

**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

Date: November 7, 2011

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Drug Name and Strengths: Subsys (Fentanyl) Sublingual Spray, 100 mcg, 200 mcg, 400 mcg,
600 mcg, 800 mcg per spray

Application Type/Number: NDA 202788

Applicant/sponsor: Insys Therapeutics

OSE RCM #: 2011-1671

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1 INTRODUCTION

This re-assessment of the proposed proprietary name, Subsys is written in response to the anticipated approval of this NDA within 90 days from the date of this review. DMEPA found the proposed name, Subsys, acceptable in OSE Review 2011-1017, dated June 7, 2011.

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 approved since the previous OSE proprietary name review. For this review we used the same search criteria described in OSE Review 2011-1017. Because none of the proposed product characteristics were altered we did not re-evaluate previous names of concern. The searches of the databases yielded four new names ((b) (4) Synagis, Safyral, (b) (4) thought to look or sound similar to Subsys 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 Subsys and lead to medication errors. This analysis determined that the name similarity between Subsys and the identified names 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 28, 2011. OPDP re-reviewed the proposed name on October 27, 2011 and had no concerns regarding the proposed name from a promotional perspective.

3 CONCLUSIONS

The re-evaluation of the proposed proprietary name, Subsys, did not identify any vulnerabilities that would result in medication errors with the additional names noted in this review. Thus, DMEPA has no objection to the proprietary name, Subsys, for this product at this time.

DMEPA considers this a final review; however, if approval of the NDA 202788 is delayed beyond 90 days from the date of this review, the Division of Analgesia and Anesthesia 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 Danyal Chaudhry, OSE project manager, at 301-796-3813.

4 REFERENCES

1. *OSE Reviews*

OSE Review # 2011-1017. Subsys Proprietary Name Review. Tobenkin, Anne. June 7, 2011.

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

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

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

USAN Stems List contains all the recognized USAN stems.

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

Proprietary Name	Active Ingredient	Similarity to Subsys	Failure Preventions
(b) (4)			

Appendix B: FMEA Table

Proposed name: Susbsys (Fentanyl) Strength: 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray Dose: 1 to 2 sprays sublingually every 4 hours as needed	Causes of Failure Mode Resulting in Medication Error: Incorrect Product Ordered/ Selected/ Dispensed or Administered Because of Name confusion	Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences
(b) (4)		

Proposed name: Susysys (Fentanyl) Strength: 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray Dose: 1 to 2 sprays sublingually every 4 hours as needed	Causes of Failure Mode Resulting in Medication Error: Incorrect Product Ordered/ Selected/ Dispensed or Administered Because of Name confusion	Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences
Safyral (Drosperinone/Ethinyl Estradiol/Levomefolate and Levomefolate) - 3 mg/0.04 mg/0.451 mg oral tablets and 0.451 oral tablets - One tablet once daily or as directed	Orthographic similarity - Both names begin with ‘S’ - Both names have a downstroke ‘y’ - Both names are similar in length Product characteristics - Route of administration (oral)	Orthographic differences - Susysys has two upstrokes vs. Safyral has three upstrokes - Susysys has one letter after the downstroke vs. Safyral has three letters after the downstroke Differing product characteristics - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. 3 mg/0.04 mg/0.451 mg oral tablets and 0.451 oral tablets, single strength, not required on prescription) - Frequency of administration (every 4 hours as needed for pain vs. once daily)
Synagis (Palivizumab) - 50 mg/0.5 mL, 100 mg/1 mL injection solution - 15 mg/kg intramuscularly once a month during Respiratory Syncytial Virus season	Phonetic - Both names begin with the sound “S” - Both names end with the sound “ys”	Orthographic differences - Susysys has two syllables vs. Synagis has three syllables - The first syllable in Susysys ends with the sound “uhb” vs. “in” in Synagis Differing product characteristics - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. 15 mg/kg, weight based regimen) - Route of administration (oral vs. intramuscular) - Frequency of administration (every 4 hours as needed for pain vs. once monthly)

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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 Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology**

Date: June 7, 2011
To: Bob Rappaport
Through: Melina Griffis, RPh, Team Leader
Carol Holquist, RPh, Director
Division of Medication Error Prevention and Analysis (DMEPA)
From: Anne Crandall, RPh, PharmD, Safety Evaluator
Division of Medication Error Prevention and Analysis (DMEPA)
Subject: Proprietary Name Review
Drug Name(s): Subsys (Fentanyl) Sublingual Spray
100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray
Application Type/Number: NDA 202788
Applicant: Insys Therapeutics
OSE RCM #: 2011-1017

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EXECUTIVE SUMMARY

This review summarizes the proprietary name evaluation of Subsys (Fentanyl) Sublingual Spray. 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. Our findings are consistent with the findings of the findings of the External Proprietary Name Risk Assessment submitted by the Applicant. Thus, DMEPA finds the proposed proprietary name, Subsys, acceptable for this product.

