CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

202100Orig1s000

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:	September 17, 2012
Reviewer:	Loretta Holmes, BSN, PharmD Division of Medication Error Prevention and Analysis
Team Leader	Irene Z. Chan, PharmD, BCPS Division of Medication Error Prevention and Analysis
Division Director	Carol A. Holquist, RPh Division of Medication Error Prevention and Analysis
Drug Name and Strength:	Quillivant XR (Methylphenidate Hydrochloride) for Extended-release Oral Suspension 25 mg/5 mL
Application Type/Number:	NDA 202100
Applicant:	NextWave Pharmaceuticals, Inc.
OSE RCM #:	2012-1780

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Quillivant XR, 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

NDA 202100 for Quillivant XR (Methylphenidate Hydrochloride) for Extended-release Oral Suspension is a 505(b)(2) application. The Reference Listed Drug (RLD) is Methylin (Methylphenidate Hydrochloride) Oral Solution (NDA 021419). The NDA was submitted on July 29, 2010 and a Complete Response (CR) action was taken on August 30, 2011. The Applicant resubmitted the NDA on March 30, 2012 in response to the CR action.

The name (b) (4) was initially proposed for this NDA. DMEPA found the proposed name, (b) (4) unacceptable (b) (4) the Applicant was notified of DMEPA's findings via teleconference on March 1, 2011. As a result, the Applicant withdrew the proposed proprietary name (b) (4) on March 7, 2011. The Applicant submitted a new Proprietary Name Review Request for the name Quillivant on March 31, 2011. The name was found acceptable in OSE Review 2011-1138, dated May 12, 2011.

Following resubmission of the NDA, a request for re-review of the proposed proprietary name Quillivant was submitted on April 17, 2012. However, in our re-review of the name in OSE Review 2012-958, dated July 16, 2012, the name was found unacceptable because it lacked a modifier that would help to convey the product's extended-release formulation and once daily administration. Thus, the Applicant submitted the name Quillivant XR on August 2, 2012 for our review.

1.2 PRODUCT INFORMATION

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

- **Active Ingredient:** Methylphenidate Hydrochloride
- **Indication of Use:** Treatment of Attention Deficit Hyperactivity Disorder (ADHD)
- **Route of administration:** Oral
- **Dosage form:** for Extended-release Oral Suspension
- **Strength:** 25 mg/5 mL (5 mg/mL)
- **Dose and Frequency of Administration:** For patients 6 years and above, the recommended starting dose is 20 mg given orally once daily in the morning. Dosage may be increased by 10 mg per day to 20 mg per day at weekly intervals. Daily dosage above 60 mg is not recommended.

- **How Supplied:** Supplied in bottles to prepare 60 mL, 120 mL, 180 mL, 240 mL, 300 mL or 360 mL. Each carton contains one bottle of Quillivant, one 12 mL oral dosing dispenser and one bottle adapter. Quillivant must be reconstituted by the pharmacist before dispensing.
- **Storage:** Store at 25ºC (77ºF); excursions permitted from 15ºC to 30ºC (59ºF to 86ºF)
- **Container and Closure Systems:** USP Type III glass with Child-Resistant Closure (CRC)
- **Status:** Quillivant XR is a Schedule II controlled substance
- **Proposed Pronunciation:** QUIL·I·VANT (\kwil-ə-vant\) XR
- **Derivation of the Name:** None provided

2 RESULTS

The following sections provide the information obtained and considered in the overall 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 Psychiatry Products (DPP) concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) SEARCH

The August 20, 2012 search of the United States Adopted Name (USAN) stems did not identify a USAN stem present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The proposed proprietary name contains two components 1) the proposed root name, Quillivant, and 2) a modifier, XR. See Section 3 *Discussion* for our evaluation of the proposed modifier.

2.2.3 FDA Name Simulation Studies

Eighty-four practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with or appear or sound similar to any currently marketed products. Across all three studies, the modifier XR was omitted by four participants. Additionally, across all three studies, the modifier was misinterpreted as SR, XT, or XT by seven participants. Thirty-one participants in the verbal study misinterpreted the name and spelled it with one "l" rather than "ll". 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, August 9, 2012 e-mail, the Division of Psychiatry Products (DPP) 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, Quillivant XR. Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Quillivant XR, identified by the primary reviewer and the Expert Panel Discussion (EPD).

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

Look Similar					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Quinalan	EPD Panel	Qutenza	EPD Panel	Amiloride	Primary SE
Quenalin	EPD Panel	Dexilant	EPD Panel	Combivent	Primary SE
Quinact	EPD Panel	Quadramet	EPD Panel	Quillaja	Primary SE
(b) (4)	EPD Panel	Quinaretic	EPD Panel	Gadavist	Primary SE
(b) (4) **	EPD Panel	Quinapril	EPD Panel	Questran	EPD Panel
Acetasol	EPD Panel	Quinaglute	EPD Panel	Gallium	Primary SE
Anatrast	EPD Panel	Beclovent	EPD Panel	Quentyl	EPD Panel
Avodart	EPD Panel	Qualaquin	EPD Panel	Oxistat	EPD Panel
Gantanol	Primary SE	Quadrahist	EPD Panel	Quintabs	EPD Panel
Gantanol DS	Primary SE	Quadrahist-D	EPD Panel	Quibron-T	EPD Panel
Quelidrine	EPD Panel	Horizant	EPD Panel	Quibron-T/SR	EPD Panel
Quadraplex	EPD Panel	Quadrinal	EPD Panel	Qual-Tussin	EPD Panel
Quicklance	EPD Panel	Octreotide	EPD Panel	Ortho-Novum	EPD Panel
Ondansetron	EPD Panel	One-Tab-Daily	EPD Panel	Qual-Tussin DC	EPD Panel
Ortho-Cept	EPD Panel	Acetasol HC	EPD Panel		

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Look and Sound Similar					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Quillaia	EPD Panel	Quelicin	EPD Panel	Guaivent	EPD Panel

Our analysis of the 47 names contained in Table 1 considered the information obtained in the previous sections along with the product characteristics. We determined all 47 names do not pose a risk for confusion as described in Appendices D and E.

2.2.6 Modifier XR

In our previous review of the name, Quillivant, in OSE Review 2012-958, dated July 16, 2012, we determined that a modifier would be required to convey the extended-release properties of this product. The Applicant selected the modifier "XR" to convey this information. Thus, we evaluated the appropriateness of the modifier "XR".

Although "XR" has been used to communicate once or twice daily administration, most products with the XR modifier are dosed once daily and the modifier "XR" has not been cited as a source of confusion postmarketing. Therefore, the use of the modifier "XR", in this circumstance, is consistent with the majority of other XR products that are currently marketed. Thus, we conclude the proposed modifier, "XR", is appropriate for this product.

2.2.7 Communication of DMEPA's Final Decision to Other Disciplines

DMEPA communicated our findings to the Division of Psychiatry Products via e-mail on August 22, 2012. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Psychiatry Product on August 22, 2012, they stated no additional concerns with the proposed proprietary name, Quillivant XR.

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 Sandra Griffith, OSE Project Manager, at 301-796-2445.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Quillivant XR, and have concluded that this name is acceptable. If any of the proposed product characteristics as stated in your August 2, 2012 submission are altered the name must be resubmitted for review.

4 REFERENCES

1. Maslov, Lena. Quillivant Proprietary Name Review. OSE Review 2011-1139, dated May 12, 2011.
2. Holmes, Loretta. Quillivant Proprietary Name Review. OSE Review 2012-958, dated July 16, 2012.
3. ***Micromedex Integrated Index (http://csi.micromedex.com)***

   Micromedex contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.
4. ***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.
5. ***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.
6. ***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.
7. ***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.
8. ***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.
9. ***U.S. Patent and Trademark Office (http://www.uspto.gov)***

   USPTO provides information regarding patent and trademarks.

10. 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.

11. 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.

12. 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.

13. Access Medicine (www.accessmedicine.com)

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

14. USAN Stems (http://www.ama-assn.org/ama/pub/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.

15. Red Book Pharmacy's Fundamental Reference

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

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

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

17. Medical Abbreviations Book

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

18. CVS/Pharmacy (www.CVS.com)

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

19. Walgreens (www.walgreens.com)

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

20. Rx List (www.rxlist.com)

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

21. 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 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.

