

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**22-246**

**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: May 4, 2009

To: Donna Griebel, M.D., Director  
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Through: Denise Toyer, PharmD, Deputy Director  
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Subject: Proprietary Name Review

Drug Name(s): Metozolv ODT (Metoclopramide Orally Disintegrating Tablets)  
5 mg and 10 mg

Application Type/Number: NDA 22-246

Applicant/Applicant: Wilmington Pharmaceuticals

OSE RCM #: 2008-1910

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

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## **EXECUTIVE SUMMARY**

This re-assessment of the proprietary name is written in response to a notification that NDA #22-246 may be approved within 90 days. DMEPA found the proposed proprietary name, Metozolv ODT, acceptable in OSE Review# 2009-1910 dated February 6, 2009 and in OSE Review# 2008-305 dated July 18, 2008. Since that review, none of Metozolv ODT's product characteristics have changed.

During this re-review we identified five new names for their similarity to Metozolv ODT. The results of the Failure Mode Effects Analysis found that the proposed name, Metozolv ODT is not vulnerable to name confusion that could lead to medication errors with any of the five names. Thus, the Division of Medication Error Prevention and Analysis does not object to the use of the proprietary name, Metozolv ODT, for this product.

DMEPA considers this a final review, however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Gastroenterology Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

## **1 BACKGROUND**

### **1.1 INTRODUCTION**

This review was written in response to a request from the Division of Gastroenterology Products, to evaluate the proprietary name for its potential to contribute to medication errors. The proposed name, Metozolv ODT, is evaluated to determine if the name could potentially be confused with other proprietary or established drug names. The proposed proprietary name, Metozolv ODT, was previously reviewed by DMEPA in 2008 (OSE Consult # 2008-305, July 18, 2008) without objection. Additionally, the same review evaluated the modifier 'ODT'. Another review of the proposed name, Metozolv ODT was completed on February 6, 2009 (OSE Review #2009-1910), without objection, however Metozolv ODT received a Complete Response Letter. Therefore, DMEPA is re-reviewing the proposed name again and considers this a final review. DMEPA will not reevaluate the modifier independent of the entire proposed proprietary name because this was conducted during the previous reviews.

### **1.2 PRODUCT INFORMATION**

Metozolv ODT is the proposed name for metoclopramide orally disintegrating tablets. Metozolv ODT is a prokinetic agent indicated for the management of diabetic gastroparesis and gastroesophageal reflux disease.

The dosage for diabetic gastroparesis is 10 mg orally at least 30 minutes before each meal and at bedtime up to 4 times per day. The usual dose for gastroesophageal reflux disease is 10 mg to 15 mg orally up to four times a day at least 30 minutes before each meal and at bedtime. Doses may vary depending upon the symptoms being treated and the clinical response. If symptoms only occur intermittently or at specific times of the day, Metozolv ODT may be used in single doses up to 20 mg prior to the provoking situation rather than continuous treatment.

The maximum dose for Metozolv ODT is 60 mg per day for gastroesophageal reflux disease and 40 mg per day for diabetic gastroparesis. Metozolv ODT will be available as 5 mg and 10 mg orally disintegrating tablets in foil-backed unit dose blister packs of 10 tablets. Each carton will contain 10 blister cards for a total of 100 orally disintegrating tablets per carton. Metozolv ODT should be stored at controlled room temperature.

## 2 METHODS AND MATERIALS

This section describes the methods and materials used by DMEPA staff conducting a proprietary name risk assessment (see 2.1 Proprietary Name Risk Assessment). The primary focus for the assessment is to identify and remedy potential sources of medication error prior to drug approval. 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>1</sup>

### 2.1 PROPRIETARY NAME RISK ASSESSMENT

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, Metozolv ODT, 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 Agency.

For the proprietary name, Metozolv ODT, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Sections 2.1.1 for detail) and held an CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.1.2). DMEPA normally conducts internal CDER prescription analysis studies and, when provided, external prescription analysis studies results are considered and incorporated into the overall risk assessment.

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 (see detail 2.1.2). The overall risk assessment is based on the findings of a Failure Modes and Effects Analysis (FMEA) of the proprietary name, and is focused on the avoidance of medication errors. FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.<sup>2</sup> FMEA is used to analyze whether the drug names identified with look- or sound-alike similarity to the proposed name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of the medication error staff to anticipate the conditions of the clinical setting that the product is likely to be used in 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. As such, DMEPA staff considers the product characteristics associated with the proposed drug throughout the risk assessment, since 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 drug name include, but are not limited to established name of the proposed product, the proposed indication, 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 considers the potential for confusion throughout the

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

<sup>2</sup> Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.<sup>3</sup>

### 2.1.1 Search Criteria

DMEPA staff considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

For this review, particular consideration was given to drug names beginning with the letter 'M' 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.<sup>4,5</sup>

Additionally, since omission of a modifier is cited in the literature as a common cause of medication errors<sup>6</sup>, the DMEPA staff consider 'Metozolv ODT' as a complete name as well as 'Metozolv,' the root term, omitting the modifying term 'ODT'.

To identify drug names that may look similar to Metozolv ODT, the staff also consider the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (11 letters), upstrokes (six; capital letter 'M', lower case letters 't', and 'l', capital letters 'O', 'D' and 'T'), downstrokes (one, lower case 'z'), cross-strokes (two lower case 't', and capital 'T'), and dotted letters (none). Additionally, several letters in Metozolv ODT may be vulnerable to ambiguity when scripted, including the letter 'M' may appear as 'N', 'H', or 'Z'; lower case 'e' may appear as a lower case 'a', 'i', 'l' or 'p'; lower case 't' may appear as lower case 'f', 'r' or 'x'; lower case 'o' may appear as a lower case 'a', 'i', letter combination lower case 'ri' or 'ro'; lower case 'z' appears as a lower case 'm', 'r', or 's'; lower case 'l' appears a lower case 'b', 'e', 'k' or 'p'; lower case 'v' may appear as a lower case 'e', 'i', 'o', 'r', 'u' or letter combination lower case 've'; and upper case 'T' may appear as upper case 'J', 'F' or 'Z'. As such, the staff also considers these alternate appearances when identifying drug names that may look similar to Metozolv ODT.

When searching to identify potential names that may sound similar to Metozolv ODT, DMEPA staff search for names with similar number of syllables in the name (6 syllables), stresses (Met-o-solve Oh-Dee-Tee, met-O-solve Oh-Dee-Tee, or met-o-Solve Oh-Dee-Tee), and placement of vowel and consonant sounds. In addition, several letters in Metozolv ODT may be subject to interpretation when spoken, including the letter 'M' may be interpreted as 'N'; the letter 't' may be interpreted as 'd' or 'n'; the letter 'o' may be interpreted as 'all' or 'a'; the letter 'z' may be interpreted as 'c', 's' or 'x'; the letter 'l' may be interpreted as the letter 'f'; and the letter 'v' may be interpreted as 'f'. We also considered how the inclusion of "ODT" may change the sound of the name. The Applicant's intended pronunciation of the proprietary name could not be expressly taken into consideration, as this was not provided with the proposed name submission.

The staff also considers the product characteristics associated with the proposed drug throughout the identification of similar drug names, since the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting. For this review, DMEPA staff were provided with the following information about the proposed product: the proposed proprietary name (Metozolv ODT), the established name (metoclopramide), proposed indication (diabetic gastroparesis and

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<sup>3</sup> Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

<sup>4</sup> Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at <http://www.ismp.org/Tools/confuseddrugnames.pdf>

<sup>5</sup> Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

<sup>6</sup> Lesar TS. Prescribing Errors Involving Medication Dosage Forms. *J Gen Intern Med.* 2002; 17(8): 579-587.

gastroesophageal reflux disease), strength (5 mg and 10 mg), dose (10 mg to 20 mg), frequency of administration (up to 4 times a day), route (oral) and dosage form of the product (oral disintegrating tablet). Appendix A provides a more detailed listing of the product characteristics that DMEPA staff generally take into consideration.

Lastly, DMEPA staff considers the potential for the proposed 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. As such, these broader safety implications of the name are considered and evaluated throughout this assessment and DMEPA staff provide additional comments related to the safety of the proposed name or product based on their professional experience with medication errors.

#### **2.1.1.1 Database and Information Sources**

The proposed proprietary name, Metozolv ODT, was provided to DMEPA staff to conduct a search 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 Metozolv ODT using the criteria outlined in 2.1.1. A standard description of the databases used in the searches is provided in Section 7. To complement the process, 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, DMEPA staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The findings of the individual Safety Evaluators were then pooled and presented to the Expert Panel.

#### **2.1.1.2 FDA Expert Panel Discussion**

An Expert Panel Discussion is held by DMEPA to gather CDER professional opinions on the safety of the product and the proprietary name, Metozolv ODT. Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed. This group is composed of the Division of Medication Errors Prevention and Analysis staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC).

The pooled results of DMEPA staff were presented 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 Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name..

#### **2.1.2 Safety Evaluator Risk Assessment of the Proposed Proprietary Name**

Based on the criteria set forth in Section 2.1, the Safety Evaluator Risk Assessment applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Modes and Effects Analysis and provide an overall risk 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.<sup>7</sup> When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed name to be confused with another drug name as a result of the name confusion and 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 look- or sound-alike drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

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<sup>7</sup> Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

In order to perform an FMEA of the proposed name, the Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is not yet marketed, the Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Appendix A. 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 evaluation, and studies, and identifies potential failure modes by asking: “Is the name Metozolv ODT 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 Metozolv ODT 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 name possesses similarity that would cause confusion at any point in the medication use system and the name is eliminated from further review.