The proposed proprietary name, Subsys, 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.

1 BACKGROUND

1.1 INTRODUCTION

This review responds to the March 14, 2011 request from Insys Therapeutics, for DMEPA's assessment of the proposed proprietary name, Subsys, regarding potential name confusion with other proprietary or established drug names, as well as promotional review. The Applicant submitted an Independent Name Assessment with the proprietary name review request. Container labels, carton and package insert labeling were submitted on March 3, 2011 and will be reviewed under a separate cover, OSE review # 2011-1019.

1.2 PRODUCT INFORMATION

The proposed indication for Subsys (Fentanyl) sublingual spray is for the management of breakthrough cancer pain in opioid-tolerant patients. Subsys will be available as 100 mcg, 200 mcg, 400 mcg, 600 mcg and 800 mcg per spray single use bottles which are contained in individually sealed child-resistant blister packages. The recommended starting dose is 100 mcg. The usual dose is 1 or 2 sprays sublingually administered at no more than every four hours. The maximum daily dose is 6400 mcg. Subsys will be supplied in a single use spray device in individually wrapped, child-resistant, protective blister packs packaged in 6, 14 and 28 cartons.

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, Subsys.

2.1 SEARCH CRITERIA

The DMEPA safety evaluators 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 ‘S’ 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 Subsys, 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 (six letters), upstrokes (two, capital letter ‘S’ and lower case letter ‘b’); downstrokes (one, ‘y’), cross-strokes (none), and dotted letters (none). Additionally, several letters in Subsys 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 Subsys

When searching to identify potential names that may sound similar to Subsys, DMEPA safety evaluators search for names with similar number of syllables (two), stresses (SUB-sys, sub-SYS), and placement of vowel and consonant sounds. Additionally, several letters in Subsys may be subject to interpretation when spoken (see Appendix B). The Applicant’s intended pronunciation of the proprietary name (sub’ sis) was taken into consideration, as this was provided with the proposed name submission, however DMEPA understands that pronunciation of the product will vary greatly from region to region and be based upon cultural background.

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, an inpatient medication order, outpatient and verbal prescription was communicated during the FDA prescription studies (see Appendix C).

2.3 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

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

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

3 RESULTS

The following sections describe the results of the proprietary name analysis that were identified during this review.

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)

3.1 DATABASE AND INFORMATION SOURCES

DMEPA safety evaluator searches of the databases and DMEPA's information sources yielded a total of 27 names as having some similarity to the name, Subsys.

Twenty-three (Galzin, Sabril, Anbesol, Ambien, Sulzee, Jujube, Colcrys, Solodyn, Sronyx, Staxyn, Sebizon, Lybrel, Symlin, Zyban, Symbyax, Sulamyd, Folutyn, Pegasys, Gilenya, Salagen, Selsun, Soliris, and (b) (4)) of the 27 names were thought to look like Subsys. Three (Subys, Subutex and Subsys) of the 27 names were thought to both look and sound like Subsys. The remaining name (Saphris) was thought to sound like Subsys.

DMEPA safety evaluators did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of April 4, 2011.

3.2 EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMEPA safety evaluators (See Section 3.1 above) and noted one additional name, Ionsys, thought to have orthographic or phonetic similarity to Subsys. The name Ionsys was added to the proprietary name analysis.

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 thirty (n=31) practitioners responded to the prescription analysis studies. None of the practitioner responses overlapped with any existing or proposed drug names, however five of the nine respondents in the verbal study misinterpreted the name as "sepsis". Sixteen (n=16) of the practitioners interpreted the name correctly as "Subsys." The remainder of the practitioners misinterpreted the drug name (n=15). The most common misinterpretation was between the letter pair 'S' and 'F', 's' and 'a' and 'y' and 'i'. See Appendix D for the complete listing of interpretations from the verbal and written prescription studies.

3.4 EXTERNAL PROPRIETARY NAME RISK ASSESSMENTS

The August 24, 2010, submission from the Applicant included a proprietary name analysis conducted by the (b) (4) (b) (4) found the proposed proprietary name, Subsys, acceptable. Their study identified and evaluated a total of two names, Pegasys and Stasis, for potential confusion with Subsys. DMEPA identified one of the two names (Pegasys) during our database searches. The remaining name, Stasis, was added to the DMEPA safety evaluator risk assessment.

3.5 COMMENTS FROM THE REVIEW DIVISION

3.5.1 Initial Phase of Review

In a response to the OSE April 4, 2011, e-mail, the Division of Anesthesia and Analgesia Products (DAAP) did not forward any comments and/or concerns on the proposed name at the initial phase of the name review.

