

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
**021936Orig1s000**

**PROPRIETARY NAME REVIEW(S)**

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**PROPRIETARY NAME REVIEW**

Division of Medication Error Prevention and Analysis (DMEPA)  
Office of Medication Error Prevention and Risk Management (OMEPRM)  
Office of Surveillance and Epidemiology (OSE)  
Center for Drug Evaluation and Research (CDER)

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<b>Date of This Review:</b>	June 30, 2014
<b>Application Type and Number:</b>	NDA 021936
<b>Product Name and Strength:</b>	Spiriva Respimat (Tiotropium Bromide) Inhalation Spray 2.5 mcg per actuation
<b>Product Type:</b>	Single Ingredient Product
<b>Rx or OTC:</b>	Rx
<b>Applicant/Sponsor Name:</b>	Boehringer Ingelheim Pharmaceuticals, Inc.
<b>Submission Date:</b>	April 14, 2014
<b>Panorama #:</b>	2014-17214
<b>DMEPA Primary Reviewer:</b>	Lissa C. Owens, PharmD
<b>DMEPA Team Leader:</b>	Kendra Worthy, PharmD
<b>DMEPA Associate Director:</b>	Lubna Merchant, M.S., PharmD

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## 1 INTRODUCTION

This review evaluates the proposed proprietary name, Spiriva Respimat, 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 Applicant did not submit an external name study for this proposed proprietary name.

### 1.1 PRODUCT INFORMATION

The following product information is provided in the April 14, 2014 proprietary name submission.

<b>Table 1. Relevant Product Information for Spiriva Respimat (Tiotropium Bromide) and Spiriva HandiHaler (Tiotropium Bromide)</b>		
<b>Product Name</b>	Spiriva Respimat	Spiriva HandiHaler
<b>Initial Approval Date</b>	N/A	2004
<b>Active Ingredient</b>	Tiotropium Bromide	Tiotropium Bromide
<b>Indication</b>	Long-term once daily maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), and for reducing COPD exacerbations.	Long-term once daily maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), and for reducing COPD exacerbations.
<b>Route of Administration</b>	Oral Inhalation	Oral Inhalation
<b>Dosage Form</b>	Inhalation Spray	Capsules for Oral Inhalation
<b>Strength</b>	2.5 mcg per actuation	18 mcg per capsule
<b>Dose and Frequency</b>	2 inhalations once daily	2 inhalations of the powder contents of one capsule once daily
<b>How Supplied</b>	Carton containing one Spiriva Respimat cartridge and one Spiriva Respimat inhaler	Carton containing Spiriva capsules and the HandiHaler device
<b>Storage</b>	25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F)	25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F)

## **2 RESULTS**

The following sections provide 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 Pulmonary, Allergy, and Rheumatology Products (DPARP) 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***

There is no USAN stem present in the proprietary name<sup>1</sup>.

#### ***2.2.2 Components of the Proposed Proprietary Name***

The proposed proprietary name, Spiriva Respimat, is comprised of two words: the root name 'Spiriva' and the modifier 'Respimat'. The Applicant indicated in their submission that the proposed name, Spiriva Respimat, is derived from its predecessor Spiriva HandiHaler (same active ingredient, same indication, different device) which was approved (NDA 021395) on January 30, 2004. The Respimat (inhalation device) name was derived from its predecessor Combivent Respimat (same device) which was approved (NDA 021747) on October 7, 2011.

This product will be added to the existing "Spiriva" product line. We have evaluated whether or not the proposed name requires the modifier, evaluated the appropriateness of the chosen modifier 'Respimat', and considered if this product should utilize a totally different proprietary name to help distinguish the product presentation from the existing product line. Our evaluation of this issue is discussed in Section 2.2.5

#### ***2.2.3 Comments from Other Review Disciplines at Initial Review***

In response to the OSE, April 28, 2014 e-mail, the Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

#### ***2.2.4 Medication Error Data Selection of Cases***

We searched the FDA Adverse Event Reporting System (FAERS) on April 18, 2014 using the criteria in Table 1, and then individually reviewed each case. We limited our analysis to cases that described errors possibly associated with name confusion. We used

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<sup>1</sup>USAN stem search conducted on April 18, 2014.

the NCC MERP Taxonomy of Medication Errors to code the type and factors contributing to the errors when sufficient information was provided by the reporter.<sup>2</sup>

<b>Table 3: FAERS Search Strategy</b>	
<b>Date Range</b>	<b>May 13, 2011 to April 18, 2014 (Spiriva)</b> <b>May 22, 2012 to April 18, 2014(Combivent Respimat)</b>
<b>Product</b>	<b>Spiriva</b> <b>Combivent Respimat</b>
<b>Event (MedDRA Terms)</b>	<b>Medication Errors [HLGT]</b> <b>Product Packaging Issues [HLT]</b> <b>Product Label Issues [HLT]</b> <b>Product Quality Issues (NEC)[HLT]</b>

The FAERS database search identified 9193 Spiriva cases. After individual review, none of the cases were relevant as they did not involve name confusion with Spiriva.

The FAERS database search identified 6 Combivent Respimat cases. After individual review, none of the cases were relevant as they did not involve name confusion.

#### ***2.2.5 FMEA of the Modifier “Respimat” for this product***

The Applicant proposes to use the modifier ‘Respimat’ to differentiate the proposed Inhalation Spray from the currently marketed, Spiriva HandiHaler formulation.

The differences between the proposed formulation and the current marketed formulation are listed in Table 1 in section 1.1.