In the second stage of the Risk Assessment, all potential failure modes are evaluated 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 ultimately not be a source of medication errors in the usual practice setting, the name is eliminated 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 that an alternate proprietary name be used. In rare instances, the FMEA findings may provide other risk-reduction strategies, such as product reformulation to avoid an overlap in strength or an alternate modifier designation may be recommended as a means of reducing the risk of medication errors resulting from drug name confusion.

DMEPA will object to the use of proposed proprietary name when the one or more of the following conditions are identified in the Safety Evaluator’s Risk Assessment:

1. 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 trade name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. 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)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains an USAN stem, particularly in a manner that is contradictory to the USAN Council’s definition.
5. DMEPA staff identify a potential source of medication error within the proposed proprietary name. 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.

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 is awarded approval first has the right to the use the name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

If none of these conditions are met, then DMEPA will not object to the use of the proprietary name. If any of these conditions are met, then DMEPA will object to the use of the proprietary 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 1 through 5 are supported either by FDA Regulation or by external healthcare authorities, including the IOM, WHO, Joint Commission, and ISMP, who have examined medication errors resulting from look- or sound-alike drug names and called for Regulatory Authorities to address the issue prior to approval.

Furthermore, 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, can be identified and remedied prior to approval to avoid patient harm.

Additionally, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to remedy post-approval. Educational efforts and so on are low-leverage strategies that have proven to have limited effectiveness at alleviating the medication errors involving drug name confusion. Higher-leverage strategies, such as drug name changes, have been undertaken 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 the approving the error-prone proprietary name. Moreover, even after Applicant's have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioner's vocabulary, and as such, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval (see limitations of the process).

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the FMEA process is used 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, and so DMEPA may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

### **3 RESULTS**

#### **3.1 PROPRIETARY NAME RISK ASSESSMENT**

##### ***3.1.1 Database and Information Sources***

The search of the internet, several standard published databases and information sources (see Section 7 References) yielded a total of sixteen names as having some similarity to the name Metozolv ODT.

Four of the five names were thought to look like Metozolv ODT. These include Maxitrol, Metamucil, Natacyn and Nafazolin. The remaining name (Mitrazol) was thought to sound like Metozolv ODT.

Additionally, we did not identify any United States Adopted Names (USAN) stems in the name, Metozolv ODT, as of April 24, 2009.

### **3.1.2 Expert Panel Discussion**

The Expert Panel reviewed the pool of names identified by DMEPA staff (see section 3.1.1. above) and did not note any additional names thought to have orthographic or phonetic similarity to Metozolv ODT. DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name.

### **3.1.3 Safety Evaluator Risk Assessment**

Eleven of the names identified for this review were evaluated in DMEPA's previous reviews for the name Metozolv ODT (OSE Reviews # 2008-305 and 2009-1910), and there have been no changes in the product characteristics for Metozolv ODT or any of the names that would change or impact that analysis. All names identified in previous reviews of Metozolv ODT are presented in Appendix B. The remaining five newly identified names were analyzed to determine if the drug names could be confused with Metozolv ODT and if the drug name confusion would likely result in a medication error.

Failure mode and effect analysis was then applied to determine if the potential name, Metozolv ODT, could potentially be confused with any of the five names and lead to medication errors. This analysis determined that the name similarity between Metozolv ODT and the identified names was unlikely to result in medication errors with any of the five products identified for the reasons presented in Appendices C-E.

## **4 DISCUSSION**

### **4.1 PROPRIETARY NAME RISK ASSESSMENT**

Our evaluation identified five new names as having some similarity to the proposed name, Metozolv ODT. However, FMEA findings indicate that the proposed name is not vulnerable to name confusion that could lead to medication errors for the reasons outlined in Appendices C-E.

## **5 CONCLUSIONS AND RECOMMENDATIONS**

The Proprietary Name Risk Assessment findings indicate that the proposed name, Metozolv ODT, is not vulnerable to name confusion that could lead to medication errors. As such, the Division of Medication Error Prevention and Analysis does not object to the use of the proprietary name, Metozolv ODT, for this product. This is considered a final review. However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, the Division of Medication Error Prevention and Analysis rescinds this Risk Assessment finding, and recommends that the name 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. Additionally, if the product approval is delayed beyond 90 day from the date of this review, the proposed name must be resubmitted for evaluation.

### **5.1 COMMENTS TO THE DIVISION**

We would be willing to meet with the Division for further discussion, if needed. Please copy DMEPA on any communication to the Applicant with regard to this review. If you have further questions or need clarifications, please contact Darryl Jenkins, project manager, at 301-796-0558.

## 5.2 COMMENTS TO THE APPLICANT

### 5.2.1 Proprietary Name

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

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

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

## 6 REFERENCES

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

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

2. ***Phonetic and Orthographic Computer Analysis (POCA)***

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. This is a database which was created for the Division of Medication Error Prevention and Analysis, FDA.

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

Drug Facts and Comparisons is a compendium organized by therapeutic course; 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>)

Provides a compilation of approved drug products with therapeutic equivalence evaluations.

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

Provides information regarding patent and trademarks.

9. **Clinical Pharmacology Online** ([www.clinicalpharmacology-ip.com](http://www.clinicalpharmacology-ip.com))

Contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. Provides a keyword search engine.

10. **Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at** ([www.thomson-thomson.com](http://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](http://www.naturaldatabase.com))

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](http://www.statref.com))

Contains full-text information from approximately 30 texts. 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>)

List contains all the recognized USAN stems.

14. **Red Book Pharmacy's Fundamental Reference**

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

15. **Lexi-Comp** ([www.lexi.com](http://www.lexi.com))

A web-based searchable version of the Drug Information Handbook.

16. **Medical Abbreviations Book**

Contains commonly used medical abbreviations and their definitions.

## APPENDICES

### Appendix A:

DMEPA staff considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compare the spelling of the proposed proprietary name with the proprietary and proper name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examines the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly *and* dissimilarly spelled drug name pairs to appear very similar to one another and the similar appearance of drug names when scripted has lead to medication errors. DMEPA staff apply their 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), along with other orthographic attributes that determine the overall appearance of the drug name when scripted (see detail in Table 1 below). Additionally, since verbal communication of medication names is common in clinical settings, DMEPA staff compare the pronunciation of the proposed proprietary name with the pronunciation of other drug names. If provided, DMEPA will consider the Applicant’s intended pronunciation of the proprietary name. However, because the Applicant has little control over how the name will be spoken in practice, DMEPA also considers a variety of pronunciations that could occur in the English language.

**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	<ul style="list-style-type: none"> <li>Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication</li> <li>Names may look similar when scripted and lead to drug name confusion in written communication</li> </ul>
	Orthographic similarity	Similar spelling Length of the name Upstrokes Downstrokes Cross-strokes Dotted letters Ambiguity introduced by	<ul style="list-style-type: none"> <li>Names may look similar when scripted, and lead to drug name confusion in written communication</li> </ul>

		scripting letters Overlapping product characteristics	
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	<ul style="list-style-type: none"> <li>Names may sound similar when pronounced and lead to drug name confusion in verbal communication</li> </ul>

**Appendix B:** All product names identified in the two previous reviews for Metozolv ODT

<b>Product name</b>	<b>Similarity to Metozolv ODT</b>	<b>Product name</b>	<b>Similarity to Metozolv ODT</b>
<b>Metaproterenol</b>	Look	<b>Ketozole</b>	Look and Sound
<b>Methoxsalen</b>	Sound	<b>Metro I.V.</b>	Look and Sound
<b>Medrol</b>	Sound	<b>Metrogel</b>	Look
<b>Metolazone</b>	Look and Sound	<b>Metopirone</b>	Look
<b>Methimazole</b>	Look	<b>Vitafol</b>	Look
<b>Nebivolol</b>	Look	<b>Ultracet</b>	Look
<b>Tovalt ODT</b>	Look and Sound	<b>Metaxalone</b>	Look and Sound
<b>Metaglip</b>	Look	<b>Midazolam</b>	Look and Sound
<b>Methazolamide</b>	Sound	<b>Metoprolol</b>	Look and Sound
<b>Mebendazole</b>	Look	<b>Mintezol</b>	Look and Sound
<b>Metoprolol HCT</b>	Look and Sound	<b>Metronidazole</b>	Look and Sound
<b>Metadol</b>	Look and Sound	<b>Nefazodone</b>	Look
<b>Metoz</b>	Look	<b>Hetrazan</b>	Look
<b>Metozol</b>	Look and Sound	<b>Neptazane</b>	Look
<b>Miconazole</b>	Look	<b>Methadose</b>	Look
<b>Metaprel</b>	Look	<b>Metozok</b>	Look
<b>Metozoc</b>	Look	<b>Mezolor</b>	Look
<b>Metocyl</b>	Look and Sound		

**Appendix C:** Products that lack orthographic and phonetic similarity to Metozolv ODT

Product name with potential for confusion	Similarity to Metozolv ODT
Metamucil	Look

**Appendix D:** Products marketed in foreign countries

Proprietary Name	Similarity to Metozolv ODT
Nafazolin (naphazoline ophthalmic drops in Slovenia)	Look

**Appendix E:** Products with no overlap in strength, dose, and route of administration

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Metozolv ODT (metoclopramide) orally disintegrating tablets	N/A	5 mg and 10 mg	5-10 mg orally up to 5 times a day for GERD 10 mg orally at least 30 minutes before each meal at at bedtime for diabetic gastroparesis
Maxitrol  (neomycin, polymyxin B, and dexamethasone)	Look	Ophthalmic ointment: Dexamethasone 0.1%, Neomycin SO <sub>4</sub> 0.35%, Polymyxin B SO <sub>4</sub> 10,000U/1g, Ophthalmic ointment  Ophthalmic suspension: Dexamethasone 0.1%, Neomycin Sulfate 0.35%,	Ointment: Place a small amount (~1/2") in the affected eye 3-4 times/day or apply at bedtime as an adjunct with drops  Suspension: Instill 1-2 drops into affected eye(s) every 3-4 hours; in severe disease, drops may be used hourly and tapered to discontinuation

