

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

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PROPRIETARY NAME REVIEW(S)



**Department of Health and Human Services
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Office of Surveillance and Epidemiology**

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Subject: Proprietary Name Review

Drug Name(s): Exparel (Bupivacaine) Extended-release Liposome Injection
150 mg/10 mL vial and 300 mg/20 mL vial

Sponsor: Pacira Pharmaceuticals, Inc.

OSE RCM #: 2010-2430

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

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EXECUTIVE SUMMARY

This review summarizes the Division of Medication Error Prevention and Analysis (DMEPA) Proprietary Name Analysis for the proposed proprietary name, Exparel (Bupivacaine) Extended-release Liposome Injection. 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, Exparel, acceptable for this product. The proposed proprietary name must be re-reviewed 90 days before the approval of the NDA. 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. The Sponsor will be notified of these findings via letter.

1 BACKGROUND

1.1 INTRODUCTION

The Applicant, Pacira Pharmaceuticals, requested an assessment of the proposed proprietary name, Exparel on November 11, 2010. DMEPA assesses a proposed name regarding its potential name confusion with other proprietary or established drug names in the usual practice settings. Additionally, DMEPA considers the Division of Drug Marketing, Advertising and Communication (DDMAC) promotional assessment of the name.

1.2 REGULATORY HISTORY

DMEPA conducted a review of the proposed name, Exparel, during the IND phase of the application (IND 069198) in OSE Review #2008-2006 dated May 15, 2009. DMEPA found the name acceptable at that time.

On September 28, 2010, the Applicant submitted new drug application (NDA 022496) as a 505(b)(2) for this product citing Marcaine (Bupivacaine Hydrochloride) Injection (NDA 016964) as the reference listed drug

1.3 PRODUCT INFORMATION

Exparel is a long-acting extended-release liposome injection of Bupivacaine indicated for (b) (4) postoperative analgesia following a single dose administration. Exparel is a sterile preservative-free aqueous suspension of multivesicular liposomes and is administered by local infiltration into the surgical wound prior to closure in patients 18 years of age or older. Exparel is intended for single-dose administration (b) (4)

(b) (4)

(b) (4)

Exparel should be injected slowly into the soft tissue via local administration into the surgical wound using a 25-gauge or larger bore needed, with appropriate technique to verify that no accidental intravascular injection has occurred (i.e., the syringe plunger should be pulled back often and the aspirate checked for blood). The maximum dose of Exparel should not exceed (b) (4) Exparel can be administered undiluted or diluted to up to 1 mg/mL (i.e. 1:14 dilution by volume) with

preservative-free 0.9% normal saline for injection. Vials of Exparel should be inverted to re-suspend the particles immediately prior to withdrawal from the vial and Exparel should be used within four hours of preparation in the syringe. Some physicochemical incompatibilities exist between Exparel and several other drugs which can result in a rapid increase in free (unencapsulated) Bupivacaine, altering Exparel characteristics. Therefore, the admixing of Exparel with other drugs prior to administration is not recommended.

Exparel is available in a (b) (4) strength and is packaged in vials of (b) (4). Exparel should be stored refrigerated between 2° to 8°C (36° to 46°F) and should not be frozen or exposed to high temperatures. Different formulations of Bupivacaine are not bioequivalent even if the milligram strength is the same. Therefore, it is not possible to convert dosing from any other formulation of Bupivacaine to Exparel.

2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment for all proprietary names. Sections 2.1, 2.2, and 2.3 identify specific information associated with the methodology for the proposed proprietary name, (b) (4).

2.1 SEARCH CRITERIA

The DMEPA safety evaluator considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Table 2.

For this review, particular consideration was given to drug names beginning with the letter ‘E’ 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 ‘Exparel’, the DMEPA safety evaluator also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (seven letters), upstrokes (two, capital letter ‘E’ and lower case letter ‘l’), downstrokes (one lower case letter ‘p’), dotted letters (none) and cross-strokes (one lower case letter ‘x’). Additionally, several letters in Exparel may be vulnerable to ambiguity when scripted (see Appendix B). As a result, the DMEPA safety evaluator also considers these alternate appearances when identifying drug names that may look similar to Exparel.

