Health Organization, Joint Commission, and Institute for Safe Medication Practices, have examined medication errors resulting from look- or sound-alike drug names and called for Regulatory Authorities to address the issue prior to approval.

Furthermore, the Division of Medication Error Prevention and Analysis contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, can be identified and remedied prior to approval to avoid patient harm.

Additionally, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to remedy post-approval. Educational efforts and so on are low-leverage strategies that have proven to have limited effectiveness at alleviating the medication errors involving drug name confusion. Higher-leverage strategies, such as drug name changes, have been undertaken in the past; but at great financial cost to the Sponsor, and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Sponsor's have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioner's vocabulary, and as such, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, we believe that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval (e.g. new form introduced like Lamisil) (see limitations of the process in Section 4).

If the Division of Medication Error Prevention and Analysis objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the FMEA process is used to identify strategies to reduce the risk of medication errors. The Division of Medication Error Prevention and Analysis is likely to recommend that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for the Division of Medication Error Prevention and Analysis to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name, and so we may be able to provide the Sponsor with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

3 RESULTS

3.1 PROPRIETARY NAME RISK ASSESSMENT

3.1.1 Database and Information Sources

The search identified 6 names as having some similarity to the name Intermezzo. Four names were thought to look like Intermezzo, which include: Intermigran, Intrinsa^{***}, Interferon, and Infergen. One name, Indomethacin, was thought to sound like Intermezzo. One name, Intermezzo, was thought to look and sound similar to Intermezzo.

Additionally, the Division of Medication Error Prevention and Analysis did not identify any USAN stems in the name Intermezzo as of November 28, 2008.

3.1.2 Expert Panel Discussion

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

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 of Proposed Proprietary Name

Independent searches by the primary Safety Evaluator did not identify any additional names thought to look similar to Intermezzo and represent a potential source of drug name confusion. As such, a total of 6 names were analyzed to determine if the drug names could be confused with Intermezzo and if the drug name confusion would likely result in a medication error.

Failure Mode and Effects Analysis was then applied to determine if the proposed name, Intermezzo, could potentially be confused with any of the 6 names and lead to medication errors. This analysis determined that the name similarity between Intermezzo and the identified names was unlikely to result in medication errors for all 6 products for reasons described/outlined in Appendices B through E.

4 DISCUSSION

4.1 PROPRIETARY NAME RISK ASSESSMENT

We evaluated 6 names for their potential similarity to Intermezzo. The results of the FMEA for the name Intermezzo found the proposed name, Intermezzo, is not vulnerable to name confusion that could lead to medication errors with any of these six names.

5 CONCLUSIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Intermezzo, is not vulnerable to name confusion that could lead to medication errors. As such, the Division of Medication Error Prevention and Analysis does not object to the use of the proprietary name, Intermezzo, for this product at this time.

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

If any of the proposed product characteristics as stated in this review are altered prior to approval of the product; the Division of Medication Error Prevention and Analysis rescinds this Risk Assessment finding, and recommends that the name, labels, and labeling be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. Additionally, if the product approval is delayed beyond 90 day from the date of this review, the proposed name must be resubmitted for evaluation.

6 RECOMMENDATIONS

6.1 COMMENTS TO THE DIVISION

We would appreciate feedback on the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. Please copy the Division of Medication Error Prevention and Analysis on any correspondence to the Applicant pertaining to this issue. If you have further questions or need clarifications, please contact Daniel Brounstein, OSE Project Manager, at 301-796-0674.

6.2 COMMENTS TO THE APPLICANT

6.2.1 Proprietary Name

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

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

7 REFERENCES

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Provides information regarding patent and trademarks.

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

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

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

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

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

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

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

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

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

List contains all the recognized USAN stems.

14. *Red Book Pharmacy's Fundamental Reference*

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

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

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

16. *Medical Abbreviations Book*

Contains commonly used medical abbreviations and their definitions.

APPENDICES

Appendix A:

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

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

Type of similarity	Considerations when searching the databases		
	Potential causes of drug name similarity	Attributes examined to identify similar drug names	Potential Effects
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<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 Downstrokes 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

Appendix B: Name evaluated in our previous review (OSE Review 06-0129)

Name	Similarity to Intermezzo	Comments
Interferon	Look	Multiple brand name products (e.g., Actimmune, Avonex, PegIntron, Intron A, and others) and varieties (e.g., Interferon Alfa-2A, Alfa-2B, Alfacon-1, Beta-1A, Gamma-1B, and others) are available. The dosing, route of administration, and dosage forms for these products differ from Intermezzo.

Appendix C: Name without convincing look-alike and/or sound-alike similarities to Intermezzo

Name	Similarity to Intermezzo
Infergen	Look
Intrinsa ^{***}	Look
Indomethacin	Sound

Appendix D: Name with multiple trademarks

Name	Similarity to Intermezzo	Comments
Intermezzo	Look and Sound	This name has multiple trademarks (U.S. and foreign), however, as best as we can determine, the Applicant is the only one to have this name trademarked for use as a drug name.

Appendix E: Foreign Name

Name	Similarity to Intermezzo	Country
Intermigran	Look	Germany. Product is no longer marketed.

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

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/s/

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