		Polymyxin B Sulfate 10000U/1mL	
Natacyn (natamycin)	Look	Ophthalmic suspension: 5 % (15 mL)	Fungal keratitis: Ophthalmic: Instill 1 drop in conjunctival sac every 1-2 hours, after 3-4 days reduce to one drop 6-8 times/day; usual course of therapy is 2-3 weeks or until resolution of active fungal keratitis (may be useful to gradually reduce dosage at 4-7 day intervals to assure elimination of organism)  Fungal blepharitis or conjunctivitis: Ophthalmic: Instill 1 drop in conjunctival sac every 4-6 hours
Mitrazol (miconazole nitrate)	Sound	Topical powder: 2%	Apply powder to the cleansed, dry, infected area twice daily

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Laura Pincock  
5/4/2009 10:19:33 AM  
DRUG SAFETY OFFICE REVIEWER

Denise Toyer  
5/4/2009 12:40:11 PM  
DRUG SAFETY OFFICE REVIEWER



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

Date: February 6, 2009

To: Donna Griebel, M.D., Director  
Division of Gastroenterology Products

Through: Kellie Taylor, PharmD, MPH, Team Leader  
Denise Toyer, PharmD, Deputy Director  
Carol Holquist, RPh, Director  
Division of Medication Error Prevention and Analysis, HFD-420

From: Laura Pincock, RPh, PharmD, Safety Evaluator  
Division of Medication Error Prevention and Analysis, HFD-420

Subject: Proprietary Name Review

Drug Name(s): Metozolv ODT (Metoclopramide Orally Disintegrating Tablets)  
5 mg and 10 mg

Application Type/Number: NDA 22-246

Applicant/Applicant: Wilmington Pharmaceuticals

OSE RCM #: 2008-1910

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

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## **EXECUTIVE SUMMARY**

The results of the Proprietary Name Risk Assessment found that the proposed name, Metozolv ODT, is not vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention and Analysis does not object to the use of the proprietary name, Metozolv ODT, for this product. This is considered a final review, however, if approval is delayed beyond 90 days from the date of this review, the proprietary name should be resubmitted for re-review.

## **1 BACKGROUND**

### **1.1 INTRODUCTION**

This review was written in response to a request from the Division of Gastroenterology Products, to evaluate the proprietary name for its potential to contribute to medication errors. The proposed name, Metozolv ODT, is evaluated to determine if the name could potentially be confused with other proprietary or established drug names. The proposed proprietary name, Metozolv ODT, was previously reviewed by DMEPA in 2008 (OSE Consult # 2008-305) without objection. Additionally, the same review evaluated the modifier 'ODT'. As such, DMEPA will not reevaluate the modifier independent of the entire proposed proprietary name in this evaluation of the proposed name. Container labels and carton labeling were also provided to be evaluated from a medications errors perspective. Review comments on the labels and labeling will be provided under separate cover in a forthcoming review (OSE Review # 2008-1946).

### **1.2 PRODUCT INFORMATION**

Metozolv ODT is the proposed name for metoclopramide orally disintegrating tablets. Metozolv ODT is a prokinetic agent indicated for the management of diabetic gastroparesis and gastroesophageal reflux disease.

The dosage for diabetic gastroparesis is 10 mg orally at least 30 minutes before each meal and at bedtime up to 4 times per day. The usual dose for gastroesophageal reflux disease is 10 mg to 15 mg orally up to four times a day at least 30 minutes before each meal and at bedtime. Doses may vary depending upon the symptoms being treated and the clinical response. If symptoms only occur intermittently or at specific times of the day, Metozolv ODT may be used in single doses up to 20 mg prior to the provoking situation rather than continuous treatment.

The maximum dose for Metozolv ODT is 60 mg per day for gastroesophageal reflux disease and 40 mg per day for diabetic gastroparesis. Metozolv ODT will be available as 5 mg and 10 mg orally disintegrating tablets in foil-backed unit dose blister packs of 10 tablets. Each carton will contain 10 blister cards for a total of 100 orally disintegrating tablets per carton. Metozolv ODT should be stored at controlled room temperature.

## **2 METHODS AND MATERIALS**

This section describes the methods and materials used by DMEPA staff conducting a proprietary name risk assessment (see 2.1 Proprietary Name Risk Assessment). The primary focus for the assessment is to identify and remedy potential sources of medication error prior to drug approval. 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>1</sup>

## 2.1 PROPRIETARY NAME RISK ASSESSMENT

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, Metozolv ODT, 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 Agency.

For the proprietary name, Metozolv ODT, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Sections 2.1.1 for detail) and held an CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.1.2). DMEPA normally conducts internal CDER prescription analysis studies and, when provided, external prescription analysis studies results are considered and incorporated into the overall risk assessment.

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 (see detail 2.1.2). The overall risk assessment is based on the findings of a Failure Modes and Effects Analysis (FMEA) of the proprietary name, and is focused on the avoidance of medication errors. FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.<sup>2</sup> FMEA is used to analyze whether the drug names identified with look- or sound-alike similarity to the proposed name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of the medication error staff to anticipate the conditions of the clinical setting that the product is likely to be used in 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. As such, DMEPA staff consider the product characteristics associated with the proposed drug throughout the risk assessment, since 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 drug name include, but are not limited to established name of the proposed product, the proposed indication, 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 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.<sup>3</sup>

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

<sup>2</sup> Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

<sup>3</sup> Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

### 2.1.1 Search Criteria

DMEPA staff considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

For this review, particular consideration was given to drug names beginning with the letter 'M' 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.<sup>4,5</sup> Additionally, since omission of a modifier is cited in the literature as a common cause of medication errors<sup>6</sup>, the DMEPA staff consider 'Metozolv ODT' as a complete name as well as 'Metozolv,' the root term, omitting the modifying term 'ODT'.

To identify drug names that may look similar to Metozolv ODT, the staff also consider the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (11 letters), upstrokes (six; capital letter 'M', lower case letters 't', and 'l', capital letters 'O', 'D' and 'T'), downstrokes (one, lower case 'z'), cross-strokes (two lower case 't', and capital 'T'), and dotted letters (none). Additionally, several letters in Metozolv ODT may be vulnerable to ambiguity when scripted, including the letter 'M' may appear as 'N', 'H', or 'Z'; lower case 'e' may appear as a lower case 'a', 'i', 'l' or 'p'; lower case 't' may appear as lower case 'f', 'r' or 'x'; lower case 'o' may appear as a lower case 'a', 'i', letter combination lower case 'ri' or 'ro'; lower case 'z' appears as a lower case 'm', 'r', or 's'; lower case l appears a lower case 'b', 'e', 'k' or 'p'; lower case 'v' may appear as a lower case 'e', 'i', 'o', 'r', 'u' or letter combination lower case 've'; and upper case 'T' may appear as upper case 'J', 'F' or 'Z'. As such, the staff also considers these alternate appearances when identifying drug names that may look similar to Metozolv ODT.

When searching to identify potential names that may sound similar to Metozolv ODT, DMEPA staff search for names with similar number of syllables in the name (6 syllables), stresses (Met-o-solve Oh-Dee-Tee, met-O-solve Oh-Dee-Tee, or met-o-Solve Oh-Dee-Tee), and placement of vowel and consonant sounds. In addition, several letters in Metozolv ODT may be subject to interpretation when spoken, including the letter 'M' may be interpreted as 'N'; the letter 't' may be interpreted as 'd' or 'n'; the letter 'o' may be interpreted as 'all' or 'a'; the letter 'z' may be interpreted as 'c', 's' or 'x'; the letter 'l' may be interpreted as the letter 'f'; and the letter 'v' may be interpreted as 'f'. We also considered how the inclusion of "ODT" may change the sound of the name. The Applicant's intended pronunciation of the proprietary name could not be expressly taken into consideration, as this was not provided with the proposed name submission.

The staff also consider the product characteristics associated with the proposed drug throughout the identification of similar drug names, since the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting. For this review, DMEPA staff were provided with the following information about the proposed product: the proposed proprietary name (Metozolv ODT), the established name (metoclopramide), proposed indication (diabetic gastroparesis and gastroesophageal reflux disease), strength (5 mg and 10 mg), dose (10 mg to 20 mg), frequency of administration (up to 4 times a day), route (oral) and dosage form of the product (oral disintegrating tablet). Appendix A provides a more detailed listing of the product characteristics that DMEPA staff generally take into consideration.

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<sup>4</sup> Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at <http://www.ismp.org/Tools/confuseddrugnames.pdf>

<sup>5</sup> Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. *Artificial Intelligence in Medicine* (2005)

<sup>6</sup> Lesar TS. Prescribing Errors Involving Medication Dosage Forms. *J Gen Intern Med.* 2002; 17(8): 579-587.

Lastly, DMEPA staff considers the potential for the proposed 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. As such, these broader safety implications of the name are considered and evaluated throughout this assessment and DMEPA staff provide additional comments related to the safety of the proposed name or product based on their professional experience with medication errors.

#### **2.1.1.1 Database and Information Sources**

The proposed proprietary name, Metozolv ODT, was provided to DMEPA staff to conduct a search 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 Metozolv ODT using the criteria outlined in 2.1.1. A standard description of the databases used in the searches is provided in Section 7. To complement the process, 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, DMEPA staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The findings of the individual Safety Evaluators were then pooled and presented to the Expert Panel.

