CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

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PROPRIETARY NAME REVIEW(S)

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

Date:	May 24, 2010
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Through:	Zachary Oleszczuk, Pharm.D., Acting Team Leader Kellie Taylor, Pharm.D., MPH, Associate Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis
From:	Tara Turner, Pharm.D., Safety Evaluator Division of Medication Error Prevention and Analysis
Subject:	Proprietary Name Review
Drug Name(s):	Advil Congestion Relief (Ibuprofen and Phenylephrine Hydrochloride) Caplets 200 mg/10 mg
Application Type/Number:	NDA 022565
Applicant:	Wyeth Consumer Healthcare
OSE RCM #:	2010-1037

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EXECUTIVE SUMMARY

This review summarizes DMEPA's proprietary Name Risk Assessment for Advil Congestion Relief (Ibuprofen and Phenylephrine Hydrochloride) Caplets. 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, Advil Congestion Relief, acceptable for this product.

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

1 BACKGROUND

1.1 INTRODUCTION

This review responds to a request from Wyeth Consumer Healthcare dated May 11, 2010 for an assessment of the proposed proprietary name, Advil Congestion Relief.

The Applicant also submitted draft container labels and carton labeling which will be evaluated in a separate forthcoming DMEPA review (OSE RCM# 2010-1079).

1.2 REGULATORY HISTORY

On August 27, 2009, the Applicant submitted "Advil Cold & Sinus PE" as the proposed proprietary name for this product. The Division of Medication Error Prevention and Analysis (DMEPA) found the proposed name unacceptable because of concerns that the "PE" modifier does not have a consistent meaning among healthcare practitioners and consumers and that the modifier is a documented source of confusion in the marketplace (see OSE RCM# 2009-1586, dated November 5, 2009). Subsequently, the Applicant conducted a study of the meaning of the "PE" modifier among healthcare practitioners and consumers. This study was submitted in support of a reconsideration request dated February 17, 2010. DMEPA's analysis of the study results concludes that the "PE" modifier does not have a consistent meaning among healthcare practitioners and consumers and that the "PE" modifier does not differentiate the proposed product from the currently marketed Advil Cold & Sinus product, which contains pseudoephedrine (see OSE RCM# 2009-1586, dated May 13, 2010). Given this data, DMEPA maintained its original objection to the proposed name, Advil Cold & Sinus PE. These findings were communicated to the Applicant via teleconference on April 2, 2010. The Applicant withdrew the proposed name, Advil Cold & Sinus PE, on April 22, 2010. On May 11, 2010, the proposed proprietary name "Advil Congestion Relief" was submitted and is the subject of the current review.

1.3 PRODUCT INFORMATION

Advil Congestion Relief is an over-the-counter combination product containing Ibuprofen 200 mg and Phenylephrine Hydrochloride 10 mg per caplet. The proposed indication is to provide temporary relief of the following symptoms associated with the common cold or flu: headache, fever, sinus pressure, nasal congestion, and minor body aches/pains. The recommended dose for adults and children 12 years of age and over is one caplet orally every 4 hours while symptoms persist. Advil Congestion Relief will be supplied in cartons of 20 count and shelf cartons of 50 packets, each containing one caplet.

1.4 APPLICANT'S DERIVATION OF PROPOSED NAME

In their proprietary name submission, the Applicant cites the following derivation of the proposed name:

> *The proprietary name Advil Congestion Relief is derived from the pain relieving properties of ibuprofen to treat headache and aches and pains associated with cold and flu. Congestion Relief is derived from the decongestant, phenylephrine HCl that is in the combination to treat another major symptom, congestion that is associated with cold and flu. Additionally this combination is labeled per the monograph ingredients headache, fever, sinus pressure, nasal congestion, and minor body aches/pains.*

The Applicant provided no assessments of the name, packaging, or labeling of Advil Congestion Relief.

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, Advil Congestion Relief.

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter 'A' 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 Advil Congestion Relief, the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. In this case, we evaluated the root name 'Advil' separately and in conjunction with the additional descriptor segments of the name ('Congestion Relief') "which are derived from the decongestant, phenylephrine HCL that is in the combination to treat a major symptom, congestion that is associated with cold and flu", according to the Applicant's submission. The modifiers 'Congestion' and 'Relief' are used for other marketed products that are used to treat chest congestion or nasal congestion or both (see Appendices B through E).

Specific attributes taken into consideration include the length of the name (21 letters; three words), upstrokes (eight: capital letters 'A', 'C', and 'R; two lower case letters 'l', lower case letters 'd', 't', and 'f'), downstrokes (two: lower case letters 'g' and 'f'), cross-strokes (two: capital letter 'A' and lower case letter 't') and dotted letters (three lower case letters 'i'). Additionally, several letters in Advil Congestion Relief may be vulnerable to ambiguity when scripted (see Appendix F). As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Advil Congestion Relief.