3.5.2 Midpoint of Review

On June 7, 2011, DMEPA notified DAAP via e-mail that we have no objection to the use of the proprietary name, Subsys. DAAP indicated that they concur with our assessment of the proposed proprietary name, Subsys.

3.6 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary safety evaluator identified three additional proprietary names which were thought to look or sound similar to Subsys and represent a potential source of drug name confusion. All three (Sufenta, Salacyn, and Solage) names were thought to look like Subsys. A total of 32 names were identified as having some potential similarity to the proposed name Subsys; 27 from safety evaluator searches, one from EPD, one from the external name study, and three from the primary safety evaluator search.

4 DISCUSSION

The proposed name, Subsys, was evaluated from a safety and promotional perspective based on the product characteristics provided by the Applicant.

4.1 PROMOTIONAL ASSESSMENT

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

4.2 SAFETY ASSESSMENT

DMEPA identified 32 names with potential similarity to the proposed name, Subsys. No other aspects of the proposed proprietary name were identified as a potential source of failure that may lead to medication error. Three of the 32 names were not evaluated further for the reasons identified in Appendix E.

Failure Mode and Effects Analysis was then applied to determine if the proposed name, Subsys, could potentially be confused with the remaining 29 names and lead to medication errors. This analysis determined that the name similarity between Subsys was unlikely to result in medication errors with any of the 29 products for the reasons presented in Appendix F. This finding was consistent with and supported by the independent risk assessment of the proprietary name submitted by the Applicant.

Additionally, DMEPA noted that study participants in the prescription studies thought the name Subsys sounded like Sepsis. Although there are phonetic similarities, confusion between Subsys and sepsis will be mitigated by dose instructions and frequency of administration following the proprietary name, Subsys, which will identify the name as a drug product, rather than a diagnosis or indication.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Colcrys, is not vulnerable to name confusion that could lead to medication errors, nor is it considered promotional. This finding was consistent with and supported by an independent risk assessment of the proprietary name submitted by the Sponsor. Thus the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Colcrys, for this product at this time.

If you have further questions or need clarifications, please contact Danyal Chaudhry, OSE Project Manager at 301-796-3813.

5.1 COMMENTS TO THE APPLICANT

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

The proposed proprietary name, Subsys, will be re-reviewed in 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. The conclusions upon re-review are subject to change.

6 REFERENCES

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

USPTO provides information regarding patent and trademarks.

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

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

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

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

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

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

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

Stat!Ref contains full-text information from approximately 30 texts; it includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, 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>)

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

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

APPENDICES

Appendix A:

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

For the proposed proprietary name, DMEPA 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 Sponsor’s intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Sponsor has little control over how the name will be spoken in clinical practice.

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 safety evaluator 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 safety evaluators 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/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of 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

DMEPA requests the Office of New Drugs (OND) responsible for the application for its 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 is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys its decision to accept or reject the name. OND is requested to concur/not concur with DMEPA's final decision.

5. External Proprietary Name Risk Assessment

DMEPA conducts an independent analysis and evaluation of the data provided, and responds to the overall findings of the assessment. When the external proprietary name risk assessment identifies potentially confusing names that were not captured in DMEPA's database searches or in the Expert Panel Discussion, these names are included in the Safety Evaluator's risk assessment and analyzed independently by the Safety

Evaluator to determine if the potentially confusing name could lead to medication errors in usual practice settings.

After the safety evaluator has determined the overall risk assessment of the proposed name, the Safety Evaluator compares the findings of the overall risk assessment to the findings of the proprietary name risk assessment submitted by the Applicant. The Safety Evaluator then determines whether the DMEPA safety evaluators' risk assessment concurs or differs with the findings. When the proprietary name risk assessments differ, the DMEPA safety evaluators provide a detailed explanation of these differences.

6. 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

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

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 Sponsor 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 Sponsor with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

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

The threshold set for objection to the proposed proprietary name may seem low to the Sponsor. 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), the Joint Commission, and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names 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 Sponsor can identify and rectify prior to approval to avoid patient harm.

