CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

202343Orig1s000

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 26, 2011
Reviewer(s):	Anne Tobenkin, PharmD Division of Medication Error Prevention and Analysis
Team Leader	Lubna Merchant, PharmD, M.S. Division of Medication Error Prevention and Analysis
Division Director	Carol Holquist, RPh. Division of Medication Error Prevention and Analysis
Drug Name(s):	Juvisync (Sitagliptin and Simvastatin) Tablets
Strengths:	100 mg/10 mg, 100 mg/20 mg, 100 mg/40 mg
Application Type/Number:	NDA 202343
Applicant/sponsor:	Merck
OSE RCM #:	2011-3271

*** 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, Juvisync, from a safety and promotional perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively.

1.1 REGULATORY HISTORY

The Applicant, Merck, submitted the proprietary name request for Juvisync Tablets on September 2, 2011. The Applicant had submitted two names previously, (b) (4) which was found unacceptable in OSE review # 2011-2427 and (b) (4) which was withdrawn by the Applicant on September 2, 2011.

Additionally, a label and labeling review (OSE review # 2011-300) was also completed on June 20, 2011. The label and labeling recommendations were sent to the Applicant.

1.2 PRODUCT INFORMATION

Juvisync is a combination product which contains Sitagliptin and Simvastatin. Juvisync is indicated for glycemic control in the setting of Type 1 diabetes and to decrease cholesterol. The proposed strengths of Juvisync include; 100 mg/10 mg, 100 mg/20 mg, and 100 mg/40 mg tablets. The recommended dose and frequency of Juvisync is one tablet by mouth once daily. Juvisync will be available in physician samples and bottles of 30, 90 and 1000 tablets and can be stored at room temperature.

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 Metabolic and Endocrinology Products concurred with the findings of DDMAC's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) SEARCH

The September 9, 2011 United States Adopted Name (USAN) stem search identified that a USAN stem is not present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

Per the Applicant and DMEPA's evaluation of the proprietary name, Juvisync, is a coined term that has no intrinsic meaning. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc) that can contribute to medication error or render the name unacceptable.

2.2.3 FDA Name Simulation Studies

Twenty nine practitioners participated in DMEPA's prescription studies. The most common misinterpretation in the written study was with the first letter 'J' for 'T' and 'L'. The most common misinterpretations in the voice study was confusion with vowels 'i' for 'a', 'e', and 'o' and 'y' for 'i'. 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, September 14, 2011 e-mail, the Division of Metabolic and Endocrinology Products (DMEP) did not forward any comments or concerns relating to the proposed name at the initial phase of the 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 name, Juvisync. Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Juvisync identified by the primary reviewer (PR), the Expert Panel Discussion (EPD), other review disciplines.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD and Other Disciplines)

Look Similar		Sound Similar		Look and Sound Similar	
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Jenloga	EPD	Nuvaring	EPD	Juvisync	EPD
Tasigna	EPD	Jantoven	EPD	Januvia	EPD
Tikosyn	EPD			(b) (4)	EPD
Tussigon	EPD				
(b) (4)	EPD				
(b) (4)	EPD				
Invega	EPD				
Invagesic	EPD				
Visudyne	EPD				
Jevantique	EPD				
Junovan	EPD				
Junifer	EPD				
Enjuvia	EPD				
(b) (4)	PR				
(b) (4)	PR				

Look Similar	
Firazyr	PR
(b) (4)	EPD

Our analysis of the twenty two names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics. We determined the 22 names will not pose a risk for confusion as described in Appendix D through E.

DMEPA communicated these findings to the Division of Metabolic and Endocrinology Products (DMEP) via e-mail on September 16, 2011. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DMEP on September 19, 2011 they stated no additional concerns with the proposed proprietary name, Juvisync.

3 CONCLUSIONS

DMEPA concludes the proposed proprietary name, Juvisync, 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.

If you have further questions or need clarifications, please contact Margarita Tossa, OSE Project Manager, at 301-796-4053.

3.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your September 09, 2011, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

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*** *(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.

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.

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

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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.

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).

