CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

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PROPRIETARY NAME REVIEW(S)

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

Date:	June 16, 2010
To:	Scott Monroe, MD, Director Division of Reproductive and Urologic Products (DRUP)
Through:	Todd Bridges, RPh, Team Leader Denise Toyer, PharmD, Deputy Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Jibril Abdus-Samad, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Staxyn (Vardenafil Hydrochloride) Orally Disintegrating Tablets, 10 mg
Application Type/Number:	NDA# 200179
Applicant:	Bayer HealthCare Pharmaceuticals, Inc.
OSE RCM #:	2010-1246

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EXECUTIVE SUMMARY

This review summarizes the DMEPA's Proprietary Name Assessment for the proposed proprietary name, Staxyn (Vardenafil Hydrochloride) Orally Disintegrating Tablets. Our evaluation did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of this review. Thus, DMEPA finds the proposed proprietary name, Staxyn, acceptable for this product. The proposed proprietary name must be re-reviewed 90 days before the approval of the NDA.

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

1 BACKGROUND

1.1 INTRODUCTION

This review responds to a request from Bayer HealthCare Pharmaceuticals, Inc., received on June 2, 2010, for an assessment of the proposed proprietary name, Staxyn, regarding potential name confusion with other proprietary or established drug names in the usual practice settings.

1.2 REGULATORY HISTORY

For this product, the Applicant initially proposed the proprietary name, (b) (4). However, the name was found unacceptable for promotional concerns. These promotional concerns and additional safety concerns were discussed during a teleconference held on December 14, 2009, and communicated to the Applicant in a letter dated January 28, 2010. Subsequently, in a letter dated February 15, 2010, the Applicant requested review of the proposed proprietary names, (b) (4) and (b) (4). A teleconference was held on April 13, 2010, to discuss safety issues with the proposed proprietary names (b) (4) and (b) (4). These concerns were also communicated to the Applicant in a letter dated May 19, 2010. The Applicant subsequently proposed a new proprietary name, (b) (4) in a letter dated April 20, 2010. In a teleconference held May 27, 2010, DMEPA communicated that the proposed name (b) (4) was unacceptable. Subsequently, the Applicant submitted the proposed proprietary name, Staxyn, for review on June 2, 2010.

1.3 PRODUCT INFORMATION

Staxyn has a proposed indication for the treatment of erectile dysfunction. The recommended dose is one tablet by mouth approximately 60 minutes before sexual activity. Staxyn should be placed on the tongue where it will disintegrate. The maximum recommended dosing frequency is one tablet per day. Staxyn is supplied as a foil blisterpacks and supplied as a 4 tablet unit or as a 40 tablet bulk pack. Staxyn should be stored at 25ºC (77ºF); excursions permitted to 15º-30ºC (59º -86ºF).

2 METHODS AND MATERIALS

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

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter 'S' when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.[1,2]

To identify drug names that may look similar to Staxyn, the DMEPA staff also consider the other orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (6 letters), upstrokes (2, capital letter 'S', lowercase 't'), down-strokes (1, lowercase 'y'), cross-strokes (1, lowercase 'x'), and dotted letters (none). Additionally, several letters in Staxyn may be vulnerable to ambiguity when scripted (see Appendix B). As such, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Staxyn.

When searching to identify potential names that may sound similar to Staxyn, the DMEPA staff search for names with similar number of syllables (2), stresses (STAX-yn or stax-YN), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary (See Appendix B). The Applicant's intended pronunciation (stæx-zin) was also taken into consideration, as it was included in the Proprietary Name Review Request. Moreover, names are often mispronounced or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

2.2 FDA PRESCRIPTION ANALYSIS STUDIES

FDA Prescription Analysis Studies were not conducted because of limited time available to complete the proprietary name review prior to the application action date.

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The DMEPA searches yielded a total of 16 names as having some similarity to the proposed proprietary name, Staxyn.

The DMEPA safety evaluators thought twelve of the names looked like Staxyn. These include Atarax, Ativan, Atreza, ATryn, (b) (4)***, Sronyx, Stadol, Stalevo, Starlix, Stavzor, (b) (4)***, and Stoxil. Two names were thought to sound like Staxyn: Afaxin and Skelaxin. The remaining two names were thought to look and sound like Staxyn: Staticin and Staxyn.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of June 7, 2010.