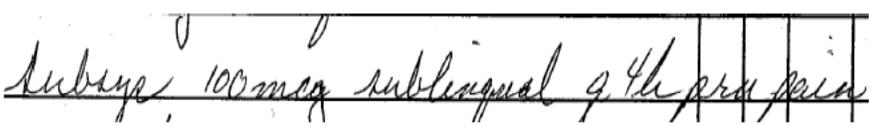
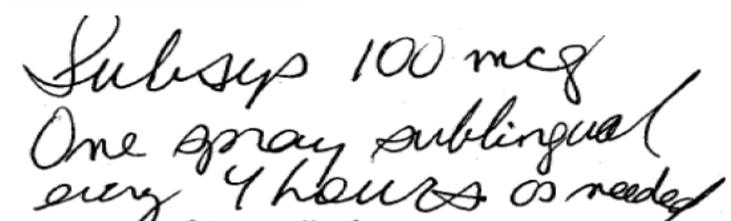
Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Sponsors have undertaken higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency's

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

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in Name: Subsys	Scripted may appear as	Spoken may be interpreted as
S	G,	"Z"
u	o, a, e	"e"
b	H, lo, lc	"v", "p"
s	r, n	"z", "c"
y	g, j,	"i"
s	r, n	"z", "c"

Appendix C. Subsys Rx Study (conducted on March 25, 2011)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
<p><u>Inpatient Medication Order :</u></p> 	<p>Subsys 100 mcg One spray sublingually every 4 hours as needed</p>
<p><u>Outpatient Prescription:</u></p> 	

Appendix D: FDA Prescription Study Responses (March 25, 2011)		
Written Outpatient	Written Inpatient	Verbal Prescription
Lubsys	Subays	Fectous
Subsys	Subsys	Sepsis
Subsys?	subsys	sepsis
Subsys	Subsya	sepsis
Subsys	Subsys	Suxis
Subsys	Subsya	Sepsis
Subsys	Subsya	Sepcist
Subsys		Sepsis
Subsys		Fepsis
Subsys		
Lubsys		
Subsys		

Appendix E: Names that did not undergo FMEA analysis	
Proprietary Name	Reason for Removal
Subsys	Application under review
Jujube	Not orthographically similar to Subsys
Subys Solution G	Not found in commonly used databases

Appendix F:				
Product name with potential for confusion	Similarity to Subsys	Strength	Usual Dose (if applicable)	Product Characteristic, Phonetic, and Orthographic Differences
Subsys (Fentanyl)	N/A	100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray	1 to 2 sprays no more then every four hours as needed	
Galzin (Zinc acetate)	Orthographic	25 mg, 50 mg oral capsules	One capsule by mouth three times daily	<p><u>Orthographic differences</u></p> <ul style="list-style-type: none"> - The second upstroke and downstroke in Subsys have a letter in between vs. The upstroke and downstroke are next to one another in Galzin - The downstroke in Subsys has one letter that follows the downstroke vs. two letters follow the downstroke in Galzin <p><u>Product characteristics</u></p> <ul style="list-style-type: none"> - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. 25 mg, 50 mg) - Dosage form (spray vs. capsule)
Sabril (Vigabatrin)	Orthographic	500 mg oral tablet, 500 mg/packet oral powder for solution	500 mg by mouth twice daily, may be increased to maximum daily dose of 3 g	<p><u>Orthographic differences</u></p> <ul style="list-style-type: none"> - Subsys has a downstroke vs. Sabril has no downstrokes - Subsys has two upstrokes vs. Sabril has three upstrokes and ends with an upstroke <p><u>Product characteristics</u></p> <ul style="list-style-type: none"> - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. 500 mg, single strength, not required on prescription) - Dosage form (spray vs. tablet, powder for solution) - Schedule of administration ('pm' or as needed vs. around the clock)

Appendix F:				
Product name with potential for confusion	Similarity to Subsys	Strength	Usual Dose (if applicable)	Product Characteristic, Phonetic, and Orthographic Differences
Subsys (Fentanyl)	N/A	100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray	1 to 2 sprays no more then every four hours as needed	
Anbesol (Benzocaine)	Orthographic	10% oral liquid and gel	Apply to affected area in the mouth up to four times daily	<p><u>Orthographic differences</u></p> <ul style="list-style-type: none"> - Subsys has a downstroke vs. Anbesol does not have a downstroke - Subsys has two upstrokes vs. Anbesol has three upstroke and ends with an upstroke <p><u>Product characteristics</u></p> <ul style="list-style-type: none"> - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. single strength, not required on prescription) - Dose (spray vs. small amount) - Prescription status (controlled substance, requires prescription vs. over the counter product)
Ambien (Zolpidem tartrate)	Orthographic	5 mg, 10 mg oral tablet	5 mg or 10 mg immediately before bedtime	<p><u>Orthographic differences</u></p> <ul style="list-style-type: none"> - Subsys has a downstroke vs. Ambien does not have a downstroke <p><u>Product characteristics</u></p> <ul style="list-style-type: none"> - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. 5 mg, 10 mg) - Frequency of administration (no more then every four hours vs. once, immediately before bedtime) - Dosage form (spray vs. tablet)