#### **2.1.1.2 FDA Expert Panel Discussion**

An Expert Panel Discussion is held by DMEPA to gather CDER professional opinions on the safety of the product and the proprietary name, Metozolv ODT. Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed. This group is composed of the Division of Medication Errors Prevention and Analysis staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC).

The pooled results of DMEPA staff were presented 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 Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name..

#### **2.1.2 Safety Evaluator Risk Assessment of the Proposed Proprietary Name**

Based on the criteria set forth in Section 2.1, the Safety Evaluator Risk Assessment applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Modes and Effects Analysis and provide an overall risk 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.<sup>7</sup> When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed name to be confused with another drug name as a result of the name confusion and 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 look- or sound-alike 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 Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is not yet marketed, the Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical

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<sup>7</sup> Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

and product characteristics listed in Appendix A. 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 evaluation, and studies, and identifies potential failure modes by asking: “Is the name Metozolv ODT 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 Metozolv ODT to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names possess similarity that would cause confusion at any point in the medication use system and the name is eliminated from further review.

In the second stage of the Risk Assessment, all potential failure modes are evaluated 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 ultimately not be a source of medication errors in the usual practice setting, the name is eliminated 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 that an alternate proprietary name be used. In rare instances, the FMEA findings may provide other risk-reduction strategies, such as product reformulation to avoid an overlap in strength or an alternate modifier designation may be recommended as a means of reducing the risk of medication errors resulting from drug name confusion.

DMEPA will object to the use of proposed proprietary name when the one or more of the following conditions are identified in the Safety Evaluator’s Risk Assessment:

1. 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 trade name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. 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)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains an USAN stem, particularly in a manner that is contradictory to the USAN Council’s definition.
5. DMEPA staff identify a potential source of medication error within the proposed proprietary name. 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.

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 is awarded approval first has the

right to the use the name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

If none of these conditions are met, then DMEPA will not object to the use of the proprietary name. If any of these conditions are met, then DMEPA will object to the use of the proprietary 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 1 through 5 are supported either by FDA Regulation or by external healthcare authorities, including the IOM, WHO, Joint Commission, and ISMP, who have examined medication errors resulting from look- or sound-alike drug names and called for Regulatory Authorities to address the issue prior to approval.

Furthermore, 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, can be identified and remedied prior to approval to avoid patient harm.

Additionally, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to remedy post-approval. Educational efforts and so on are low-leverage strategies that have proven to have limited effectiveness at alleviating the medication errors involving drug name confusion. Higher-leverage strategies, such as drug name changes, have been undertaken 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 the approving the error-prone proprietary name. Moreover, even after Applicant's have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioner's vocabulary, and as such, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval (see limitations of the process).

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the FMEA process is used 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, and so DMEPA may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

### **3 RESULTS**

#### **3.1 PROPRIETARY NAME RISK ASSESSMENT**

##### ***3.1.1 Database and Information Sources***

The search of the internet, several standard published databases and information sources (see Section 7 References) yielded a total of seventeen names as having some similarity to the name Metozolv ODT.

Fifteen of the seventeen names were thought to look like Metozolv ODT. These include Metoprolol, Metolazone, Metrogel, Metaprel, Metronidazole, Methadose, Metaproterenol, Methimazole, Metozok, Methazolamide, Midazolam, Mezolor, Metazoc, Metaglip, and Mintezol. One of the seventeen names (Medrol) was thought to sound like Metozolv ODT. The one remaining name, Metozyl, was thought to look and sound similar to Metozolv ODT.

Additionally, we did not identify any United States Adopted Names (USAN) stems in the name, Metozolv ODT, as of January 17, 2009.

### ***3.1.2 Expert Panel Discussion***

The Expert Panel reviewed the pool of names identified by DMEPA staff (see section 3.1.1. above) and did not note any additional names thought to have orthographic or phonetic similarity to Metozolv ODT. DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name.

### ***3.1.3 Safety Evaluator Risk Assessment***

Eleven of the names identified for this review were evaluated in DMEPA's previous review for the name Metozolv ODT (OSE Review # 2008-305), and there have been no changes in the product characteristics for Metozolv ODT or any of the names that would change or impact that analysis. The remaining six newly identified names were analyzed to determine if the drug names could be confused with Metozolv ODT and if the drug name confusion would likely result in a medication error.

Failure mode and effect analysis was then applied to determine if the potential name, Metozolv ODT, could potentially be confused with any of the six names and lead to medication errors. This analysis determined that the name similarity between Metozolv ODT and the identified names was unlikely to result in medication errors with any of the six products identified for the reasons presented in Appendices C-D.

## **4 DISCUSSION**

### **4.1 PROPRIETARY NAME RISK ASSESSMENT**

Our evaluation identified six names has having some similarity to the proposed name, Metozolv ODT, However, FMEA findings indicate that the proposed name is not vulnerable to name confusion that could lead to medication errors for the reasons outlined in Appendices C-D.

## **5 CONCLUSIONS AND RECOMMENDATIONS**

The Proprietary Name Risk Assessment findings indicate that the proposed name, Metozolv ODT, is not vulnerable to name confusion that could lead to medication errors. As such, the Division of Medication Error Prevention and Analysis does not object to the use of the proprietary name, Metozolv ODT, for this product. This is considered a final review. However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, the Division of Medication Error Prevention and Analysis rescinds this Risk Assessment finding, and recommends that the name 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. Additionally, if the product approval is delayed beyond 90 day from the date of this review, the proposed name must be resubmitted for evaluation.

### **5.1 COMMENTS TO THE DIVISION**

We would appreciate feedback on the final outcome of this review. We would be willing to meet with the Division for further discussion, if needed. Please copy DMEPA on any communication to the Applicant with regard to this review. If you have further questions or need clarifications, please contact Cheryle Milburn, project manager, at 301-796-2084.

## 5.2 COMMENTS TO THE APPLICANT

### 5.2.1 Proprietary Name

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

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

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

## 6 REFERENCES

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

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

2. ***Phonetic and Orthographic Computer Analysis (POCA)***

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. This is a database which was created for the Division of Medication Error Prevention and Analysis, FDA.

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

Drug Facts and Comparisons is a compendium organized by therapeutic course; 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>)

Provides a compilation of approved drug products with therapeutic equivalence evaluations.

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

Provides information regarding patent and trademarks.

**9. Clinical Pharmacology Online ([www.clinicalpharmacology-ip.com](http://www.clinicalpharmacology-ip.com))**

Contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. Provides a keyword search engine.

**10. Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at ([www.thomson-thomson.com](http://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](http://www.naturaldatabase.com))**

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](http://www.statref.com))**

Contains full-text information from approximately 30 texts. 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>)**

List contains all the recognized USAN stems.

**14. Red Book Pharmacy's Fundamental Reference**

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

**15. Lexi-Comp ([www.lexi.com](http://www.lexi.com))**

A web-based searchable version of the Drug Information Handbook.

**16. Medical Abbreviations Book**

Contains commonly used medical abbreviations and their definitions.

**APPENDICES**

**Appendix A:**

DMEPA staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compare the spelling of the proposed proprietary name with the proprietary and proper name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examine 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* dissimilarly spelled drug name pairs to appear very similar to one another and the similar appearance of drug names when scripted has lead to medication errors. DMEPA staff apply their 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), along with other orthographic attributes that determine the overall appearance of the drug name when scripted (see detail in Table 1 below). Additionally, since verbal communication of medication names is common in clinical settings, DMEPA staff compare the pronunciation of the proposed proprietary name with the pronunciation of other drug names. If provided, DMEPA will consider the Applicant’s intended pronunciation of the proprietary name. However, because the Applicant has little control over how the name will be spoken in practice, DMEPA also considers a variety of pronunciations that could occur in the English language.

**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	<ul style="list-style-type: none"> <li>Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication</li> <li>Names may look similar when scripted and lead to drug name confusion in written communication</li> </ul>
	Orthographic similarity	Similar spelling Length of the name Upstrokes Downstrokes Cross-strokes Dotted letters Ambiguity introduced by	<ul style="list-style-type: none"> <li>Names may look similar when scripted, and lead to drug name confusion in written communication</li> </ul>

		scripting letters Overlapping product characteristics	
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	<ul style="list-style-type: none"> <li>Names may sound similar when pronounced and lead to drug name confusion in verbal communication</li> </ul>

**Appendix B:** All product names identified in the previous review for Metozolv ODT

<b>Product name</b>	<b>Similarity to Metozolv ODT</b>	<b>Product name</b>	<b>Similarity to Metozolv ODT</b>
<b>Metaproterenol</b>	Look	<b>Ketozole</b>	Look and Sound
<b>Methoxsalen</b>	Sound	<b>Metro I.V.</b>	Look and Sound
<b>Medrol</b>	Sound	<b>Metrogel</b>	Look
<b>Metolazone</b>	Look and Sound	<b>Metopirone</b>	Look
<b>Methimazole</b>	Look	<b>Vitafof</b>	Look
<b>Nebivolol</b>	Look	<b>Ultracet</b>	Look
<b>Tovalt ODT</b>	Look and Sound	<b>Metaxalone</b>	Look and Sound
<b>Metaglip</b>	Look	<b>Midazolam</b>	Look and Sound
<b>Methazolamide</b>	Sound	<b>Metoprolol</b>	Look and Sound
<b>Mebendazole</b>	Look	<b>Mintezol</b>	Look and Sound
<b>Metoprolol HCT</b>	Look and Sound	<b>Metronidazole</b>	Look and Sound
<b>Metadol</b>	Look and Sound	<b>Nefazodone</b>	Look
<b>Metoz</b>	Look	<b>Hetrazan</b>	Look
<b>Metozol</b>	Look and Sound	<b>Neptazane</b>	Look
<b>Miconazole</b>	Look		

