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APPLICATION NUMBER:

22580Orig1s000

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: June 14, 2012

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Drug Name and Strength(s): Qsymia (Phentermine and Topiramate) Extended-release
Capsules, 3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg,
15 mg/92 mg

Application Type/Number: NDA 022580

Applicant/Sponsor: Vivus Inc.

OSE RCM #: 2012-1268

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

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Qsymia, from a safety and promotional perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively.

1.1 REGULATORY HISTORY

The proposed proprietary name, Qsymia (Phentermine and Topiramate) Extended-release Capsules is the subject of a 505 (b)(1) application, NDA 022580 submitted to the FDA on December 29, 2009. The name, Qsymia, is the fourth proposed proprietary name for the product submitted by the Applicant on May 31, 2012.

The first proposed proprietary name, Qnexa (Phentermine and Topiramate) Extended release, was found acceptable by DMEPA in OSE Review 2009-2013, dated February 17, 2010. The applicant received a complete response letter from the Agency dated, October 28, 2010. On February 2, 2012, the Applicant submitted a request for proprietary name review as part of a class 2 resubmission. On April 17, 2012, in OSE RCM# 2012-187, DMEPA found the proposed proprietary name, Qnexa unacceptable (b) (4)

A second proprietary name, Qsiva, was proposed and subsequently withdrawn by the Applicant after DMEPA expressed concern that the proposed name could be confused with (b) (4). The Applicant proposed a third proprietary name, (b) (4) but this name was found by the Office of Prescription Drug Promotion (OPDP) and the Division of Metabolism and Endocrinology Products (DMEP) (b) (4). This concern was communicated to the Applicant during a May 25, 2012 teleconference and the firm subsequently withdrew the name from consideration.

1.2 PRODUCT INFORMATION

The following product information is provided in the February 2, 2012 proprietary name submission.

- Active Ingredient: Phentermine and Topiramate Extended-release
- Indication of Use: Adjunct to diet and exercise to aid in weight loss in obese patients or overweight patients
- Route of Administration: Oral
- Dosage Form: Extended-release Capsules
- Strength: 3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, and 15 mg/92 mg
- Dose and Frequency: The recommended starting dose is 3.75 mg/23 mg by mouth once daily. The dose can be titrated up to a maximum dose of 15 mg/92 mg by mouth once daily.

- How Supplied: Bottles containing 14 and 30 capsules
- Distribution: This product may have specialized distribution depending on the ETASUs agreed upon in the REMS. However, we considered the potential for confusion with and without specialized distribution in the event that ETASUs for the distribution of this product are not needed.
- Storage: Store at room temperature (15°C to 25°C; 59°F to 77°F)
- Container and Closure Systems: HDPE bottles (b) (4)

2 RESULTS

The following sections provide the information obtained and considered in the evaluation of the proposed proprietary name.

2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Metabolism and Endocrinology Products (DMEP) concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following aspects of the name were considered in the overall safety evaluation.

2.2.1 *United States Adopted Names (USAN) SEARCH*

The June 1, 2012 search of the United States Adopted Name (USAN) stems did not identify that a USAN stem is present in the proposed proprietary name.

2.2.2 *Components of the Proposed Proprietary Name*

This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 *FDA Name Simulation Studies*

Eighteen practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with or appear or sound similar to any currently marketed products. In the written studies, 2 of 10 participants correctly interpreted the prescription. Common misinterpretations in the written studies include: 'Os', 'Op' for 'Qs' and 'Opz' for 'Qsy' respectively. In the voice study, participants commonly misinterpreted 'G' and 'J' for 'Q'. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.4 *Comments from Other Review Disciplines*

In response to the OSE, May 31, 2012 e-mail, the Division of Metabolism and Endocrinology Products (DMEP) did not forward any comments or concerns relating to the proposed name at the initial phase of the proprietary name review.

2.2.5 Failure Mode and Effects Analysis of Similar Names

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in the proposed proprietary name, Qsymia. **Table 1** lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Qsymia identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, Other Disciplines, and FDA Name Simulation Studies.

Look Similar					
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
Aczone	EPD	Arzerra	EPD	Aspirin	EPD
Gemzar	EPD	Oscimin	EPD	Orzel	EPD
(b) (4)	EPD	Quixin	EPD		
Sound Similar					
None					
Look and Sound Similar					
(b) (4)	EPD	Cimzia	EPD		

Our analysis of the 10 names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics. We determined 10 names will not pose a risk for confusion as described in Appendix D through E.

2.2.7 Communication of DMEPA’s Final Decision to Other Disciplines

DMEPA communicated our findings to the Division of Metabolism and Endocrinology Products (DMEP) via e-mail on June 4, 2012. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Metabolism and Endocrinology Products on June 4, 2012, they stated they have no additional concerns with the proposed proprietary name, Qsymia.

3 CONCLUSIONS

The proposed proprietary name is acceptable from both a promotional and safety perspective.

If you have further questions or need clarifications, please contact Ermias Zerislassie, OSE project manager, at 301-796-0097.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Qsymia, and have concluded that this name is acceptable. However, if any of the proposed product characteristics as stated in your February 2, 2012 submission are altered, DMEPA rescinds this finding and the name must be resubmitted for review.

Additionally, the proposed proprietary name must be re-reviewed 90 days prior to approval of the NDA. The conclusions upon re-review are subject to change.

4 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. This database also lists the orphan drugs.

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

USPTO provides information regarding patent and trademarks.

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

Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common,

combination, nutraceutical and nutritional products. It also provides a keyword search engine.

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

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

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

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

11. *Access Medicine (www.accessmedicine.com)*

Access Medicine® from McGraw-Hill contains full-text information from approximately 60 titles; it includes tables and references. Among the titles are: Harrison's Principles of Internal Medicine, Basic & Clinical Pharmacology, and Goodman and Gilman's The Pharmacologic Basis of Therapeutics.

12. *USAN Stems (<http://www.ama-assn.org/ama/pub/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml>)*

USAN Stems List contains all the recognized USAN stems.

13. *Red Book (www.thomsonhc.com/home/dispatch)*

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

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

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

15. *Medical Abbreviations (www.medilexicon.com)*

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

16. *CVS/Pharmacy (www.CVS.com)*

This database contains commonly used over the counter products not usually identified in other databases.

17. *Walgreens (www.walgreens.com)*

This database contains commonly used over the counter products not usually identified in other databases.

18. Rx List (www.rxlist.com)

RxList is an online medical resource dedicated to offering detailed and current pharmaceutical information on brand and generic drugs.

19. Dogpile (www.dogpile.com)

Dogpile is a [Metasearch](#) engine that searches multiple search engines including Google, Yahoo! and Bing, and returns the most relevant results to the search.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment considers the promotional and safety aspects of a proposed proprietary name. The promotional review of the proposed name is conducted by OPDP. OPDP evaluates proposed proprietary names to determine if they are overly fanciful, so as to misleadingly imply unique effectiveness or composition, as well as to assess whether they contribute to overstatement of product efficacy, minimization of risk, broadening of product indications, or making of unsubstantiated superiority claims. OPDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, we consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.). DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.¹

Following the preliminary screening of the proposed proprietary name, DMEPA gathers to discuss their professional opinions on the safety of the proposed proprietary name. This meeting is commonly referred to the Center for Drug Evaluation and Research (CDER) Expert Panel discussion. DMEPA also considers other aspects of the name that may be misleading from a safety perspective. DMEPA staff conducts a prescription simulation studies using FDA health care professionals. When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name 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 misleading nature of the proposed proprietary name with a focus on the avoidance of medication errors.

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. DMEPA considers the product characteristics associated with the proposed product throughout the risk assessment because the product characteristics of the

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

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. DMEPA considers how these product characteristics may or may not be present in communicating a product name throughout the medication use system. Because drug name confusion can occur at any point in the medication use process, DMEPA 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.²

The DMEPA considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA compares the proposed proprietary name with the proprietary and established name of existing and proposed drug products and names currently under review at the FDA. DMEPA 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. DMEPA examines the phonetic similarity using patterns of speech. 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. The orthographic appearance of the proposed name is evaluated using a number of different handwriting samples. DMEPA applies expertise gained from root-cause analysis of postmarketing 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).

² 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/Similar shape 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, DMEPA 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 searches 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. A standard description of the databases used in the searches is provided in the reference section of this review. To complement the process, the DMEPA uses 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, DMEPA reviews 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. DMEPA also evaluates if there are characteristics included in the composition that may render the name unacceptable from a safety perspective (abbreviation, dosing interval, etc.).

2. Expert Panel Discussion

DMEPA gathers CDER professional opinions on the safety of the proposed product and discussed the proposed proprietary name (Expert Panel Discussion). The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Office of Prescription Drug Promotion (OPDP). We also consider input from other review disciplines (OND, ONDQA/OBP). 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 database and information searches to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend additional 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 Simulation 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 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 record their interpretations of the orders which are recorded electronically.