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

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

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

3.2 EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMEPA staff (See Section 3.1 above) and did not find additional names thought to have orthographic or phonetic similarity to Staxyn. Additionally, the Expert Panel anticipates wrong drug medications errors when vardenafil orally disintegrating tablets become available as a generic product.

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name.

3.3 COMMENTS FROM THE DIVISION OF REPRODUCTIVE AND UROLOGIC PRODUCTS (DRUP)

3.3.1 Initial Phase of Review

In response to an e-mail from OSE dated June 11, 2010, DRUP did not forward any comments or concerns on the proposed name at the initial phase of the name review.

3.3.2 Midpoint Review

On June 15, 2010, DMEPA notified the DRUP via e-mail, that we that we had no objections to the proposed proprietary name, Staxyn. Per e-mail correspondence from DRUP on June 15, 2010, they indicated they had no comments regarding this decision.

3.4 SAFETY EVALUATOR RISK ASSESSMENT OF THE PROPOSED PROPRIETARY NAME

Independent searches by the primary Safety Evaluator did not yield additional names which look or sound similar to Staxyn and represent a potential source of drug name confusion.

Thus, we identified and evaluated a total of 16 names for their similarity to the proposed name: all 16 names identified in section 3.1.

4 DISCUSSION

This proposed name, Staxyn, was evaluated from promotional and safety perspectives based on the product characteristics provided by the Applicant. We sought input from pertinent disciplines involved with the review of this application and considered it accordingly.

4.1 PROMOTIONAL ASSESSMENT

DDMAC did not have promotional concerns with the proposed name, Staxyn. DRUP and DMEPA concurred with DDMAC's assessment.

4.2 SAFETY ASSESSMENT

DMEPA identified 16 names for their potential similarity to the proposed name, Staxyn. Two of the 16 names lacked orthographic and/or phonetic similarity to Staxyn and four names were determined to no longer be active and therefore were not evaluated further (see Appendices C and D). Additionally, the name Staxyn, which is the subject of this review, was identified in our database search and thus eliminated from further analysis.

Failure Mode and Effect Analysis (FMEA) was applied to determine if the proposed proprietary name could potentially be confused with the remaining nine names. This analysis determined that the name similarity between Staxyn and the remaining names nine names was unlikely to result in medication errors for the reasons presented in Appendices E through I. Additionally, our analysis did not identify other aspects of the name that would contribute to error.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment indicates that the proposed name, Staxyn, is not vulnerable to name confusion that could lead to medication errors, nor is the name considered promotional. Thus, DMEPA has no objection to the proposed name, Staxyn, for this product at this time.

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMEPA rescinds this Risk Assessment finding and the name must be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. Furthermore, if the approval of this application is delayed beyond 90 days from the signature date of this review, the proposed name must be re-reviewed.

For questions or clarifications, please contact Karen Townsend, OSE Regulatory Project manager, at 301-796-5413.

5.1 COMMENTS TO THE APPLICANT

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

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

6 REFERENCES

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

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

2. Phonetic and Orthographic Computer Analysis (POCA)

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

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

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

4. AMF Decision Support System [DSS]

DSS is a government database used to track individual submissions and assignments in review divisions.

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

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

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

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

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

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

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

USPTO provides information regarding patent and trademarks.

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

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

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

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

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

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

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

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

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

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

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

APPENDICES

Appendix A:

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

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity and hold a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name. DMEPA staff also conducts internal CDER prescription analysis studies. When provided, DMEPA considers external prescription analysis study results and incorporate into the overall risk assessment.

[3] National Coordinating Council for Medication Error Reporting and Prevention. http://www.nccmerp.org/aboutMedErrors html. Last accessed 10/11/2007.

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and focuses on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail. [4] DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. Accordingly, the DMEPA staff considers the product characteristics associated with the proposed drug throughout the risk assessment because the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA staff considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.[5] DMEPA provides the product characteristics considered for this review in section one.

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

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

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

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

Type of similarity	**Considerations when searching the databases**		
	Potential causes of drug name similarity	*Attributes examined to identify similar drug names*	*Potential Effects*
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• 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, the DMEPA staff also considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to

the safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

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

2. CDER Expert Panel Discussion

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

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

3. FDA Prescription Analysis Studies

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of the 123 participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants send their interpretations of the orders via e-mail to DMEPA.

4. Comments from the OND Review Division or Office of Generic Drugs

DMEPA requests the Office of New Drugs (OND) or Office of Generic Drugs (OGD) Regulatory Division responsible for the application for their comments or concerns with the proposed proprietary name and any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with DDMAC's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND or 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 concur/not concur with DMEPA's final decision.