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

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

When searching to identify potential names that may sound similar to Advil Congestion Relief, the DMEPA staff searches for names with similar number of syllables (7), stresses (AD-vil con-GEST-ion re-LIEF or ad-VIL con-GEST-ion re-LIEF), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary (see Appendix F). The Applicant's intended pronunciation ('ad-(,)vil\ kən-'jes-chən\ ri-'lēf) was also taken into consideration, as it was included in the Proprietary Name Review Request. However, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

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. Advil Congestion Relief Study (conducted on May 13, 2010)

HANDWRITTEN PRESCRIPITON AND MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order: 	"Advil Congestion Relief 1 PO every 4 hours prn"
Outpatient Prescription: 	

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The DMEPA searches yielded a total of 30 names as having some similarity to the proposed proprietary name, Advil Congestion Relief.

Four of the names were thought to look like Advil Congestion Relief (Cognex, Loestrin, Elavil, and Zicam Extreme Congestion Relief). The remaining 26 names (Advil Cold & Sinus Relief, Advil Cold & Sinus, Advil Allergy Sinus, Advil Cold and Sinus, Advil, Advil Allergy and Sinus, Advil Multi-Symptom Cold, [redacted] (b) (4) Zyrtec-D Allergy and Congestion, Tavist Allergy/Sinus/Headache, [redacted] (b) (4) Advil Liqui-Gels, Advil Migraine Liqui-Gels, Advil PM, Children's Advil, Children's Advil Allergy Sinus, Children's Advil-Flavored, Junior Strength Advil, Pediatric Advil, Cetirizine Hydrochloride Hives Relief, Children's Cetirizine Hydrochloride Hives

Relief, Children's Zyrtec Hives Relief, Claritin Hives Relief, Claritin Hives Relief Reditab, Imodium Multi-Symptom Relief, and Zyrtec Hives Relief) were thought to look and sound similar to Advil Congestion Relief.

Additionally, DMEPA staff identified a United States Adopted Names (USAN) stem in the proposed proprietary name, as of May 13, 2010. The stem is –gest-, which represents progestins.

3.2 CDER EXPERT PANEL DISCUSSION

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

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 42 practitioners responded to the studies and all practitioners correctly identified the name as Advil Congestion Relief. Additionally, one participant stated "This must be an OTC product. Congestion Relief is certainly promotional". See Appendix G for the complete listing of interpretations from the verbal and written prescription studies.

Although one participant stated that the name appears promotional, DMEPA notes that the modifier "Congestion Relief" is already currently marketed in several OTC product lines. Additionally, DDMAC, the Division of Nonprescription Clinical Evaluation, and DMEPA did not find the name to be promotional.

3.4 COMMENTS FROM THE DIVISION OF NONPRESCRIPTION CLINICAL EVALUATION (DNCE)

Due to time constraints, a teleconference was held between DNCE and DMEPA on May 14, 2010, during which DNCE representatives indicated they have no issues with the proposed name, Advil Congestion Relief.

3.5 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator identified 17 additional names which were thought to look or sound similar to Advil Congestion Relief and represent a potential source of drug name confusion. Four names (Acuvail, Advacal, Advicor, and Advair) were thought to look similar to Advil Congestion Relief. The remaining 13 names (Cogentin, Relafen, Advil Cold & Sinus Liqui-Gels, Advil PM Liqui-Gels, Advil Migraine, Advil Flu and Body Ache, Advil Junior Strength, Children's Advil Cold, Infants' (b) (4)) were thought to look and sound similar to Advil Congestion Relief.

Additionally, we note that seven of the names identified by DMEPA searches are variations of the approved Advil product line (Advil Cold & Sinus Relief, Advil Cold and Sinus, Advil Allergy and Sinus, Children's Advil-Flavored, Advil Migraine Liqui-Gels, Junior Strength Advil, and Pediatric Advil). We assume that these names were reported incorrectly during the search process. The correct versions of these names are already accounted for in the evaluation of the Advil product line.

As such, a total of 40 names were analyzed to determine if the drug names could be confused with Advil Congestion Relief and if the drug name confusion would likely result in a medication error.

Twelve of the 40 names were evaluated and found to lack convincing orthographic and/or phonetic similarity and were eliminated from further analysis (see Appendix H).

Failure mode and effects analysis (FMEA) was then applied to determine if the proposed name, Advil Congestion Relief, could potentially be confused with any of the 28 remaining names and lead to medication errors. This analysis determined that the name similarity between Advil Congestion Relief and the identified names was unlikely to result in medication errors with nine of the products identified for the reasons presented in Appendices K through N.

The remaining 19 names are marketed or proposed names for the Advil product line and could be confused with Advil Congestion Relief. Fifteen names represent Advil products that are currently marketed (see Appendix I). Four names represent Advil products that have never been marketed (see Appendix J). The Advil product line is discussed in detail in Section 4.

4 DISCUSSION

Advil Congestion Relief is the proposed proprietary name for Ibuprofen and Phenylephrine caplets. This product represents an extension of the current Advil product line. 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 had no concerns regarding the proposed name from a promotional perspective and did not offer and additional comments relating to the proposed name. The Division of Nonprescription Clinical Evaluation and DMEPA concurred with the promotional assessment.

4.2 SAFETY ASSESSMENT

Forty names were evaluated for their similar appearance and/or sound to the proposed name. Our analysis indicates that the proposed name is not likely to result in name confusion that could lead to medication errors with 21 of the names identified. The remaining 19 names are marketed or proposed names for the Advil product line and are discussed below.

When evaluating the proposed name, DMEPA also identified the factors outlined below that could lead to confusion. However, these factors did not render the name unacceptable for the reasons discussed below.