When searching to identify potential names that may sound similar to Exparel, DMEPA staff searches for names with similar number of syllables (three), stresses (EX par el, ex PAR el and ex par EL), and placement of vowel and consonant sounds. The Sponsor’s intended pronunciation of the proprietary name (eks-puh-rel) was also taken into consideration. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary (See Appendix B). Moreover, names are often mispronounced or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

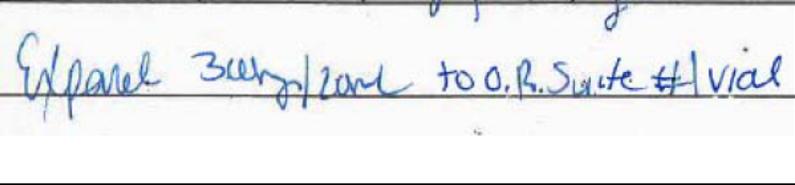
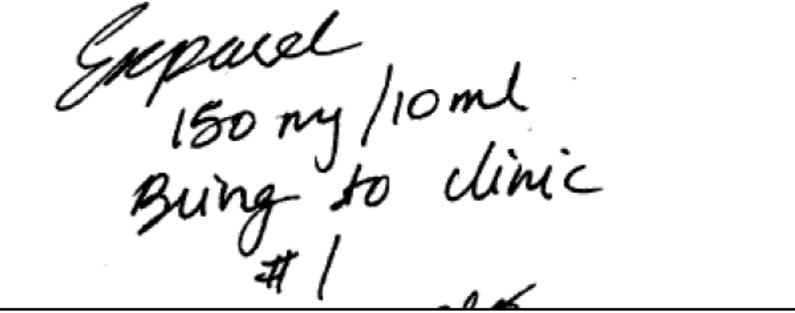
¹ Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at <http://www.ismp.org/Tools/confuseddrugnames.pdf>

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

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. Exparel Rx Study (conducted on December 7, 2010)

HANDWRITTEN MEDICATION ORDER	VERBAL PRESCRIPTION
<p><u>Inpatient Medication Order :</u></p> 	<p>Exparel 150 mg/10 mL vial Bring to clinic Dispense one vial</p>
<p><u>Outpatient Medication Order:</u></p> 	

3 RESULTS

The following sections describe findings of DMEPA database searches, Expert Panel Discussion (EPD) and Safety Evaluator Risk Assessment.

3.1 DATABASE AND INFORMATION SOURCES

The DMEPA safety evaluator searches yielded a total of 18 names as having some similarity to the name, Exparel.

Thirteen of the 18 names (Cefprozil, Easprin, Elspar, Enoxaparin, Enpresse, Enteral, Eskalith, Espocol, Estradiol, Ethiodol, Exjade, Factrel and Synarel) were thought to look like Exparel. Five names (Enalapril, Enbrel, Estriol, Exterol and Isuprel) were thought to look and sound like Exparel.

A search of the United States Adopted Names (USAN) stems list on January 10, 2011, did not identify any USAN stems in the proposed proprietary name, Exparel.

3.2 EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMEPA safety evaluator (See Section 3.1 above) and did not note any additional names thought to have orthographic or phonetic similarity to Exparel.

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 34 practitioners responded to the prescription studies. None of the responses overlapped with currently marketed products. Twelve (n=12) respondents interpreted the name correctly as ‘Exparel’, with correct interpretation occurring in both the inpatient written study and the voice study. The remainder of the responses misinterpreted the drug name. Common misinterpretations included the letter ‘x’ being interpreted as the letter ‘n’ and the letter ‘r’ being interpreted as the letter ‘c’. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 COMMENTS FROM THE REVIEW DIVISION

3.4.1 Initial Phase of Review

In response to the OSE November 26, 2010 e-mail, the Division of Anesthesia and Analgesia Products (DAAP) stated that they have no issues with the proposed name.

3.4.2 Midpoint of Review

On February 3, 2011, DMEPA notified DAAP via e-mail that we had no objections to the proposed proprietary name, Exparel. Per e-mail correspondence from DAAP on February 4, 2011, they indicated that they had no additional comments or concerns with our assessment of the proposed proprietary name, Exparel.

3.5 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator resulted in the identification of seven additional names including Campral, Clozaril, Desyrel, Drixoral, Estrogel and (b) (4) thought to look similar to Exparel, and Resporal, thought to like and sound similar to Exparel and represent a potential source of drug name confusion.