4. Comments from Other Review Disciplines

DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for 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 OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, considers all aspects of the name that may be misleading or confusing, conducts a Failure Mode and Effects Analysis, and provides an overall decision on acceptability dependent on their 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.³ 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

³ Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

characteristics listed in Section 1.2 of this review. 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? And are there any components of the name that may function as a source of error beyond sound/look-alike?”

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 or because of some other component of the name. If the answer to the question is no, the Safety Evaluator is not convinced that the names possess similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

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

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

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

Moreover, 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 Overall Risk Assessment:

- a. OPDP finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with OPDP’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 but involve a naming characteristic that when incorporated into a proprietary name, may be confusing, misleading, cause or contribute to medication errors.

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 generally recommends that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for 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 Applicant/Sponsor. However, the safety concerns set forth in criteria a through e above 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, confusing, or misleading 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 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

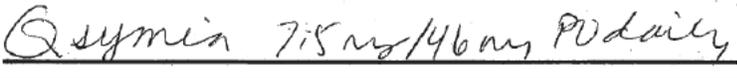
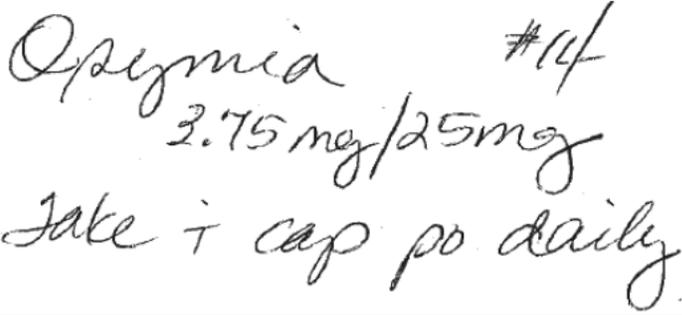
past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Sponsors' have changed a product's proprietary name in the post-approval 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, Qsymia	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'Q'	A, D, O, Qu, U	K, Qu, T
Lower case 'q'	g, j, qu, z	k, qu
Lower case 's'	G, 5, g, n, p, r	x
Lower case 'y'	f, p, u, v, x, z	e, i, u
Lower case 'm'	m, mm, n, v, w, wi, vi onc, z	
Lower case 'i'	e	
Lower case 'a'	el, ci, cl, d, o, u	Any vowel

Appendix C: Prescription Simulation Samples and Results

Figure 1. Qsymia Study (Conducted on May 31, 2012)

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Medication Order:</u></p>  <p><u>Outpatient Prescription:</u></p> 	<p>Qsymia 3.75 mg/23 mg Take 1 capsule by mouth daily #14</p>

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

84 People Received Study 16 People Responded				
Study Name: Qsymia				
Total	5	6	5	16
INTERPRETATION	INPATIENT	VOICE	OUTPATIENT	TOTAL
GISIMIA	0	1	0	1
GUCEMIA	0	1	0	1
JASIMIA	0	1	0	1
OPYMIA	0	0	2	2
OPYMIA 3.75 MG/25 MG	0	0	1	1
OPZMIA	0	0	1	1
OSYMIA	1	0	1	2
QSIMMEA	0	1	0	1
QSYMIA	2	0	0	2
QSYMIN	2	0	0	2
QUESEMIA	0	1	0	1
QUSIMIA	0	1	0	1

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

Proprietary Name	Active Ingredient	Similarity to Osvmia	Failure preventions
(b) (4)			

Appendix E: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

<p>Proposed name: Qsymia (Phentermine and Topiramate) Extended-release Dosage Form: capsule</p> <p>Strength(s): 3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, 15 mg/92 mg</p> <p>Usual Dose: 7.5 mg/46 mg once daily OR Take 1 capsule by mouth daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Aczone Gel (Dapsone)</p> <p>Strength: 5%</p> <p>Usual dose: Apply to affected area twice daily</p>	<p><u>Orthographic similarity to Qsymia</u> When scripted the letter string ‘Qsy’ may look similar to ‘Acz’ when ‘z’ is scripted as a downstroke. Also, when ‘z’ is scripted as a downstroke the names have a similar shape.</p> <p><u>Dosage form</u> Both products are available as a single dosage form. Thus the dosage form maybe omitted when prescribed.</p>	<p><u>Orthographic differences</u> When scripted the letter string ‘mia’ may look different than ‘one’.</p> <p><u>Route of administration</u> Oral administration compared to topical application</p> <p><u>Strength</u> Single strength vs. multiple strengths and no overlap in strengths. Thus, the strength of Aczone may be omitted, but the strength of Qsymia must be specified.</p>

Appendix E: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

<p>Proposed name: Qsymia (Phentermine and Topiramate) Extended-release Dosage Form: capsule</p> <p>Strength(s): 3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, 15 mg/92 mg</p> <p>Usual Dose: 7.5 mg/46 mg once daily OR Take 1 capsule by mouth daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Arzerra Solution for Injection (Ofatumumab)</p> <p>Dosage form: Solution for Injection</p> <p>Strength: 100 mg per 5 mL</p> <p>Usual dose: Administer 300 mg intravenously once followed 1 week later by 2000 mg intravenously weekly for 7 weeks</p>	<p><u>Orthographic similarity to Qsymia</u> When scripted the letter strings ‘Qsy’ and ‘Arz’ may look similar. When scripted both names appear similar in shape and length, 6 letters compared to 7 letters.</p> <p><u>Dosage form</u> Both products are available as a single dosage form. Thus the dosage form maybe omitted when prescribed.</p> <p><u>Frequency of Administration</u> Both products are administered once daily.</p>	<p><u>Orthographic differences</u> When scripted the letter string ‘mia’ may look different than ‘erra’.</p> <p><u>Route of administration</u> Oral administration compared to intravenous administration</p> <p><u>Strength and Dosing</u> Single strength vs. multiple strengths and no overlap in strengths. Arzerra is part of chemotherapy regimen and the strength must be specified. Qsymia is available is multiple strengths thus the strength must be specified.</p> <p><u>Setting of Use</u> Qsymia is part of a REMS and the distribution of Qsymia will be restricted to specialty pharmacies. Arzerra is dispensed in a hospital.</p>

Appendix E: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

<p>Proposed name: Qsymia (Phentermine and Topiramate) Extended-release Dosage Form: capsule</p> <p>Strength(s): 3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, 15 mg/92 mg</p> <p>Usual Dose: 7.5 mg/46 mg once daily OR Take 1 capsule by mouth daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Aspirin Tablets Dosage form: Enteric coated Tablets Strength: 81 mg, 325 mg Usual dose: Take 1 tablet by mouth daily</p>	<p><u>Orthographic similarity to Qsymia</u> When scripted the letter strings ‘Qsy’ and ‘Asp’ may look similar. When scripted both names appear similar in shape and length, 6 letters compared to 7 letters.</p> <p><u>Dosage form</u> Both products are available as a single dosage form.</p> <p><u>Frequency of Administration</u> Both products are administered once daily.</p> <p><u>Route of administration</u> Both products are administered orally.</p>	<p><u>Orthographic differences</u> When scripted the letter string ‘mia’ may look different than ‘irin’.</p> <p><u>Strength</u> There are no overlapping product strengths between products. The product strength must be specified with both products.</p>

Appendix E: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

<p>Proposed name: Qsymia (Phentermine and Topiramate) Extended-release Dosage Form: capsule</p> <p>Strength(s): 3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, 15 mg/92 mg</p> <p>Usual Dose: 7.5 mg/46 mg once daily OR Take 1 capsule by mouth daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Cimzia Injection (Certolizumab Pegol)</p> <p>Dosage form: Solution for Injection</p> <p>Strength: 200 mg</p> <p>Usual dose: Inject 400 mg subcutaneously on weeks 0, 2, 4 then every 4 weeks.</p>	<p><u>Orthographic similarity to Qsymia</u> When scripted the letters ‘Q’ and ‘C’ may look similar. The names have a similar shape and are identical in length, comprised of 6 letters.</p> <p><u>Phonetic similarity to Qsymia</u> When spoke the letter string ‘sym’ may sound similar to ‘cim’.</p> <p><u>Dosage form</u> Both products are available as a single dosage form. Thus the dosage form maybe omitted when prescribed.</p> <p><u>Frequency of administration</u> Both products are administered once daily.</p>	<p><u>Phonetic differences</u> When spoken the ‘Q’ in Qsymia sounds distinctive from ‘C’ in Cimzia.</p> <p><u>Dose</u> Qsymia is a single unit for use product compared to Cimzia requires 2 units (injections) for use.</p> <p><u>Route of administration</u> Oral administration compared to subcutaneous administration</p> <p><u>Strength</u> Single strength vs. multiple strengths and no overlap in strengths. Qsymia is available is multiple strengths thus the strength must be specified.</p>