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[1] National Coordinating Council for Medication Error Reporting and Prevention. http://www nccmerp.org/aboutMedErrors 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.[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**		
	Potential Causes of Drug Name Similarity	*Attributes Examined to Identify Similar Drug Names*	*Potential Effects*
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name/Similar shape Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, 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 gather 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 Division of Drug Marketing, Advertising, and Communications (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 posses similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

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

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

The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not 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 Quillivant	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'Q'	'G', 'O', 'A', 'D'	'K', 'G'
lower case "q"	g, j, z	'k', 'g'
lower case 'u'	'n', 'v', 'w'	Any vowel
lower case 'i'	'e', 'l'	Any vowel
lower case 'l'	'b', 'e', 's', 'i'	
Letter string 'll'	'u', 'il', 'li', 'el', 'le', 'tt'	
lower case 'i'	'e', 'l'	Any vowel
lower case 'v'	'r', 'u', 'y', z', 'x', 'n'	'f'
lower case 'a'	'ci', 'cl', 'd', 'o', 'el, 'u', 'n'	Any vowel
lower case 'n'	'm', 'u', 'x', 'r', 'h', 's'	'm', 'dn', 'kn', 'mn, 'pn'
Lower case 't'	'f', 'd', 'b' 'r', 'x', 'a'	'd'
Capital 'X'	'd', 'f', 'K', 'P', 't', 'U', 'V', 'Y'	'KS', 'KZ', 'S', 'Z'
Capital 'R'	'B', 'Pr', 'K'	

Appendix C: Prescription Simulation Samples and Results

Figure 1. Quillivant XR Study (Conducted on August 10, 2012)

Handwritten Requisition Medication Order	Verbal Prescription
Inpatient Medication Order: Quillivant XR 40mg PO QAM	"Quillivant XR 6 mL po qam" "Dispense # 180 mL"
Outpatient Prescription: Quillivant XR 6 ml PO QAm 180mL	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

				184 People Received Study
				96 People Responded
Study Name: Quillivant XR				
Total	**30**	**36**	**30**	
INTERPRETATION	**INPATIENT**	**VOICE**	**OUTPATIENT**	**TOTAL**
?	0	1	0	1
CLOVAC SR	0	1	0	1
CLUILLIVANT XR	0	0	2	2
ONILLIVANT XR	0	0	1	1
OUILLIVANT XR	1	0	2	3
QUELAVANCE XR	0	1	0	1
QUILAVANT XR	0	8	0	8
QUILAVEN	0	1	0	1
QUILAVENT SR	0	1	0	1
QUILAVENT XR	0	2	0	2
QUILEVANT XR	0	1	0	1
QUILEVENT XR	0	1	0	1
QUILIVAN XR	0	2	0	2
QUILIVANT SR	0	1	0	1
QUILIVANT XR	0	7	0	7
QUILIVEN SR	0	1	0	1
QUILIVENT XR	0	3	0	3
QUILLERANT XR	1	0	0	1
QUILLERIANT XL	0	0	1	1
QUILLIRANT	0	0	1	1
QUILLIRANT XR	1	0	0	1
QUILLIVANT	1	0	3	4
QUILLIVANT XR	25	0	18	43
QUILLIVANT XR	0	0	1	1

QUILLIVANT XT	1	0	1	2
QUILLIVENT XR	0	1	0	1
QUILVANT	0	1	0	1
QUIVALENT XR	0	1	0	1
QUIVANT XR	0	1	0	1
QULAVET XR	0	1	0	1

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

No.	Proprietary Name	Active Ingredient	Similarity to Quillivant XR	Failure preventions
1.	Oxistat	Oxiconazole Nitrate	Look	Lacks sufficient orthographic similarity.
2.	Quentyl	Dicyclomine HCl, USP	Look	Lacks sufficient orthographic similarity.
3.	Quinaglute	Quinidine Gluconate Extended-release	Look	Lacks sufficient orthographic similarity.
4.	Quillaja	N/A	Look	Quillaja is a large evergreen tree with shiny thick leaves. The inner bark has commercial and medicinal uses. Also known as Quillaia.
5.	Quillaia	N/A	Look and Sound	Quillaja is a large evergreen tree with shiny thick leaves. The inner bark has commercial and medicinal uses. Also known as Quillaja.
6.	Quinact	Quinidine Gluconate	Look	Discontinued without generic equivalent available.
7.	Anatrast	Barium Sulfate	Look	Discontinued without generic equivalent available.
8.	Quibron-T	Theophylline	Look	Discontinued without generic equivalent available.
9.	Quibron-T/SR	Theophylline	Look	Discontinued without generic equivalent available.
10.	Guaivent	Guaifenesin and Phenylpropanolamine	Look and Sound	Discontinued without generic equivalent available.
11.	Gantanol	Sulfamethoxazole	Look	Discontinued without generic equivalent available.
12.	Gantanol DS	Sulfamethoxazole	Look	Discontinued without generic equivalent available.
13.	Beclovent	Beclomethasone	Look	Discontinued without generic equivalent available.
14.	Gallium	Gallium	Look	Lacks sufficient orthographic similarity

No.	Proprietary Name	Active Ingredient	Similarity to Quillivant XR	Failure preventions
				(b) (4)
16.	Quelidrine Cough	Phenylephrine HCl, Ammonium Chloride, Ipecac Syrup, Dextromethorphan HBr, Chlorpheniramine Maleate, and Ephedrine HCl	Look	This name was found in Micromedex with the ingredient information provided. Unable to find dosing information in Micromedex or our other standard drug information databases.
17.	Quadrahist	Chlorpheniramine Maleate, Phenylephrine, Phenylpropanolamine, Phenyltoloxamine	Look	This is a discontinued product. Unable to find dosing information in our standard drug information databases. According to SAEGIS, the year of last recorded sales of this product was 2000.[4]
18.	Quadrahist-D	Pheniramine Maleate, Phenylpropanolamine HCl, Phenyltoloxamine Citrate, Pyrilamine Maleate	Look	This is a discontinued product. Unable to find dosing information in our standard drug information databases. According to SAEGIS, the year of last recorded sales of this product was 2004.[4]
19.	Quadrinal	Ephedrine HCl, Phenobarbital, Potassium Iodide, Theophylline	Look	This is a discontinued product. Unable to find dosing information in our standard drug information databases. According to SAEGIS, the year of last recorded sales of this product was 2000.[4]
20.	Qual-Tussin	Chlorpheniramine Maleate, Dextromethorphan HBr, Guaifenesin, Phenylephrine HCl	Look	This is a discontinued product. No generic equivalents identified. According to SAEGIS, the year of last recorded sales of this product was 2007.[4]
21.	Qual-Tussin DC	Guaifenesin, Hydrocodone Bitartrate, Phenylephrine HCl	Look	This is a discontinued product. No generic equivalents identified. According to SAEGIS, the year of last recorded sales of this product was 2004.[4]
22.	Quadraplex	Unknown	Look	This name was found at cvs.com. No product characteristic information specific to this product could be found there or in our standard drug information databases.
23.	Horizant	Gabapentin Enacarbil	Look	Lacks sufficient orthographic similarity

[4] **Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at (www.thomson-thomson.com). Accessed on August 20, 2012.**

No.	Proprietary Name	Active Ingredient	Similarity to Quillivant XR	Failure preventions
24.	Quicklance	N/A	Look	This is not a drug product. It is a lancet device.
25.	Octreotide	Octreotide	Look	Lacks sufficient orthographic similarity.
26.	Ondansetron	Ondansetron	Look	Lacks sufficient orthographic similarity.
27.	One-Tab-Daily	Unknown (ingredient information not available)	Look	Lacks sufficient orthographic similarity.
28.	Ortho-Cept	Ethinyl Estradiol and Desogestrel	Look	Lacks sufficient orthographic similarity.
29.	Ortho-Novum	Norethindrone and Ethinyl Estradiol	Look	Lacks sufficient orthographic similarity.

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.

No.	Proposed name: Quillivant XR	Strength: 25 mg/5 mL (5 mg/mL)	Usual dosage: 20 mg (4 mL) to 60 mg (12 mL) orally once daily in the morning
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
1.	Quinalan (Quinidine Gluconate) Extended-release Tablet 324 mg (Proprietary name discontinued, however, generic products are still available) Usual Dose 324 mg to 648 mg orally every 8 to 12 hours	Orthographic Both names start with the letter string 'Qui-' and share the letter string '-an' in similar positions. Route of Administration Orally	Orthographic The root name Quillivant contains 4 upstrokes vs. the name Quinalan contains 2 upstrokes. Additionally, the upstroke 'l' in Quinalan is located at a different position than the two upstrokes 'll' in Quillivant. Strength Quillivant strength is 25 mg/5 mL vs. 324 mg Usual Dose 20 mg (4 mL) to 60 mg (12 mL) vs. 324 mg to 648 mg Frequency of Administration Once daily vs. every 8 hours to 12 hours.

No.	Proposed name: Quillivant XR	Strength: 25 mg/5 mL (5 mg/mL)	Usual dosage: 20 mg (4 mL) to 60 mg (12 mL) orally once daily in the morning
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
2.	Quenalin (Diphenhydramine) Oral Solution 12.5 mg/5 mL Usual Dose: Adults and Adolescents: 25 mg to 50 mg orally three to four times per day, at 4 hour to 6 hour intervals, as needed. Maximum dose is 300 mg/day.	Orthographic Both names start with the letter string 'Qu-' and contain the letter 'n' in similar positions. Additionally, the letter 'e' in Quenalin may appear similar to the corresponding first letter 'i' in Quillivant when scripted. Overlap Strength and Dose Quillivant XR may de dispensed as 300 mg bottle and Quenalin has a maximum dose of 300 mg per day. Route of Administration Orally	Orthographic The root name Quillivant contains 4 upstrokes vs. the name Quinalan contains 2 upstrokes and upstrokes are not located in same positions. Additionally, the letter string '-ll-' in Quillivant lacks orthographic similarity to the corresponding letter string '-na-' in Quenalin when scripted. Frequency of Administration Once daily vs. every 4 hours to 6 hours

(b) (4)

[redacted]

No.	Proposed name: Quillivant XR	Strength: 25 mg/5 mL (5 mg/mL)	Usual dosage: 20 mg (4 mL) to 60 mg (12 mL) orally once daily in the morning
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
4.	Acetasol (Glacial Acetic Acid) Otic Solution, 2% (Proprietary name discontinued, however, generic products are still available) <u>Usual Dose</u> Instill 4 drops to 6 drops into external ear canal every 2 to 3 hours.	<u>Orthographic</u> The letter strings 'Quil-' and '-iv-' in Quillivant may appear similar to the corresponding letter strings 'Acet-' and '-so-' in Acetasol when scripted. <u>Numerical overlap in dose</u> Quillivant XR may be dosed as 4 mL and Acetasol is dosed at the strength of 4 drops	<u>Orthographic</u> The root name Quillivant appears longer than the name Acetasol (10 letters vs. 8 letters) Additionally, the second letter 'l' and the letter string '-ant' in Quillivant lack orthographic similarity to the corresponding letters 'a' and 'l' in Acetasol. <u>Frequency of Administration</u> Once daily vs. every 2 to 3 hours (Acetasol) or three to four times daily (Acetasol HC) An order for Acetasol would have to state which ear(s) the drops should be placed into.
5.	*Acetasol HC* (Glacial Acetic Acid and Hydrocortisone) Otic Solution, 2%/1% <u>Usual Dose</u> Instill 3 drops to 5 drops into external ear canal three to four times daily		