Thus, DMEPA identified and evaluated 25 names for their potential similarity to the proposed name, Exparel. Eighteen (n=18) names from the database searches and seven (n=7) names from the safety evaluator searches.

4 DISCUSSION

This proposed name, Exparel, 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 did not have promotional concerns with the proposed name, Exparel. The Division of Anesthesia and Analgesia Products (DAAP) and DMEPA concurred with DDMAC’s assessment.

4.2 SAFETY ASSESSMENT

DMEPA identified and evaluated 25 names for their potential similarity to the proposed name, Exparel. No other aspects of the name were identified as a source of potential confusion and error.

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Five of the 25 names were eliminated from further evaluation for the following reasons: one name was found to be a device, one name was found to be a compounding agent, two names are discontinued products with no generic products available on the market and one product is available in the United Kingdom only. (See Appendices D for details).

Failure mode and effect analysis (FMEA) was then applied to determine if the proposed proprietary name could potentially be confused with the remaining 20 names and lead to medication errors. This analysis determined that the name similarity between Exparel and all 20 of the identified names was unlikely to result in medication error for the reasons presented in Appendix E.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Exparel, is not vulnerable to name confusion that could lead to medication errors, nor is it considered promotional. Thus, the Division of Medication Error Prevention and Analysis has no objections to the proprietary name, Exparel, at this time. The Sponsor will be notified via letter.

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.

5.1 COMMENTS TO THE SPONSOR

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

The proposed proprietary name must 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.

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

6 REFERENCES

Previous OSE Reviews

Miller, C.A., Exparel Proprietary Name Review, OSE #2008-2006 dated May 15, 2009.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

USPTO provides information regarding patent and trademarks.

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

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

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

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

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

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

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

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

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

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

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

APPENDICES

Appendix A:

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

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.

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 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.

Table 2. Criteria used to identify drug names that look- or sound-similar to a proposed proprietary name.

Type of similarity	Considerations when searching the databases		
	Potential causes of drug name similarity	Attributes examined to identify similar drug names	Potential Effects
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	<ul style="list-style-type: none"> Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

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

throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

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

2. CDER Expert Panel Discussion

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

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

3. 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 staff's risk assessment concurs or differs with the findings. When the proprietary name risk assessments differ, the DMEPA staff provides 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

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

would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

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

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

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

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

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

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the 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 the name Exparel	Scripted may appear as	Spoken may be interpreted as
Capital ‘E’	Capital C	Any vowel
Letters ‘Ex’	En, Er, Cen, Cex	‘S’ sound
Lower case ‘p’	f, g, j, q, or x	‘B’ sound
Lower case ‘a’	Any lowercase letter that does not have a upstroke or downstroke	Any vowel sound
Lower case ‘r’	Any lowercase letter that does not have a upstroke or downstroke	
Lower case ‘e’	i, l, t	Any vowel
Lower case ‘l’	e, i, t, b	

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME:		STRENGTH:	USUAL DOSE:
Exparel Bupivacaine (b) (4) liposome injection		(b) (4) (b) (4) (b) (4)	(b) (4)
FAILURE MODE:		CAUSES:	PREVENTION OF FAILURE MODE
Name Confusion		(Potential reasons for name confusion that could lead to medication error)	(Reasons why the risk of medication error is minimized)
1	Campral (Acamprosate Calcium) Tablets Strength: 333 mg Dose: Two tablets (668 mg) three times daily	Orthographic similarities: The first letter ‘C’ can appear like the first letter ‘E’, the letter ‘m’ can appear like the letter ‘x’, both names contain the downstroke letter ‘p’ and the upstroke letter ‘l’ similarly placed in the names. Overlapping product characteristics: Possible numeric overlap in dose	Multiple strengths versus one strength No overlap in dose Route of administration: Oral versus wound infiltration Frequency of administration: Three times daily versus one time use during operative procedure
2	Cefprozil (Cefprozil) Tablets and Oral Suspension Strength: 250 mg and 500 mg tablets 125 mg/5 mL and 250/5 mL oral suspension Dose: 250 mg to 500 mg every twelve hours 7.5 mg/kg to 20 mg/kg every twelve to twenty-four hours	Orthographic similarities: The first letter ‘C’ can appear like the first letter ‘E’, both names contain a downstroke letter ‘p’ similarly placed and end with the upstroke letter ‘l’.	Orthographic differences in the names, along with multiple varying product characteristics listed below, minimize the potential for confusion. Orthographic differences: Exparel contains seven letters while Cefprozil contains nine letters making the name appear longer when scripted. Cefprozil also contains the letter ‘f’, which can be presented as an upstroke or a downstroke, in the third letter position of the name in conjunction with the downstroke letter ‘p’ presented in both names. Differentiating product characteristics: Dosage form: Oral tablet or suspension versus injection No overlap in strength or dose Route of administration: Oral versus wound infiltration Frequency of administration: Once or twice daily versus one time use during operative procedure