Appendix F:				
Product name with potential for confusion	Similarity to Subsys	Strength	Usual Dose (if applicable)	Product Characteristic, Phonetic, and Orthographic Differences
Subsys (Fentanyl)	N/A	100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray	1 to 2 sprays no more then every four hours as needed	
Sulzee (Sulfacetamide and Sulfur) Discontinued but generics available	Orthographic	100 mg/10 mg/g topical wash	Wash affected area as needed	<p><u>Orthographic differences</u></p> <ul style="list-style-type: none"> - The second upstroke and downstroke in Subsys have a letter in between vs. the upstroke and downstroke are next to one another in Sulzee - Subsys has one letter after the upstroke vs. Sulzee has two letters after the upstroke <p><u>Product characteristics</u></p> <ul style="list-style-type: none"> - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. single strength, not required on prescription) - Route of administration (sublingual vs. topical) - Dose (spray vs. amount to affected area) - Dosage form (Spray vs. wash)

Appendix F:				
Product name with potential for confusion	Similarity to Subsys	Strength	Usual Dose (if applicable)	Product Characteristic, Phonetic, and Orthographic Differences
Subsys (Fentanyl)	N/A	100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray	1 to 2 sprays no more then every four hours as needed	
Colcris (Colchicine)	Orthographic	0.6 mg oral tablet	<ul style="list-style-type: none"> - Gout prophylaxis: 0.6 mg by mouth once or twice daily - Gout treatment: one tablet by mouth, followed by another tablet one hour later then continue on prophylaxis schedule - Familial Mediterranean Fever: 0.3 mg to 2.4 mg by mouth daily 	<p><u>Orthographic differences</u></p> <ul style="list-style-type: none"> - The beginning letter, 'S' in Subsys does not resemble 'C' in Colcris <p><u>Product characteristics</u></p> <ul style="list-style-type: none"> - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. 0.6 mg single strength, not required on prescription. Additionally although 600 mcg could be interpreted as 0.6 mg, all fentanyl doses are recognized in mcg strengths, therefore it is unlikely 0.6 mg would be used) - Frequency of administration (every 4 hours as needed vs. once or twice daily around the clock) - Dosage form (spray vs. tablet)
Solodyn (Minocycline hydrochloride)	Orthographic	45 mg, 55 mg, 65 mg, 80 mg, 90 mg, 105 mg, 115 mg, 135 mg oral tablets	1 mg/kg (45 mg to 135 mg) by mouth once daily	<p><u>Orthographic differences</u></p> <ul style="list-style-type: none"> - Subsys has two upstrokes vs. Solodyn has three upstrokes - Subsys has a letter in between the upstroke and the downstroke vs. Solodyn has the upstroke and downstroke next to one another <p><u>Product characteristics</u></p> <ul style="list-style-type: none"> - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. 45 mg, 55 mg, 65 mg, 80 mg, 90 mg, 105 mg, 115 mg, 135 mg) - Frequency of administration (up to every four hours vs. once daily) - Dosage form (spray vs. tablet)

Appendix F:				
Product name with potential for confusion	Similarity to Subsys	Strength	Usual Dose (if applicable)	Product Characteristic, Phonetic, and Orthographic Differences
Subsys (Fentanyl)	N/A	100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray	1 to 2 sprays no more than every four hours as needed	
Sronyx (Levonorgestrel and Ethinyl estradiol)	Orthographic	0.1 mg/0.02 mg oral tablet, 28 tablet dispenser	One tablet by mouth once daily	<p><u>Orthographic differences</u></p> <ul style="list-style-type: none"> - Subsys has two upstrokes vs. Sronyx has one upstroke - Subsys does not have a cross-stroke vs. Sronyx ends with a cross-stroke <p><u>Product characteristics</u></p> <ul style="list-style-type: none"> - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. single strength, not required on prescription) - Frequency of administration (once daily vs. up to every four hours) - Dosage form (spray vs. tablet)
Staxyn (Vardenafil hydrochloride)	Orthographic	10 mg orally disintegrating tablets	One tablet by mouth 60 minutes prior to sexual activity	<p><u>Orthographic differences</u></p> <ul style="list-style-type: none"> - Subsys has no cross-strokes vs. Staxyn has two cross-strokes - Subsys has a letter between the two upstrokes vs. Staxyn has the upstrokes next to one another <p><u>Product characteristics</u></p> <ul style="list-style-type: none"> - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. single strength, not required on prescription) - Frequency of administration (up to every four hours vs. one time) - Dosage form (spray vs. orally disintegrating tablet)