[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 (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

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

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 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

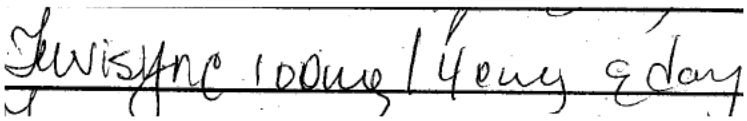
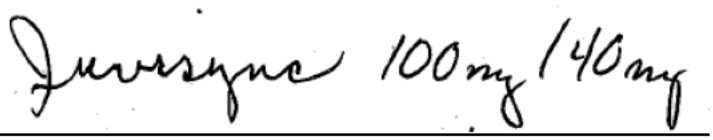
past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Sponsors' have changed a product's proprietary name in the post-approval 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: Letters with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, NAME	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'J'	T, F, I	"G"
lower case 'u'	a, o, e, i	"ew", "oo"
lower case 'v'	n, r, s	"b"
lower case 'i'	e, r	"y", "ee"
lower case 's'	r, n	"z", "c"
lower case 'y'	g, j	"i"
Lower case 'n'	r, m, s	
Lower case 'c'	e, i	"k", "ck"

Appendix C: Prescription Simulation Samples and Results

Figure 1. Rx Simulation Study (Conducted on September 9, 2011)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order: 	Juvisync 100 mg/40 mg One po qdaily
Outpatient Prescription: 	

FDA Prescription Simulation Responses.

Inpatient Medication Order	Outpatient Prescription	Voice Prescription
TURISYNC	JUVISYNC	JUVESINC
TEVISYNC	JUVESYNC	JUVOSAKE
TUVISYNC	JURVISYNC	JURISYNC
TUVISCYNC	INVYSYNC	JUVESYNC
TUVISYNC	JUVISYNE	JUVASINC
TUVISYNC	JUVISYNC	JUVESYNC
TERVISYNC	JUVISYNC	JUVASINK
LUVISYNC		JUVISYNC
JEWISYNC		JUVESYNC
TUVISYNC		JUVISYNC
TUVISYNC		
LEVISYNC		

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 Name of drug	Failure preventions
[redacted]			(b) (4)
Juvisync	Sitaglitpin and Simvastatin	Orthographic and Phonetic	Proposed proprietary name for the product in this review
Junifer	N/A	Orthographic	Foreign drug product, not marketed in the U.S.
Junovan	Mifamurtide	Orthographic	Name found unacceptable in OSE review # 2006-759, OSE found alternate proprietary name, Mepactid, acceptable in OSE review # 2007-1291
[redacted]			(b) (4)

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

Proposed name: Juvisync (Sitagliptin and Simvastatin) **Strength and Dosage Form: 100 mg/10 mg, 100 mg/20 mg, 100 mg/40 mg tablets** **Usual Dose: One tablet by mouth once daily**	**Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion**	**Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences**
Jenloga (Clonidine) - 0.1 mg, 0.2 mg extended-release tablets - One tablet by mouth once daily for once week and then titrate to twice daily	**Orthographic similarities** - Both names begin with 'J' - Both names are similar in length - Both names a down stroke **Product characteristics** - Route of administration (oral) - Dosage form (tablet) - Frequency of administration (once daily)	**Orthographic differences which make the names appear different when scripted** - Juvisync has one upstroke vs. Jenloga has two upstrokes - Juvisync has two letters after the downstroke vs. Jenloga has one letter **Product characteristic differences** - Strength (100 mg/10 mg, 100 mg/20 mg, 100 mg/40 mg vs. 0.1 mg, 0.2 mg) - Frequency of administration (once daily vs. twice daily, once daily administration only occurs for one week and only for titration purpose)
Tasigna (Nilotinib) - 150 mg, 200 mg oral capsules - two capsules by mouth twice daily	**Orthographic similarities** - 'T' and 'J' appear similar when scripted - Both names have one downstroke that is similarly situated **Product characteristics** - Route of administration (oral) - Dosage form (oral solid: capsule, tablet) - Obtainable strength (200 mg)	**Orthographic differences which make the names appear different when scripted** - Juvisync appears longer when scripted **Product characteristic differences** - Frequency of administration (once daily vs. twice daily) - Strength (100 mg/10 mg, 100 mg/20 mg, 100 mg/40 mg vs. 150 mg, 200 mg; Juvisync prescription must designate, at a minimum, the Simvastatin strength which does not overlap with Tasigna strengths)