No.	Proposed name: Quillivant XR	Strength: 25 mg/5 mL (5 mg/mL)	Usual dosage: 20 mg (4 mL) to 60 mg (12 mL) orally once daily in the morning
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
6.	Avodart (Dutasteride) Capsules, 0.5 mg <u>Usual Dose</u> 0.5 mg orally once daily	<u>Orthographic</u> The letter string 'Quil-' may appear similar to the corresponding letter string 'Avod-' when scripted. <u>Overlap in Strength/Dose</u> Quillivant XR may be administered at the dose of 5 mL or 50 mg, which may overlap with the Avodart's dose of 0.5 mg, especially if the leading zero is omitted (e.g., .5 mg) <u>Route of Administration</u> Orally <u>Frequency of Administration</u> Once daily	<u>Orthographic</u> The root name Quillivant appears longer than the name Avodart (10 letters vs. 7 letters). Quillivant contains 4 upstroke letters including the adjacent letters 'll' whereas Avodart contains three upstroke letters and no adjacent upstroke letters.

No.	Proposed name: Quillivant XR	Strength: 25 mg/5 mL (5 mg/mL)	Usual dosage: 20 mg (4 mL) to 60 mg (12 mL) orally once daily in the morning
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
7.	Qutenza (Capsaicin) Topical Patch, 8% <u>Usual Dose</u> Use up to 4 patches per application. Apply for 60 minutes and do not use more often than every 3 months.	<u>Orthographic</u> Both names start with the letter string 'Qu-'. Additionally, the letter strings 'Quil-' and '-va-'in Quillivant appears to be similar to the letter strings 'Qut-' and '-za' in Qutenza when scripted. <u>Numerical Overlap in Dose</u> Quillivant XR may be administered at the dose of 4 mL and Qutenza is dosed at up to 4 patches	<u>Orthographic</u> The root name Quillivant appears longer than the name Qutenza (10 letters vs. 7 letters). Additionally, the name Quillivant contains 4 upstrokes vs. the name Qutenza contains 2 upstrokes. Additionally, the letter string '-li-' in Quillivant lacks orthographic similarity to the letter string '-en-' in Qutenza when scripted. <u>Frequency of Administration</u> Once daily vs. every 3 months
8.	Quadramet (Samarium sm 153 lexidronam) Injection <u>Usual Dose</u> 1 mCi/kg intravenously over 1 minute.	<u>Orthographic</u> Both names start with the letter string 'Qu-'. Additionally, the letter string '-vant' in Quillivant may be scripted to appear similar to the letter string '-met' in Quadramet.	<u>Orthographic</u> The root name Quillivant contains 2 upstrokes in the middle of the name (letter string 'll') vs. the name Quadramet contains 1 upstroke (letter 'd'). Additionally, the letter string '-illi-' in Quillivant lacks orthographic similarity to the letter string '-adra-' in Quadramet when scripted. <u>Usual Dose</u> 20 mg (4 mL) to 60 mg (12 mL) vs. 1 mCi/kg <u>Route of Administration</u> Orally vs. intravenously

No.	Proposed name: Quillivant XR	Strength: 25 mg/5 mL (5 mg/mL)	Usual dosage: 20 mg (4 mL) to 60 mg (12 mL) orally once daily in the morning
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
9.	Dexilant (Dexlansoprazole) Delayed-release Capsule, 30 mg and 60 mg <u>Usual Dose</u> 30 mg to 60 mg orally once daily	<u>Orthographic</u> Both names share the letter string '-ant' at the end of the names. Additionally, the letter strings 'Quil-' may appear similar to the corresponding letter string 'Dexil-' when scripted. <u>Overlap in Strength/Dose</u> Both products may be administered at the doses of 30 mg and 60 mg <u>Route of Administration</u> Orally <u>Frequency of Administration</u> Once daily	<u>Orthographic</u> The root name Quillivant appears longer than the name Dexilant (10 letters vs. 8 letters). Additionally, the letter string '-liv-' in Quillivant lacks similarity to the corresponding letter string '-ant' when scripted.

No.	Proposed name: Quillivant XR	Strength: 25 mg/5 mL (5 mg/mL)	Usual dosage: 20 mg (4 mL) to 60 mg (12 mL) orally once daily in the morning
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
10.	Quinaretic (Quinapril and Hydrochlorothiazide) Tablet, 10 mg/12.5 mg, 20 mg/12.5 mg, and 20 mg/25 mg Usual Dose 10 mg/12.5 mg to 20 mg/25 mg (maximum of 40 mg of quinapril and 25 mg of hydrochlorothiazide per day)	Orthographic Both names start with the letter string 'Qui-' Additionally, the letter string '-iv-' and the letter 'n' in Quillivant may appear similar to the corresponding letter strings '-re-' and '-ic' in Quinaretic when scripted. Partial Overlap in Strength/Dose Quillivant XR may be administer at the doses of 20 mg, or 25 mg, which overlaps with Quinaretic's partial strength of Quinapril (i.e., 20 mg) and Hydrochlorothiazide (i.e., 25 mg) Route of Administration Orally Frequency of Administration Once daily	Orthographic The root name Quillivant contains 4 upstroke vs. the name Quinaretic contains 2 upstrokes. Additionally, the letter string '-ll-' in Quillivant lacks orthographic similarity to the letter string '-na-' in Quinaretic when scripted. Prescribing: Quinaretic would have to be prescribed with both strengths of the active ingredients included on a prescription.

No.	Proposed name: Quillivant XR	Strength: 25 mg/5 mL (5 mg/mL)	Usual dosage: 20 mg (4 mL) to 60 mg (12 mL) orally once daily in the morning
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
11.	Quinapril Tablet, 10 mg, 20 mg, 30 mg, 40 mg , and 50 mg Usual Dose 10 to 20 mg orally once daily. 40 mg to 80 mg should be administered in two divided doses (i.e., twice daily)	Orthographic Both names start with the letter string 'Qui-' Additionally, the letter string '-va-' in Quillivant may appear similar to the corresponding letter string '-ri- in Quinapril when scripted. Overlap in Strength/Dose Both products can be dosed at 20 mg, 30 mg, 40 mg, or 50 mg doses Route of Administration Orally Frequency of Administration Both products can be administered once daily	Orthographic The root name Quillivant contains 4 upstrokes vs. the name Quinapril which contains 2 upstrokes and 1 downstroke. Additionally, the letter string '-lli-' in Quillivant lacks orthographic similarity to the letter string '-nap-' in Quinapril when scripted.

No.	Proposed name: Quillivant XR	Strength: 25 mg/5 mL (5 mg/mL)	Usual dosage: 20 mg (4 mL) to 60 mg (12 mL) orally once daily in the morning
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
12.	Questran (Cholestyramine) Powder for Oral Suspension, 4 g <u>Usual Dose</u> 4 g orally administered once or twice daily before meals, may increase up to 16 g per day in two divided doses	<u>Orthographic</u> The letter strings 'Qui-' and '-iva-' in Quillivant may appear similar to the corresponding letter strings 'Que-' and '-ran' when scripted. <u>Overlap in Strength/Dose</u> Quillivant XR can be dosed as 4 mL or 40 mg, which overlaps with Questran strength of 4 g. <u>Route of Administration</u> Orally <u>Frequency of Administration</u> Both products can be administered once daily	<u>Orthographic</u> The root name Quillivant appears longer than the name Questran (10 letters vs. 8 letters). Additionally, the name Quillivant contains 4 upstrokes vs. the name Questran contains 2 upstrokes.

No.	Proposed name: Quillivant XR	Strength: 25 mg/5 mL (5 mg/mL)	Usual dosage: 20 mg (4 mL) to 60 mg (12 mL) orally once daily in the morning
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
13.	Amiloride HCl Tablet, 5 mg Usual Dose 5 mg to 20 mg orally once daily	Orthographic The letter string 'Quil-' may appear similar to the letter string 'Amil-' when scripted. Overlap in Strength/Dose Both products can be dosed at 20 mg Route of Administration Orally Frequency of Administration Both products can be administered once daily	Orthographic The root name Quillivant contains 4 upstrokes vs. the name Amiloride contains 3 upstrokes. Additionally, the letter string '-livant' lacks orthographic similarity to the letter string '-oride' in Amiloride.

No.	Proposed name: Quillivant XR	Strength: 25 mg/5 mL (5 mg/mL)	Usual dosage: 20 mg (4 mL) to 60 mg (12 mL) orally once daily in the morning
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
14.	Gadavist (Gadobutrol) Injection, 1 mmol Gadobutrol/mL (Equivalent to 604.72 mg/mL) Usual Dose 0.1 mmol/kg as intravenous bolus injection	Orthographic Both names end with the letter 't'. Additionally, the letter strings 'Quil-' and '-iv-' in Quillivant may appear similar to the corresponding letter strings 'Gad-' and '-vi-' in Gadavist Overlap in Dose Quillivant XR can be administered at doses between 20 mg and 60 mg, which may overlap with achievable Gadavist dose (e.g., 10 mmol for 100 kg person)	Orthographic The root name Quillivant appears longer than the name Gadavist (10 letters vs. 8 letters). Additionally, the name Quillivant contains 4 upstrokes vs. the name Gadavist which contains 3 upstrokes. Additionally, Quillivant contains two adjacent upstroke letters 'll' whereas Gadavist does not. Context of Use Gadavist is an imaging agent for use in diagnostic MRI whereas Quillivant XR would not be used in this context.