Appendix F:				
Product name with potential for confusion	Similarity to Subsys	Strength	Usual Dose (if applicable)	Product Characteristic, Phonetic, and Orthographic Differences
Subsys (Fentanyl)	N/A	100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray	1 to 2 sprays no more than every four hours as needed	
Sebizon (Sulfacetamide sodium)	Orthographic	10% topical lotion	Apply to affected area two to four times daily until infection has cleared	<i>Product characteristics</i> <ul style="list-style-type: none"> - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. single strength, not required on prescription) - Route of administration (sublingual vs. topical) - Dose (spray vs. amount to cover area) - Dosage form (spray vs. lotion)
Lybrel (Levonorgestrel and Ethinyl estradiol)	Orthographic	90 mcg/20 mcg oral tablet	One tablet by mouth once daily	<i>Orthographic differences</i> <ul style="list-style-type: none"> - Subsys has two upstrokes vs. Lybrel has three upstrokes and ends in an upstroke - The downstroke in Subsys is situated at the end of the name vs. the beginning of the name in Lybrel <i>Product characteristics</i> <ul style="list-style-type: none"> - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. single strength, not required on prescription) - Dosage form (spray vs. tablet) - Frequency of administration (up to every four hours vs. once daily)

Appendix F:				
Product name with potential for confusion	Similarity to Subsys	Strength	Usual Dose (if applicable)	Product Characteristic, Phonetic, and Orthographic Differences
Subsys (Fentanyl)	N/A	100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray	1 to 2 sprays no more then every four hours as needed	
Symlin (Pramlintide acetate)	Orthographic	1000 mcg/mL injection; 1.5 mL, 2.7 mL multidose pen 600 mcg/mL injection; 5 mL vial	- Type 2 Diabetes: 60 mcg to 120 mcg subcutaneously prior to meals - Type 1 Diabetes: 15 mcg to 60 mcg subcutaneously prior to meals	<u>Orthographic differences</u> - The downstroke is situated at the end of the name Subsys vs. the beginning of the name in Symlin - There are three letters after the upstroke in Subsys vs. two letter in Symlin <u>Product characteristics</u> - Dose (1 or 2 sprays vs. 15 mcg, 30 mcg, 45 mcg, 60 mcg, or 120 mcg) - Route of administration (sublingual vs. subcutaneous) - Frequency of administration (up to every 4 hours as needed vs. prior to meals)
Zyban (Bupropion hydrochloride)	Orthographic	150 mg oral tablet	150 mg by mouth for three days then 150 mg by mouth twice daily	<u>Orthographic differences</u> - The downstroke in Subsys appears at the end of the name vs. the beginning of the name in Zyban <u>Product characteristics</u> - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. single strength, not required on prescription) - Dosage form (spray vs. tablet) - Frequency of administration (up to every 4 hours as needed vs. once or twice a day)

Appendix F:				
Product name with potential for confusion	Similarity to Subsys	Strength	Usual Dose (if applicable)	Product Characteristic, Phonetic, and Orthographic Differences
Subsys (Fentanyl)	N/A	100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray	1 to 2 sprays no more than every four hours as needed	
Symbyax (Olanzapine and Fluoxetine hydrochloride)	Orthographic	3 mg/25 mg, 6 mg/25 mg, 6 mg/50 mg, 12 mg/25 mg, 12 mg/50 mg oral tablets	One tablet by mouth once daily in the evening	<p><u>Orthographic differences</u></p> <ul style="list-style-type: none"> - Subsys has one downstroke vs. Symbyax has two downstrokes - Subsys does not have a cross-stroke vs. Symbyax ends with a cross-stroke <p><u>Product characteristics</u></p> <ul style="list-style-type: none"> - Strength(100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. 3 mg/25 mg, 6 mg/25 mg, 6 mg/50 mg, 12 mg/25 mg, 12 mg/50 mg)
Sulamyd (Sulfacetamide sodium) Discontinued, generic available	Orthographic	10% ophthalmic solution	One to two drops in the conjunctival sac(s) of the affected eye(s) every two to three hours	<p><u>Orthographic differences</u></p> <ul style="list-style-type: none"> - Subsys has two upstrokes vs. Sulamyd has three upstrokes and ends with an upstroke <p><u>Product characteristics</u></p> <ul style="list-style-type: none"> - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. single strength, not required on prescription) - Route of administration (sublingual vs. ophthalmic) - Dose (spray vs. drop)