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME:		STRENGTH:	USUAL DOSE:
Exparel Bupivacaine (b) (4) liposome injection		(b) (4) (b) (4) (b) (4)	(b) (4)
FAILURE MODE:		CAUSES:	PREVENTION OF FAILURE MODE
Name Confusion		(Potential reasons for name confusion that could lead to medication error)	(Reasons why the risk of medication error is minimized)
3	Clozaril (Clozapine) Tablets Strength: 25 mg and 100 mg Dose: 12.5 mg to 100 mg once or twice daily	Orthographic similarities: The letter ‘C’ can appear like the letter ‘E’, the third letter ‘z’ can appear like the letter ‘p’ if scripted with a downstroke, and the letters ‘aril’ are similar to the letters ‘arel’.	Orthographic differences in the names, along with multiple varying product characteristics listed below, minimize the potential for confusion. Orthographic differences: There is an upstroke letter ‘l’ in the second letter position of Clozaril that is not present in the name Exparel. Differentiating product characteristics: Dosage form: Tablet versus Injection No overlap in strength or dose Route of administration: Oral versus Wound infiltration Frequency of administration: Once or twice daily versus one time use during operative procedure
4	Desyrel (Trazodone Hydrochloride) Tablet Strength: 150 mg and 300 mg Dose: 150 mg to 300 mg per day in divided doses	Orthographic similarities: The downstroke letter ‘y’ can appear like the downstroke letter ‘p’ when scripted and both names end with the letters ‘rel’ Overlapping product characteristics: Numeric overlap in strength and dose (150 mg and 300 mg)	Orthographic differences in the names, along with multiple varying product characteristics listed below, minimize the potential for confusion. Orthographic differences: The first letter ‘D’ appears different than the first letter ‘E’ when scripted. Differentiating product characteristics: Dosage form: Oral tablet versus Injection Route of administration: Oral versus wound infiltration Frequency of administration: Divided daily doses versus one time use during operative procedure

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME:		STRENGTH:	USUAL DOSE:
Exparel Bupivacaine (b) (4) liposome injection		(b) (4) (b) (4) (b) (4)	(b) (4)
FAILURE MODE:		CAUSES:	PREVENTION OF FAILURE MODE
Name Confusion		(Potential reasons for name confusion that could lead to medication error)	(Reasons why the risk of medication error is minimized)
5	Drixoral (Dexbrompheniramine Maleate and Pseudoephedrine Sulfate) Tablet Strength: 6 mg/120 mg Dose: One tablet every six to eight hours	Orthographic similarities: Both names contain a cross-stroke letter 'x' and end similarly with 'oral' versus 'arel'.	Orthographic differences in the names along with multiple varying product characteristics listed below minimize the potential for confusion. Orthographic differences: The first letter 'D' appears different than the first letter 'E', the letter 'x' appears in different letter positions of the names (fourth versus second), and there is a downstroke letter 'p' in the name Exparel that is not present in the name Drixoral Differentiating product characteristics: Dosage form: Tablet versus Injection No overlap in strength or dose Route of administration: Oral versus wound infiltration Frequency of administration: Every six to eight hours versus one time use during operative procedure
6	Easprin (Aspirin) Delayed-release tablets Strength: 975 mg Dose: One tablet three to four times daily	Orthographic similarities: Both names begin with the letter 'E' and contain the downstroke letter 'p' and the letter 'r' similarly placed in the names.	Orthographic differences in the names along with multiple varying product characteristics listed below minimize the potential for confusion. There is a cross-stroke letter 'x' in the second letter position and an upstroke letter 'l' in the last letter position of the name Exparel that are not present in the name Easprin. Differentiating product characteristics: Dosage form: Tablet versus Injection No overlap in strength or dose Route of administration: Oral versus Wound infiltration Frequency of administration: Three to four times daily versus one time use during operative procedure