No.	Proposed name: Quillivant XR	Strength: 25 mg/5 mL (5 mg/mL)	Usual dosage: 20 mg (4 mL) to 60 mg (12 mL) orally once daily in the morning
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
15.	Quelicin (Succinylchloline) Injection: 200 mg/10 mL (20 mg/mL) 1000 mg/10 mL (100 mg/mL) Usual Dose: Intravenous administration Adults: Average dose is 0.6 mg/kg intravenously (range 0.3 mg/kg to 1.1 mg/kg) administered over 10 seconds to 30 seconds. Additional doses may be administered in accordance with patient's response. Intramuscular Adults, Older Children, and Infants: A dose of up to 3 mg/kg to 4 mg/kg intramuscularly may be administered, but the total dose must not exceed 150 mg	Orthographic The letter string 'Quilliva-' may appear similar to the name Quelicin when scripted. Phonetic The letter string 'Quilli-' in Quillivant is phonetically similar to the letter string 'Queli-' in Quelicin Overlap in Strength/Dose Quillivant XR may be administered at the dose of 20 mg, which overlaps with Quelicin strength and concentration of 200 mg/10 mL (20 mg/mL) or 1000 mg/10 mL. Additionally, the achievable doses of both products may overlap as well (e.g., Quelicin administered at dose of 1 mg/kg for 40 kg, 50 kg, or 60 kg person)	Orthographic The root name Quillivant appears longer than the name Quelicin (10 letters vs. 8 letters). Additionally, the name Quillivant contains 4 upstrokes vs. the name Quelicin contains 2 upstrokes. Furthermore, Quillivant ends with an upstroke and cross-stroke letter ('t') whereas Quelicin does not. Phonetic The letter string '-vant' lack phonetic similarity to the letter string '-cin' Route of Administration Orally vs. intravenously or intramuscularly

No.	Proposed name: Quillivant XR	Strength: 25 mg/5 mL (5 mg/mL)	Usual dosage: 20 mg (4 mL) to 60 mg (12 mL) orally once daily in the morning
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
16.	Combivent (Albuterol and Ipratropium) Inhalation Aerosol 103 mcg/18 mcg per actuation. Usual Dose 2 to 3 inhalations every 6 hours.	Orthographic The letter string 'Qu-' and the letter string '-ivant' in Quillivant may appear similar to the letter string 'Co-' and '-ivent' when scripted. Additionally, the first letter 'l' may in Quillivant appear similar to the letter 'b' in Combivent when scripted.	Orthographic The root name Quillivant contains 4 upstrokes vs. the name Combivent which contains 3 upstrokes. Additionally, the first letter 'i' in Quillivant lacks orthographic similarity to the letter 'm' in Combivent when scripted. Usual Dose 20 mg (4 mL) to 60 mg (12 mL) vs. 2 inhalations to 3 inhalations Frequency of Administration Once daily vs. every 6 hours
17.	Qualaquin (Quinine Sulfate) Capsules Strength: 324 mg Dosage: 648 mg orally every 8 hours	Orthographic: The beginning letter strings "Quil" vs. Qual" look similar when scripted. Route of administration: Both products are administered orally.	Orthographic: The root name "Quillivant" contains four upstroke letters and no downstroke letters whereas Qualaquin has two upstroke letters and one downstroke letter which helps to differentiate the names. Dose: 20 mg to 60 mg vs. 648 mg The products do not overlap in dose. Frequency of administration: Once daily vs. every 8 hours

No.	Proposed name: Quillivant XR	Strength: 25 mg/5 mL (5 mg/mL)	Usual dosage: 20 mg (4 mL) to 60 mg (12 mL) orally once daily in the morning
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
18.	Quintabs (Vitamin A 5,000 IU, Vitamin C 300 mg, Vitamin D 400 IU, Vitamin 50 IU, Vitamin B1 30 mg, Vitamin B2 30 mg, Niacin 100 mg, Vitamin B6 30 mg, Folic Acid 400 mcg, Vitamin B12 30 mcg, Biotin 30 mcg, and Pantothenic Acid 30 mg) Tablets Strength: Not applicable Dosage: 1 tablet orally once daily	Orthographic: Both names begin with the letters "Qui" and contain an upstroke letter in the fifth position. Dose: There is the potential for the dose of both products to have numerical overlap (e.g., 1 teaspoonful vs. 1 tablet)	Orthographic: Quillivant contains four upstroke letters whereas Quintabs contains three. Additionally, the adjacent upstroke letters "ll" in Quillivant helps to differentiate it from Quintabs. Dosage units: mL, mg, or teaspoonsful vs. tablet

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

/s/

LORETTA HOLMES
09/20/2012

CAROL A HOLQUIST on behalf of IRENE Z CHAN
09/20/2012
Signing on behalf of Irene Chan

CAROL A HOLQUIST
09/20/2012

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

Proprietary Name Review

Date:	July 16, 2012
Reviewer:	Loretta Holmes, BSN, PharmD Division of Medication Error Prevention and Analysis
Team Leader	Irene Z. Chan, PharmD, BCPS Division of Medication Error Prevention and Analysis
Division Director	Carol A. Holquist, RPh Division of Medication Error Prevention and Analysis
Drug Name and Strength:	Quillivant (Methylphenidate Hydrochloride) for Extended-release Oral Suspension 25 mg/5 mL
Application Type/Number:	NDA 202100
Applicant:	NextWave Pharmaceuticals, Inc.
OSE RCM #:	2012-958

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

CONTENTS

1 INTRODUCTION

This review evaluates the proposed proprietary name, Quillivant, 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

NDA 202100 for Quillivant (Methylphenidate Hydrochloride) for Extended-release Oral Suspension is a 505(b)(2) application. The Reference Listed Drug (RLD) is Methylin (Methylphenidate Hydrochloride) Oral Solution (NDA 021419). The NDA was submitted on July 29, 2010 and a Complete Response action was taken on August 30, 2011. The Applicant submitted a Complete Response on March 30, 2012.

The name (b) (4) was initially proposed for this NDA. DMEPA found the proposed name, (b) (4) unacceptable due to (b) (4) and the Applicant was notified of DMEPA's findings via teleconference on March 1, 2011. As a result, the Applicant withdrew the proposed proprietary name (b) (4) on March 7, 2011. The Applicant submitted a new Proprietary Name Review Request for the name Quillivant on March 31, 2011. The name was found acceptable in OSE Review 2011-1138, dated May 12, 2011. Following resubmission of the NDA, a request for re-review of the proposed proprietary name Quillivant was submitted on April 17, 2012.

1.2 PRODUCT INFORMATION

The following product information is provided in the April 17, 2012 proprietary name submission.

- **Active Ingredient:** Methylphenidate Hydrochloride
- **Indication of Use:** Treatment of Attention Deficit Hyperactivity Disorder (ADHD)
- **Route of administration:** Oral
- **Dosage form:** for Extended-release Oral Suspension
- **Strength:** 25 mg/5 mL (5 mg/mL)
- **Dose and Frequency of Administration:** For patients 6 years and above, the recommended starting dose is 20 mg given orally once daily in the morning. Dosage may be increased by 10 mg per day to 20 mg per day at weekly intervals. Daily dosage above 60 mg is not recommended.
- **How Supplied:** Supplied in bottles to prepare 60 mL, 120 mL, 180 mL, 240 mL, 300 mL or 360 mL. Each carton contains one bottle of Quillivant, one 12 mL oral dosing dispenser and one bottle adapter. Quillivant must be reconstituted by the pharmacist before dispensing.
- **Storage:** Store at 25ºC (77ºF); excursions permitted from 15ºC to 30ºC (59ºF to 86ºF)

- **Container and Closure Systems:** USP Type III glass with Child-Resistant Closure (CRC)
- **Proposed Pronunciation:** QUIL·I·VANT (\kwil-ə-vant\)
- **Derivation of the Name:** None provided

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 Psychiatry Products 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 28, 2012 search of the United States Adopted Name (USAN) stems did not identify a USAN stem present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

According to the Applicant, the proposed proprietary name has no derivation. This proposed proprietary name is comprised of a single word that does not contain any components that are misleading or can contribute to medication errors.

Quillivant is an extended-release for oral suspension formulation of methylphenidate. The Applicant does not include a modifier with the name (e.g., ER, XR, XL) to convey that Quillivant is an extended-release dosage form. There are currently marketed methylphenidate immediate-release oral solutions available in 1 mg per mL and 2 mg per mL strengths marketed by another firm under the proprietary name Methylin. Therefore, we have evaluated whether or not the proposed name requires a modifier to signal the extended-release nature of the product (see Discussion – Section 3).

2.2.5 FDA Name Simulation Studies

Thirty-three practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with or appear or sound similar to any currently marketed products. All of the participants in the verbal study spelled the name incorrectly with one letter "l" rather than two. Additionally, two participants in the outpatient study interpreted the letters "ll" as the letters "tt". Furthermore, eight participants in the inpatient and outpatient studies (inclusively) interpreted the letter "n" as the letter "r". 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, April 27, 2012 e-mail, the Division of Psychiatry Products (DPP) 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, Quillivant. Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Quillivant, identified by the Expert Panel Discussion (EPD) and not identified in our previous review of Quillivant. None of the product characteristics have changed since our last review of the name Quillivant; however, we re-looked at our previous names of concern and verified that they are not vulnerable to confusion with our proposed proprietary name, Quillivant.