Appendix E: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

<p>Proposed name: Qsymia (Phentermine and Topiramate) Extended-release Dosage Form: capsule</p> <p>Strength(s): 3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, 15 mg/92 mg</p> <p>Usual Dose: 7.5 mg/46 mg once daily OR Take 1 capsule by mouth daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Gemzar (Gemcitabine)</p> <p>Dosage form: Powder for Injection and Solution for Injection</p> <p>Strength: 200 mg, 1000 mg, 2000 mg, 200 mg/5.26 mL, 1000 mg/26.3 mL, 2000 mg/52.6 mL</p> <p>Usual dose: Administer 1000 mg/m² intravenously on days 1, 8, 15 of a 28 day cycle</p> <p>Calculated dose: 1600 mg to 1900 mg</p>	<p><u>Orthographic similarity to Qsymia</u> When scripted the letters 'Q' and 'G' may look similar. Both names have a similar shape and are identical in length, comprising of 6 letters.</p> <p><u>Frequency of administration</u> Both products are administered once daily.</p>	<p><u>Orthographic differences</u> When scripted the names have a different shape. Qsymia has a downstroke in the third position compared to Gemzar has a downstroke in the fourth position.</p> <p><u>Route of administration</u> Oral administration compared to intravenous administration</p> <p><u>Strength</u> There are no overlapping product strengths between products. The product strength must be specified with both products.</p>

Appendix E: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

<p>Proposed name: Qsymia (Phentermine and Topiramate) Extended-release Dosage Form: capsule</p> <p>Strength(s): 3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, 15 mg/92 mg</p> <p>Usual Dose: 7.5 mg/46 mg once daily OR Take 1 capsule by mouth daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Oscimin Tablet (Hyoscyamine)</p> <p>Dosage form: Tablet</p> <p>Strength: 0.125 mg</p> <p>Usual dose: Take 1-2 tablets by mouth every 4 hours</p>	<p><u>Orthographic similarity to Qsymia</u> When scripted the letters ‘Qs’ and ‘Os’ look similar.</p> <p><u>Dosage form</u> Both products are available as a single dosage form. Thus the dosage form maybe omitted when prescribed.</p> <p><u>Route of administration</u> Both products are administered orally.</p>	<p><u>Orthographic differences</u> When scripted the names have different shapes. Oscimin does not contain any upstrokes or downstrokes giving it a relatively flat shape. Qsymia has a downstroke in the third position.</p> <p><u>Dose</u> Qsymia is a single unit for use product compared to Oscimin which requires up to two units for use.</p> <p><u>Frequency of Administration</u> Once daily administration compared to administration up to six times daily</p> <p><u>Strength</u> Single strength vs. multiple strengths and no overlap in strengths. Thus, the strength of Oscimin may be omitted, but the strength of Qsymia must be specified.</p>

Appendix E: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

<p>Proposed name: Qsymia (Phentermine and Topiramate) Extended-release Dosage Form: capsule</p> <p>Strength(s): 3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, 15 mg/92 mg</p> <p>Usual Dose: 7.5 mg/46 mg once daily OR Take 1 capsule by mouth daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Orzel Capsules (UFT)</p> <p>Dosage form: Capsule</p> <p>Strength: 100 mg, 224 mg</p> <p>Usual dose: Take 5 capsules by mouth daily</p> <p>Calculated dose: 480 mg to 570 mg</p>	<p><u>Orthographic similarity to Qsymia</u> When scripted the letter string ‘Qsy’ may look similar to ‘Orz’ when ‘z’ is scripted as a downstroke. When scripted both names appear similar in length, 5 letters compared to 6 letters.</p> <p><u>Dosage form</u> Both products are available as a single dosage form. Thus the dosage form maybe omitted when prescribed.</p> <p><u>Route of administration</u> Both products are administered orally.</p>	<p><u>Orthographic differences</u> When scripted the letter string ‘mia’ may look different than ‘el’.</p> <p><u>Dose</u> Qsymia is a single unit for use product compared to Orzel which requires multiple units for use.</p> <p><u>Strength</u> There are no overlapping product strengths between products. The product strength must be specified with both products.</p>

Appendix E: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

<p>Proposed name: Qsymia (Phentermine and Topiramate) Extended-release Dosage Form: capsule</p> <p>Strength(s): 3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, 15 mg/92 mg</p> <p>Usual Dose: 7.5 mg/46 mg once daily OR Take 1 capsule by mouth daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Quixin Ophthalmic Drops (Levofloxacin)</p> <p>Dosage form: Ophthalmic drops</p> <p>Strength: 0.5%</p> <p>Usual dose: Instill 1-2 drops in affected eye(s) every 1-4 hours</p>	<p><u>Orthographic similarity to Qsymia</u> Both names begin with the letter 'Q'. Also Qsymia and Quixin are identical in length, comprised of 6 letters.</p> <p><u>Dosage form</u> Both products are available as a single dosage form. Thus the dosage form maybe omitted when prescribed.</p>	<p><u>Orthographic differences</u> When scripted Qsymia has a different shape than Quixin. Qsymia contains a downstroke in the third position whereas a potential downstroke by the 'x' in Quixin is in the fourth position.</p> <p><u>Route of administration</u> Oral administration compared to ophthalmic drops</p> <p><u>Frequency of Administration</u> Qsymia is administered once daily compared to application greater than 4 times daily.</p> <p><u>Strength</u> Single strength vs. multiple strengths and no overlap in strengths. Thus, the strength of Quixin may be omitted, but the strength of Qsymia must be specified</p>

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

/s/

KEVIN WRIGHT
06/14/2012

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06/14/2012

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

Proprietary Name Review

Date: April 16, 2012

Reviewer: Kevin Wright, PharmD, Safety Evaluator
Division of Medication Error and Prevention Analysis

Team Leader: Yelena Maslov, PharmD
Division of Medication Error and Prevention Analysis

Deputy Director: Kellie Taylor, PharmD, MPH
Division of Medication Error and Prevention Analysis

Division Director: Carol Holquist, RPh.
Division of Medication Error and Prevention Analysis

Drug Name and Strength(s): Qnexa (phentermine and topiramate extended-release)
capsules
3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg,
15 mg/92 mg

Application Type/Number: NDA 022580

Applicant/Sponsor: Vivus Inc.

OSE RCM #: 2012-187

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

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EXECUTIVE SUMMARY

This review summarizes DMEPA's proprietary name risk assessment of Qnexa for Phentermine and Topiramate extended-release capsules. Our evaluation found the proprietary name, Qnexa is vulnerable to confusion rendering the name unacceptable based on orthographic and phonetic similarities with marketed products, B-nexa, Ranexa and Prenexa. Thus, DMEPA finds the proposed proprietary name, Qnexa, unacceptable for this product.

1 INTRODUCTION

This review evaluates the proposed proprietary name, Qnexa (Phentermine and Topiramate extended-release), from a promotional and safety perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively.

1.1 REGULATORY HISTORY

The proposed proprietary name, Qnexa (Phentermine and Topiramate extended release), was found acceptable by DMEPA in OSE Review 2009-2013, dated February 17, 2010 under NDA 022580. The applicant received a complete response letter from the Agency dated, October 28, 2010. On February 2, 2012, the Sponsor submitted a request for proprietary name review as part of a class 2 resubmission.

1.2 PRODUCT INFORMATION

The following product information is provided in the February 2, 2012 proprietary name submission.

- Active Ingredient: Phentermine and Topiramate extended release
- Indication of Use: Adjunct to diet and exercise to aid in weight loss in obese patients or overweight patients
- Route of Administration: Oral
- Dosage Form: Extended-release Capsules
- Strengths: 3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, and 15 mg/92 mg
- Dose and Frequency: The recommended starting dose is 3.75 mg/23 mg by mouth once daily. The dose can be titrated up to a maximum dose of 15 mg/92 mg by mouth once daily.
- How Supplied: Bottles containing 14 and 30 capsules
- Storage: Store at room temperature (15°C to 25°C; 59°F to 77°F)

2 RESULTS

PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Metabolic and Endocrine Products (DMEP) concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following aspects of the name were considered in the overall safety evaluation.

2.2.1 *United States Adopted Names (USAN) SEARCH*

On March 13, 2012 the United States Adopted Name (USAN) stem search, identified that an USAN stem is not present in the proposed proprietary name.

2.2.2 *Components of the Proposed Proprietary Name*

This proprietary name comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that is misleading or can contribute to medication error.

2.2.3 *Medication Error Data Selection of Cases*

On February 20, 2012, DMEPA received a report from ISMP that described a confusion between Prenexa and Ranexa where a written prescription for Ranexa 500 mg was dispensed instead of Prenexa.¹ The patient took Ranexa for one year thinking that it was a prenatal vitamin. This report prompted DMEPA to search AERS database for medication errors involving confusion between Ranexa and Prenexa which would be relevant for this review since both names contain the share letter string '-nexa'.

The February 21, 2012 search of the Adverse Event Reporting System (AERS) database used the following search terms: [REDACTED] (b) (4)

[REDACTED] along with the HLTG Term Medication Errors, HLT Product Label Issues, and PT Product Name Confusion.

Each report was reviewed for relevancy and duplication. Duplicates were merged into a single case. The NCC MERP Taxonomy of Medication Errors was used to code the case outcome and error root causes when provided by the reporter.

The search yielded no relevant cases related to confusion of Ranexa to Prenexa.