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

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

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

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

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names 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:

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

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

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

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

a. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].

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

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

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

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

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

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

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

confusion is a predictable and a preventable source of medication error that, in many instances, the Agency and/or Applicant can identify and rectify prior to approval to avoid patient harm.

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

Appendix B: Potential orthographic or phonetic misinterpretation of the letters in the name Staxyn

Letters in Name, Staxyn	Scripted may appear as	Spoken may be interpreted as
Capital 'S'	A, G	C
lowercase 't'	f, k, x	d
lowercase 'a'	c, ci, ce, o, or u	any vowel
lowercase 'x'	f, k, r, t	ks, z
lowercase 'y'	g, u	i, e
lowercase 'n'	h, m, r, s, u	m

Appendix C: Names lacking significant orthographic or phonetic similarities

Proprietary Name	Similarity to Staxyn	Source
Stadol	Look	EPD
Stalevo	Look	EPD

Appendix D: Proprietary names no longer active

Proprietary Name	Similarity to Staxyn	Status
Afaxin (Vitamin A Palmitate)	Look	Discontinued per DARRTS and Drugs @ FDA, not available in Red Book, and no generics available (ANDA 083187)
(b) (4)**	Look	ANDA 075803 approved on March 20, 2002 with proprietary name *Lessina*
(b) (4)***	Look	NDA 021548 approved on October 20, 2003 with proprietary name *Lexiva*
Stoxil (Idoxuridine)	Look	Discontinued per Drugs @ FDA, not available in Red Book, and no generics available

Appendix E: Products with different strength and frequency of administration

Product name with potential for confusion	Similarity to Staxyn	Strength, Dosage Form	Frequency of Administration
Staxyn (Vardenafil)		**10 mg orally disintegrating tablets**	**once daily**
Stavzor (Valproic Acid)	Look	125 mg, 250 mg, 500 mg tablets	2 times daily

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

Appendix F: Products with different product characteristics

Product name with potential for confusion	**Similarity to Staxyn**	**Strength, Dosage Form**	**Usual Dose**	**Differing product characteristics**
Staxyn (Vardenafil)		**10 mg tablets**	**Take 1 tablet orally daily 60 minutes prior to sexual activity**	***Dose*: 1 tablet** ***Strength*: One strength available)** ***Dosage Form*: tablet** ***Route of Administration*: oral** ***Frequency of Administration*: once daily** ***Usual Practice setting*: Outpatient**
A Tryn (Antithrombin)	Look	1750 International Units/vial, for inj	*Loading dose*: [(100 - baseline AT activity level) divided by 2.3] x body weight (kg) = International Units of AT required *Maintenance infusion*: [(100 - baseline AT activity level) divided by 10.2] x body weight (kg) = International Units of AT required/hr	*Dose*: 100 units/mL *Dosage Form*: injection *Route of Administration*: Intravenous *Usual practice setting*: Inpatient
Staticin (Erythromycin) *discontinued product, only generic available*	Look/Sound	2% solution	Apply to affected area twice daily	*Dosage Form*: solution *Route of Administration*: topical *Frequency of administration*: twice daily

Appendix G: Products with orthographic differences and different patient populations

Failure Mode: Name confusion	**Causes: (could be multiple)**	**Rationale why medications errors are unlikely to occur in usual practice setting**
Staxyn (Vardenafil)	**10 mg orally disintegrating tablets**	**Usual dose: Take 1 tablet orally daily 60 minutes prior to sexual activity**
Sronyx (Ethinyl Estradiol and Levonorgestrel) 20 mcg/0.1 mg tablets Usual Dose: Take 1 tablet orally daily	Orthographic similarity: Both names contain 6 letters; both names share 2 letters in same position ('S', 'y'); share a letter that appears similar when scripted ('o' vs. 'a') Both can be prescribed without a strength. Both can be prescribed with dose instructions as 'once daily' or 'as directed'.	Orthographic Difference: Staxyn contains the upstroke 't' in the second letter position. The crosstroke 'x' is in different positions in both names. Patient Population: Sronyx is an oral contraceptive prescribed for women and Staxyn will be prescribed for men. Multiple failure modes must occur for a medication error to occur (name confusion, omission of strength, wrong patient population).