4.2.1 Use of "Congestion Relief" Modifiers

As part of our FMEA we evaluated the potential for medication errors to occur due to misinterpretation of the modifiers "Congestion Relief".

4.2.1.1 USAN Stem

We note that the modifier "Congestion" contains the USAN stem –gest-, which represents progestins. Inclusion of a USAN stem in a proprietary name typically renders a name unacceptable. However, in this case the modifier "Congestion" is an English word used to describe a pharmacological class of nonprescription products. We have no expectation that the word "Congestion" should be spelled differently to avoid containing a USAN stem. Additionally, the word congestion is used in several over-the-counter proprietary names. Therefore, although the proposed name contains the USAN stem -gest-, we accept the use of the USAN stem within the proprietary name in this particular circumstance.

4.2.1.2 Precedence

We note that the proposed name includes the modifiers "Congestion Relief" and that no data was provided to support that the modifiers would not inadvertently introduce a source of error. However, we also note that these modifiers as a whole or separately are used for other marketed nonprescription products to represent an intended use (e.g. treatment of nasal congestion, chest congestion, or both). From our searches we found that oral products intended to treat chest congestion typically contain guaifenesin or dextromethorphan or both. Oral products that are intended to treat nasal congestion typically contain phenylephrine or pseudoephedrine. There appears to be no established association with the modifier "congestion" or "relief" and a particular active ingredient. However, there does appear to be consistency for use of these modifiers to describe an ailment or indication the product is intended to treat. The Applicant's intended meaning of the modifier follows this trend because the proposed product contains phenylephrine, which is classified as a nasal decongestant.

Therefore, although this Applicant has not provided data to support the use of the proposed modifiers, DMEPA believes that the use of these modifiers in the nomenclature of similar marketed products adequately supports their use for the proposed product. Thus, in consideration of the total data available, DMEPA does not believe the modifier "Congestion Relief" represent a safety concern.

4.2.2 Differentiation within the Advil product line

When evaluating the proposed name, DMEPA identified 19 names that were currently marketed or proposed names for the Advil product line. In our previous reviews of the proposed name, Advil Cold & Sinus PE, one of our concerns was that the "PE" modifier would not provide adequate differentiation from the currently marketed Advil Cold & Sinus product, which contains pseudoephedrine. However, we note that within the currently marketed Advil product line there are no products that contain the modifiers "Congestion" or "Relief" in their names. Therefore, we do not have the same concern with the proposed name, Advil Congestion Relief. We believe that the modifier "Congestion Relief" provides adequate differentiation for the proposed product within the context of the currently marketed Advil product line.

5 CONCLUSIONS AND RECOMMENDATIONS

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

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

If you have further questions or need clarifications, please contact Catherine Carr, Regulatory Project Manager, at 301-796-2311.

5.1 COMMENTS TO THE APPLICANT

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

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

6 REFERENCES

6.1 OSE REVIEWS

Turner, T. Proprietary Name Review of Advil Cold & Sinus PE. OSE Review # 2009-1586, November 5, 2009.

Turner, T. Proprietary Name Review of Advil Cold & Sinus PE. OSE Review # 2009-1586, May 13, 2010.

6.2 DATABASES

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

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

2. Phonetic and Orthographic Computer Analysis (POCA)

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

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

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

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

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

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

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

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

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

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

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

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

Provides information regarding patent and trademarks.

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

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

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

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

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

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

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

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

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

List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

Contains commonly used medical abbreviations and their definitions.

APPENDICES

Appendix A:

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

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

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

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

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

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

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

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

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

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

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

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

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

Lastly, the DMEPA staff also considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a

variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

DMEPA staff conducts searches of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the DMEPA staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel.

2. CDER Expert Panel Discussion

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

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

3. FDA Prescription Analysis Studies

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

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

4. Comments from the OND review Division or Generic drugs

DMEPA requests the Office of New Drugs (OND) or Office of Generic Drugs (OGD) Regulatory Division responsible for the application for their comments or concerns with the proposed proprietary

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

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

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

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

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

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

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

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

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

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

The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not

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

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:

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 PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].
2. 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)].
3. 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.
4. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
5. 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: Drug products that contain "Congestion Relief" in their Trade Name from Walgreens (www.walgreens.com)

Product	Active Ingredient(s)	Rx or OTC
Zicam Extreme Congestion Relief	Oxymetazoline	OTC
Walgreens Mucus Relief PE Sinus Congestion	Guaifenesin and Phenylephrine	OTC
Walgreens Mucus Relief Chest Congestion	Guaifenesin	OTC
TheraFlu Warming Relief Cold & Chest Congestion	Acetaminophen/Guaifenesin/Phenylephrine	OTC

Appendix C: Drug products that contain "Congestion Relief" in their Trade Name from Clinical Pharmacology

Product	Active Ingredient(s)	Rx or OTC
Equaline 24 hour Allergy and Congestion Relief	Loratadine and Pseudoephedrine	OTC
Goodsense Allergy and Congestion Relief 24 hour	Loratadine and Pseudoephedrine	OTC
Vicks Formula 44D Cough and Head Congestion Relief	Dextromethorphan and Pseudoephedrine	OTC
Vicks Formula 44E Pediatric Cough and Congestion Relief	Dextromethorphan and Guaifenesin	OTC
Vicks Formula 44E Cough and Congestion Relief	Dextromethorphan and Guaifenesin	OTC
Zicam Extreme Congestion Relief	Oxymetazoline	OTC