¹ This document contains proprietary data from the Institute for Safe Medication Practices (ISMP) which cannot be shared outside of the FDA. Users wanting this information must contact a designated individual in the Division of Medication Error Prevention who will gain approval from ISMP. **

2.2.4 FDA Name Simulation Studies

Twenty-four practitioners participated in DMEPA’s prescription studies. The interpretations did not overlap with or appear or sound similar to any currently marketed products. In the written studies, 13 of 16 participants correctly interpreted the prescription. In the voice study only 1 participant correctly interpreted the prescription. Common misinterpretations in the voice study include: ‘Ka’, ‘Ki’ and ‘Tu’ for ‘Q’. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.5 Comments from Other Review Disciplines

In response to the OSE email dated, March 1, 2012, the Division of Metabolic and Endocrine Products (DMEP) did not forward any comments or concerns relating to the proposed name at the initial phase of the proprietary name review. However, in an email correspondence dated March 12, the Office of Drug Evaluation II (ODE II) expressed concern regarding potential confusion between Qnasl and Qnexa.

These concerns were mitigated by differences in product characteristics (dosage form, route of administration, strength).

2.2.6 Failure Mode and Effects Analysis of Similar Names

Our analysis reviewed 26 names thought to present a risk of confusion with Qnexa and concluded through Failure Mode and Effects Analysis the similarity between Qnexa and 23 of the 26 names identified names was unlikely to result in medication errors. However, it was determined that name confusion may occur between the following name pairs Bnexa-Qnexa, Prenexa-Qnexa, and Ranexa-Qnexa.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, Other Disciplines, FDA Name Simulation Studies, and External Name Study if applicable)

Look Similar					
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
Avage	EPD	Abreva	EPD	Aceon	EPD
Adoxa	EPD	Anexsia	EPD	Arava	EPD
Avinza	EPD	Avonex	EPD	Conex	EPD
Duexa	EPD	Gynix	EPD	Kionex	Primary Safety Evaluator
Onetab	EPD	Orencia	EPD	Ovcon	EPD
Qnaze	EPD	Quide	EPD	Quixin	EPD
Umecta	EPD	Zmax	EPD		

Sound Similar					
(b) (4)	EPD				

Look and Sound Similar					
Qnasl	EPD	Ranexa	EPD	(b) (4)	EPD
Prenexa	EPD	B-nexa	EPD		

We determined 23 of the 26 total names will not pose a risk for confusion as described in Appendix D and E. However, the proposed name could be confused with B-nexa, Prenexa, and Ranexa. The rationale for the risk of confusion is described in Section 3.1, *Comments to the Applicant*.

2.2.7 Communication of DMEPA’s Final Decision to Other Disciplines

In email correspondence dated April 9, 2012 DMEPA expressed concerns regarding potential confusion between Qnexa and B-nexa, Prenexa, or Ranexa. The DMEP concurred with DMEPA’s findings in the email on April 10, 2012.

The following sections provide the information obtained and considered in the evaluation of the proposed proprietary name.

3 CONCLUSIONS AND RECOMMENDATIONS

The proposed proprietary name is not acceptable from a safety perspective. The proposed name, Qnexa, is vulnerable to name confusion with B-nexa, Prenexa and Ranexa. Therefore, the decision to deny the name will be communicated to the Applicant via letter (See Section 3.1).

If you have further questions or need clarifications, please contact Ermias Zerislassie, OSE project manager, at 301-796-0097.

3.1 COMMENTS TO THE APPLICANT

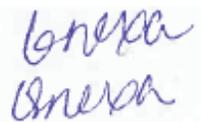
We have completed our review of this proposed proprietary name and have concluded that this name is unacceptable due to three safety concerns related to the potential for confusion between Qnexa and B-nexa, Prenexa, and Ranexa. We have concerns that the proposed proprietary name Qnexa could be confused with these products due to orthographic and phonetic similarities and shared product characteristics.

B-nexa (ginger, vitamin B 6, and folic acid) tablets and Prenexa (multivitamin with iron) tablets are prescription prenatal vitamins used for nutrition supplementation during pregnancy. Both products are single use products administered orally once a day. Ranexa (ranolazine extended release) is indicated in the treatment of chronic angina. Ranexa is marketed as a 500 mg and 1000 mg oral tablet and the drug is dosed twice daily.

The following section discusses the similarities between Qnexa and the aforementioned products in detail.

A. B-NEXA AND QNEXA ORTHOGRAPHIC AND PHONETIC SIMILARITY

Qnexa has significant orthographic and phonetic similarity to B-nexa. The orthographic similarity of this name pair is attributed to the fact that the names differ by only one letter. Both product names end in the suffix 'nexa' and the letter 'Q' may be misinterpreted for the letter 'B' when scripted (See sample below).



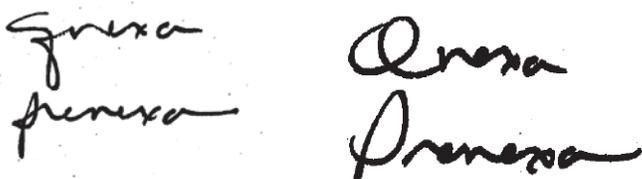
Additionally, both names are phonetically similar to each other. B-nexa (bé-nek-suh) and Qnexa (kyoo-nek-suh) are comprised of 3 syllables with the stroke on the second syllable. Both products end with the letter string 'nexa' and the letter 'B' may be misinterpreted for the letter 'Q' when spoken.

The pair's shared product characteristics include dosage form (solid oral form), usual dose (one), frequency (once daily), and route of administration (oral).

Even though the B-nexa product has only been recently introduced into the marketplace, drug usage data indicates that in 2012 prescriptions are being issued bearing the name, B-nexa.

B. PRENEXA AND QNEXA ORTHOGRAPHIC AND PHONETIC SIMILARITY

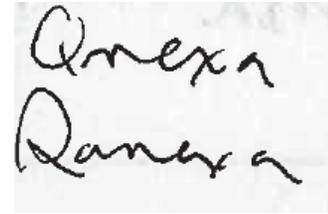
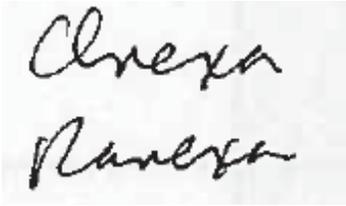
Qnexa has significant orthographic similarity to Prenexa. With respect to the orthographic similarity, both products end with the suffix 'nexa' and are similar in length. The minor orthographic differences in the names may not sufficiently distinguish the name pair given the other orthographic similarities noted previously and the shared product characteristics (See samples below).



The pair's shared product characteristics include dosage form (solid oral form), usual dose (one), frequency (once daily) and route of administration (oral). We note that drug usage database indicates that prescriptions are issued bearing the name, Prenexa.

C. RANEXA AND QNEXA ORTHOGRAPHIC AND PHONETIC SIMILARITY

Qnexa has significant orthographic similarity to the currently marketed product, Ranexa. With respect to the orthographic similarity, both products end with the suffix 'nexa' and are similar in length. The minor orthographic differences in the names may not sufficiently distinguish the name pair given the other orthographic similarities noted previously and the shared product characteristics (See samples below)



The pair's shared product characteristics include dosage form (solid oral form), usual dose (one), and route of administration (oral).

D. ANALYSIS OF PRODUCT CHARACTERISTIC DIFFERENCES

We carefully considered whether your restricted distribution system or the difference in distribution system, strength, and frequency for your product compared to B-nexa, Prenexa, and Ranexa would minimize the potential for error between Qnexa and these products. We concluded these aspects will not eliminate the potential for the name confusion and medication errors.

Although the strengths of your product are not similar to the strength of B-nexa, Prenexa or Ranexa, we are concerned that this difference will not adequately prevent confusion between the above name pairs. We have identified post-marketing reports of confusion between products marketed in different strengths when strong orthographic or phonetic similarity exists. As an example, a recent report from ISMP describes confusion between Prenexa and Ranexa where a written prescription for Ranexa 500 mg was dispensed instead of Prenexa.² The patient took Ranexa for one year thinking that it was a prenatal vitamin. This error occurred despite the differences in products strengths (Ranexa is available in 500 mg and 1000 mg and Prenexa a single strength prenatal multivitamin) and frequency of administration (Ranexa should be administered twice daily vs. Prenexa should be administered once daily). Thus, the distinct differences in strength and frequency of administration were insufficient to prevent a medication error arising from name similarity. As it relates to Qnexa, we think that similar errors could occur between B-nexa and Qnexa, Prenexa and Qnexa or Ranexa and Qnexa since the Qnexa name is composed of similar letters and components.