Appendix F:				
Product name with potential for confusion	Similarity to Subsys	Strength	Usual Dose (if applicable)	Product Characteristic, Phonetic, and Orthographic Differences
Subsys (Fentanyl)	N/A	100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray	1 to 2 sprays no more than every four hours as needed	
Folotyn (Pralatrexate)	Orthographic	20 mg/mL, 40 mg/mL injection	30 mg/m ² intravenous push over three to five minutes once a week for six weeks in seven week cycles	<p><u>Orthographic differences</u></p> <ul style="list-style-type: none"> - Subsys has two upstrokes vs. Folotyn has three upstrokes - Subsys has a letter in between the upstroke and downstroke vs. Folotyn has an upstroke and downstroke next to one another - Subsys has no cross-strokes vs. Folotyn has a cross-stroke <p><u>Product characteristics</u></p> <ul style="list-style-type: none"> - Frequency of administration (up to every four hours as needed vs. once a week) - Route of administration (sublingual vs. intravenous) - Dose (one or two sprays vs. 30 mg/m², weight based dose) - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. 20 mg/mL, 40 mg/mL)
Pegasys (Peginterferon alfa-2b)	Orthographic	180 mcg single use vial or prefilled syringe	135 mcg or 180 mcg subcutaneous injection once weekly	<p><u>Orthographic differences</u></p> <ul style="list-style-type: none"> - Subsys has one downstroke vs. Pegasys has two downstrokes - Subsys has two upstrokes vs. Pegasys has one upstroke <p><u>Product characteristics</u></p> <ul style="list-style-type: none"> - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. single strength, not required on prescription) - Route of administration (sublingual vs. subcutaneous) - Frequency of administration (up to every four hours vs. once weekly)

Appendix F:				
Product name with potential for confusion	Similarity to Subsys	Strength	Usual Dose (if applicable)	Product Characteristic, Phonetic, and Orthographic Differences
Subsys (Fentanyl)	N/A	100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray	1 to 2 sprays no more than every four hours as needed	
Gilenya (Fingolimod hydrochloride)	Orthographic	0.5 mg oral capsule	One capsule by mouth once daily	<u>Product characteristics</u> - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. single strength, not required on prescription) - Frequency of administration (up to every four hours vs. once daily) - Dosage form (spray vs. capsule)
Salagen (Pilocarpine hydrochloride)	Orthographic	5 mg, 7.5 mg oral tablets	5 mg by mouth twice daily 5 mg to 10 mg by mouth three times a day 5 mg by mouth four times daily	<u>Orthographic differences</u> - Subsys has one letter after downstroke vs. Salagen has two letters after the downstroke <u>Product characteristics</u> - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. 5 mg, 7.5 mg) - Dosage form (spray vs. tablet)
Selsun (Pyrrithione zinc)	Orthographic	Topical shampoo	Massage on scalp twice weekly	<u>Orthographic differences</u> - Subsys has a downstroke vs. Selsun has no downstroke <u>Product characteristics</u> - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. single strength, not required on prescription) - Frequency of administration (up to every 4 hours as needed vs. twice weekly) - Route of administration (sublingual vs. scalp) - Dosage form (spray vs. shampoo)

Appendix F:

Product name with potential for confusion	Similarity to Subsys	Strength	Usual Dose (if applicable)	Product Characteristic, Phonetic, and Orthographic Differences
Subsys (Fentanyl)	N/A	100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray	1 to 2 sprays no more than every four hours as needed	
Soliris (Eculizumab)	Orthographic	300 mg/30 mL injection, single use vial	600 mg diluted in 120 mL or 900 mg diluted in 180 mL infused intravenously over 35 minutes every seven days	<u>Orthographic differences</u> - Subsys has a downstroke vs. Soliris does not have a downstroke <u>Product characteristics</u> - Dose (one or two sprays vs. 600 mg or 900 mg) - Frequency of administration (up to every four hours as needed vs. every seven days) - Route of administration (spray vs. intravenous)

(b) (4)

Appendix F:				
Product name with potential for confusion	Similarity to Subsys	Strength	Usual Dose (if applicable)	Product Characteristic, Phonetic, and Orthographic Differences
Subsys (Fentanyl)	N/A	100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray	1 to 2 sprays no more then every four hours as needed	
Ionsys (Fentanyl hydrochloride)	Orthographic	Dermal system that administers 40 mcg per dose and contains up to 80 doses	Patient activated system provides doses as needed, apply new patch every 24 hours, only to be used on hospitalized patients, must be discontinued at discharge	<u>Orthographic differences</u> - The 'S' in Subsys does not resemble the 'I' in Ionsys - Subsys has two upstrokes vs. Ionsys has one upstroke <u>Product characteristics</u> - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. single strength, not required on prescription) - Frequency of administration (up to every 4 hours vs. apply patch every 24 hours) - Route of administration (sublingual vs. topical) - Dosage form (spray vs. patch)