Table 1: Collective List of Potentially Similar Names (identified by EPD)

Look Similar					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Quelidrine	EPD Panel	Quadrahist	EPD Panel	Quintabs	EPD Panel
Sound Similar					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
None					

Look and Sound Similar					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Qualaquin	EPD Panel				

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

2.2.7 Communication of DMEPA's Final Decision to Other Disciplines

DMEPA communicated our findings to the Division of Psychiatry Products via e-mail on July 10, 2012. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Psychiatry Products on July 13, 2012, they stated no additional concerns with the proposed proprietary name, Quillivant.

3 DISCUSSION

As proposed, the Applicant does not include a modifier with the name (e.g., ER, XR, XL) to convey that Quillivant is an extended-release dosage form. There are currently marketed methylphenidate immediate-release oral solutions available in 1 mg/mL and 2 mg/mL strengths marketed by another firm under the proprietary name Methylin, along with generic products marketed under the established name, methylphenidate hydrochloride. Methylin, the branded product, is typically administered two to three times daily, with the dose individualized to the needs of the patient. Quillivant will be available in a 5 mg/mL strength, which does not overlap with the currently marketed immediate release oral solutions, and if approved, it will be the first marketed methylphenidate extended-release oral suspension.

There are also other currently marketed extended-release methylphenidate products, but these are only available as solid oral dosage forms. Currently, all of the extended-release methylphenidate products on the market have a modifier as part of the proprietary name (e.g., ER, LA, CD, or SR) except for Concerta. However, there are no overlapping strengths between Concerta and the currently marketed immediate-release methylphenidate products, which is a key differentiating product characteristic for Concerta.

There is no marketed immediate-release product with the root name, Quillivant, that this product needs to distinguish itself from; therefore, a modifier may not be necessary. However, we considered whether the lack of modifier raises a potential safety concern, specifically if practitioners or patients were to assume Quillivant is an immediate-release dosage form because no modifier is present in the proprietary name to signal the extended-release nature of the product. We are primarily concerned with wrong frequency errors involving the administration of the extended-release dosage form at intervals more frequent than labeled, (e.g. taking Quillivant twice a day).

First we determined there are five currently marketed extended release oral suspensions: Delsym (Dextromethorphan Polistirex) Extended-release suspension, 30 mg/5 mL; Tussionex Pennkinetic (Hydrocodone Polistirex and Chlorpheniramine Polistirex) Extended-release suspension, 10 mg/8 mg per 5 mL (there are also two generics available but these are marketed under the established name); and Zmax (Azithromycin) powder for suspension, 2 g per bottle. With the exception of Zmax, which is administered as a one time dose, the remaining products are administered twice daily, which differs from Quillivant, which is administered once a day. Therefore, previous experience with these products cannot directly inform our review of Quillivant.

Next, we identified other extended-release products (not limited to oral suspensions) approved without a modifier in the proprietary name and reviewed documented errors relating to wrong frequency of administration. Wrong frequency errors involved the administration of the extended-release dosage form at intervals more frequent than labeled, (e.g. taking a once daily drug twice a day). Wrong frequency errors occurred despite the presence of clear labeling directives to administer the products at the given intervals. Additionally, based on the case narratives we were unable to determine a definitive root cause of the errors.

Although a clear pattern did not emerge from our review of names without modifiers, our medication error postmarketing experience with drug products marketed without a modifier in the proprietary name leads us to believe that the failure to include a modifier that conveys the extended-release properties of the drug may predispose the product to wrong frequency errors. Therefore, in some circumstances, a modifier in the proprietary name of an extended-release product may help reduce the risk of this type of error.

In this case, Quillivant does not have direct overlapping strengths with the immediate-release methylphenidate oral solutions (5 mg/mL vs. 1 mg/mL or 2 mg/mL). Prescriptions for Quillivant will not necessarily include the product strength since this is a single strength product. Instead, the desired dose is sufficient, and the doses can overlap between the immediate-release and extended-release oral suspension formulations of methylphenidate. A provider that is researching available methylphenidate oral suspension products may overlook the extended release properties of Quillivant in the absence of a signal indicating Quillivant differs from the currently marketed Methylin products (or available generics). Although there is no modifier that consistently conveys once daily administration, the use of a modifier may signal to healthcare practitioners that this product may differ in regards to formulation and frequency of administration as compared to the currently marketed immediate-release methylphenidate oral solutions which may help to minimize errors involving the wrong frequency of administration with this product.

Additionally, a modifier may be used to communicate that this product is an extended-release dosage form and cannot be interchanged with the immediate-release methylphenidate oral solution products. We recognized there were limitations to this approach since there is postmarketing evidence that modifiers have been omitted or overlooked; however, given the increased risks associated with Quillivant, we believe the addition of the modifier could add an incremental measure of safety. Therefore, DMEPA requests the Applicant add an appropriate modifier to the proposed name, Quillivant.

4 CONCLUSIONS

The proposed proprietary name, Quillivant, is acceptable from a promotional perspective but not acceptable from a safety perspective. The proposed name is vulnerable to confusion with the currently marketed methylphenidate immediate-release oral solutions because it does not contain a modifier that conveys its extended-release properties. This decision will be communicated to the Applicant via letter (see Section 4.1).

If you have further questions or need clarifications, please contact Sandra Griffith, OSE Project Manager, at 301-796-2445.

4.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Quillivant, and have concluded that this name is unacceptable for the following reasons:

As proposed, the name does not include a modifier (e.g., ER, XR, XL) to convey that Quillivant is an extended-release dosage form. There are currently marketed methylphenidate immediate-release oral solutions available in 1 mg/mL and 2 mg/mL strengths marketed by another firm under the proprietary name Methylin, along with generic products marketed under the established name, methylphenidate hydrochloride. Methylin, the branded product, is typically administered two to three times daily, with the dose individualized to the needs of the patient.

There are also currently marketed extended-release methylphenidate products, but these are only available as solid oral dosage forms. Currently, all of the extended-release methylphenidate products on the market have a modifier as part of the proprietary name (e.g., ER, LA, CD, or SR) except for Concerta. However, there are no overlapping strengths between Concerta and the currently marketed immediate-release methylphenidate products, which is a key differentiating product characteristic for Concerta.

There is no marketed immediate-release product with the root name, Quillivant, that this product needs to distinguish itself from; therefore, a modifier may not be necessary. However, we considered whether the lack of modifier raises a potential safety concern, specifically if practitioners or patients were to assume Quillivant is an immediate-release

dosage form because no modifier is present in the proprietary name to signal the extended-release nature of the product. We are primarily concerned with wrong frequency errors involving the administration of the extended-release dosage form at intervals more frequent than labeled, (e.g. taking Quillivant twice a day).

First we determined there are five currently marketed extended release oral suspensions: Delsym (Dextromethorphan Polistirex) Extended-release suspension, 30 mg/5 mL; Tussionex Pennkinetic (Hydrocodone Polistirex and Chlorpheniramine Polistirex) Extended-release suspension, 10 mg/8 mg per 5 mL (there are also two generics available but these are marketed under the established name); and Zmax (Azithromycin) powder for suspension, 2 g per bottle. With the exception of Zmax, which is administered as a one time dose, the remaining products are administered twice daily, which differs from Quillivant, which is administered once a day. Therefore, previous experience with these products cannot directly inform our review of Quillivant.

Next, we identified other extended-release products (not limited to oral suspensions) approved without a modifier in the proprietary name and reviewed documented errors relating to wrong frequency of administration. Wrong frequency errors involved the administration of the extended-release dosage form at intervals more frequent than labeled, (e.g. taking a once daily drug twice a day). Wrong frequency errors occurred despite the presence of clear labeling directives to administer the products at the given intervals. Additionally, based on the case narratives we were unable to determine a definitive root cause of the errors.

Although a clear pattern did not emerge from our review of names without modifiers, our medication error postmarketing experience with drug products marketed without a modifier in the proprietary name leads us to believe that the failure to include a modifier that conveys the extended-release properties of the drug may predispose the product to wrong frequency errors. Therefore, in some circumstances, a modifier in the proprietary name of an extended-release product may help reduce the risk of this type of error.

In this case, Quillivant does not have direct overlapping strengths with the immediate-release methylphenidate oral solutions (5 mg/mL vs. 1 mg/mL or 2 mg/mL). Prescriptions for Quillivant will not necessarily include the product strength since this is a single strength product. Instead, the desired dose is sufficient, and the doses can overlap between the immediate-release and extended-release oral suspension formulations of methylphenidate. A provider that is researching available methylphenidate oral suspension products may overlook the extended release properties of Quillivant in the absence of a signal indicating Quillivant differs from the currently marketed Methylin products (or available generics). Although there is no modifier that consistently conveys once daily administration, the use of a modifier may signal to healthcare practitioners that this product may differ in regards to formulation and frequency of administration as compared to the currently marketed immediate-release methylphenidate oral solutions which may help to minimize errors involving the wrong frequency of administration with this product.

Additionally, a modifier may be used to communicate that this product is an extended-release dosage form and cannot be interchanged with the immediate-release methylphenidate oral solution products. We recognized there were limitations to this

approach since there is postmarketing evidence that modifiers have been omitted or overlooked; however, given the increased risks associated with Quillivant, we believe the addition of the modifier could add an incremental measure of safety. Therefore, DMEPA requests you add an appropriate modifier to the proposed name, Quillivant.