**Appendix C:** Products that lack orthographic and phonetic similarity to Metozolv ODT

<b>Product name with potential for confusion</b>	<b>Similarity to Metozolv ODT</b>
Methadose (methadone)	Look
Metaprel (metaproterenol syrup), also no longer marketed	Look

**Appendix D:** Products marketed in foreign countries

<b>Proprietary Name</b>	<b>Similarity to Metozolv ODT</b>
Metozok (metoprolol marketed in Estonia)	Look
Metozoc (metoprolol marketed in Finland, Norway, Denmark)	Look
Mezolor (unknown pharmaceutical registered in Mexico)	Look
Metocyl (metoclopramide marketed in unknown foreign country)	Look and Sound

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

Date: July 9, 2008

To: Donna Griebel, MD  
Director, Division of Gastroenterology Products

Through: Todd Bridges, RPh, Team Leader  
Denise Toyer, PharmD, Deputy Director  
Carol Holquist, RPh, Director  
Division of Medication Error Prevention

From: Zachary Oleszczuk, PharmD, Safety Evaluator  
Division of Medication Error Prevention

Subject: Proprietary Name Review

Drug Name(s): Metozolv ODT (Metoclopramide Orally Disintegrating Tablets)

Application Type/Number: NDA 22-246 (IND 70,578)

Applicant: Wilmington Pharmaceuticals

OSE RCM #: 2008-305

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## **EXECUTIVE SUMMARY**

The results of the Proprietary Name Risk Assessment found that the proposed name, Metozolv ODT has some similarity to other proprietary and established drug names, but the findings of the FMEA indicates that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors in the United States of America. Thus, the Division of Medication Error Prevention has no objection to the use of the proprietary name, Metozolv ODT for this product.

If any of the proposed product characteristics as stated in this review are altered prior to approval of the product, the Division of Medication Error Prevention rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review. Furthermore, this name must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approval of other proprietary or established names from the signature date of this document.

## **1 BACKGROUND**

### **1.1 INTRODUCTION**

This consult was written in response to a request from the Division of Gastroenterology Products (DGP) to evaluate the product for its potential to contribute to medication errors. The proposed name, Metozolv ODT, is evaluated to determine if the name could potentially be confused with other proprietary or established drug names.

### **1.2 PRODUCT INFORMATION**

Metozolv ODT is the proposed name for metoclopramide orally disintegrating tablets. Metozolv ODT is a prokinetic agent indicated for the management of diabetic gastroparesis and gastroesophageal reflux disease.

The dosage for diabetic gastroparesis is 10 mg by mouth at least 30 minutes before each meal and at bedtime up to 4 times per day. The usual dose for gastroesophageal reflux disease is 10 mg to 15 mg by mouth up to four times a day at least 30 minutes before each meal and at bedtime. Doses may vary depending upon the symptoms being treated and the clinical response. If symptoms only occur intermittently or at specific times of the day, Metozolv ODT may be used in single doses up to 20 mg prior to the provoking situation rather than continuous treatment.

The maximum dose for Metozolv ODT is 60 mg per day for gastroesophageal reflux disease and 40 mg per day for diabetic gastroparesis. Metozolv ODT will be available as 5 mg and 10 mg orally disintegrating tablets in foil-backed unit dose blister packs of 10 tablets. Each carton will contain 10 blister cards for a total of 100 orally disintegrating tablets per carton.

## 2 METHODS AND MATERIALS

This section consists of three sections which describe the methods and materials used by the Division of Medication Error Prevention staff conducting a proprietary name risk assessment (see 2.1 Proprietary Name Risk Assessment) and a medication error risk assessment (see 2.2 Medication Error Risk Assessment). The primary focus for all of the assessments is to identify and remedy potential sources of medication error prior to drug approval. Our Division 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>1</sup>

### 2.1 PROPRIETARY NAME RISK ASSESSMENT

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, Metozolv ODT, and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, and ANDA products currently under review by the Agency. Additionally, the modifier, 'ODT', was assessed for resemblance to any numbers, dosing instructions, or medical abbreviations. Furthermore, the Division of Medication Error Prevention evaluated the appropriateness of the proposed modifier, considered the potential for modifier's omission or interpretation, and verified that the modifier does not appear on the error-prone abbreviation list maintained by the Institute of Safe Medication Practices (ISMP).

For the proprietary name, Metozolv ODT, the Medication Error Staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see section 2.1.1 for detail) and held a CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see section 2.1.3). Additionally, we conducted a search of the Adverse Event Reporting System (AERS) database to search for any additional names that may potentially be confused with the proposed proprietary name (see section 2.2). The Division of Medication Error Prevention also conducts internal CDER prescription analysis studies (see 2.1.2), and, when provided, external prescription analysis studies results are considered and incorporated into the overall risk assessment.

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 (see detail 2.4). The overall risk assessment is based on the findings of a Failure Modes and Effects Analysis (FMEA) of the proprietary name, and is focused on the avoidance of medication errors. FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.<sup>2</sup> FMEA is used to analyze whether the drug names identified with look- or sound-alike similarity to the proposed name could cause confusion that subsequently leads to medication errors in the clinical setting. The Division of Medication Error Prevention 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> Our Division uses the clinical expertise of the Medication Error Staff to anticipate the conditions of the clinical setting that the product is likely to be used in based on the characteristics of the proposed product.

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

<sup>2</sup> Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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

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. As such, the Staff consider the product characteristics associated with the proposed drug throughout the risk assessment, since 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 drug name include, but are not limited to established name of the proposed product, the proposed indication, 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, we consider 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.<sup>4</sup>

### **2.1.1 Search Criteria**

The Medication Error Staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

For this review, particular consideration was given to drug names beginning with the letter ‘M’ 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.<sup>5,6</sup> Additionally, since omission of a modifier is cited in the literature as a common cause of medication errors<sup>7</sup>, the Medication Error Prevention Staff consider ‘Metozolv ODT’ as a complete name as well as ‘Metozolv,’ the root term, omitting the modifying term ‘ODT’.

To identify drug names that may look similar to Metozolv ODT, the Staff also consider the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (11 letters), upstrokes (six; capital letter ‘M’, lower case letters ‘t’, and ‘l’, capital letters ‘O’, ‘D’ and ‘T’), downstrokes (one, lower case ‘z’), cross-strokes (two lower case ‘t’, and capital ‘T’), and dotted letters (none). Additionally, several letters in Metozolv ODT may be vulnerable to ambiguity when scripted, including the letter ‘M’ may appear as ‘N’, ‘H’, or ‘Z’; lower case ‘e’ may appear as a lower case ‘a’, ‘i’, ‘l’ or ‘p’; lower case ‘t’ may appear as lower case ‘f’, ‘r’ or ‘x’; lower case ‘o’ may appear as a lower case ‘a’, ‘i’, letter combination lower case ‘ri’ or ‘ro’; lower case ‘z’ appears as a lower case ‘m’, ‘r’, or ‘s’; lower case l appears a lower case ‘b’, ‘e’, ‘k’ or ‘p’; lower case ‘v’ may appear as a lower case ‘e’, ‘i’, ‘o’, ‘r’, ‘u’ or letter combination lower case ‘ve’; and upper case ‘T’ may appear as upper case ‘J’, ‘F’ or ‘Z’. As such, the Staff also considers these alternate appearances when identifying drug names that may look similar to Metozolv ODT.

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<sup>4</sup> Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

<sup>5</sup> Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at <http://www.ismp.org/Tools/confuseddrugnames.pdf>

<sup>6</sup> Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

<sup>7</sup> Lesar TS. Prescribing Errors Involving Medication Dosage Forms. *J Gen Intern Med.* 2002; 17(8): 579-587.

When searching to identify potential names that may sound similar to Metozolv ODT, the Medication Error Staff search for names with similar number of syllables in the name (6 syllables), stresses (Met-o-solve Oh-Dee-Tee, met-O-solve Oh-Dee-Tee, or met-o-Solve Oh-Dee-Tee), and placement of vowel and consonant sounds. In addition, several letters in Metozolv ODT may be subject to interpretation when spoken, including the letter 'M' may be interpreted as 'N'; the letter 't' may be interpreted as 'd' or 'n'; the letter 'o' may be interpreted as 'all' or 'a'; the letter 'z' may be interpreted as 'c', 's' or 'x'; the letter 'l' may be interpreted as the letter 'f'; and the letter 'v' may be interpreted as 'f'. We also considered how the inclusion of "ODT" may change the sound of the name. The Applicant's intended pronunciation of the proprietary name could not be expressly taken into consideration, as this was not provided with the proposed name submission.

The Staff also consider the product characteristics associated with the proposed drug throughout the identification of similar drug names, since the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting. For this review, the Medication Error Staff were provided with the following information about the proposed product: the proposed proprietary name (Metozolv ODT), the established name (metoclopramide), proposed indication (Diabetic Gastroparesis and Gastroesophageal reflux disease), strength (5 mg and 10 mg), dose (10 mg to 20 mg), frequency of administration (up to 4 times a day), route (oral) and dosage form of the product (oral disintegrating tablet). Appendix A provides a more detailed listing of the product characteristics the Medication Error Staff general take into consideration.

Lastly, the Medication Error Staff also consider the potential for the proposed name to inadvertently function as a source of error for reasons other than name confusion. Postmarketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. As such, these broader safety implications of the name are considered and evaluated throughout this assessment and the Medication Error Staff provide additional comments related to the safety of the proposed name or product based on their professional experience with medication errors.