In addition to this report, we also considered other reports of confusion between products marketed with differing strengths when strong orthographic or phonetic similarity exists. For example, we identified confusion between the products Kapidex (dexlansoprazole delayed-release capsules) and Casodex (bicalutamide tablets) as well as Kapidex and Kadian (morphine extended-release). Casodex is marketed in a 50 mg tablet and Kadian is marketed in 10 mg, 20 mg, 30 mg, 50 mg, 60 mg, 80 mg, 100 mg, and 200 mg capsules, while Kapidex was marketed in 15 mg and 60 mg capsules. These products

² This document contains proprietary data from the Institute for Safe Medication Practices (ISMP) which cannot be shared outside of the FDA. Users wanting this information must contact a designated individual in the Division of Medication Error Prevention who will gain approval from ISMP.**

were confused with each other due to strong proprietary name similarity despite differences in the strengths and required a name change of Kapidex post-approval to Dexilant. This post-marketing experience adds to our concern with Qnexa, since the proposed name is very similar to Ranexa and Prenexa.

Additionally, we have taken into consideration that Qnexa may be distributed via mail pharmacies that are certified to dispense this product. However, we determined that your proposed distribution system will not minimize the potential for errors between Qnexa and B-nexa, Prenexa, or Ranexa because the same mail order pharmacies that may distribute Qnexa may also distribute these products. Additionally, we have reports of name confusion with other products marketed under restricted distribution systems and therefore our safety concern is not diminished with your product.

We acknowledge that this conclusion differs from the March 5, 2010 letter finding your name conditionally acceptable. This difference is accounted for by the introduction of the new product and the recently reported medication errors. Our previous evaluation of the proposed name Qnexa completed on February 17, 2010, did not identify the name B-nexa, because B-nexa was launched in January, 2012. Thus, at the time of the previous review, B-nexa did not exist. Additionally, our previous evaluations of Qnexa did not identify the name Prenexa and as a result, the name was not evaluated for orthographic or phonetic similarities with Qnexa.

With respect to the potential for confusion with Ranexa, our previous evaluation did consider the potential for Qnexa to be confused with Ranexa. At the time of our evaluation, we determined that differences in strength and dosing between the two products should minimize the potential for confusion between the pair. However, our post-marketing surveillance of medication errors reported since the time of that review demonstrates that such differences may not prevent confusion between products with similar proprietary names. In light of this new information, we now believe that the similarity between Ranexa and Qnexa poses a safety concern.

We note that you have not proposed an alternate proprietary name for review. If you intend to have a proprietary name for this product, we recommend that you submit a new request for a proposed proprietary name review and include the alternate name. (See the Guidance for Industry, *Complete Submission for the Evaluation of Proprietary Names*, <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf> and “PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2008 through 2012”.)

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Ermias Zerislassie, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0097. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager Pooja Dharia at (301) 796-5332.

4. 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. This database also lists the orphan drugs.

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

USPTO provides information regarding patent and trademarks.

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

Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common,

combination, nutraceutical and nutritional products. It also provides a keyword search engine.

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

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

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

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

11. *Access Medicine (www.accessmedicine.com)*

Access Medicine® from McGraw-Hill contains full-text information from approximately 60 titles; it includes tables and references. Among the titles are: Harrison's Principles of Internal Medicine, Basic & Clinical Pharmacology, and Goodman and Gilman's The Pharmacologic Basis of Therapeutics.

12. *USAN Stems (<http://www.ama-assn.org/ama/pub/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml>)*

USAN Stems List contains all the recognized USAN stems.

13. *Red Book (www.thomsonhc.com/home/dispatch)*

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

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

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

15. *Medical Abbreviations (www.medilexicon.com)*

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

16. *CVS/Pharmacy (www.CVS.com)*

This database contains commonly used over the counter products not usually identified in other databases.

17. *Walgreens (www.walgreens.com)*

This database contains commonly used over the counter products not usually identified in other databases.

18. Rx List (www.rxlist.com)

RxList is an online medical resource dedicated to offering detailed and current pharmaceutical information on brand and generic drugs.

19. Dogpile (www.dogpile.com)

Dogpile is a [Metasearch](#) engine that searches multiple search engines including Google, Yahoo! and Bing, and returns the most relevant results to the search.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment considers the promotional and safety aspects of a proposed proprietary name. The promotional review of the proposed name is conducted by OPDP. OPDP evaluates proposed proprietary names to determine if they are overly fanciful, so as to misleadingly imply unique effectiveness or composition, as well as to assess whether they contribute to overstatement of product efficacy, minimization of risk, broadening of product indications, or making of unsubstantiated superiority claims. OPDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, we consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.). 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

Following the preliminary screening of the proposed proprietary name, DMEPA gathers to discuss their professional opinions on the safety of the proposed proprietary name. This meeting is commonly referred to the Center for Drug Evaluation and Research (CDER) Expert Panel discussion. DMEPA also considers other aspects of the name that may be misleading from a safety perspective. DMEPA staff conducts a prescription simulation studies using FDA health care professionals. When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name 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 misleading nature of the proposed proprietary name with a focus on the avoidance of medication errors.

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. DMEPA considers the product characteristics associated with the proposed product 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.

³ National Coordinating Council for Medication Error Reporting and Prevention. <http://www.nccmerp.org/about/MedErrors.html>. Last accessed 10/11/2007.

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. DMEPA considers how these product characteristics may or may not be present in communicating a product name throughout the medication use system. Because drug name confusion can occur at any point in the medication use process, DMEPA 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.⁴

The DMEPA considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA compares the proposed proprietary name with the proprietary and established name of existing and proposed drug products and names currently under review at the FDA. DMEPA 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. DMEPA examines the phonetic similarity using patterns of speech. 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. The orthographic appearance of the proposed name is evaluated using a number of different handwriting samples. DMEPA applies expertise gained from root-cause analysis of postmarketing 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).

⁴ 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/Similar shape 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, DMEPA 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 searches 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. A standard description of the databases used in the searches is provided in the reference section of this review. To complement the process, the DMEPA uses 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, DMEPA reviews 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. DMEPA also evaluates if there are characteristics included in the composition that may render the name unacceptable from a safety perspective (abbreviation, dosing interval, etc.).

2. Expert Panel Discussion

DMEPA gathers CDER professional opinions on the safety of the proposed product and discussed the proposed proprietary name (Expert Panel Discussion). The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Office of Prescription Drug Promotion (OPDP). We also consider input from other review disciplines (OND, ONDQA/OBP). 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 database and information searches to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend additional 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 Simulation 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 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 record their interpretations of the orders which are recorded electronically.

4. Comments from Other Review Disciplines

DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for 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 OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, considers all aspects of the name that may be misleading or confusing, conducts a Failure Mode and Effects Analysis, and provides an overall decision on acceptability dependent on their 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.⁵ 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

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

characteristics listed in Section 1.2 of this review. 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? And are there any components of the name that may function as a source of error beyond sound/look-alike?”

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 or because of some other component of the name. If the answer to the question is no, the Safety Evaluator is not convinced that the names possess similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

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

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

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

Moreover, 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 Overall Risk Assessment:

- a. OPDP finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with OPDP’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 but involve a naming characteristic that when incorporated into a proprietary name, may be confusing, misleading, cause or contribute to medication errors.

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 generally recommends that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for 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 Applicant/Sponsor. However, the safety concerns set forth in criteria a through e above 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, confusing, or misleading 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 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

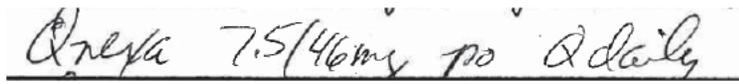
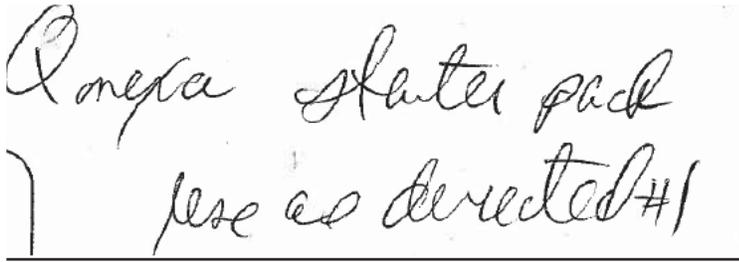
past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Sponsors' have changed a product's proprietary name in the post-approval 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, Qnexa	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'Q'	O, A, D, U	K, T
Lower case 'q'	g, j, z	k
Lower case 'n'	m, u, x, r, h, s	dn, gn, kn, mn, pn
Lower case 'e'	a, i, l, p	Any vowel
Lower case 'x'	a, d, skinny f, k, n, p, r, t, v, y	ks, kz, s, z
Lower case 'a'	el, ci, cl, d, o, u	Any vowel

Appendix C: Prescription Simulation Samples and Results

Figure 1. Qnexa Study (Conducted on 02/21/12)

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Medication Order:</u></p> 	<p>Qnexa Starter Pack Use as directed #1</p>
<p><u>Outpatient Prescription:</u></p> 	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

84 People Received Study 24 People Responded				
Study Name: Qnexa				
Total	9	8	7	
INTERPRETATION	INPATIENT	VOICE	OUTPATIENT	TOTAL
KANEXA	0	1	0	1
KANEXA STARTER PACK	0	1	0	1
KINEXA	0	2	0	2
KINEXA STARTER PACK	0	1	0	1
KINEXIA STARTERPAK	0	1	0	1
ONEXA	1	0	1	2
ONEXA STARTER PACK	0	0	1	1
OREXA	1	0	0	1
QNEXA	7	0	2	9
QNEXA STARTER PACK	0	1	3	4
TUNEXA STARTER PACK	0	1	0	1