Appendix H: Products with phonetic differences and different frequency of administration

Failure Mode: Name confusion	**Causes: (could be multiple)**	**Rationale why medications errors are unlikely to occur in usual practice setting**
Staxyn (Vardenafil)	**10 mg orally disintegrating tablets**	**Usual dose: Take 1 tablet orally daily 60 minutes prior to sexual activity**
Skelaxin (Metaxalone) 800 mg tablets Usual Dose: Take 1 tablet 3 to 4 times daily as needed	Phonetic Similarity: Both names have similar sounding syllables ('Stax-in' vs. 'lax-in') Single strength product that can be prescribed without a strength	Phonetic Differences: Skelaxin contain 3 syllables (Ske-lax-in) while Staxyn contains 2 syllables (Stax-in) Frequency of Administration: Skelaxin is generally as prescribed multiple times per day on an as needed basis.

Appendix I: Products with orthographic differences and different frequency of administration

Failure Mode: Name confusion	**Causes: (could be multiple)**	**Rationale why medications errors are unlikely to occur in usual practice setting**
Staxyn (Vardenafil)	**10 mg orally disintegrating tablets**	**Usual dose: Take 1 tablet orally daily 60 minutes prior to sexual activity**
Atarax (Hydroxyzine Hydrochloride) 10 mg, 25 mg, 50 mg, 100 mg tablets Usual Dose: Take 1 tablet orally 3 to 4 times daily as needed	Orthographic similarity: Both names share the same length (6 letters); contain 2 letters in the same position (‘ta’); share a letter that may appear similar when scripted (‘A’ vs. ‘S’) Numerical Similarity: 10 mg vs. 10 mg	Orthographic differences: Staxyn contains a downstroke toward the end of the name. Additionally the ending of the names differ (‘-rax’ vs. ‘-xyn') Frequency of Administration: Atarax is generally as prescribed multiple times per day on an as needed basis
10 mg/5 mL solution Usual Dose: Take 5 mL to 2.5 mL orally 3 to 4 times daily as needed		
Ativan (Lorazepam) 0.5 mg, 1 mg, 2 mg tablets Usual Dose: Take 1 tablet orally daily	Orthographic similarity: Both names share the same length (6 letters); contain 2 letters in the same position (‘t’, ‘n’); share 2 letters that may appear similar when scripted (‘A’ vs. ‘S’, ‘i’ vs. ‘a’) Numeric similarity 1 mg vs. 10 mg	Orthographic difference: The middle portion of the names help distinguish these names (‘-va-’ vs. ‘-xy-’), especially since Staxyn contains the downstroke ‘y’. Frequency of Administration: Ativan is generally as prescribed multiple times per day on an as needed basis. Medication orders for parenteral Ativan must contain route of administration (intravenous or intramuscular) and the usual practice setting will be inpatient.
2 mg/mL, 4 mg/mL injections Usual Dose: Inject 2 mg to 4 mg intramuscularly or intravenously		

continued Appendix I: Products with orthographic differences and different frequency of administration

Failure Mode: Name confusion	**Causes: (could be multiple)**	**Rationale why medications errors are unlikely to occur in usual practice setting**
Staxyn (Vardenafil)	**10 mg orally disintegrating tablets**	**Usual dose: Take 1 tablet orally daily 60 minutes prior to sexual activity**
Atreza Atropine) 0.4 mg Usual Dose: Take 1 tablet every 4 to 6 hours	Orthographic similarity: Both names share the same length (6 letters); contain a letter in the same position ('t'); share a letters that may appear similar when scripted ('A' vs. 'S'); contain a downstroke in same position ('z' vs. 'y') Both products can be prescribed without a strength	Orthographic differences: Staxyn contains an additional crosstroke 'x', thus the middle portions of the names do not look alike ('-re-' vs. '-ax-') Frequency of Administration: Atreza is prescribed 3 times daily. The maximum dose of Staxyn is one tablet daily
Starlix (Nateglinide) 60 mg, 120 mg Usual Dose: Take 1 tablet orally 3 times daily with meals	Orthographic similarity: Both names share 3 letters in the same position ('Sta-')	Orthographic difference: Starlix contains an additional upstroke ('l') toward the end of the name while Staxyn contains a downstroke ('y'). Frequency of Administration: Starlix is prescribed 3 times daily. The maximum dose of Staxyn is one tablet daily. A prescription for Starlix must include the strength (60 mg or 120 mg)

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200179	ORIG-1	BAYER HEALTHCARE PHARMACEUTICALS INC	VARDENAFIL HCL

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