### ***2.1.2 CDER 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 Metozolv ODT 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 a total of 123 healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The results are used by the Safety Evaluator to identify any orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of Metozolv ODT 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 prescriptions are optically scanned and one prescription is delivered to a random sample of 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 the medication error staff.

**Figure 1. Metozolv ODT Study (conducted on March 25, 2008)**

HANDWRITTEN PRESCRIPTION AND MEDICATION ORDER	VERBAL PRESCRIPTION
<p><u>Outpatient Prescription:</u></p> <p>Metozolv ODT 10mg # 120 TI tabs po qid</p>	<p>Metozolv ODT 10 mg Take two tablets by mouth qid</p>
<p><u>Inpatient Medication Order:</u></p> <p><del>1 Metozolv ODT 10mg</del> <del>2 tabs po qid</del></p>	

**2.1.3 Database and information sources**

The proposed proprietary name, Metozolv ODT, was provided to the Medication Error Staff of the Division of Medication Error Prevention to conduct a search 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 Metozolv ODT using the criteria outlined in 2.1.1. Additionally, the modifier ‘ODT’ was assessed for resemblance to any numbers, dosing instructions, or medical abbreviations. A standard description of the databases used in the searches is provided in Section 6.2. To complement the process, the Medication Error 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 Medication Error Staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The findings of the individual Safety Evaluators were then pooled and presented to the Expert Panel.

**2.1.4 CDER Expert Panel Discussion**

An Expert Panel Discussion is held by the Division of Medication Error Prevention to gather CDER professional opinions on the safety of the product and the proprietary name, Metozolv ODT. Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed. This group is composed of Medication Error Prevention Staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC).

The pooled results of the medication error staff were presented 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 Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

### **2.1.5 Medication Error Risk Assessment**

The active ingredient for Metozolv ODT, metoclopramide, has been marketed since 1980. Because metoclopramide is already out on the market, the Division of Medication Error Prevention conducted a search of the Adverse Event Reporting System (AERS) database to determine if there are any medication errors associated with name confusion which may be indicative of potential name confusion with Metozolv ODT. The Division of Medication Error Prevention performed an updated AERS search for medication errors involving metoclopramide or Reglan (metoclopramide), the reference listed drug.

The MedRA High Level Group Term (HLGT) “Medication Errors” and Preferred Term (PT) “Pharmaceutical product complaint” were used as search criteria for Reactions. The search criteria used for Products were active ingredients “Metocl%”, trade names “Metocl%” and “Regla%” and verbatim substance search “metoc%”.

The cases were manually reviewed to determine if a medication error occurred. Those cases that did not describe a medication error were excluded from further analysis. The cases that did describe a medication error were categorized by type of error. Our Division reviewed the cases within each category to identify factors that contributed to the medication errors, and to ascertain if these risks might apply to the proposed Metozolv ODT.

### **2.1.6 Safety Evaluator Risk Assessment of the Proposed Proprietary Name**

Based on the criteria set forth in Section 2.1.1, the Safety Evaluator Risk Assessment applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Modes and Effects Analysis and provide an overall risk 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.<sup>8</sup> When applying FMEA to assess the risk of a proposed proprietary name, the Division of Medication Error Prevention seeks to evaluate the potential for a proposed name to be confused with another drug name as a result of the name confusion and 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 look- or sound-alike 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 Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is not yet marketed, the Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Appendix A. 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.

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<sup>8</sup> Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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 evaluation, and studies, and identifies potential failure modes by asking: “Is the name Metozolv ODT 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 Metozolv ODT to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names possess similarity that would cause confusion at any point in the medication use system and the name is eliminated from further review.

In the second stage of the Risk Assessment, all potential failure modes are evaluated 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 ultimately not be a source of medication errors in the usual practice setting, the name is eliminated 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 that an alternate proprietary name be used. In rare instances, the FMEA findings may provide other risk-reduction strategies, such as product reformulation to avoid an overlap in strength or an alternate modifier designation may be recommended as a means of reducing the risk of medication errors resulting from drug name confusion.

The Division of Medication Error Prevention will object to the use of proposed proprietary name when the one or more of the following conditions are identified in the Safety Evaluator’s Risk Assessment:

1. 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 trade name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. The Division of Medication Error Prevention 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)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains an USAN stem, particularly in a manner that is contradictory to the USAN Council’s definition.
5. Medication Error Staff identify a potential source of medication error within the proposed proprietary name. 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.

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

If none of these conditions are met, then we will not object to the use of the proprietary name. If any of these conditions are met, then we will object to the use of the proprietary 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 1 through 5 are supported either by FDA Regulation or by external healthcare authorities, including the Institute of Medicine, World Health Organization, Joint Commission, and Institute for Safe Medication Practices, have examined medication errors resulting from look- or sound-alike drug names and called for Regulatory Authorities to address the issue prior to approval.

Furthermore, we contend 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, can be identified and remedied prior to approval to avoid patient harm.

Additionally, postmarketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to remedy post-approval. Educational efforts and so on are low-leverage strategies that have proven to have limited effectiveness at alleviating the medication errors involving drug name confusion. Higher-leverage strategies, such as drug name changes, have been undertaken 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 the approving the error-prone proprietary name. Moreover, even after Applicant's have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioner's vocabulary, and as such, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, we believe that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval (see limitations of the process).

If our Division objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the FMEA process is used to identify strategies to reduce the risk of medication errors. We are likely to recommend that the Applicant 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, and so we may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

### **3 RESULTS**

#### **3.1 PROPRIETARY NAME RISK ASSESSMENT**

##### ***3.1.1 Database and information sources***

Medication Error Prevention Staff conducted a search of the internet, several standard published databases and information sources (see Section 7 References) for existing drug names which sound-alike or look-alike to Metozolv ODT to a degree where potential confusion between drug names could occur and result in medication errors in the usual clinical practice settings. In total, 29 names were identified as having some similarity to the name Metozolv ODT.

Fifteen of the 29 names were thought to look like Metozolv ODT; these names include: Metaglip, Metrogel, Tovalt ODT, Neptazane, Miconazole, Methimazole, Nebivolol, Nefazodone, Metopirone, Vitafol, Metoz, Hatrazan, Ultracet, Mebendazole, and Metaproterenol. One name, Methoxsalen, was thought to sound similar to Metozolv ODT. Thirteen of the 29 names were thought to look and sound similar to Metozolv ODT; these names include: Medrol, Methazolamide, Metoprolol, Metronidazole, Mintezol, Metro I.V., Metolazone, Metaxalone, Metozol, Ketozole, Midazolam, Metoprolol HCT, and Metadol.

The proposed modifier 'ODT' did not resemble any numbers, or dosing instructions. However, the proposed modifier 'ODT' may be used as a medical abbreviation for O-Desmethyltramadol, Occlusive Dressing Technique, Octadecanethiol, Octadecyltitania Stationary Phase, Oculodynamic Methodology, Oculodynamic Test, Oculodynamic Text, Oculodynamic Tract, Odor Detection Test, Odor Detection Threshold, Of Lower Extremity Discomfort, Olympic Distance Triathlon Performance, On Direct Testing, Once-Daily Tobramycin, Optical Doppler Tomography, Orally Dispersible Tablets, Order-Disorder Transition, Organ Donation And Transplant, Oscillatory Displacement Threshold, Osteochondrosis Dissecans Of The Talus, or Right Occipitotransverse<sup>9</sup>.

The proposed modifier 'ODT' does not appear on the ISMP "List of Error Prone Abbreviations, Symbols, and Dose Designations." Additionally, six products (Aricept ODT, Fazacllo ODT, Orapred ODT, Reglan ODT, Tovalt ODT, and Zofran ODT) listed in the Orange Book contained the Modifier 'ODT' in their proprietary names. The six proprietary names found in the Orange Book and the proposed proprietary names use the "ODT" modifier to describe the "orally disintegrating tablets" dosage form.

The proposed proprietary name, Metozolv ODT, does not contain a USAN stem as of the last date searched, March 23, 2008.

### ***3.1.2 CDER Expert Panel Discussion***

The Expert Panel reviewed the pool of names identified by the Medication Error Prevention Staff (see section 3.1.1 above), and did not provide any additional names orthographically or phonetically similar to Metozolv ODT or Metozolv. Two safety evaluators commented on the modifier ODT in the proposed name. Both safety evaluators commented that ODT can be interpreted in several different ways and included the examples "occipitodextra transerve", "optical doppler tomography", "oral disintegrating tablet", and "once daily tobramycin".

However, assessment of the modifier 'ODT' revealed that the modifier does not resemble any numbers or dosing instructions and the modifier does not appear on the error-prone abbreviation list maintained by the Institute of Safe Medication Practices (ISMP). Therefore, the Division of Medication Error Prevention views the modifier as appropriate.

One safety evaluator expressed concern that since Metozolv ODT is indicated for diabetic gastroparesis, the 'met' in the name could possibly mislead healthcare professionals to think the product contains metformin. However, 'met' is not a recognized stem from the United States Adopted Names Council. Additionally, when 'met' is used to indicate metformin in a formulation the product is usually a combination product. For example, Metaglip is a combination product that contains both metformin and glipizide.

Additionally, one safety evaluator commented that the proposed name reminds them of the word "dissolve".

DDMAC had no objection regarding the proposed name from a promotional perspective, but did comment that Metozolv ODT sounds and looks like metronidazole.

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<sup>9</sup> Medilexicon, <http://www.medilexicon.com/medicalabbreviations.php>, May 28, 2008

### **3.1.3 CDER Prescription Analysis Studies**

A total of 30 practitioners responded, none of the responses overlapped with existing or proposed drug names. One participant (n=1) in the outpatient prescription study interpreted the name correctly as "Metozolv ODT". The remainder of the responses (n=29) misinterpreted the drug name. The majority of misinterpretations occurred in the voice prescription study, with '-zolv' in Metozolv ODT reported as '-solve', the lower case 't' reported as 'd' and the 'o' reported as 'i' or 'a'. Two participants omitted the modifier 'ODT', one participant from the inpatient written prescription study and one patient from the voice prescription study.