Appendix D: Drug products that contain "Congestion Relief" in their Trade Name from CVS (www.cvs.com)

Product	Active Ingredient(s)	Rx or OTC
Goodsense Allergy & Congestion Relief	Loratadine and Pseudoephedrine	OTC
Good Neighbor Allergy & Congestion Relief 24 Hour	Loratadine and Pseudoephedrine	OTC
Zicam Extreme Congestion Relief	Oxymetazoline	OTC
CVS Maximum Congestion Relief	Oxymetazoline	OTC
CVS Chest Congestion Relief	Guaifenesin	OTC
CVS Chest Congestion Relief DM	Dextromethorphan and Guaifenesin	OTC
CVS Chest Congestion Relief PE	Guaifenesin and Phenylephrine	OTC
TheraFlu Warming Relief Cold & Chest Congestion	Acetaminophen/Guaifenesin/Phenylephrine	OTC

Appendix E: Drug products that contain "Congestion" in their Trade Name from Google search

Product	Active Ingredient(s)	Rx or OTC
Vicks Formula 44 Custom Care Congestion	Phenylephrine	OTC
Vicks Vapo Syrup Severe Congestion Head & Chest Congestion Relief	Phenylephrine	OTC
Vicks Formula 44D Cough & Head Congestion	Pseudoephedrine and Dextromethorphan	OTC
Vicks Formula 44E Cough & Chest Congestion	Dextromethorphan and Guaifenesin	OTC
Tylenol Cold Head Congestion Severe	Phenylephrine	OTC
Tylenol Cold Severe Congestion Daytime	Pseudoephedrine	OTC
Tylenol Sinus Congestion & Pain Severe	Phenylephrine	OTC
Tylenol Sinus Congestion & Pain Daytime	Phenylephrine	OTC
Tylenol Sinus Congestion & Pain Nighttime	Phenylephrine	OTC
Tylenol Sinus Severe Congestion Daytime	Pseudoephedrine	OTC
Tylenol Cold Head Congestion Daytime	Phenylephrine	OTC
Tylenol Cold Head Congestion Nighttime	Phenylephrine	OTC
Triaminic Chest & Nasal Congestion	Phenylephrine and Guaifenesin	OTC
Robitussin Cough & Chest Congestion DM Max	Dextromethorphan and Guaifenesin	OTC
Robitussin Cough & Chest Congestion DM	Dextromethorphan and Guaifenesin	OTC
Robitussin To Go Cough & Chest Congestion DM	Dextromethorphan and Guaifenesin	OTC

Robitussin Cough & Chest Congestion Sugar-Free DM	Dextromethorphan and Guaifenesin	OTC
Robitussin Chest Congestion	Guaifenesin	OTC
Theraflu Cold & Chest Congestion Warming Relief	Phenylephrine; Guaifenesin; Acetaminophen	OTC
Theraflu Flu & Chest Congestion	Guaifenesin and Acetaminophen	OTC
Alka-Seltzer Plus Mucus & Congestion	Dextromethorphan and Guaifenesin	OTC
Coricidin HBP Chest Congestion & Cough	Dextromethorphan and Guaifenesin	OTC
Sudafed Congestion	Pseudoephedrine	OTC
Sudafed PE Congestion	Phenylephrine	OTC
Sudafed PE Day & Night Congestion	Phenylephrine	OTC
Dimetapp Nighttime Cold & Congestion	Phenylephrine and Diphenhydramine	OTC

Appendix F: Letters with possible orthographic or phonetic misinterpretation

Letters in Name, Advil Congestion Relief	**Scripted may appear as**	**Spoken may be interpreted as**
Capital ‘A’	Capital ‘C’ or ‘I’	Any vowel
Lower case ‘d’	‘cl’	‘t’
Lower case ‘v’	‘u’, ‘n’, or ‘r’	‘f’
Lower case ‘i’	‘e’ or ‘l’	Any vowel
Lower case ‘l’	‘e’, ‘i’, or ‘b’	
Capital ‘C’	Capital ‘A’	‘k’
Lower case ‘o’	‘a’, ‘e’, ‘u’, or number ‘0’	Any vowel
Lower case ‘n’	‘m’, ‘u’, ‘x’, ‘r’, ‘h’, or ‘s’	‘dn’, ‘gn’, ‘kn’, ‘mn’, or ‘pn’
Lower case ‘g’	‘q’ or ‘j’	‘j’
Lower case ‘e’	‘i’ or ‘l’	Any vowel
Lower case ‘s’	‘n’ or ‘g’	‘x’ or ‘z’
Lower case ‘t’	‘l’, ‘r’, ‘x’, or ‘b’	‘d’, ‘pt’
Capital ‘R’	Capital ‘B’, ‘P’, or ‘K’	‘wr’
Lower case ‘f’	‘b’	‘v’ or ‘ph’

Appendix G: Advil Congestion Relief Prescription Study Responses (conducted on May 13, 2010)