Appendix F:				
Product name with potential for confusion	Similarity to Subsys	Strength	Usual Dose (if applicable)	Product Characteristic, Phonetic, and Orthographic Differences
Subsys (Fentanyl)	N/A	100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray	1 to 2 sprays no more then every four hours as needed	
Saphris (Asenapine maleate)	Orthographic and phonetic	5 mg, 10 mg sublingual tablets 5 mg, 10 mg black cherry sublingual tablets	5 mg to 10 mg by mouth twice daily	<p><u>Orthographic differences</u></p> <ul style="list-style-type: none"> - The downstroke in Subsys is located at the end of the name vs. the downstroke in Saphris which is in the beginning - The upstroke in Subsys precedes the downstroke and there is a letter in between the upstroke and downstroke vs. the upstroke directly follows the downstroke in Saphris <p><u>Phonetic differences</u></p> <ul style="list-style-type: none"> - The first syllable “Sub” in Subsys does not sound like the first syllable “Saph” in Saphris - The last syllable in Subsys does not have an “r” sound vs. the last syllable in Saphris starts with an “r” sound <p><u>Product characteristics</u></p> <ul style="list-style-type: none"> - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. 5 mg, 10 mg) - Dosage form (spray vs. tablet)

Appendix F:				
Product name with potential for confusion	Similarity to Subsys	Strength	Usual Dose (if applicable)	Product Characteristic, Phonetic, and Orthographic Differences
Subsys (Fentanyl)	N/A	100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray	1 to 2 sprays no more than every four hours as needed	
Stasis (Multivitamin)	Orthographic and phonetic	Oral capsule	One capsule by mouth once daily	<p><u>Orthographic differences</u></p> <ul style="list-style-type: none"> - Subsys has a downstroke vs. Stasis does not have a downstroke - Subsys has a letter in between the two upstrokes vs. Stasis has two consecutive upstrokes <p><u>Phonetic differences</u></p> <ul style="list-style-type: none"> - The first syllable sound “Sub” in Subsys differs from the first syllable “Sta” in Stasis <p>Product characteristics</p> <ul style="list-style-type: none"> - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. single strength, not required on prescription) - Frequency of administration (up to every four hours vs. once daily) - Dosage form (capsule vs. spray)
Sufenta (Sufentanil citrate)	Orthographic	50 mcg/mL; 1 mL, 2 mL, 5 mL ampules	Intravenous or epidural route	<p><u>Orthographic differences</u></p> <ul style="list-style-type: none"> - Subsys has two upstrokes vs. Sufenta has three upstrokes - Subsys has a downstroke at the end of the name vs. Sufenta has a downstroke in the middle of the name - Subsys has no cross-strokes vs. Sufenta a cross-stroke <p><u>Product characteristics</u></p> <ul style="list-style-type: none"> - Route of administration (sublingual vs. intravenous or epidural) - Dosage form (single dose spray bottle vs. glass ampule)

Appendix F:				
Product name with potential for confusion	Similarity to Subsys	Strength	Usual Dose (if applicable)	Product Characteristic, Phonetic, and Orthographic Differences
Subsys (Fentanyl)	N/A	100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray	1 to 2 sprays no more than every four hours as needed	
Salacyn (Salicylic acid)	Orthographic	6% topical cream, lotion	Apply thoroughly to affected area at bedtime and cover the treated area	<u>Product characteristics</u> <ul style="list-style-type: none"> - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. single strength, not required on prescription) - Route of administration (sublingual vs. topical) - Frequency of administration (up to every four hours vs. once at bedtime) - Dosage form (spray vs. cream, lotion) - Dose (one to two sprays vs. enough to cover affected area)
Solage (Mequinol and Tretinoin)	Orthographic	2%/0.01% topical solution	Apply to affected area using applicator tip twice daily in the morning and evening	<u>Product characteristics</u> <ul style="list-style-type: none"> - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. single strength, not required on prescription) - Route of administration (sublingual vs. topical) - Dose (spray vs. use tip to affected area) - Dosage form (spray vs. solution)

Appendix F:				
Product name with potential for confusion	Similarity to Subsys	Strength	Usual Dose (if applicable)	Product Characteristic, Phonetic, and Orthographic Differences
Subsys (Fentanyl)	N/A	100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray	1 to 2 sprays no more than every four hours as needed	
Subutex (Buprenorphine hydrochloride and Naloxone hydrochloride)	Orthographic and phonetic	2 mg/0.5 mg, 8 mg/2 mg oral tablets	One to two tablets (up to 16 mg) under the tongue once daily	<p><u>Orthographic differences</u></p> <ul style="list-style-type: none"> - Subsys has a downstroke vs. Subutex has no downstroke - Subsys has two upstrokes vs. Subutex has three upstrokes - Subsys does not have a cross-stroke vs. Subutex has two cross-strokes <p><u>Product characteristics</u></p> <ul style="list-style-type: none"> - Frequency of administration (once daily) - Strength (100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg per spray vs. 2 mg/0.5 mg, 8 mg/2 mg)

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/s/

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