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME:		STRENGTH:	USUAL DOSE:
Exparel Bupivacaine (b) (4) liposome injection		(b) (4) (b) (4) (b) (4)	(b) (4)
FAILURE MODE:		CAUSES:	PREVENTION OF FAILURE MODE
Name Confusion		(Potential reasons for name confusion that could lead to medication error)	(Reasons why the risk of medication error is minimized)
7	Elspar (Asparaginase) For Injection Strength: 10,000 international units (IU) per vial Dose: 6,000 IU/m ² three times weekly IV or IM	Orthographic similarities: Both names begin with the letter ‘E’ and contain the downstroke letter ‘p’ similarly placed in the names. Overlapping product characteristics: Similar dosage form: Injection versus Powder for Injection Numeric overlap in the dose (600 mg versus 6000 IU)	Orthographic differences in the names along with a different frequency of administration minimize the potential for confusion. Orthographic differences: Elspar contains six letters while Exparel contains seven letters and appears longer when scripted due to the cross-stroke letter ‘x’ in the second letter position that is not present in Elspar. Additionally, there is an upstroke letter ‘l’ in the last letter position of Exparel that is not present in the name Elspar. Differentiating product characteristics: Frequency of administration: Three times weekly versus one time use during operative procedure
8	Enalapril (Enalapril Maleate) Tablet Strength: 2.5 mg, 5 mg, 10 mg, 20 mg Dose: 2.5 mg to 40 mg once daily	Orthographic and phonetic similarities: Both names begin with the letter ‘E’, contain a downstroke letter ‘p’ and end similarly with the letters ‘ril’ versus ‘rel’. The first ‘E’ sound the last syllable sound ‘pril’ versus ‘prel’ sound similar. Overlapping product characteristics: Numeric overlap in dose (20 mg versus 20 mL and 40 mg versus 40 mL)	Orthographic differences in the names along with multiple varying product characteristics listed below minimize the potential for confusion. Orthographic differences: There are seven letters in the name Exparel while there are nine letters in the name Enalapril, making it appear longer when scripted. The downstroke letter ‘p’ appears in different locations of the name (third letter position versus sixth letter position). There is an upstroke letter ‘l’ in the fourth letter position of Enalapril that is not present in the name Exparel. Additionally, there are three syllables in Exparel while there are four syllables in Enalapril and the middle sounds ‘nala’ sounds different than ‘xpar’ when pronounced. Differentiating product characteristics: Dosage form: Tablet versus Injection Route of administration: Oral versus wound infiltration

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME:		STRENGTH:	USUAL DOSE:
Exparel Bupivacaine (b) (4) liposome injection		(b) (4) (b) (4) (b) (4)	(b) (4)
FAILURE MODE:		CAUSES:	PREVENTION OF FAILURE MODE
Name Confusion		(Potential reasons for name confusion that could lead to medication error)	(Reasons why the risk of medication error is minimized)
9	Enbrel (Etanercept) Injection Strength: 25 mg/vial and 50 mg/vial Dose: 25 mg to 50 mg once or twice weekly; Peds: 0.8 mg/kg per week	Orthographic similarities: Both names begin with the letter 'E' and end with the letters 'rel' Overlapping product characteristics: Dosage form: Injection	Orthographic differences in the names along with multiple varying product characteristics listed below minimize the potential for confusion. Orthographic differences: There is a downstroke letter 'p' in the third letter position of Exparel not present in Enbrel and there is an upstroke letter 'b' in Enbrel that is not present in Exparel, providing orthographic distinction. Differentiating product characteristics: No overlap in strength or dose Frequency of administration: Once or twice weekly versus one time use during operative procedure
10	Enoxaparin (Enoxaparin Sodium) Injection Strength: 30 mg/0.3 mL, 40 mg/0.4 mL, 60 mg/0.6 mL, 80 mg/0.8 mL and 100 mg/mL Dose: 30 mg to 40 mg once daily; 30 mg every twelve hours or 1 mg/kg every twelve hours	Orthographic similarities: Both names begin with the letter 'E' and contain a downstroke letter 'p' Overlapping product characteristics: Numeric overlap in strength and dose (30 mg versus 300 mg, 60 mg versus 600 mg, and 40 mg versus 40 mL) Dosage form: Injection	Orthographic differences in the names along with multiple varying product characteristics listed below minimize the potential for confusion. Orthographic differences: Exparel has seven letters in the name Exparel while there are ten letters in the name Enoxaparin, making the name appear longer when scripted. Although both names contain a downstroke letter 'p', the letter appears in the third letter position of the name Exparel while it appears in the sixth letter position of the Enoxaparin. Additionally, there is an upstroke letter 'l' in the last letter position of Exparel that is not present in the name Enoxaparin. Differentiating product characteristics: Frequency of administration: Once daily or every twelve hours versus one time administration during an operative procedure.