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. (See the Guidance for Industry, *Contents of a 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".

5 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 Pharmacy's Fundamental Reference***

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

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

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

15. ***Medical Abbreviations Book***

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

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 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.

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[1] National Coordinating Council for Medication Error Reporting and Prevention. http://www nccmerp.org/aboutMedErrors 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.[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**		
	Potential Causes of Drug Name Similarity	*Attributes Examined to Identify Similar Drug Names*	*Potential Effects*
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name/Similar shape Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, 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 gather 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 Division of Drug Marketing, Advertising, and Communications (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 posses similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

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

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

The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not 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 Quillivant	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'Q'	'G', 'O', 'A', 'D'	'K', 'G'
lower case "q"	g, j, z	'k', 'g'
lower case 'u'	'n', 'v', 'w'	Any vowel
lower case 'i'	'e', 'l'	Any vowel
lower case 'l'	'b', 'e', 's', 'i'	
Letter string 'll'	'u', 'il', 'li', 'el', 'le', 'tt'	
lower case 'i'	'e', 'l'	Any vowel
lower case 'v'	'r', 'u', 'y', z', 'x', 'n'	'f'
lower case 'a'	'ci', 'cl', 'd', 'o', 'el, 'u', 'n'	Any vowel
lower case 'n'	'm', 'u', 'x', 'r', 'h', 's'	'm', 'dn', 'kn', 'mn, 'pn'
Lower case 't'	'f', 'd', 'b' 'r', 'x', 'a'	'd'

Appendix C: Prescription Simulation Samples and Results

Figure 1. Quillivant Study (Conducted on May 4, 2012)

Handwritten Requisition Medication Order	Verbal Prescription
Inpatient Medication Order: Quillivant 10ms PO QAM	"Quillivant 2 mL by mouth every morning. Dispense #60 mL bottle"
Outpatient Prescription: Quillivant 2mL PO QAM Disp: 60mL bottle	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

	84 People Received Study
	33 People Responded

Study Name: **Quillivant**

Total	10	10	13	
INTERPRETATION	**INPATIENT**	**VOICE**	**OUTPATIENT**	**TOTAL**
QINTTIVANT	0	0	1	1
QUILAVANT	0	5	0	5
QUILIVANT	0	5	0	5
QUILLIVANT	7	0	7	14
QUILLIVART	3	0	4	7
QUNLLIVART	0	0	1	1
QINTTIVANT	0	0	1	1
QUILAVANT	0	5	0	5

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 Quillivant	Failure Preventions
Quelidrine Cough (Phenylephrine Hydrochloride 5 mg, Ammonium Chloride 40 mg, Ipecac Syrup 0.005 ML, Dextromethorphan HBr 10 mg, Chlorpheniramine Maleate 2 mg, and Ephedrine Hydrochloride 5 mg) per 5 mL Oral Solution	Look	This name was found in Micromedex with the ingredient information provided. Unable to find dosing information in our other standard drug information databases.
Quadrahist Quadrahist-D (Pheniramine, Phenyltoloxamine, Pseudoephedrine, and Pyrilamine) Strengths: 8 mg/8 mg/40 mg/8 mg 16 mg/8 mg/80 mg/16 mg	Look	This name was found in Red Book Online, however, no information regarding the product was available in the database. Unable to find the active ingredient(s) or dosing information in our standard drug information databases. Ingredient information for Quadrahist-D was found via a Google search at http://www.drugs.com/imprints/ethex-057-1649.html and http://www.drugs.com/imprints/ethex-056-1648.html but dosing information was not available on these web pages.

Appendix E: Summary Findings of the FMEA

Proposed name: **Quillivant**	**Strength:** **25 mg/5 mL (5 mg/mL)**	**Usual dosage:** **10 mg (2 mL) to 60 mg (12 mL) orally once daily in the morning**
Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
Quintabs (Vitamin A 5,000 IU, Vitamin C 300 mg, Vitamin D 400 IU, Vitamin 50 IU, Vitamin B1 30 mg, Vitamin B2 30 mg, Niacin 100 mg, Vitamin B6 30 mg, Folic Acid 400 mcg, Vitamin B12 30 mcg, Biotin 30 mcg, and Pantothenic Acid 30 mg) Tablets Strength: Not applicable Dosage: 1 tablet orally once daily	Orthographic: Both names begin with the letters "Qui" and contain an upstroke letter in the fifth position. Dose: There is the potential for the dose of both products to have numerical overlap (e.g., 1 teaspoonful vs. 1 tablet)	Orthographic: Quillivant contains three upstroke letters ("ll" and "t") whereas Quintabs contains two ("t" and "b"). Additionally, the adjacent upstroke letters "ll" in Quillivant helps to differentiate it from Quintabs. Dosage units: mL, mg, or teaspoonsful vs. tablet
Qualaquin (Quinine Sulfate) Capsules Strength: 324 mg Dosage: 648 mg orally every 8 hours	Orthographic: The names begin with letters that may look similar when written ("Quil" vs. "Qual"). Dose: There is the potential for both products to have numerical overlap in dose (e.g., 2 mL or 2 teaspoonsful vs. 2 capsules)	Orthographic: Quillivant contains three upstroke letters ("ll" and "t") whereas Qualaquin only has one ("l"). Additionally, Qualaquin contains the downstroke letter "q" whereas Quillivant does not contain any downstroke letters. Dosage units: mL, mg, or teaspoonsful vs. capsule Frequency of administration: Once daily vs. every 8 hours

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/s/

LORETTA HOLMES
07/16/2012

IRENE Z CHAN
07/16/2012

CAROL A HOLQUIST
07/16/2012

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

Proprietary Name Review

Date:	May 12, 2011
Reviewer(s):	Yelena Maslov, Pharm.D., Safety Evaluator Division of Medication Error Prevention and Analysis
Team Leader	Zachary Oleszczuk, Pharm.D., Team Leader Division of Medication Error Prevention and Analysis
Division Director	Carol Holquist, R.Ph., Director Division of Medication Error Prevention and Analysis
Drug Name(s):	Quillivant (Methylphenidate HCl) Extended-release Powder for Oral Suspension, 25 mg/5 mL
Application Type/Number:	NDA 202100
Applicant/sponsor:	Next Wave Pharmaceuticals
OSE RCM #:	2011-1138

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CONTENTS

1 INTRODUCTION

This review evaluates the proposed proprietary name, Quillivant, 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. The proposed product characteristics are provided in Appendix B.

1.1 REGULATORY HISTORY

Quillivant (Methylphenidate HCl) Extended-release Powder for Oral Suspension is the subject of a 505(b)(2) application submitted to the FDA on July 29, 2010, that references Methylin (Methylphenidate HCl) Oral Solution (NDA 02419). The Applicant submitted a Proprietary Name Review Request for the name (b) (4), on January 11, 2011. DMEPA found the proposed name, (b) (4) unacceptable due to phonetic similarity to (b) (4) and the Applicant was notified of DMEPA's findings via teleconference on March 1, 2011. As a result, the Applicant withdrew the proposed proprietary name (b) (4) on March 7, 2011. The Applicant submitted a new Proprietary Name Review Request for the name Quillivant on March 31, 2011.

2 RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

DDMAC determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Psychiatry Products concurred with the findings of DDMAC's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

2.2.1 United States Adopted Names (USAN) Search

The United States Adopted Name (USAN) stem search conducted on April 29, 2011, by the safety evaluator identified that a USAN stem is not present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

There are no components of the proposed proprietary name that can contribute to medication error or render the name unacceptable.

2.2.4 FDA Name Simulation Studies

Thirty eight practitioners participated in DMEPA's prescription studies. See Appendix D for samples and complete listing of interpretations from the verbal and written prescription studies.

None of the responses overlapped with other drug names. Twenty two respondents interpreted the proposed proprietary name correctly as "Quillivant", with eleven correct interpretations occurring with inpatient orders (n=11) and eleven correct interpretations

occurring with outpatient orders (n=11). The remaining sixteen participants misinterpreted the name, Quillivant. The most common interpretation occurred with 10 participants misinterpreting the letter string '-ll-' as a single letter 'l' during the voice study.

2.2.5 Comments from Other Review Disciplines

In response to the OSE, April 21, 2011 e-mail, the Division of Psychiatry Products (DPP) did not forward any comments or concerns relating to the proposed name at the initial phase of the name review.

2.2.6 Failure Mode and Effects Analysis of Similar Names

Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Quillivant (see Appendix C). These names were identified by the primary reviewer and DMEPA's Expert Panel.

Table 1: Collective List of Potentially Similar Names (Primary Reviewer and EPD Panel)

Look Similar		Look and Sound Similar	
Name	***Source***	***Name***	***Source***
Quinalan	EPD Panel	Quillaia	EPD Panel
Quenalin	EPD Panel	Quelicin	EPD Panel
Quinact	EPD Panel	Guaivent	EPD Panel
[redacted] (b) (4)			
Acetasol	EPD Panel		
Anatrast	EPD Panel		
Avodart	EPD Panel		
Oxistat	EPD Panel		
Quibron-T	EPD Panel		
Quentyl	EPD Panel		
Qutenza	EPD Panel		
Dexilant	EPD Panel		
Quadramet	EPD Panel		
Quinaretic	EPD Panel		

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Quinapril	EPD Panel		
Quinaglute	EPD Panel		
Beclovent	EPD Panel		
Questran	EPD Panel		
Gallium	Primary SE		
Gantanol/ Gantanol DS	Primary SE		
Amiloride	Primary SE		
Combivent	Primary SE		
Quillaja	Primary SE		
Gadavist	Primary SE		

Our analysis of the 28 names contained in Table 1 considered the information obtained in the previous sections along with the product characteristics for the names indentified in Tables 1above. We determined the twenty-eight names will not pose a risk for confusion as described in Appendix E through F.