Outpatient Prescription	Voice Prescription	Inpatient Prescription
Advil Congestion Relief	Advil congestion relief	Advil Congestion Relief
Advil congestion relief	Advil congestion relief	Advil Congestion Relief
Advil congestion relief	Advil Congestion Relief	Advil Congestion Relief
Advil congestion relief	Advil Congestion Relief	Advil Congestion Relief
Advil Congestion Relief	Advil congestion relief	Advil Congestion Relief
Advil Congestion Relief	Advil Congestion Relief	Advil Congestion Relief
Advil congestion relief	Advil Congestion Relief	Advil Congestion relief
Advil congestion relief	Advil Congestion Relief	Advil Congestion Relief
Advil Congestion Relief	Advil congestion relief	Advil congestion relief
Advil Congestion Relief	Advil congestion relief	Advil Congestion Relief
Advil Congestion Relief		Advil Congestion Relief (This must be an OTC product. 'Congestion Relief' is certainly promotional.)
Advil Congestion Relief		Advil congestion relief,
Advil congestion relief		
Advil Congestion Relief		
Advil Congestion Relief		
Advil Congestion Relief		
Advil congestion relief		
Advil Congestion Relief		
Advil congestion relief		
Advil Congestion Relief		

Appendix H: Names lacking convincing look-alike or sound-alike similarities with Advil Congestion Relief

Proprietary Name	Source
Loestrin	EPD
Cetirizine Hydrochloride Hives Relief	EPD
Children's Cetirizine Hydrochloride Hives Relief	EPD
Children's Zyrtec Hives Relief	EPD
Claritin Hives Relief	EPD
Claritin Hives Relief Reditab	EPD
Imodium Multi-Symptom Relief	EPD
Zyrtec Hives Relief	EPD
Zyrtec-D Allergy & Congestion	EPD
Tavist Allergy/Sinus/Headache	EPD
[redacted]	(b) (4)

Appendix I: **Proposed product (Advil Congestion Relief) compared to Advil product line** (from www.advil.com; Drugs@FDA; Clinical Pharmacology; and DARRTS)

Proprietary Name	Legend Status	Active Ingredients	Formulation	Dosage Strength	Dosing Frequency and Route of Administration
Advil Congestion Relief	OTC	Ibuprofen/ phenylephrine	Caplets	200 mg/ 10 mg	1 caplet orally every 4 hours while symptoms persist
Advil Cold & Sinus	OTC (behind the counter)	Ibuprofen/ pseudoephedrine	Caplets	200 mg/ 30 mg	1 caplet orally every 4 to 6 hours while symptoms persist
Advil Cold & Sinus Liqui-Gels	OTC (behind the counter)	Ibuprofen/ pseudoephedrine	Liquid-filled capsules	200 mg/ 30 mg	1 capsule orally every 4 to 6 hours while symptoms persist
Advil Allergy Sinus	OTC (behind the counter)	Ibuprofen/ chlorpheniramine/ pseudoephedrine	Caplets	200 mg/ 2 mg/30 mg	1 caplet orally every 4 to 6 hours while symptoms persist.
Advil	OTC	Ibuprofen	Tablets Caplets Gel Caplets	200 mg	1 tablet/caplet/gel caplet orally every 4 to 6 hours while symptoms persist
Advil Liqui-Gels	OTC	Ibuprofen	Liquid-filled capsules	200 mg	1 capsule orally every 4 to 6 hours while symptoms persist
Advil PM	OTC	Ibuprofen/ diphenhydramine citrate	Caplets	200 mg/ 38 mg	2 caplets orally at bedtime
Advil PM Liqui-Gels	OTC	Ibuprofen/ diphenhydramine hydrochloride	Liquid-filled capsules	200 mg/ 25 mg	2 capsules orally at bedtime
Advil Migraine	OTC	Ibuprofen	Capsules	200 mg	2 capsules orally with a glass of water

Advil Flu and Body Ache	OTC	Ibuprofen/pseudoephedrine HCl	Tablets	200 mg/ 30 mg	No information
Advil Multi-Symptom Cold	OTC	Ibuprofen/chlorpheniramine maleate/pseudoephedrine HCl	Tablets	200 mg/ 2 mg/30 mg	No information
Advil Junior Strength	OTC	Ibuprofen	Tablets; Chewable Tablets	100 mg	No information
Children's Advil	OTC	Ibuprofen	Suspension	100 mg/ 5 mL	Per dosing chart; repeat dose every 6 to 8 hours, if needed
Children's Advil Cold	OTC (behind the counter)	Ibuprofen/ pseudoephedrine hydrochloride	Suspension	100 mg/ 15 mg per 5 mL	Per dosing chart; repeat dose every 6 hours, if needed
Children's Advil Allergy Sinus (not currently marketed per annual report)	OTC (behind the counter)	Ibuprofen/ pseudoephedrine HCl/ chlorpheniramine maleate	Suspension	100 mg/ 15 mg/ 1 mg per 5 mL	Per dosing chart; if needed, repeat dose every 6 hours while symptoms persist
Infants' Advil (same as Pediatric Advil)	OTC	Ibuprofen	Concentrated Drops	50 mg/ 1.25 mL	Per dosing chart; repeat dose every 6 to 8 hours, if needed

Appendix J: Advil products that have never been marketed in the U.S. (from DARRTS)

Proprietary Name	Active Ingredient(s)	Dosage Form	Status
(b) (4)			