Three participants from the inpatient prescription studies misinterpreted the 'ODT' modifier. One participant interpreted the modifier to be 'ODJ' and two participants interpreted the modifier to be 'ODF'. See Appendix B for the complete listing of interpretations from the verbal and written prescription studies. The misinterpretations of the prescriptions analysis studies resulted in modifiers 'ODJ' and 'ODF'. The modifier 'ODJ' did not result in any possible matches as a medical abbreviation. The modifier 'ODF' resulted in the following medical abbreviations: Observer Data Files, Ophthalmic Drug Films, Oppositional Defiant Feature, Orodigitofacial, Osteoclast Differentiation Factor, Otocyst-Derived Factor, Ouabain Displacing Factor, Outer Dense Fibers, Outpatient Drug-Free, Overall Defensive Functioning, and Oviductal Fluid. If the modifier 'ODT' is misinterpreted, the risk for medication error is reduced by the possible resulting medical abbreviations not being appropriate in the context of a medication order.

### **3.1.4 Adverse Event Reporting**

For this review, the Division of Medication Error Prevention performed an updated search of the FDA Adverse Event Reporting System (AERS) for medication errors submitted for Metoclopramide and Reglan (the trade name of metoclopramide) since the previous reviews dated January 10, 2005; August 10, 2005; and October 11, 2005 (see OSE reviews 04-0262, 05-0148-2, and 05-0420 respectively). These reviews completed a review of cases submitted through October 1, 2005. The searches completed in the previous reviews identified four look-alike names to metoclopramide (Mercaptopurine, Metaproterenol, Methyclothiazide, and Metolazone). A risk assessment for Mercaptopurine was completed in OSE review 05-0148-2 and for the remaining three aforementioned names in OSE review 04-2062.

For this review, an updated AERS search was performed with the dates October 1, 2005 through April 04, 2008. This search yielded 18 cases of medication errors associated with the active ingredient metoclopramide. Of the 18 cases, two cases involved an omitted dose or half tablets being dispensed instead of whole tablets of metoclopramide and were not relevant to this review.

The remaining sixteen cases were related to name or label confusion with metoclopramide (see Appendix G). All cases of name or label confusion were domestic cases. Thirteen (n=13) of the sixteen cases involved confusion between metoclopramide injection and other products for injection (Methylprednisolone injection, Enalaprilat injection, and Fosphenytoin injection). In all thirteen cases the reporter stated that the products had similar labels or the vials were similar. In 7 cases the drug never reached the patient whereas in 6 cases there was no reported outcome. Since Metozolv ODT will not be available as an injectable formulation the labels and packaging will differ from the products involved in the thirteen cases identified. Therefore, the characteristics of these cases are not relevant to the proposed product.

The remaining three (n=3) cases involved oral metoclopramide. There was one case of confusion between metoclopramide and Prograf which resulted in a patient having a low Prograf serum level. The case did not have enough information to determine the cause of the medication error; therefore the characteristics of this case can not be extrapolated to a new formulation of metoclopramide.

The second case of confusion occurred between dexamethasone and metoclopramide, which occurred because a nurse called the pharmacy for metoclopramide even though a written prescription was clearly for dexamethasone. When the written prescription arrived to the pharmacy the pharmacist never verified that metoclopramide was written on the prescription. There was not enough information to determine why the nurse requested metoclopramide when dexamethasone was ordered. The error never reached the patient. The case did not have enough information to determine the cause of the medication error; therefore the characteristics of this case can not be extrapolated to a new formulation of metoclopramide.

The final medication error case for oral metoclopramide involved confusion with metoprolol. In this case the error reached the patient. The reporter stated that the error occurred because of the similar names of the two products. The error may have contributed to or resulted in temporary harm to the patient and required intervention. Although the AERS search identified one error related to confusion between the generic name of the proposed product, metoclopramide and metoprolol FMEA determined that potential confusion between the proprietary name Metozolv ODT and metoprolol would be minimal (see Appendix F).

### ***3.1.5 Safety evaluator risk assessment***

Independent searches by the primary safety evaluator did not result in any additional names thought to look or sound similar to Metozolv ODT and represent a potential source of drug name confusion. As such, a total of 29 names were analyzed to determine if the drug names could be confused with Metozolv ODT and if the drug name confusion would likely result in a medication error.

All of the identified names were determined to have some orthographic and/or phonetic similarity to Metozolv ODT, and thus determined to present some risk for confusion. Failure modes and effects analysis (FMEA) was then applied to determine if the proposed name, Metozolv ODT, could potentially be confused with any of the 29 names and lead to medication error.

Eleven of the names identified: Metaproterenol, Methoxsalen, Medrol, Metolazone, Methimazole, Nebivolol, Tovalt ODT, Metaglip, Methazolamide, Mebendazole, and Metoprolol HCT, were not considered further because they lack convincing orthographic and/or phonetic similarities with Metozolv ODT (see Appendix C).

Three of the 29 names (Metozol, Metadol, and Metoz), are foreign drug products that do not appear in common references such as Clinical pharmacology, Drugs@FDA, The Orange Book, Lexi-Comp, or Rxlist.com and thus FMEA determined that medication errors were unlikely to occur in the United States of America (see Appendix D).

For eight of the names (Miconazole, Ketozole, Metro I.V., Metrogel, Metopirone, Vitafof, Ultracet, and Metaxalone) FMEA determined that medication errors were unlikely because the products do not overlap in strength or dose with Metozolv ODT and have minimal orthographic and/or visual similarity to Metozolv ODT (see Appendix E).

Seven of the names (Midazolam, Metoprolol, Mintezol, Metronidazole, Nefazodone, Hetrazan, and Neptazane) had numerical overlap with Metozolv ODT in either dosage or strength, but analysis of the failure mode did not determine the effect of this similarity to result in medication errors in the usual practice setting. Minimal orthographic/phonetic similarities in addition to other differentiating characteristics such as directions for use, duration of use, and the need for trailing zero's to have a direct overlap in either strength or dose minimizes the risk for error in the usual practice setting (see Appendix G).

## **4 DISCUSSION**

The results of the Proprietary Name Risk Assessment found that the proposed name, Metozolv ODT, has some similarity to other proprietary and established drug names, but the findings of the FMEA process indicate that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors.

The findings of the Proprietary Name Risk Assessment are based upon current understanding of factors that contribute to medication errors involving name confusion. Although we believe the findings of the Risk Assessment to be robust, our findings do have limitations. First, because our assessment involves a limited number of practitioners, it is possible that the analysis did not identify a potentially confusing name. Also, there is some possibility that our Risk Assessment failed to consider a circumstance in which confusion could arise. However, the Division of Medication Error Prevention believes that these limitations are sufficiently minimized by the use of an Expert Panel and the CDER Prescription studies, that involved 123 CDER practitioners.

However, our risk assessment also faces limitations beyond the control of the Agency. First, our risk assessment is based on current health care practices and drug product characteristics, future changes to either could increase the vulnerability of the proposed name to confusion. Since these changes cannot be predicted for or accounted by the current Proprietary Name Risk Assessment process, such changes limit our findings. To help counterbalance this impact, the Division of Medication Error Prevention recommends that the proprietary name be re-submitted for review if approval of the product is delayed beyond 90 days.

Overall, our Risk Assessment is limited by our current understanding of medication errors and causality. The successful application of Failure Modes and Effect Analysis depends upon the learning gained for a spontaneous reporting program. It is quite possible that our understanding of medication error causality would benefit from unreported medication errors; and, that this understanding could have enabled the Staff to identify vulnerability in the proposed name, packaging, and labeling that was not identified in this assessment. To help minimize this limitation in future assessments, we encourage the Sponsor to provide the Agency with medication error reports involving their marketed drug products regardless of adverse event severity.

## **5 CONCLUSIONS AND RECOMMENDATIONS**

The Proprietary Name Risk Assessment findings indicate that the proposed name, Metozolv ODT, does not appear to be vulnerable to name confusion that could lead to medication errors in the United States of America. As such, the Division of Medication Prevention does not object to the use of the proprietary name, Metozolv ODT, for this product.

Additionally, DDMAC has no objections to the proposed name, Metozolv ODT, from a promotional perspective.

### **5.1 COMMENTS TO THE DIVISION**

The Division of Medication Error Prevention does not object to the use of the proprietary name, Metozolv ODT for this product.

If any of the proposed product characteristics as stated in this review are altered prior to approval of the product, the Division of Medication Error Prevention rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review. Furthermore, this name must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approval of other proprietary or established names from the signature date of this document.

Container labels, carton and insert labeling were not submitted prior to completion of this review. Please forward the container labels for review and comment when they become available.

The Division of Medication Error Prevention would appreciate feedback on the final outcome of this review. Please copy the Division of Medication Error Prevention on any communication to the Sponsor with regard to this review. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Cheryle Milburn, Project Manager, at 301-796-2084.

## **5.2 COMMENTS TO THE APPLICANT**

1. The Division of Medication Error Prevention has no objections to the use of the proprietary name, Metozolv ODT, for this product. If any of the proposed product characteristics as stated in this review are altered prior to approval of the product, the Division of Medication Error Prevention rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review. Additionally, this name must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approval of other proprietary or established names from the signature date of this document.
2. Submit all container labels for review and comment when they become available.