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME:		STRENGTH:	USUAL DOSE:
Exparel Bupivacaine (b) (4) liposome injection		(b) (4) (b) (4) (b) (4)	(b) (4)
FAILURE MODE:		CAUSES:	PREVENTION OF FAILURE MODE
Name Confusion		(Potential reasons for name confusion that could lead to medication error)	(Reasons why the risk of medication error is minimized)
11	Enpresse (Ethinyl Estradiol and Levonorgestrel) Tablet Strength: One 21-day or 28-day packet containing 0.03 mg, 0.04 mg, and 0.03 mg Ethinyl Estradiol and 0.05 mg, 0.75 mg, and 0.125 mg of Levonorgestrel Dose: One tablet once daily	Orthographic similarities: Both names begin with the letter ‘E’, the second letter ‘n’ can appear like the second letter ‘x’ and both names contain a downstroke letter ‘p’ in the third letter position of the names.	Orthographic differences in the names along with multiple varying product characteristics listed below minimize the potential for confusion. Orthographic differences: The endings of the name appear different ‘esse’ versus ‘arel’ providing orthographic distinction when scripted. Differentiating product characteristics: Dosage form: Tablet versus Injection No numeric overlap in strength or dose Route of administration: Oral versus wound infiltration Frequency of administration: Once daily versus one time administration during operative procedure
12	Eskalith (Lithium Carbonate) Capsules and Tablets Strength: 300 mg Dose: 300 mg to 600 mg three times daily	Orthographic similarities: Both names begin with the letter ‘E’, the second letter ‘s’ can appear like the second letter ‘x’ and the last upstroke letter ‘h’ can appear like the last upstroke letter ‘l’ when scripted. Overlapping product characteristics: Dose Overlap: 300 mg and 600 mg	Orthographic differences in the names along with multiple varying product characteristics listed below minimize the potential for confusion. Orthographic differences: There is an upstroke letter ‘k’ in the third letter position of Eskalith while there is a downstroke letter ‘p’ in the third letter position of Exparel. Additionally, there is an upstroke letter ‘l’ in the fifth letter position and an upstroke cross-stroke letter ‘t’ in the next to the last letter position of Eskalith that are not present in the name Exparel, providing added orthographic distinction. Differentiating product characteristics: Dosage form: Tablet or capsule versus injection Route of administration: Oral versus wound infiltration Frequency of administration: Three times daily versus one time use during an operative procedure

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME: Exparel Bupivacaine (b) (4) liposome injection	STRENGTH: (b) (4) (b) (4) (b) (4)	USUAL DOSE: (b) (4)
FAILURE MODE: Name Confusion	CAUSES: (Potential reasons for name confusion that could lead to medication error)	PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)
<p>13</p> <p>Especol (Fructose, Dextrose and Phosporic Acid) Oral Solution</p> <p>Strength: 1.87 grams, 1.87 grams and 21.5 mg per 5 mL</p> <p>Dose: 5 mL to 30 mL every three hours as needed for nausea</p>	<p>Orthographic and phonetic similarities:</p> <p>Both names begin with the letter ‘E’, the second letter ‘s’ can appear like the second letter ‘x’, both names contain the downstroke letter ‘p’ in the third letter position and both names end similarly with ‘ol’ versus ‘el’. Additionally, both names have three syllables and the first syllable ‘Es’ can sound like the first syllable ‘Ex’, the second syllable ‘pe’ can sound like the second syllable ‘par’ and the ending of the last syllable ‘ol’ can sound like ‘el’.</p> <p>Overlapping product characteristics:</p> <p>Potential dose overlap with (b) (4)</p>	<p>Multiple varying product characteristics listed below minimize the potential for confusion.</p> <p>Orthographic differences:</p> <p>Dosage form: Oral solution versus injection</p> <p>Route of administration: Oral versus wound infiltration</p> <p>Frequency of administration: Every three hours versus one time administration during an operative procedure</p>