Appendix K: Natural Medicine Product (with a different context of use than Advil Congestion Relief)

Proprietary Name	Similarity to Advil Cold & Sinus PE	Description	Use
AdvaCal	Look	**Advacal**: 3 capsules contain calcium 500 mg (from calcium hydroxide and calcium oxide) **Advacal Calcium Chewable Wafers**: 2 wafers contain calcium 400 mg (from calcium hydroxide and calcium oxide); Stevia leaf 700 mcg; Hijiki Seaweed extract (hizikia fusiforme, heat treated) 320 mcg **Advacal Ready-to-Drink Calcium**: each packet contains calcium 300 mg (from calcium hydroxide and calcium oxide); Hijiki Seaweed extract (hizikia fusiforme, heat treated) 1 mg	Nutritional supplement

Appendix L: Products with no overlap in strength or dose

Advil Congestion Relief (ibuprofen/phenylephrine HCl)		**Caplets: 200 mg/10 mg**	**One caplet orally every 4 hours while symptoms persist; no more than 6 caplets in a 24 hours period**
Product name with potential for confusion	**Similarity to Proposed Proprietary Name**	**Strength**	**Usual Dose (if applicable)**
Cogentin (Benztropine Mesylate)	Look and Sound	Tablets: 0.5 mg, 1 mg, 2 mg Injection: 1 mg/mL *Brand name tablets discontinued; generics available	**For the treatment of Parkinsonism or Parkinson's disease:** The recommended initial dose is 0.5 mg to 1 mg orally or via intramuscular injection at bedtime. Increase in 0.5 mg increments at 5 to 6 day intervals if necessary. The dosage range is 0.5 mg to 6 mg and must be individualized according to age and weight. **For the treatment of drug-induced extrapyramidal symptoms (except tardive dyskinesia):** The recommended dose is 1 mg to 4 mg via intravenous or intramuscular injection or orally once or twice daily.
Relafen (Nabumetone)	Look and Sound	Tablets: 500 mg, 750 mg *Brand name product discontinued; generics available	Initially, 1000 mg orally once daily or 500 mg orally twice daily. Adjust according to patient response. Maximum dose is 2000 mg per day.
Advicor (Niacin extended-release/Lovastatin) Tablets	Look	500 mg/20 mg; 750 mg/20 mg; 1000 mg/20 mg; 100 mg/40 mg	Start at the lowest initial dose, a single 500 mg/20 mg tablet orally once daily at bedtime.

Advair (Fluticasone Propionate and Salmeterol Xinafoate)	Look	Diskus: 100/50, 250/50, 500/50 HFA: 45/21, 115/21, 230/21	Diskus: For maintenance treatment of asthma: 1 inhalation of the appropriate strength twice daily (strength is based on asthma severity) For maintenance treatment of COPD: 1 inhalation of 250/50 twice daily HFA: For maintenance treatment of asthma: For patients not adequately controlled on an inhaled corticosteroid, the recommended dose is 2 inhalations twice daily of the appropriate strength (based on current inhaled corticosteroid dosage) For patients not currently on inhaled corticosteroids, the recommended starting dosage is 2 inhalations of 45/21 or 115/21 twice daily

Appendix M: Products with Overlapping Strength but Other Differentiating Product Characteristics

Product name with potential for confusion	Similarity to Product Name	Strength	Usual Dose	Other Differentiating Product Characteristics
Advil Congestion Relief (ibuprofen/phenylephrine HCl)		**Caplets: 200 mg/10 mg**	**One caplet orally every 4 hours while symptoms persist; no more than 6 caplets in a 24 hours period**	
Cognex (Tacrine Hydrochloride)	Look	Tablets: 10 mg, 20 mg, 30 mg, 40 mg	Initially, 10 mg orally four times per day; maintain for a minimum of four weeks. Increase to 20 mg orally four times per day if patient tolerates. Maximum dose is 160 mg per day administered in four divided doses.	**Dose:** 10 mg to 20 mg vs. one caplet **Frequency of administration:** Four times per day vs. every four hours
Elavil (Amitriptyline Hydrochloride)	Look	Tablets: 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg Injection: 10 mg/mL *Brand name products discontinued; generics available only for the tablets	Initially, 25 mg to 75 mg orally per day given as a single dose at bedtime or in divided doses. Titrate, if needed, up to 200 mg per day by increasing the daily dose 25 mg to 50 mg at weekly intervals. Maximum dose for adult outpatients is 200 mg per day; maximum dose for adult hospitalized patients is 300 mg per day	**Dose:** 25 mg to 75 mg vs. one caplet **Frequency of administration:** Single dose at bedtime or in divided doses vs. every four hours

Appendix N: Single Strength Products with Differentiating Product Characteristics