DMEPA communicated these findings to the Division of Psychiatry Products via e-mail on April 29, 2011. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Psychiatry Products on May 3, 2011, they stated no additional concerns with the proposed proprietary name, Quillivant.

3 CONCLUSIONS

DMEPA concludes the proposed proprietary name, Quillivant, is acceptable from both a promotional and safety perspective. However, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

Additionally, the proposed proprietary name must be re-reviewed if approval of this NDA is delayed beyond 90 days.

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.

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. ***Access Medicine Database (http://www.accessmedicine.com/drugs.aspx)***

    Access Medicine contains full-text information from approximately 60 medical titles: it includes tables and references. Among the database titles are: Goodman and Gilman's The Pharmacological Basis of Therapeutics, Current Medical Diagnosis and Treatment, Tintinalli's Emergency Medicine, and Hurst's the Heart.

13. ***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.

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.

17. ***LabelDataPlus Database (http://www.labeldataplus.com/index.php?ns=1)***

    LabelDataPlus database covers a total of 36773 drug labels. This includes Human prescription drug labels as well as Active Pharmaceutical Ingredients (APIs), OTC

(Application and Monograph) drugs, Homeopathic drugs, Unapproved drugs, and Veterinary drugs.

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 DDMAC. DDMAC 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. DDMAC 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 product characteristics considered for this review appears in Appendix B1 of this review.

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).

Table 1. Criteria Used to Identify Drug Names that Look- or Sound-Similar to a Proposed Proprietary Name.

Type of Similarity	**Considerations when Searching the Databases**		
	Potential Causes of Drug Name Similarity	*Attributes Examined to Identify Similar Drug Names*	*Potential Effects*
	Similar spelling	Identical prefix	• Names may appear similar

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

Look-alike		Identical infix Identical suffix Length of the name Overlapping product characteristics	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	• Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, 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 gather 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 Division of Drug Marketing, Advertising, and Communications (DDMAC). 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 DDMAC'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 characteristics listed in Appendix B1 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***

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

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

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

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

The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not 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. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].

b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].

c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.

d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.

e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug

product 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: Product Characteristics Provided for Quillivant

Quillivant
(\kwil-ə-vant\)
(Methylphenidate) Extended Release Powder for Suspension
NDA#202100

Indication: Treatment of ADHD
Route: oral
Dosage Form: powder for suspension
Strengths: 25 mg/5 mL (5 mg/mL)
Dosage/Administration: Adults and children over 6 years of age: starting dose 20 mg once daily, can titrate upwards up to 60 mg or downwards to 10 mg.
How Supplied: Once reconstituted total content of each container is 300 mg (60 mL), 600 mg (120 mL), 900 mg (180 mL), 1200 mg (240 mL), 1500 mg (300 mL), and 1800 mg (360 mL)

Appendix C: Letters with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Quillivant	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'Q'	'G', 'O', 'A', 'D'	'K', 'G'
lower case 'u'	'n', 'v', 'w'	any vowel
lower case 'i'	'e', 'l'	any vowel
lower case 'l'	'b', 'e', 's', 'i'	
Letter string 'll'	'u', 'il', 'li', 'el', 'le'	
lower case 'v'	'r', 'u', 'y', z', 'x', 'n'	'f'
lower case 'a'	'el, 'd', 'o', 'u', 'n'	Any vowel
lower case 'n'	'm', 'u', 'x', 'r', 'h', 's'	'm', 'dn', 'kn', 'mn, 'pn'
Lower case 't'	'f', 'd', 'b' 'r', 'x', 'a'	'd'

Appendix D: Prescription Simulation Samples and Results

Figure 1. Quillivant Study (Conducted on 03/25/2011)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order: Quillivant 20mg po qday.	Quillivant 30 mg orally once daily
Outpatient Prescription: Quillivant 30 mg orally once daily #1 month supply	

FDA Prescription Simulation Responses.

Inpatient Medication Order	Outpatient Prescription	Voice Prescription
Quillivant	Quillevant	Quilivint
Quillivant	Quillevent	Quilifant
Quillivant	Quillivant	Quilivent
Quillivant	Quillivant	Quilivent
Quillivant	Quillivant	Quilivin
Quillivant	Quillivant	Quilivint
Quillivant	Quillivant	Quilivent
Quillivant	Quillivant	Quilivin
Quillivant	Quillivant	qualivent
Quillivant	Quillivant	Quilivin
quillivant	Quillivant	
	Quillivant	
	Quillivant	
	Quillivent	
	Quillivent	
	Quillivent	
	Quillirant	

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

Proprietary Name	Active Ingredient	Similarity to Quillivant	Failure preventions
Oxistat	Oxiconazole Nitrate	Look alike	Lacks sufficient orthographic similarity
Quentyl	Dicyclomine HCl, USP	Look alike	Lacks sufficient orthographic similarity
Quinaglute	Quinidine Gluconate Extended-release	Look alike	Lacks sufficient orthographic similarity
Quillaja	None	Look alike	Not a drug, a tree, whose bark possesses medicinal properties.
Quillaia	Soap Bark	Look alike	Proprietary name for bark of Quillaja tree in Sweden
Quinact	Quinidine Gluconate	Look alike	Discontinued without generic equivalent available
Anatrast	Barium Sulfate	Look alike	Discontinued without generic equivalent available
Quibron-T	Anhydrous Theophylline	Look alike	Discontinued without generic equivalent available
Guaivent	Guaifenesin and Phenylpropanolamine	Look alike and sound alike	Discontinued without generic equivalent available
Gantanol	Sulfamethoxazole	Look alike	Discontinued without generic equivalent available
Beclovent	Beclomethasone	Look alike	Discontinued without generic equivalent available
Ganite	Gallium	Look alike	Discontinued without generic equivalent available
			(b) (4)

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

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

Proposed name: Quillivant	**Strength(s): 25 mg/5 mL supplied as: 300 mg (60 mL), 600 mg (120 mL), 900 mg (180 mL), 1200 mg (240 mL), 1500 mg (300 mL), and 1800 mg (360 mL)**	**Usual dose: 10 mg (2 mL), 20 mg (4 mL), 30 mg (6 mL), 40 mg (8 mL), 50 mg (10 mL), and 60 mg (12 mL)**
Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
[redacted] (b) (4)		
Quenalin (Diphenhydramine) Oral Solution: 12.5 mg/5 mL Usual Dose: Adults and Adolescents: 25 mg to 50 mg orally three to four times per day, at 4 hour to 6 hour intervals, as needed. Maximum dose is 300 mg/day.	Orthographic Both names start with the letter string 'Qu-' and contain letter 'n' in similar positions. Additionally, the letter 'e' in Quenalin may appear similar to the corresponding first letter 'i' in Quillivant when scripted. Overlap Strength and Dose Quillivant may de dispensed as 300 mg bottle and Quenalin has a maximum dose of 300 mg per day. Route of Administration Orally	Orthographic The name Quillivant contains 4 upstrokes vs. the name Quinalan contains 2 uptrokes and upstrokes are not located in same positions. Additionally, the letter string '-ll-' in Quillivant lacks orthographic similarity to the corresponding letter string '-na-' in Quenalin when scripted. Frequency of Administration Once daily vs. every 4 hours to 6 hours

(b) (4)		
Acetasol* (Acetic Acid) Otic Solution, 2% *Proprietary name discontinued, however, generic products are still available <u>Usual Dose</u> Instill 4 drops to 6 drops into external ear canal every 2 to 3 hours. Acetasol HC (Acetic Acid and Hydrocortisone) Otic Solution, 2%/1% <u>Usual Dose</u> Instill 3 drops to 5 drops into external ear canal three to four times daily	<u>Orthographic</u> The letter strings 'Quil-' and '-iv-' in Quillivant may appear similar to the corresponding letter strings 'Acet-' and '-so-' in Acetasol when scripted. <u>Overlap Strength and Dose</u> Quillivant may be dosed as 2 mL and Acetasol is dosed at the strength of 2%	<u>Orthographic</u> The name Quillivant appears longer than the name Acetasol (10 letters vs. 8 letters) Additionally, the second letter 'l' and the letterstring '-ant' in Quillivant lack orthographic similarity to the corresponding letters 'a' and 'l' in Acetasol. <u>Route of Administration</u> Oral vs. otic <u>Usual Dose</u> 10 mg (2 mL) to 60 mg (12 mL) vs. 4 drops to 6 drops (Acetasol) or 3 drops to 5 drops (Acetasol HC) <u>Frequency of Administration</u> Once daily vs. every 2 to 3 hours (Acetasol) or three to four times daily (Acetasol HC)