Although, there are several similarities between the proposed and marketed Spiriva products, the dosage form and formulation differ and may cause wrong formulation errors or a delay in therapy if the same proprietary name is used. Given the need to distinguish the proprietary nomenclature of these products and the Applicant’s proposal to use the Spiriva name with the addition of a modifier, we considered the following:

- (1) Whether a modifier could adequately distinguish the two products,
- (2) Whether the modifier proposed is appropriate,
- (3) Whether marketing the product under a unique name is appropriate.

#### ***Safety assessment of the modifier***

It is not uncommon for modifiers to be used to denote a specific formulation or packaging configuration (e.g., Advair Diskus and Advair HFA) as part of a product line extension. The applicant states that the modifier ‘Respimat’ denotes the inhalation device and is currently used with the marketed product ‘Combivent Respimat’.

<sup>2</sup> The National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) Taxonomy of Medication Errors. Website <http://www.nccmerp.org/pdf/taxo2001-07-31.pdf>.

Given the applicant's proposal to use a modifier, we evaluated the potential risk of confusion within the Spiriva product line. Our postmarketing surveillance of Spiriva did not identify any name confusion with the existing Spiriva product. We note that by adding a modifier to 'Spiriva', the existing dosage form (capsules for inhalation), are further differentiated from the Inhalation Spray formulation. If a prescription is written for 'Spiriva Respimat', it is unlikely Spiriva Handihaler will be dispensed. Thus, the name offers a distinguishing factor that is not currently seen within the current product line.

In our search of the FAERS database, we did not identify any cases of name confusion reported with the use of this modifier. The Respimat device used with this product is identical to the Respimat device used with Combivent Respimat. Therefore, we believe the modifier Respimat is appropriate for this product as there is precedence for it in the marketplace. Additionally, we do not anticipate any confusion between Combivent Respimat and Spiriva Respimat given the root names are quite different.

However, we also note that omission and oversight of a modifier is cited in literature<sup>2</sup> as a common cause of medication error. Postmarketing experience shows that the introduction of product line extensions result in medication errors if the modifier is omitted and the product characteristics are similar or overlap. We note that in this instance a delay in therapy may occur.

### ***Safety of using a unique name to market this product***

An alternative to using a modifier to distinguish this product from the currently marketed product is to use a totally different root name. However, introducing a total new proprietary name for this product also carries a risk of medication errors. Specifically, marketing the new product under a unique name may lead to additional medication errors such as therapeutic duplication and overdoses. These errors may have greater associated safety risks than the omission or oversight of the modifier. Therefore, for the aforementioned reasons listed DMEPA finds that the proprietary name 'Spiriva Respimat,' although not free from the risk of error, offers a safer approach to naming this product.

### ***2.2.6 Communication of DMEPA's Analysis at Midpoint of Review***

DMEPA communicated our findings to the Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) via e-mail on June 9, 2014. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DPARP on June 16, 2014, they stated no additional concerns with the proposed proprietary name, Spiriva Respimat.

## **3 CONCLUSIONS**

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

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<sup>2</sup> Lesar TS. Prescribing Errors Involving Medication Dosage Forms. *J Gen Intern Med.* 2002; 17(8): 579-587.

If you have further questions or need clarifications, please contact Nichelle Rashid, OSE project manager, at 301-796-3904.

### **3.1 COMMENTS TO THE APPLICANT**

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

If any of the proposed product characteristics as stated in your April 14, 2014 submission are altered, the name must be resubmitted for review.

## 4 REFERENCES

1. *USAN Stems* (<http://www.ama-assn.org/ama/pub/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/approved-stems.page>)

USAN Stems List contains all the recognized USAN stems.

## APPENDICES

### Appendix A

FDA's Proprietary Name Risk Assessment considers the promotional and safety aspects of a proposed proprietary name.

1. **Promotional Assessment:** For prescription drug products, the promotional review of the proposed name is conducted by OPDP. For over-the-counter (OTC) drug products, the promotional review of the proposed name is conducted by DNCE. OPDP or DNCE 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 or DNCE provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment:** The safety assessment is conducted by DMEPA, and includes the following:
  - a. Preliminary Assessment: 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.) See prescreening checklist below in Table 2\*. 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.<sup>3</sup>

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

**\*Table 2- Prescreening Checklist for Proposed Proprietary Name**

	Affirmative answers to these questions indicate a potential area of concern.
Y/N	Does the name have obvious Similarities in Spelling and Pronunciation to other Names?
Y/N	Are there Manufacturing Characteristics in the Proprietary Name?
Y/N	Are there Medical and/or Coined Abbreviations in the Proprietary Name?
Y/N	Are there Inert or Inactive Ingredients referenced in the Proprietary Name?
Y/N	Does the Proprietary Name include combinations of Active Ingredients
Y/N	Is there a United States Adopted Name (USAN) Stem in the Proprietary Name?
Y/N	Is this the same Proprietary Name for Products containing Different Active Ingredients?
Y/N	Is this a Proprietary Name of a discontinued product?

- b. The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support the FDA's postmarket safety surveillance program for drug and therapeutic biologic products. The informatic structure of the FAERS database adheres to the international safety reporting guidance issued by the International Conference on Harmonisation. Adverse events and medication errors are coded to terms in the Medical Dictionary for Regulatory Activities (MedDRA) terminology. Product names are coded using the FAERS Product Dictionary. More information about FAERS can be found at:

<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm>

- c. 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.

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.

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/s/  
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LISSA C OWENS  
06/30/2014

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