Product name with potential for confusion	Similarity to Product Name	Strength	Usual Dose	Other Differentiating Product Characteristics
Advil Congestion Relief (ibuprofen/phenylephrine HCl)		**Caplets: 200 mg/10 mg**	**One caplet orally every 4 hours while symptoms persist; no more than 6 caplets in a 24 hours period**	
Zicam Extreme Congestion Relief (Oxymetazoline Hydrochloride)	Look	Liquid nasal gel: 0.05%	Pump 2 or 3 times in each nostril without tilting the patient's head. Do not use more often than once every 10 to 12 hours. Do not exceed 2 doses in any 24 hour period.	**Dosage form:** Liquid nasal gel vs. caplet **Route of administration:** Intranasal vs. oral **Dose:** 2 or 3 pumps vs. one caplet **Frequency of administration:** Once every 10 to 12 hours vs. every 4 hours
Acuvail (Ketorolac Tromethamine)	Look	Ophthalmic solution: 0.45%	One drop should be applied by the patient to the affected eye twice daily beginning 1 day prior to cataract surgery and continued through the first 2 weeks of the postoperative period.	**Dosage form:** Ophthalmic solution vs. caplet **Route of administration:** Ophthalmic vs. oral **Frequency of administration:** Twice daily vs. every 4 hours

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22565	ORIG-1	WYETH CONSUMER HEALTHCARE	ADVIL COLD & SINUS PE(IBUPROFEN 200MG/PH

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

/s/

ZACHARY A OLESZCZUK
05/24/2010

KELLIE A TAYLOR
05/24/2010

CAROL A HOLQUIST
05/25/2010

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

Date:	May 13, 2010
To:	Andrea Leonard-Segal, M.D., Director Division of Nonprescription Clinical Evaluation
Through:	Zachary Oleszczuk, Pharm.D., Acting Team Leader Kellie Taylor, Pharm.D., M.P.H., Associate Director Carol Holquist, R.Ph., Director Division of Medication Error Prevention and Analysis
From:	Tara Turner, Pharm.D., Safety Evaluator Chi-Ming Tu, Pharm.D., Safe Medication Management Fellow Division of Medication Error Prevention and Analysis
Subject:	Proprietary Name Review
Drug Name(s):	Advil Cold & Sinus PE (Ibuprofen and Phenylephrine Hydrochloride) Caplets 200 mg/10 mg
Application Type/Number:	NDA 022565
Applicant:	Wyeth Consumer Healthcare
OSE RCM #:	2009-1586

CONTENTS

EXECUTIVE SUMMARY

The Division of Medication Error Prevention and Analysis (DMEPA) previously evaluated the proposed proprietary name, Advil Cold & Sinus PE, in OSE Review #2009-1586, dated November 5, 2009, and found the name unacceptable because of concerns that the "PE" modifier does not have a consistent meaning among consumers or healthcare practitioners and the modifier is a documented source of confusion in the current marketplace. The Applicant did not provide data to support that the "PE" modifier is clear and is not a source of error and so DMEPA concluded that the "PE" modifier is not acceptable for this product.

(b) (4)

[redacted]

1 BACKGROUND

1.1 INTRODUCTION

(b) (4)

[redacted]

In our previous review of the proposed name Advil Cold & Sinus PE (OSE Review #2009-1586, dated November 5, 2009) DMEPA identified drug names with the modifier "PE" for products that contain phenylephrine and other drug products that contain pseudoephedrine (see Appendix B). DMEPA also identified literature that describes post-marketing cases of confusion between non-prescription products utilizing the "PE" modifier where the meaning of "PE" has been misinterpreted as phenylephrine or pseudoephedrine[1]. At the time of the previous review the Applicant did not provide data to support that the "PE" modifier is clear and is not a source of error and thus DMEPA concluded that the proposed proprietary name, Advil Cold & Sinus PE, was unacceptable.

DMEPA also stated in our previous review that if the Applicant wishes to pursue the name Advil Cold & Sinus PE, then healthcare practitioner and consumer studies assessing the meaning of "PE" and whether this modifier provides adequate differentiation from the current Advil Cold & Sinus product should be submitted. DMEPA also asked the Applicant to assess the proposed labeling techniques for differentiating between the currently marketed Advil Cold & Sinus product and the proposed Advil Cold & Sinus PE product.

(b) (4)

1.3 PRODUCT INFORMATION

Advil Cold & Sinus PE is an over-the-counter combination product containing ibuprofen 200 mg and phenylephrine hydrochloride 10 mg per caplet. The proposed indication is to provide temporary relief of the following symptoms associated with the common cold or flu: headache, fever, sinus pressure, nasal congestion, and minor body aches/pains. The recommended dose for adults and children 12 years of age and over is one caplet orally every 4 hours while symptoms persist. Advil Cold & Sinus PE will be supplied in cartons of 20 count and shelf cartons of 50 packets, each containing one caplet.

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[1] Institute of Safe Medication Practices. Separation Anxiety. Medication Safety Alert! Community/Ambulatory Care Edition. June 2006. Volume 5, Issue 6, Page 3.

(b) (4)

5 CONCLUSIONS AND RECOMMENDATIONS

(b) (4)

These findings were communicated to the Applicant via telephone on April 2, 2010. The Applicant withdrew the name on April 22, 2010.