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

Avodart (Dutasteride) Capsules, 0.5 mg Usual Dose 0.5 mg orally once daily	Orthographic The letter string 'Quil-' may appear similar to the corresponding letter string 'Avod-' when scripted. Overlap in Strength/Dose Quillivant may be administered at the dose of 5 mL or 50 mg, which may overlap with the Avodart's dose of 0.5 mg, especially if preceding zero is omitted (e.g., .5 mg) Route of Administration Orally Frequency of Administration Once daily	Orthographic The name Quillivant appears longer than the name Avodart (10 letters vs. 7 letters). Additionally, although the letter strings '-ant' and '-art' appear similar to each other when scripted, they are located in different positions.
Qutenza (Capsaicin) Topical Patch, 8% Usual Dose Use up to 4 patches per applicant. Apply for 60 minutes and do not use more often than every 3 months.	Orthographic Both names start with the letter string 'Qu-'. Additionally, the letter strings 'Quil-' and '-va-'in Quillivant appears to be similar to the letter strings 'Qut-' and '-za' in Qutenza when scripted. Overlap in Strength/Dose Quillivant may be administered at the dose of 8 mL and Qutenza is dosed at the strength of 8%	Orthographic The name Quillivant appears longer than the name Qutenza (10 letters vs. 7 letters). Additionally, the name Quillivant contains 4 upstrokes vs. the name Qutenza contains 2 upstrokes. Additionally, the letter string '-li-' in Quillivant lacks orthographic similarity to the letter string '-en-' in Qutenza when scripted. Route of Administration Orally vs. topically Usual Dose 10 mg (2 mL) to 60 mg (12 mL) vs. up to 4 patches

Quadramet (Samarium sm 153 lexidronam) Injection <u>Usual Dose</u> 1 mCi/kg intravenously over 1 minute.	<u>Orthographic</u> Both names start with the letter string 'Qu-'. Additionally, the letter string '-vant' in Quillivant may be scripted to appear similar to the letter string '-met' in Quadramet.	<u>Orthographic</u> The name Quillivant contains 2 upstrokes in the middle of the name (letter string 'll') vs. the name Quadramet contains 1 upstroke (letter 'd'). Additionally, the letter string '-illi-' in Quillivant lacks orthographic similarity to the letter string '-adra-' in Quadramet when scripted. <u>Usual Dose</u> 10 mg (2 mL) to 60 mg (12 mL) vs. 1 mCi/kg <u>Route of Administration</u> Orally vs. intravenously
Dexilant (Dexlansoprazole) Delayed-release Capsule, 30 mg and 60 mg <u>Usual Dose</u> 30 mg to 60 mg orally once daily	<u>Orthographic</u> Both names share the letter string '-ant' at the end of the names. Additionally, the letter strings 'Quil-' may appear similar to the corresponding letter string ' Dexil-' when scripted. <u>Overlap in Strength/Dose</u> Both products may be administered at the doses of 30 mg to 60 mg <u>Route of Administration</u> Orally <u>Frequency of Administration</u> Once daily	<u>Orthographic</u> The name Quillivant appears longer than the name Dexilant (10 letters vs. 8 letters). Additionally, the letter string '-liv-' in Quillivant lacks similarity to the corresponding letter string '-ant' when scripted.

Quinaretic (Quinapril and Hydrochlorothiazide) Tablet, 10 mg/12.5 mg, 20 mg/12.5 mg, and 20 mg/25 mg Usual Dose 10 mg/12.5 mg to 20 mg/25 mg (maximum of 40 mg of quinapril and 25 mg of hydrochlorothazide per day)	Orthographic Both names start with the letter string 'Qui-' Additionally, the letter string '-iv-' and the letter 'n' in Quillivant may appear similar to the corresponding letter strings '-re-' and '-ic' in Quinaretic when scripted. Partial Overlap in Strength/Dose Quillivant may be administer at the doses of 10 mg, 20 mg, or 25 mg, which overlaps with Quinapretic's partial strength of Quinapril (i.e., 10 mg and 20 mg) and Hydrochlorothiazdie (i.e., 25 mg) Route of Administration Orally Frequency of Administration Once daily	Orthographic The name Quillivant contains 4 upstroke vs. the name Quinaretic contains 2 upstrokes. Additionally, the letter string '-ll-' in Quillivant lacks orthographic similarity to the letter string '-na-' in Quinaretic when scripted.
Quinapril Tablet, 10 mg, 20 mg, 30 mg, 40 mg , and 50 mg Usual Dose 10 to 20 mg orally once daily. 40 mg to 80 mg should be administered in two divided doses (i.e., twice daily)	Orthographic Both names start with the letter string 'Qui-' Additionally, the letter string '-va-' in Quillivant may appear similar to the corresponding letter string '-ri- in Quinapril when scripted. Overlap in Strength/Dose Both products can be dosed at 10 mg, 20 mg, 30 mg, 40 mg, or 50 mg doses Route of Administration Orally Frequency of Administration Both products can be administered once daily	Orthographic The name Quillivant contains 4 upstroke vs. the name Quinapril contains 2 upstrokes and 1 downstroke. Additionally, the letter string '-lli-' in Quillivant lacks orthographic similarity to the letter string '-nap-' in Quinapril when scripted.

Questran (Chlestyramine) Powder for Oral Suspension, 4 g Usual Dose 4 g orally administered once to twice daily before meals, may increase up to 16 g per day in two divided doses	Orthographic The letter strings ‘Qui-’ and ‘-iva-’ in Quillivant may appear similar to the corresponding letter strings ‘Que-’ and ‘-ran’ when scripted. Overlap in Strength/Dose Quillivant can be dosed as 4 mL or 40 mg, which overlaps with Questran strength of 4 g. Route of Administration Orally Frequency of Administration Both products can be administered once daily	Orthographic The name Quillivant appears longer than the name Questran (10 letters vs. 8 letters). Additionally, the name Quillivant contains 4 upstrokes vs. the name Questran contains 2 upstrokes.
Amiloride HCl Tablet, 5 mg Usual Dose 5 mg to 20 mg orally once daily	Orthographic The letter string ‘Quil-’ may appear similar to the letter string ‘Amil-’ when scripted. Overlap in Strength/Dose Both products can be dosed at 10 mg and 20 mg Route of Administration Orally Frequency of Administration Both products can be administered once daily	Orthographic The name Quillivant contains 4 upstrokes vs. the name Amiloride contains 3 upstrokes. Additionally, the letter string ‘-livant’ lacks orthographic similarity to the letter string ‘-oride’ in Amiloride

Gadavist (Gadobutrol) Injection, 1 mmol Gadobutrol/mL (Equivalent to 604.72 mg/mL) Usual Dose 0.1 mmol/kg as intravenous bolus injection	Orthographic Both names end with the letter 't'. Additionally, the letter strings 'Quil-' and '-iv-' in Quillivant may appear similar to the corresponding letter strings'Gad-' and '-vi-' in Gadavist Overlap in Dose Quillvaint can be administered at doses between 10 mg and 60 mg, which may overlap with achievable Gadavist dose (e.g., 10 mmol for 100 kg person)	Orthographic The name Quillivant appears longer than the name Gadavist (10 letters vs. 8 letters). Additionally, the name Quillivant contains 4 upstrokes vs. the name Questran contains 3 upstrokes. Additionally, the send letter 'l' in the name Quillivant lacks orthographic similarity to the corresponding letter 'a' in Gadavist. Strength 25 mg/5 mL vs. 1 mmol Gadobutrol/mL (Equivalent to 604.72 mg/mL) Route of Administration Orally vs. intravenously Frequency of Administration Once daily vs. once
Quelicin (Succinylchloline) Injection: 200 mg/10mL (20 mg/mL) 1000 mg/10 mL (100 mg/mL) Usual Dose: Intravenous administration Adults: Average dose is 0.6 mg/kg intravenously (range 0.3 mg/kg to 1.1 mg/kg) administered over 10 seconds to 30 seconds. Additional doses may administered in accordance with patient's response. Intramuscular Adults, Older Children, and Infants: A dose of up to 3mg/kg to 4 mg/kg intramuscularly may be administered, but the total dose must not exceed 150 mg	Orthographic The letter string 'Quilliva-' may appear similar to the name Quelicin when scripted. Phonetic The letter string 'Quilli-' in Quillivant is phonetically similar to the letter string 'Queli-' in Quilicin Overlap in Strength/Dose Quillvant may be administered at the doses of 10 mg and 20 mg, which overlaps with Quelicin strength and concentration of 200 mg/10 mL (20 mg/mL) or 1000 mg/10 mL. Additionally, the achievable doses of both products may overlap as well (e.g., Quelicin administered at dose of 1 mg/kg for 40 kg, 50 kg, or 60 kg person)	Orthographic The name Quillivant appears longer than the name Quelicin (10 letters vs. 8 letters). Additionally, the name Quillivant contains 4 upstrokes vs. the name Quelicin contains 2 upstrokes. Phonetic The letter string '-vant' lack phonetic similarity to the letter string '-cin' Route of Administration Orally vs. intravenously or intramuscularly Frequency of Administration Once daily vs. over 10 seconds to 30 seconds

Combivent (Albuterol and Ipratropium) Inhalation Aerosol 103 mcg/18 mcg per actuation. <u>Usual Dose</u> 2 to 3 inhalations every 6 hours.	<u>Orthographic</u> The letter string ‘Qu-’ and the letter string ‘-ivant’ in Quillivant may appear similar to the letter string ‘Co-’ and ‘-ivent’ when scripted. Additionally, the first letter ‘l’ may in Quillivant appear similar to the letter ‘b’ in Combivent when scripted.	<u>Orthographic</u> The name Quillivant contains 4 upstrokes vs. the name Combivent contains 3 upstrokes. Additionally, the first letter ‘i’ in Quillivnat lacks orthographic similarity to the letter ‘m’ in Combivent when scripted. <u>Strength</u> 25 mg/5 mL vs. 103 mcg/18 mcg per actuation <u>Usual Dose</u> 10 mg (2 mL) to 60 mg (12 mL) vs. 2 inhalations to 3 inhalations <u>Frequency of Administration</u> Once daily vs. every 6 hours

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