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

Proprietary Name	Active Ingredient	Similarity to Qnexa	Failure preventions
Avage	Tazarotene	Look	The pair have sufficient orthographic and/or phonetic differences
Conex	Guaifenesin/ phenylephrine/ pseudoephedrine	Look	The pair have sufficient orthographic and/or phonetic differences
Duexa	Famotidine/ibuprofen	Look	Proposed proprietary name found unacceptable by DMEPA (OSE # 2009-2447). Product approved under new proprietary name, Duexis.
Gynix	Clotrimazole	Look	The pair have sufficient orthographic and/or phonetic differences
Onetab	Guaifenesin/ phenylephrine	Look	The pair have sufficient orthographic and/or phonetic differences
Qnaze	Beclomethasone dipropionate	Look	Proposed Proprietary Name found unacceptable by DMEPA (OSE# 2010-2011). Product approved under new proprietary name, Qnasl.
Q-next		Look & Sound	Product is not a drug (instant message tool for mobile devices)

Appendix E: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

<p>Proposed name: Qnexa (phentermine and topiramate extended-release) Dosage Form(s): capsule</p> <p>Strength(s): 3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, 15 mg/92 mg</p> <p>Usual Dose: 7.5 mg/46 mg once daily OR Take as directed</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Aceon (perindopril) tablets Dosage form: tablets Strength: 2 mg, 4 mg, 8 mg Usual dose: Take 2 mg orally twice daily</p>	<p><u>Orthographic similarity to Qnexa</u> When scripted the letter string ‘Qne’ looks similar to ‘Ace’. Qnexa and Aceo are identical in length.</p> <p><u>Frequency of Administration</u> Both products can be administered once daily to twice daily.</p>	<p><u>Strength</u> There are no overlapping product strengths between products. The product strength must be specified with both products.</p>
<p>Avonex powder for injection (interferon beta-1a) Dosage form: powder for injection Strength: 30 mcg Usual and Frequency: Inject 30 mcg intramuscularly once a week</p>	<p><u>Orthographic similarity to Qnexa</u> Qnexa and Avonex are similar in length and share the letter string, ‘nex’.</p>	<p><u>Orthographic differences</u> When scripted the letters ‘xa’ look different from ‘nex’.</p> <p><u>Frequency of administration</u> Once daily compared to once a week</p> <p><u>Strength</u> Single strength vs. multiple strengths and no overlap in strengths. Thus, the strength of Avonex may be omitted, but the strength of Qnexa must be specified.</p>

<p>Proposed name: Qnexa (phentermine and topiramate extended-release) Dosage Form(s): capsule</p> <p>Strength(s): 3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, 15 mg/92 mg</p> <p>Usual Dose: 7.5 mg/46 mg once daily OR take as directed</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Canasa suppository (mesalamine)</p> <p>Dosage form: suppository</p> <p>Strength: 500 mg, 1000 mg</p> <p>Usual dose: Insert one suppository rectally twice daily for 1-3 hours OR use as directed.</p>	<p><u>Phonetic similarity to Qnexa:</u> When spoken the letter strings 'nasa' and 'nexa' may sound similar.</p> <p><u>Frequency of Administration</u> Both products can be administered once daily to twice daily.</p> <p><u>Dosage form</u> Both products are available as a single dosage form. Thus the dosage form maybe omitted when prescribed.</p>	<p><u>Phonetic differences</u> When spoken 'Q' sounds different from 'Ca'.</p> <p><u>Strength</u> There are no overlapping product strengths between Qnexa and Canasa. The product strength must be specified with both products.</p>
<p>Kionex (sodium polystyrene sulfonate)</p> <p>Dosage form: rectal enema suspension, powder for suspension</p> <p>Strength: 15 g/60 mL,</p> <p>Usual dose: 15 g orally given 1-4 times per day OR 30-50 g per rectally as a rectal enema every 1-2 hours</p>	<p><u>Phonetic similarity to Qnexa</u> Both names came the letter string 'nex'.</p>	<p><u>Phonetic differences</u> When spoken the beginning of Qnexa, 'Que' sounds different from the letter string, 'Kio'.</p>

<p>Proposed name: Qnexa (phentermine and topiramate) extended-release</p> <p>Dosage Form(s): capsule</p> <p>Strength(s): 3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, 15 mg/92 mg</p> <p>Usual Dose: 7.5 mg/46 mg once daily OR take as directed</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Orencia (abatacept)</p> <p>Dosage form: powder for injection, solution for injection</p> <p>Strength: 125 mg/mL solution for injection, 250 mg powder for injection</p> <p>Usual dose:</p> <p>Greater than 100 kg: 1000 mg intravenously over 30 minutes every 2 weeks</p> <p>60-100 kg: 750 intravenously over 30 minutes every 2 weeks</p> <p>Less than 60 kg: 500 mg intravenously over 30 minutes every 2 weeks</p>	<p><u>Orthographic similarity to Qnexa</u> When scripted the letter string ‘Qne’ may look like ‘Ore’.</p> <p><u>Dosage form</u> Both products are available as a single dosage form. Thus the dosage form maybe omitted when prescribed.</p>	<p><u>Orthographic differences</u> When scripted the letter ‘x’ looks different from the letter string ‘nci’.</p> <p><u>Strength and Dosing</u> Qnexa is available in multiple strengths, and would need to be specified when prescribing. Orencia is dosed on body weight. There are no overlapping strengths or doses.</p>
<p>Ovcon (norethindrone/ethinyl estradiol)</p> <p>Dosage form: tablet</p> <p>Usual dose: Take 1 tablet orally daily OR Use as directed</p>	<p><u>Orthographic similarity to Qnexa</u> When scripted the letter string ‘Qne’ may look like ‘Ovc’. Qnexa and Ovcon are identical in length, 5 letters.</p> <p><u>Dosage form</u> Both products are available as oral dosage forms.</p> <p><u>Frequency</u> Both products are dosed once daily.</p> <p><u>Route of administration</u> Both product are available as oral dosage forms.</p>	<p><u>Strength</u> Single strength vs. multiple strengths and no overlap in strengths. Thus, the strength of Ovcon may be omitted, but the strength of Qnexa must be specified.</p>

<p>Proposed name: Qnexa (phentermine and topiramate extended-release) Dosage Form(s): capsule</p> <p>Strength(s): 3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, 15 mg/92 mg</p> <p>Usual Dose: 7.5 mg/46 mg once daily OR take as directed</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Qnasl nasal spray (beclomethasone dipropionate) Dosage form: nasal spray Strength: 80 mcg per actuation Usual dose: Two nasal sprays in each nostril daily</p>	<p><u>Orthographic similarity to Qnexa</u> When scripted the letter string 'Qnex' may look similar to 'Qnas'. Qnexa and Qnasl are identical in length, 5 letters.</p> <p><u>Phonetic similarity to Qnexa</u> When spoken the letters 'Qne' sound similar to 'Qna'.</p> <p><u>Dosage form</u> Both products are available as a single dosage form. Thus the dosage form maybe omitted when prescribed.</p> <p><u>Frequency</u> Both products are dosed once daily.</p>	<p><u>Strength</u> Single strength vs. multiple strengths and no overlap in strengths. Thus, the strength of Qvar may be omitted, but the strength of Qnexa must be specified</p>

<p>Proposed name: Qnexa (phentermine and topiramate extended-release) Dosage Form(s): capsule</p> <p>Strength(s): 3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, 15 mg/92 mg</p> <p>Usual Dose: 7.5 mg/46 mg once daily OR take as directed</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Umecta (urea)</p> <p>Dosage: nail film suspension, topical emulsion</p> <p>Usual dose: Apply to affected area twice daily or Use as directed</p>	<p><u>Orthographic similarity to Qnexa</u> When scripted the letter string ‘Qne’ looks similar to ‘Ume’.</p> <p><u>Frequency of Administration</u> Both products can be administered once daily to twice daily.</p>	<p><u>Strength</u> Single strength vs. multiple strengths and no overlap in strengths. Thus, the strength of Umecta may be omitted, but the strength of Qnexa must be specified.</p>
<p>Zmax (azithromycin extended release) for oral suspension</p> <p>Dosage form: oral suspension</p> <p>Strength: 100 mg/5 mL, 200 mg/5 mL</p> <p>Usual dose: Give 2 teaspoonfuls orally on day 1, then 1 teaspoonful on days 2-5.</p>	<p><u>Orthographic similarity to Qnexa</u> When scripted the letter string ‘nex’ and ‘max’ may look similar. The names Qnexa and Zmax are similar in length, 5 letters compared to 4 letters, respectively.</p> <p><u>Frequency</u> Both products are dosed once daily</p> <p><u>Route of Administration</u> Both products are administered orally.</p>	<p><u>Orthographic differences</u> When scripted the letter ‘Q’ looks different from the letter ‘Z’.</p> <p><u>Strength</u> There are no overlapping product strengths between products. The product strength must be specified with both products.</p>

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

/s/

YELENA L MASLOV on behalf of KEVIN WRIGHT
04/16/2012

YELENA L MASLOV
04/16/2012

KELLIE A TAYLOR
04/16/2012

CAROL A HOLQUIST
04/16/2012



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

Date: February 17, 2010

To: Mary Parks, MD, Director
Division of Metabolism and Endocrinology Drugs

Thru: Melina Griffis, RPh, Team Leader
Denise Toyer, PharmD, Deputy Director
Carol Holquist, RPh, Director
Division of Medication Error Prevention and Analysis (DMEPA)

From: Anne Crandall, PharmD, Safety Evaluator
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name(s): Qnexa (Phentermine and Topiramate) Controlled Release Capsules,
3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, 15 mg/92 mg

Application Type/Number: IND # 068651
NDA # 022580

Sponsor: Vivus

OSE RCM #: 2009-2013

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

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EXECUTIVE SUMMARY

Qnexa is the proposed proprietary name for Phentermine and Topiramate tablets. This proposed name was evaluated from a safety and promotional perspective based on the product characteristics provided by the Applicant. We sought input from pertinent disciplines involved with the review of this application and considered it accordingly. 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, Qnexa, acceptable for this product.