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME: Exparel Bupivacaine (b) (4) liposome injection	STRENGTH: (b) (4) (b) (4) (b) (4)	USUAL DOSE: (b) (4)
FAILURE MODE: Name Confusion	CAUSES: (Potential reasons for name confusion that could lead to medication error)	PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)
<p>14 Estradiol</p> <p>(Estradiol) Transdermal Patch</p> <p>Strength: 0.025 mg, 0.0375 mg, 0.06mg, 0.075 mg, 0.05 mg and 0.1 mg per 24 hours</p> <p>Dose: One patch – Apply once weekly</p>	<p>Orthographic similarities:</p> <p>Both names begin with the letter ‘E’, the second letter ‘s’ can appear like the second letter ‘x’ and ending letters ‘iol’ can appear like the ending letters ‘rel’.</p> <p>Overlapping product characteristics:</p> <p>Numeric overlap in dose (b) (4)</p>	<p>Orthographic differences in the names along with multiple varying product characteristics listed below minimize the potential for confusion.</p> <p>Orthographic differences:</p> <p>There is an upstroke/cross-stroke letter ‘t’ in the third letter position of Estradiol while there is a downstroke letter ‘p’ in the third letter position of Exparel. Additionally, there is an upstroke letter ‘d’ in Estradiol that is not present in Exparel.</p> <p>Differentiating product characteristics:</p> <p>Dosage form: Topical transdermal patch versus injection</p> <p>Route of administration: Topical versus wound infiltration</p> <p>Frequency of administration: Once weekly versus one time administration during an operative procedure</p>

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME:		STRENGTH:	USUAL DOSE:
Exparel Bupivacaine (b) (4) liposome injection		(b) (4) (b) (4) (b) (4)	(b) (4)
FAILURE MODE:		CAUSES:	PREVENTION OF FAILURE MODE
Name Confusion		(Potential reasons for name confusion that could lead to medication error)	(Reasons why the risk of medication error is minimized)
15	Estrogl (Estradiol) Gel Strength: 0.06 % Dose: 1.25 grams single dose (Depress pump twice for 93-gram pump and three times for 25-gram or 50-gram pump daily)	Orthographic similarities: Both names begin with the letter 'E', the second letter 's' can appear like the second letter 'x' and both names end with the letters 'el'.	Orthographic differences in the names along with multiple varying product characteristics listed below minimize the potential for confusion. Orthographic differences: There is a downstroke letter 'p' in the third letter position of Estrogl while there is an upstroke/cross-stroke letter 't' in the third letter position of Estrogl. There is also a downstroke letter 'g' in the sixth letter position of Estrogl that is not present in Exparel. Differentiating product characteristics: Dosage form: Topical gel versus injection No overlap in strength or dose Route of administration: Topical versus wound infiltration Frequency of administration: Daily versus one time administration during an operative procedure
16	Exjade (Deferasirox) Tablets for Oral suspension Strength: 125 mg, 250 mg, 500 mg Dose: 20 mg/kg once daily	Orthographic similarities: Both names begin with the letters 'Ex' and the third downstroke letter 'j' can appear like the third downstroke letter 'p'.	Orthographic differences in the names along with multiple varying product characteristics listed below minimize the potential for confusion. There is an upstroke letter 'l' in the last letter position of Exparel that is not present in Exjade. Differentiating product characteristics: Dosage form: Tablet versus injection No overlap in strength or dose Route of administration: Oral versus wound infiltration Frequency of administration: Once daily versus one time use during operative procedure