Proposed name: Juvisync (Sitagliptin and Simvastatin) **Strength and Dosage Form: 100 mg/10 mg, 100 mg/20 mg, 100 mg/40 mg tablets** **Usual Dose: One tablet by mouth once daily**	**Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion**	**Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences**
Tikosyn (Dofetilide) - 125 mcg, 250 mcg, 500 mcg oral capsules - one capsules by mouth twice daily	**Orthographic similarities** - 'T' and 'J' appear similar when scripted - Both names have one downstroke - Both names are similar in length **Product characteristics** - Route of administration (once daily) - Dosage form (oral solid: capsule, tablet)	**Orthographic differences which make the names appear different when scripted** - Juvisync has one upstroke vs. Tikosyn has two upstrokes - Juvisync has two letters after the downstroke vs. Tikosyn has one letter the downstroke **Product characteristic differences** - Strength (100 mg/10 mg, 100 mg/20 mg, 100 mg/40 mg vs. 125 mcg, 250 mcg, 500 mcg) - Frequency of administration (once daily vs. twice daily)
Tussigon (Homatropine and Hydrocodone) - 1.5 mg/5 mg oral tablet - ½ to one tablet by mouth every 4 to 6 hours as needed, not to exceed 6 tablets per day	**Orthographic similarities** - 'T' and 'J' appear similar when scripted - Both names have one upstroke and one downstroke **Product characteristics** - Route of administration (oral) - Dosage form (tablet) - Dose (one)	**Product characteristic differences which make the names appear different when scripted** - Strength (100 mg/10 mg, 100 mg/20 mg, 100 mg/40 mg vs. 1.5 mg/5 mg, single strength, not required on prescription) - Frequency of administration (once daily vs. every4 to 6 hours as needed)
(b) (4)		

Proposed name: Juvisync (Sitagliptin and Simvastatin) **Strength and Dosage Form: 100 mg/10 mg, 100 mg/20 mg, 100 mg/40 mg tablets** **Usual Dose: One tablet by mouth once daily**	**Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion**	**Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences**
Invega (Paliperidone) - 1.5 mg, 3 mg, 6 mg, 9 mg extended-release oral tablet - 1.5 mg to 12 mg by mouth once daily	**Orthographic similarities** - 'I' and 'J' appear similar when scripted - Both names have one upstroke and one downstroke **Product characteristics** - Route of administration (oral) - Frequency of administration (once daily) - Dose (one) - Dosage form (tablet)	**Orthographic differences which make the names appear different when scripted** - Juvisync is eight letters vs. Invega is six letters making it appear shorter when scripted **Product characteristic differences** - Strength (100 mg/10 mg, 100 mg/20 mg, 100 mg/40 mg vs. 1.5 mg, 3 mg, 6 mg, 9 mg)
Invagesic (Aspirin, Caffeine and Orphenadrine) - 385 mg/30 mg/25 mg or 770 mg/60 mg/50 mg oral tablets - ½ to 2 tablets by mouth three to four times a day	**Orthographic similarities** - 'I' and 'J' appear similar when scripted - Both names have one upstroke and one downstroke **Product characteristics** - Dosage form (tablet) - Route of administration (oral) - Dose (one)	**Orthographic differences which make the names appear different when scripted** - Juvisync has two letters after the downstroke vs. Invagesic has four letters after the downstroke **Product characteristic differences** - Strength (100 mg/10 mg, 100 mg/20 mg, 100 mg/40 mg vs. 385 mg/30 mg/25 mg, 770 mg/60 mg/50 mg) - Frequency of administration (once daily vs. three to four times a day)
Visudyne (Verteporfin) - 15 mg per vial - 6 mg/m2 intravenous infusion followed by light therapy	**Orthographic similarities** - 'J' and 'V' appear similar when scripted - Both letters have one downstroke that is similarly situated	**Orthographic differences which make the names appear different when scripted** - Juvisync has one upstroke vs. Visudyne has two upstrokes **Product characteristic differences** - Route of administration (oral vs. intravenous) - Dose (one tablet vs. 6 mg/m^2, weight based dose) - Frequency of administration (once daily vs. one time in clinic, immediately followed by light therapy) - Dosage form (tablet vs. injection)

Proposed name: Juvisync (Sitagliptin and Simvastatin) **Strength and Dosage Form:** **100 mg/10 mg,** **100 mg/20 mg,** **100 mg/40 mg tablets** **Usual Dose: One tablet by mouth once daily**	**Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion**	**Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences**
Jevantique (Norethindrone and Ethinyl estradiol) - 1 mg/5 mcg oral tablets, 28 day pack - One tablet by mouth once daily or as directed	**Orthographic similarities** - Both names begin with 'J' - Both names have one down downstroke that is similarly situated **Product characteristics** - Route of administration (oral) - Frequency of administration (once daily) - Dosage form (tablet) - Dose (one)	**Orthographic differences which make the names appear different when scripted** - Juvisync has eight letters vs. Jevantique has ten letters - Juvisync has one upstroke vs. Jevantique has two upstrokes **Product characteristic differences** - Strength (100 mg/10 mg, 100 mg/20 mg, 100 mg/40 mg vs. 1 mg/5 mcg, single strength)
Enjuvia (Synthetic conjugated estrogen) - 0.3 mg, 0.45 mg, 0.625 mg, 0.9 mg, 1.25 mg oral tablets - One tablet by mouth once daily	**Orthographic similarities** - Both names are similar in length - Both names have one downstroke and one upstroke **Product characteristics** - Frequency of administration (once daily) - Route of administration (oral) - Dosage form (tablet) - Dose (one)	**Orthographic differences which make the names appear different when scripted** - Juvisync has only two letters following the downstroke which appears at the end of the name vs. Enjuvia has a downstroke at the third letter with four letters following the downstroke **Product characteristic differences** - Strength (100 mg/10 mg, 100 mg/20 mg, 100 mg/40 mg vs. 0.3 mg, 0.45 mg, 0.625 mg, 0.9 mg, 1.25 mg)