If any of the proposed product characteristics as stated in the review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change. In addition, the proposed name must be submitted for review at the time of NDA submission.

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from Vivus Inc. dated September 30, 2009 for an assessment of the proposed proprietary name, Qnexa, regarding potential name confusion with other proprietary or established drug names in the usual practice setting.

1.2 PRODUCT INFORMATION

Qnexa (Phentermine and Topiramate) is a combination of two drugs indicated as an adjunct to diet and exercise to aid in weight loss in obese patients or overweight patients. Phentermine first received approval by the FDA as an appetite suppressant in 1959. Compounds similar to Phentermine, Fenfluramine and Dexfenfluramine were voluntarily taken off the market at the request of the FDA due to a finding of heart valve disease in patients taking Fenfluramine and Dexfenfluramine. Topiramate is an anti-epileptic drug with a known side effect of anorexia.

The recommended starting dose of Qnexa is 3.75 mg/23 mg by mouth once daily. The dose can be titrated up to a maximum dose of 15 mg/92 mg by mouth once daily. Qnexa capsules are available in four strengths: 3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, and 15 mg/92 mg. Qnexa is supplied in bottles containing 30 capsules (b) (4) to be used in the initial phase and during titrations.

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, Qnexa.

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter 'Q' 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}

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)

To identify drug names that may look similar to 'Qnexa', the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (five letters), upstrokes (1, capital letter 'Q'), downstrokes (none), dotted letters (none) and cross-strokes (two, upper case 'Q' and lower case letter 'x').

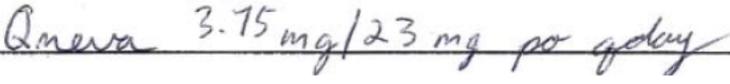
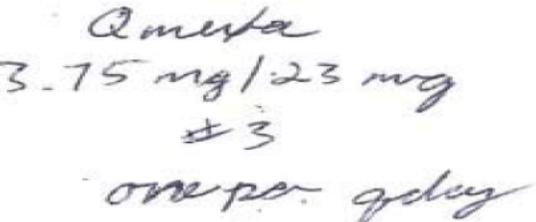
Because the letter 'Q' is typically followed by the letter 'u', the search included names that began with 'Qu', as the name when read or heard could be transcribed or interpreted with a 'u'. In addition to 'Q', several letters in Qnexa may be vulnerable to ambiguity when scripted (see Appendix B). As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Qnexa.

When searching to identify potential names that may sound similar to Qnexa, the DMEPA staff searches for names with similar number of syllables (three), stresses (Q-nex-a, q-NEX-a or q-nex-A), and placement of vowel and consonant sounds. Pronunciation of Qnexa (q-nex-a) was submitted by the Applicant. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary (See Appendix B). Furthermore, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

2.2 FDA PRESCRIPTION ANALYSIS STUDIES

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

Figure 1. Qnexa Study (conducted on November 9, 2009)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
<p><u>Inpatient Medication Order:</u></p> 	<p>Qnexa 3.75 mg/23 mg One po qday Number 3</p>
<p><u>Outpatient Prescription:</u></p> 	

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The searches yielded a total of 19 names as having some similarity to the name Qnexa.

Fifteen of the 19 names (Quixin, Onxol, Onexacin, (b) (4), Quinine, Anexsia, Lexiva, Nexavar, Q flex, Qvar, Genexa, Iquix, Quide, Zolinza, and Qnexa,) were thought to look like Qnexa. One name (Ranexa) was thought to look and sound like Qnexa. The remaining three names (Kionex, Qutenza and Lunesta) were thought to sound similar to Qnexa.

A search of the United States Adopted Name stem list on November 10, 2009 did not identify any United States Adopted Names (USAN) stem within the proposed name, Qnexa.

3.2 EXPERT PANEL DISCUSSION

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

DDMAC had no concerns regarding the proposed name from a promotional perspective and offered no additional comments.

3.3 FDA PRESCRIPTION ANALYSIS STUDIES

A total of 23 practitioners responded. None of the respondents interpreted the name correctly as 'Qnexa'. Common misinterpretations included the letter 'x' mistaken for 'v' and 't' and the vowel 'u' or 'i' added after the 'Q'. The 'n' was mistaken for 'm' in the inpatient and the outpatient study. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 COMMENTS FROM THE DIVISION OF METABOLISM AND ENDOCRINOLOGY PRODUCTS (DMEP)

3.4.1 Initial Phase of the Review

In response to the OSE e-mail on January 12, 2009, the Division of Metabolism and Endocrinology Products did not forward any comments or concerns on the proposed proprietary name at the initial phase of the review.

3.4.2 Midpoint of Review

DMEPA notified DMEP via e-mail on January 14, 2009, that we object to the proposed proprietary name Qnexa. Per e-mail correspondence from DMEP on January 18, 2009, they indicated they concur with our assessment of the proposed proprietary name, Qnexa.

3.6 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator identified six additional names (Arava, Abreva, Adoxa, Ornex, Avinza and Celexa) thought to look similar and represent a potential source of confusion to Qnexa.

A total of 25 names were identified as names with some similarity to Qnexa.

4 DISCUSSION

The Proposed name, Qnexa, was evaluated from promotional and safety perspectives.

4.1 PROMOTIONAL ASSESSMENT

DDMAC did not have promotional concerns with the proposed name, Qnexa. The Division of Metabolism and Endocrinology Products and DMEPA concurred with DDMAC's assessment.

4.2 SAFETY REVIEW

During the safety review of the proprietary name Qnexa, DMEPA did not identify aspects of the name other than identifying names that are orthographically or phonetically similar that would render the name unacceptable. DMEPA identified and evaluated 25 names for their potential similarity to the proposed proprietary name Qnexa. All 25 names were determined to have some orthographic and/or phonetic similarity

to Qnexa, and thus determined to present some risk for confusion. Four names (Onexacin, Qnexa, Quide, and (b) (4)) were excluded from further analysis because the products are not marketed in the U.S., discontinued with no generic availability, or the same name as that which is the subject of this review (See Appendices D through F).

FMEA was then applied to determine if the proposed name, Qnexa, could potentially be confused with the remaining 21 names and lead to medication errors. This analysis determined that the name similarity between Qnexa was unlikely to result in medication errors with any of the 21 products for the reason presented in Appendices H through J. This assessment was shared with the review Division who concurred with our assessment.

5 CONCLUSIONS AND RECOMMENDATIONS

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

However, if any of the proposed product characteristics as stated in this review are altered prior to submission of the NDA, DMEPA rescinds this Risk Assessment finding and the name must be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change.

We are willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Mildred Wright, OSE Project Manager at 301-796-1027.

5.1 COMMENTS TO THE APPLICANT

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

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

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

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, 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.