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

<p>PROPOSED NAME: Exparel Bupivacaine (b) (4) liposome injection</p>	<p>STRENGTH: (b) (4) (b) (4) (b) (4)</p>	<p>USUAL DOSE: (b) (4)</p>
<p>FAILURE MODE: Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>
<p>17</p>	<p>(b) (4)</p>	

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

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME: Exparel Bupivacaine (b) (4) liposome injection	STRENGTH: (b) (4) (b) (4) (b) (4)	USUAL DOSE: (b) (4)
FAILURE MODE: Name Confusion	CAUSES: (Potential reasons for name confusion that could lead to medication error)	PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)
<p>18 Isuprel (Isoproterenol Hydrochloride) Injection</p> <p>Strength: 0.2 mg and 1 mg ampules</p> <p>Dose: 0.02 mg to 0.06 mg initial dose (0.5 mL to 1 mL diluted solution); 5 mcg/min intravenous; 0.2 mg intramuscular, subcutaneous or intracardiac</p>	<p>Orthographic and phonetic similarities:</p> <p>The first letter ‘I’ can appear like the first letter ‘E’ when scripted, both names contain a downstroke letter ‘p’ and end with the letters ‘rel’. Both names end with the ‘el’ sound.</p> <p>Overlapping product characteristics:</p> <p>Injection dosage form</p>	<p>Orthographic and phonetic differences in the names along with multiple varying product characteristics listed below minimize the potential for confusion.</p> <p>There is variation in the ‘Is’ pronounced with a hard ‘I’ sound and a soft ‘s’ versus the soft ‘Eh’ sound and hard ‘x’ in ‘Ex’, along with the second syllable hard ‘u’ sound versus ‘ah’ sound.</p> <p>There is variation in the placement of certain similar letters that provide orthographic distinction including the downstroke letter ‘p’ in the third versus fourth letter position and the letters ‘par’ in Exparel versus ‘pr’ in Isuprel.</p> <p>Differentiating product characteristics:</p> <p>There is no numeric overlap in dose: 0.5 mL to 1 mL for Isuprel versus (b) (4) for Exparel</p> <p>There is no overlap in strengths between the two products and there is a considerable variation in the associated volume to be administered between the two products (0.5 mL to 1 mL for Isuprel versus a much larger volume (b) (4) for Exparel).</p>

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME:		STRENGTH:	USUAL DOSE:
Exparel Bupivacaine (b) (4) liposome injection		(b) (4) (b) (4) (b) (4)	(b) (4)
FAILURE MODE:		CAUSES:	PREVENTION OF FAILURE MODE
Name Confusion		(Potential reasons for name confusion that could lead to medication error)	(Reasons why the risk of medication error is minimized)
19	Resporal (Dexbrompheniramine Maleate and Pseudoephedrine Sulfate) Tablet Strength: 6 mg/120 mg Dose: One tablet every six to eight hours	Orthographic and phonetic similarities: The letters ‘sp’ can appear like the letters ‘xp’ and both names have similar endings ‘ral’ versus ‘rel’. Both names have three syllables ‘esporal’ sounds similar to ‘xparel’ when pronounced.	Orthographic and phonetic differences in the names along with multiple varying product characteristics listed below minimize the potential for confusion. Orthographic and phonetic differences: The first letter ‘R’ in Resporal appears and sounds different than the first letter ‘E’ in Exparel. Differentiating product characteristics: Dosage form: Tablet versus injection No overlap in strength or dose Route of administration: Oral versus wound infiltration Frequency of administration: Every six to eight hours versus one time use during an operative procedure
20	Synarel (Nafarelin Acetate) Nasal Spray Strength: 2 mg/mL 200 mcg per actuation Dose: 400 mcg daily; 200 mcg (one spray) in nostril in the morning and one spray in the evening	Orthographic similarities: The downstroke letter ‘y’ in Synarel can appear like the downstroke letter ‘p’ in Exparel and both names end with the letters ‘arel’. Overlapping product characteristics:	Orthographic differences in the names along with multiple varying product characteristics listed below minimize the potential for confusion. Orthographic differences: The first letter ‘S’ in synarel appears different when scripted than the first letter ‘E’ in Exparel. Differentiating product characteristics: Dosage form: Topical nasal spray versus injection No overlap in strength or dose Route of administration: Topical/nasally versus Frequency of administration: Twice daily versus one time use during an operative procedure

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/s/

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