Proposed name: Juvisync (Sitagliptin and Simvastatin) **Strength and Dosage Form:** **100 mg/10 mg,** **100 mg/20 mg,** **100 mg/40 mg tablets** **Usual Dose: One tablet by mouth once daily**	**Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion**	**Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences**
Januvia (Sitagliptin) - 25 mg, 50 mg, 100 mg oral tablets - One tablet by mouth once daily	**Orthographic similarities** - Both names begin with 'J' - Both names are similar in length **Phonetic similarities** - Both names begin with the sound "J" **Product characteristics** - Strength (100 mg) - Frequency of administration (once daily) - Route of administration (oral) - Dose (one) - Dosage form (tablet) - Drug Product (Sitagliptin)	**Orthographic differences which make the names appear different when scripted** - Juvisync has a downstroke vs. Januvia does not have a downstroke **Phonetic differences** - Juvisync has the sound "vee" in the second syllable vs. the sound "new" in Januvia - Juvisync ends with the sound "sink" vs. the sound "via" in Januvia **Product characteristic differences** - Strength (100 mg/10 mg, 100 mg/20 mg, 100 mg/40 mg vs. 25 mg, 50 mg 100 mg; Juvisync prescription must designate, at a minimum, the Simvastatin strength which does not overlap with Januvia strengths)
Nuvaring (Etonogestrel and Ethinyl estradiol) - 0.12 mg/0.015 mg per day intravaginal ring - One ring inserted vaginally once every 3 weeks	**Phonetic similarities** - Both names are three syllables - Both names have the sound "uva" vs. "uvi" in the first two syllables - Both names end with a similar sound "ing" vs. "ink"	**Phonetic differences** - Juvasync begins with the sound "Joo" vs. "Noo" in Nuvaring - The final syllable in Juvisync starts with the sound "sin" vs. "rin" in Nuvaring **Product characteristic differences** - Strength (100 mg/10 mg, 100 mg/20 mg, 100 mg/40 mg vs. 0.12 mg/0.015 mg, single strength, not required on prescription) - Dosage form (table vs. ring) - Route of administration (oral vs. intravaginal) - Frequency of administration (once daily vs. every three weeks)

Proposed name: Juvisync (Sitagliptin and Simvastatin) **Strength and Dosage Form: 100 mg/10 mg, 100 mg/20 mg, 100 mg/40 mg tablets** **Usual Dose: One tablet by mouth once daily**	**Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion**	**Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences**
Jantoven (Warfarin) - 1 mg, 2 mg, 2.5 mg, 3 mg, 4 mg, 5 mg, 6 mg, 7.5 mg, 10 mg	**Phonetic similarities** - Both names are three syllables - Both names begin with the sound "J" **Product characteristics** - Frequency of administration (once daily) - Route of administration (one) Dosage form (tablet) - Dose (one) - Strength (10 mg)	**Phonetic differences** - The first syllable in Juvisync ends with the sound "oo" vs. "ahn" in Jantoven - The second syllable in Juvisync has the sound "vee" vs. "toe" in Jantoven - The final syllable has the sound "sink" in Juvisync vs. "ven" in Jantoven
(b) (4)		
Firazyr (Icatibant) - 30 mg pre-filled syringe - 30 mg or one syringe once as needed for symptoms, no more then 3 syringes in one day	**Orthographic similarities** - 'F' and 'J' appear similar when scripted - Both names have one upstroke and one downstroke - Both names are similar in length	**Orthographic differences which make the names appear different when scripted** - Juvisync has two letters after the downstroke vs. Firazyr has one letter after downstroke **Product differences** - Strength (100 mg/10 mg, 100 mg/20 mg, 100 mg/40 mg vs. 30 mg, single strength, not required on prescription) - Route of administration (oral vs. subcutaneously) - Frequency of administration (once daily vs. one time for symptoms as needed) - Dosage form (tablet vs. pre-filled syringe)

Proposed name: Juvisync (Sitagliptin and Simvastatin) Strength and Dosage Form: 100 mg/10 mg, 100 mg/20 mg, 100 mg/40 mg tablets Usual Dose: One tablet by mouth once daily	Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences
(b) (4)		

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/s/

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