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

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 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. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

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

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

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

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

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

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

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

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

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

- a. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC’s findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made

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

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

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

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

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

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

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in Name, Qneva	Scripted may appear as	Spoken may be interpreted as
Capital 'Q'	'A', 'Qu' 'G' or 'O'	"KU", "CU", "QU"
Lower case 'n'	'r', 's' or 'u'	"M"
Lower case 'e'	'o', 'a', or 'i'	"I"
Lower case 'x'	'v', 'n', or 's'	"CKS"
Lower case 'a'	'u' or 'o'	"AH"

Appendix C: FDA Prescription 11/09 Study Responses

Inpatient Medication Order	Outpatient Prescription	Voice Prescription
Qneva	Qumexa	Qunexa
Queva	Qineta	
Queva	Qmeva	
Qneva	Qmexa	
Qneva	Qmexa	
Queva	Qmexa	
Qneva		
Qmeva		
Qmexa		

Appendix D: Name is the application under review

Proprietary Name	Established Name	Applicant	Website
Qnexa	Phentermine/Topiramate	Esai	United States Patent and Trade Office (USPTO)

Appendix E: Product discontinued, no generic available

Proprietary Name	Established Name	NDA
Quide	Piperacetazine	013615

Appendix F: Product approved with different name

Proprietary Name (Established Name)	Approved Name	NDA
(b) (4)		

Appendix G: Products with no numeric overlap in dose or strength

Product name with potential for confusion	Similarity to Qnexa	Strength	Usual Dose
Qnexa (Phentermine and Topiramate)		3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, 15 mg/92 mg oral capsules	One capsule by mouth once daily
Quixin (Levofloxacin)	Look	0.5% ophthalmic solution	Day 1 and 2: Instill one to two drops in the affected eye(s) every 2 hours while awake Day 3 through 7: Instill one to two drops in the affected eye(s) every 4 hours while awake

Product name with potential for confusion	Similarity to Qnexa	Strength	Usual Dose
Qnexa (Phentermine and Topiramate)		3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, 15 mg/92 mg oral capsules	One capsule by mouth once daily
Onxol (Paclitaxel)	Look	6 mg/mL injection solution available in 5 mL, 25 mL and 50 mL vials	135 mg/m ² to 175 mg/m ² intravenously every 3 weeks *All patients must be pre-medicated with Dexamethasone prior to Onxol therapy
Quinine USP	Look	324 mg oral capsule	Two capsules every 8 hours for 7 days
Lexiva (Fosamprenavir calcium)	Look	700 mg oral tablet 50 mg/mL oral suspension, 225 mL bottle	Adults: 1400 mg by mouth twice daily or 1400 mg once daily if taken with Ritonavir once daily 700 mg by mouth twice with Ritonavir twice daily Pediatrics: 30 mg/kg twice daily or 18 mg/kg if taken with Ritonavir
Nexavar (Sorafenib)	Look	200 mg oral tablet	400 mg by mouth twice daily, if toxicity occurs, decrease to 400 mg once daily or every other day
QFlex (Acetaminophen and Phenyltolxamine)	Look	600 mg/66 mg extended-release oral tablet	1 tablet by mouth twice daily
Qvar (Beclomethasone dipropionate)	Look	40 mcg, 80 mcg canister with actuator	1 to 4 inhalations by mouth twice daily
Genexa LA (guaifenesin and Phenylephrine) * DISCONTINUED	Look	400 mg/30 mg oral capsule	One tablet every 12 hours
Iquix (Levofloxacin)	Look	1.5% ophthalmic solution	Days 1 to 3: Instill one to two drops in the affected eye(s) every 30 minutes to 2 hours while awake Days 4 through treatment completion: Instill one to two drops in the affected eye every 1 to 4 hours while awake
Qutenza (Capsaicin)	Look	8% (179 mg) topical patch	Apply up to 4 patches to area for 60 minutes
Lunesta (Eszopiclone)	Sound	1 mg, 2 mg, 3 mg oral tablet	1 mg to 3 mg by mouth immediately before bedtime

Product name with potential for confusion	Similarity to Qnexa	Strength	Usual Dose
Qnexa (Phentermine and Topiramate)		3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, 15 mg/92 mg oral capsules	One capsule by mouth once daily
Zolinza (Vorinostat)	Look	100 mg oral capsule	300 mg to 400 mg once daily, or 300 mg for 5 consecutive days each week
Arava (Leflunomide)	Look	10 mg, 20 mg, 100 mg oral tablet	Loading dose: 100 mg by mouth once daily for 3 days Maintenance dose: 10 mg to 20 mg by mouth once daily
Abreva (Docosanol)	Look	10% topical cream	Apply 5 times daily to affected area
Adoxa (Doxycycline)	Look	50 mg, 75 mg, 100 mg oral tablet or 150 mg oral capsule	Adults: 300 mg by mouth once, 100 mg by mouth every 12 hours, 100 mg by mouth once daily, 200 to 400 mg per day divided in 2 doses Pediatric: 1 mg/kg to 8 mg/kg by mouth divided into 1 or 2 doses per day
Ranexa (Ranolazine)	Look and Sound	500 mg, 1000 mg oral tablet	500 mg to 1000 mg by mouth twice daily

Appendix H: Products with overlapping strength, numeric similarity in dose or strong orthographic similarity but multiple differentiating product characteristics

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Other differentiating product characteristics
Qnexa (Phentermine and Topiramate)		3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, 15 mg/92 mg oral capsules	Usual Dose: One capsule by mouth once daily	
Anexsia (Hydrocodone and acetaminophen)	Orthographic	5 mg/325 mg, 7.5 mg/325 mg, 10 mg/660 mg, 5 mg/500 mg, 7.5 mg/650 mg oral tablet	1 to 2 tablets every 4 to 6 hours as needed, total 24 hour dose not to exceed 4000 mg acetaminophen	<i>Frequency of administration</i> (Qnexa is dosed once daily vs. Anexsia is dosed every 4 to 6 hours) <i>Strength</i> (Both drugs have 7.5 mg, however because Anexsia has two different strengths of 7.5 mg, the acetaminophen strength would have to be designated as 325 mg or 650 mg which would clearly distinguish Qnexa and Anexsia because Qnexa strength that coincides with 7.5 mg is 46 mg)
Celexa (Citalopram)	Orthographic	10 mg, 20 mg , 40 mg oral tablet 10 mg/5 mL oral solution	10 mg to 60 mg by mouth once daily	<i>Obtainable dose</i> (60 mg) Although obtainable, 60 mg of the Phentermine component is four times the maximum recommended dose of Qnexa.
Kionex (Sodium polystyrene sulfonate, USP)	Phonetic	15 g per 4 teaspoonsful, 1 pound ground powder 480 mL of suspension Sodium content: 65 mEq/60 mL Potassium content: 1 mEq/4 mL	15 g to 60 g as a suspension (4 to 16 level teaspoons) by mouth four times daily	<i>Frequency of administration</i> (once daily vs. four times daily) <i>Dosage form</i> (capsule vs. suspension and powder) <i>Dose</i> (mg vs. g/mL)
Ornex (Acetaminophen/ Pseudoephed- rine)	Orthographic	325 mg/30 mg oral tablet	1 to 2 tablets by mouth every 4 to 6 hours as needed for symptoms	<i>Strength</i> (3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, 15 mg/92 mg vs. 325 mg/30 mg, single strength) <i>Frequency</i> (once daily vs. 4 to 6 times per day)

Appendix I: Name with orthographic similarity or obtainable strength with product characteristic or orthographic differences

Failure Mode: Name confusion	Causes (could be multiple)	Rationale
Qnexa (Phentermine and Topiramate)	3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, 15 mg/92 mg oral capsules	Usual Dose: 1 capsule by mouth once daily
<p>Avinza (Morphine sulfate extended release)</p> <p>30 mg, 45 mg, 60 mg, 75 mg, 90 mg, 120 mg oral capsule</p> <p>30 mg to 1600 mg by mouth per day. Doses should not exceed 1600 mg per day and dose should be administered once daily</p>	<p><i>Orthographic similarities include:</i></p> <p>Similar initial letter ('Q' and 'A' appear similar when scripted)</p> <p>Similar length (Qnexa has 5 letters vs. Avinza has six letters)</p> <p><i>Product characteristics include:</i></p> <p>Frequency of administration (once daily)</p> <p>Route of administration (oral)</p> <p>Dosage form (capsule)</p> <p>Obtainable dose (30 mg)</p>	<p>Medication errors are unlikely to occur due to orthographic and product differences.</p> <p><i>Rationale:</i></p> <p><i>1. Orthographic differences</i></p> <ul style="list-style-type: none"> - Qnexa contains no down-strokes vs. Avinza contains one down-stroke, 'z', if scripted. - Qnexa contains three letters between 'Q' and 'a' vs. Avinza contains four letters between 'A' and 'a' which makes the name more lengthy when scripted. - Qnexa contains two cross-strokes, capital letter 'Q' and lower case 'x' compared to Avinza which contains no cross-strokes. <p><i>2. Product characteristics</i></p> <ul style="list-style-type: none"> - The obtainable dose of Qnexa 30 mg exceeds the maximum recommended dose of Qnexa. Additionally, if a prescription is written for Qnexa 15 mg (without the Topiramate strength) and is misinterpreted as Avinza 15 mg the strength is not available with this extended release product.. - Avinza is a C II (Controlled substance, category 2). If a prescription for Avinza 30 mg was mistaken for Qnexa 30 mg, the provider would have to double the amount of capsules in the prescription. The requested number of capsules on the prescription would have to match exactly with the directions. If the number did not match, the provider must be called to rectify the prescription. Additionally, because of the status of Avinza as a C II, no refills can be ordered on the prescription. Additionally, 30 mg exceeds the maximum recommended dose of Qnexa.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
IND-68651	ORIG-1	VIVUS INC	PHENTERMINE/TOPIRAMATE; VI-0521
NDA-22580	ORIG-1	VIVUS INC	QNEXA (phentermine IR + topiramate modified release) CAPSULE; VI-0521

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/s/

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02/17/2010

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