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Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22565	ORIG-1	WYETH CONSUMER HEALTHCARE	ADVIL COLD & SINUS PE(IBUPROFEN 200MG/PH

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

/s/

TARA P TURNER
05/13/2010

ZACHARY A OLESZCZUK
05/14/2010

KELLIE A TAYLOR
05/14/2010

CAROL A HOLQUIST
05/14/2010

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

Date:	November 5, 2009
To:	Andrea Leonard-Segal, M.D., Director Division of Nonprescription Clinical Evaluation
Through:	Kellie Taylor, Pharm.D., M.P.H., Team Leader Denise Toyer, Pharm.D., Deputy Director Carol Holquist, R.Ph., Director Division of Medication Error Prevention and Analysis
From:	Tara Turner, Pharm.D., Safety Evaluator Division of Medication Error Prevention and Analysis
Subject:	Proprietary Name Review
Drug Name(s):	Advil Cold & Sinus PE (Ibuprofen and Phenylephrine Hydrochloride) Caplets 200 mg/10 mg
Application Type/Number:	NDA 022565
Applicant:	Wyeth Consumer Healthcare
OSE RCM #:	2009-1586

CONTENTS

1 BACKGROUND

1.1 INTRODUCTION

This review is written in response to a request from Wyeth Consumer Healthcare dated August 26, 2009 for an assessment of the proposed proprietary name, Advil Cold & Sinus PE.

The Applicant also submitted draft container labels and carton labeling for our review. The labels and labeling will be evaluated separately under OSE Review # 2009-1591.

1.2 PRODUCT INFORMATION

Advil Cold & Sinus PE is an over-the-counter combination product containing ibuprofen 200 mg and phenylephrine hydrochloride 10 mg per caplet. The proposed indication is to provide temporary relief of the following symptoms associated with the common cold or flu: headache, fever, sinus pressure, nasal congestion, and minor body aches/pains. The recommended dose for adults and children 12 years of age and over is one caplet orally every 4 hours while symptoms persist. Advil Cold & Sinus PE will be supplied in cartons of 20 count and shelf cartons of 50 packets, each containing one caplet.

1.3 APPLICANT'S RATIONALE FOR PROPOSED NAME

(b) (4)

2 RESULTS AND DISCUSSION

In our searches, DMEPA identified drug names with the modifier 'PE' for products that contain phenylephrine and other drug products that contain pseudoephedrine (see Appendix B). Further, we identified literature that describes post-marketing cases of confusion between non-prescription products utilizing the 'PE' modifier where the meaning of 'PE' has been misinterpreted as phenylephrine or

pseudoephedrine[1]. This confusion has resulted in medication errors in which patients mistakenly purchased the wrong drug.

We are concerned there is no consistent meaning of 'PE' among consumers or healthcare practitioners, especially given the documented post-marketing cases involving the 'PE' modifier and confusion as to whether this modifier meant 'pseudoephedrine' or 'phenylephrine'. Therefore, the 'PE' modifier may not provide sufficient differentiation from the currently marketed Advil Cold & Sinus product, which contains pseudoephedrine.

3 CONCLUSIONS AND RECOMMENDATIONS

In the absence of data to support that the 'PE' modifier has a clear meaning and is not a source of error, the Division of Medication Error Prevention and Analysis finds the use of the proposed proprietary name, Advil Cold & Sinus PE, for this product unacceptable.

We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Karen Townsend, Regulatory Project Manager, at 301-796-5413.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Advil Cold & Sinus PE, and have concluded that this name is unacceptable for the following reasons:

The modifier 'PE' has been used for products that contain phenylephrine and pseudoephedrine. The literature describes post-marketing cases of confusion between non-prescription products utilizing the 'PE' modifier where the meaning of 'PE' has been misinterpreted as phenylephrine or pseudoephedrine. This confusion has led to medication errors in which patients mistakenly purchased the wrong drug.

We are concerned there is no consistent meaning of 'PE' among consumers or healthcare practitioners, especially given the documented post-marketing cases involving the 'PE' modifier and confusion as to whether this modifier meant 'pseudoephedrine' or phenylephrine'. Therefore, the 'PE' modifier may not provide sufficient differentiation from the currently marketed Advil Cold & Sinus product, which contains pseudoephedrine. You have not provided data to support that the 'PE' modifier is clear and is not a source of error. In the absence of this data, we must conclude that at this time 'PE' is not acceptable for this product. If you wish to pursue this name you should submit healthcare practitioner and consumer studies assessing the meaning of 'PE' and whether this modifier provides adequate differentiation from the current Advil Cold & Sinus product.

You have not proposed an alternate proprietary name for review. If you intend to have a proprietary name for this product, we recommend that you submit a new request for a proposed proprietary name review. (See the draft Guidance for Industry, *Complete Submission for the Evaluation of Proprietary Names*, HTTP://www.fda.gov/cder/guidance/7935dft.pdf and "PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2008 through 2012".)

DMEPA scheduled a teleconference for October 28, 2009 to discuss our concerns with you. However, technical difficulties prevented this teleconference from occurring. We are willing to discuss our concerns further, if requested, following receipt of this letter.

[1] Institute of Safe Medication Practices. Separation Anxiety. Medication Safety Alert! Community/Ambulatory Care Edition. June 2006. Volume 5, Issue 6, Page 3.

1 Page has been withheld in full immediately following this page as B4 (CCI/TS)

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22565	ORIG-1	WYETH CONSUMER HEALTHCARE	ADVIL COLD & SINUS PE(IBUPROFEN 200MG/PH

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

/s/

TARA P TURNER
11/05/2009

KELLIE A TAYLOR
11/05/2009

DENISE P TOYER
11/05/2009

CAROL A HOLQUIST
11/06/2009