## **6 REFERENCES**

### **6.1 REVIEWS**

1. *OSE Review #04-0262 2 Proprietary Name and Labeling Review for Reglan RPT (metoclopramide orally disintegrating tablets), Jahng, J; January 10, 2005.*
2. *OSE Review #05-0148-2 Proprietary Name and Labeling Review for Reglan ODT (metoclopramide orally disintegrating tablets), Duffy, F; August 10, 2005.*
3. *OSE Review #05-0420 Labeling Review Reglan ODT (metoclopramide orally disintegrating tablets), Bridges, T; October 11, 2005.*

## 6.2 DATABASES

### 1. *Adverse Events Reporting System (AERS)*

AERS is a database application in CDER FDA that contains adverse event reports for approved drugs and therapeutic biologics. These reports are submitted to the FDA mostly from the manufactures that have approved products in the U.S. The main utility of a spontaneous reporting system that captures reports from health care professionals and consumers, such as AERS, is to identify potential postmarketing safety issues. There are inherent limitations to the voluntary or spontaneous reporting system, such as underreporting and duplicate reporting; for any given report, there is no certainty that the reported suspect product(s) caused the reported adverse event(s); and raw counts from AERS cannot be used to calculate incidence rates or estimates of drug risk for a particular product or used for comparing risk between products.

### 2. *Micromedex Integrated Index (<http://weblern/>)*

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

### 3. *Phonetic and Orthographic Computer Analysis (POCA)*

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. This is a database which was created for DMEDP, FDA.

### 4. *Drug Facts and Comparisons, online version, St. Louis, MO (<http://weblern/>)*

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

### 5. *AMF Decision Support System [DSS]*

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

### 6. *Division of Medication Error Prevention proprietary name consultation requests*

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

### 7. *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 and generic drugs and therapeutic biological products; prescription and over-the-counter human drugs and therapeutic biologics, discontinued drugs and “Chemical Type 6” approvals.

### 8. *Electronic online version of the FDA Orange Book (<http://www.fda.gov/cder/ob/default.htm>)*

Provides a compilation of approved drug products with therapeutic equivalence evaluations.

**9. USPTO (<http://www.uspto.gov>)**

Provides information regarding patent and trademarks.

**10. Clinical Pharmacology Online (<http://weblern/>)**

Contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. Provides a keyword search engine.

**11. Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at [www.thomson-thomson.com](http://www.thomson-thomson.com)**

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

**12. Natural Medicines Comprehensive Databases (<http://weblern/>)**

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

**13. Stat!Ref (<http://weblern/>)**

Contains full-text information from approximately 30 texts. 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.

**14. USAN Stems (<http://www.ama-assn.org/ama/pub/category/4782.html>)**

List contains all the recognized USAN stems.

**15. Red Book Pharmacy's Fundamental Reference**

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

**16. Lexi-Comp ([www.pharmacist.com](http://www.pharmacist.com))**

A web-based searchable version of the Drug Information Handbook.

**17. Medical Abbreviations Book**

Contains commonly used medical abbreviations and their definitions.

## APPENDICES

### Appendix A:

The Medication Error Staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. The Division of Medication Error Prevention also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. The Medication Error Staff also examine 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* dissimilarly spelled drug name pairs to appear very similar to one another and the similar appearance of drug names when scripted has lead to medication errors. The Medication Error Staff apply their expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (i.e. 'T' may look like 'F,' lower case 'a' looks like a lower case 'u,' etc), along with other orthographic attributes that determine the overall appearance of the drug name when scripted (see detail in Table 1 below). Additionally, since verbal communication of medication names is common in clinical settings, the Medication Error Staff compare the pronunciation of the proposed proprietary name with the pronunciation of other drug names. If provided, we will consider the Applicant's intended pronunciation of the proprietary name. However, because the Applicant has little control over how the name will be spoken in practice, we also consider a variety of pronunciations that could occur in the English language.

**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	<ul style="list-style-type: none"> <li>Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication</li> <li>Names may look similar when scripted and lead to drug name confusion in written communication</li> </ul>
	Orthographic similarity	Similar spelling Length of the name Upstrokes Downstrokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	<ul style="list-style-type: none"> <li>Names may look similar when scripted, and lead to drug name confusion in written communication</li> </ul>
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	<ul style="list-style-type: none"> <li>Names may sound similar when pronounced and lead to drug name confusion in verbal communication</li> </ul>

**Appendix B:**

CDER Prescription Study Responses for Metozolv ODT

<b>Outpatient Prescription</b>	<b>Voice Prescription</b>	<b>Inpatient Medication Order</b>
Metizol ODT	Medasolve ODT	Metoralv ODF
Metozol ODT	Medazolve ODT	Metozake ODT
Metozol ODT	Medisolve ODT	Metozalo ODF
Metozole ODT	Medosolv ODT	Metrorab ODT
Metozole ODT	Menasolve ODT	Metrozalv ODT
Metozoli ODT	Menozol ODT	Mitoralv
Metozolv ODT	Metasolve	Mitozab ODJ
Metozolve ODT	Metasolve ODT	Mitozalv ODT
Metrizole ODT	Metasolve ODT	
	Metazaf ODT	
	Metosolve ODT	
	Metosolve ODT	
	Metozole ODT	

**Appendix C:** Products that lack orthographic and phonetic similarity to Metozolv ODT.

<b>Product name with potential for confusion</b>	<b>Similarity to Metozolv ODT</b>
Metaproterenol	Look
Methoxsalen	Sound
Medrol	Sound
Metolazone	Look and Sound
Methimazole	Look
Nebivolol	Look
Tovalt ODT	Look and Sound
Metaglip	Look
Methazolamide	Sound
Mebendazole	Look
Metoprolol HCT	Look and Sound

**Appendix D:** Proprietary names of foreign drugs.

<b>Proprietary Name</b>	<b>Similarity to Metozolv ODT</b>	<b>Strength</b>	<b>Usual Dose</b>	<b>Country</b>
Metadol (Methadone)	Look and Sound	Tablets: 1 mg, 5 mg, 10 mg and 25 mg  Oral Solution: 1 mg/mL and 10mg/mL	2.5 to 10 mg orally every 3 or 4 hours as necessary.	Canada
Metoz (Metolazone)	Look	Tablets: 2.5mg, 5 mg, and 10 mg	2.5 mg to 20 mg by mouth once daily.	India
Metozol	Look and Sound	Unavailable - Foreign Product	Unavailable - Foreign Product	Brazil

**Appendix E:** Products with no numerical overlap in strength and dose.

Product name with potential for confusion	Similarity to Metozolv ODT	Strength	Usual Dose (if applicable)	Source
<b>Metozolv ODT (metoclopramide orally disintegrating tablet)</b>		<b>Tablets: 5 mg and 10 mg</b>	<b>Usual dose:</b> <u>Diabetes Gastroparesis:</u> 10 mg by mouth at least 30 minutes before each meal and at bedtime up to 4 times per day. <u>Gastroesophageal Reflux Disease:</u> 10 mg to 15 mg by mouth up to four times a day at least 30 minutes before each meal and at bedtime.	
Miconazole	Look	Vaginal suppositories: 100 mg, 200 mg, and 1200 mg  Vaginal cream: 2%  Topical cream, ointment, gel, powder, and spray: 2%	Insert 1 suppository intravaginally once daily at bedtime for 5 to 7 days  Insert 1 applicatorful intravaginally once daily at bedtime for 3 to 7 days.  Apply to affected areas twice daily (morning and evening) for up to 7 days or as needed.	Drugs@FDA Clinical Pharmacology Facts and Comparison
Ketozone (Ketoconazole)	Look and Sound	Topical Cream: 2%	Apply once daily to cover the affected and immediate surrounding area.	Google.com Orang Book
Metro I.V. (Metonidazole)	Look and Sound	Injection: 500 mg	500 mg intravenously three times per day	Drugs@FDA
Metrogel (metronidazole gel)	Look	Topical gel: 1%	Apply a thin film once daily to entire affected area.	Rxlist.com Drugs@FDA

Metopirone (metyrapone, USP)	Look	Capsule: 250 mg	30 mg/kg at midnight the night prior to drawing blood for ACTH function tests.	Facts and Comparisons Rxlist.com
Vitafol (Ascorbic Acid 60mg, Calcium Carbonate 313mg, Cholecalciferol 400IU, Cyanocobalamin 5mcg, Ferrous Fumarate 197mg, Folic Acid 1mg, Niacinamide 15mg, Pyridoxine 2.5mg, Riboflavin 1.8mg, Thiamine Mononitrate 1.1mg, Vitamin A Acetate 6,000IU, Vitamin E 30IU)	Look	Tablet	1 tablet by mouth daily	Clinical Pharmacology
Ultracet (tramadol and acetaminophen)	Look	Tablets: 37.5 mg tramadol and 325 mg of acetaminophen	2 tablets orally every 4 to 6 hours up to 8 tablets per day	Facts and Comparisons
Metaxalone (Skelaxin)	Look and Sound	Tablets: 800 mg	800 mg by mouth three to four times a day. 800 mg	Rxlist.com Drugs@FDA Clinical Pharmacology

**Appendix F:** Potential confusing name with numerical overlap in strength or dose

<b>Failure Mode:</b> <b>Name confusion</b>	<b>Causes</b> <b>(could be multiple)</b>	<b>Effects</b>
<b>Metozolv ODT</b> <b>(metoclopramide</b> <b>orally disintegrating</b> <b>tablet)</b>	<b>Tablets: 5 mg and</b> <b>10 mg</b>	<b>Usual dose:</b> <u>Diabetes Gastroparesis:</u> 10 mg by mouth at least 30 minutes before each meal and at bedtime up to 4 times per day. <u>Gastroesophageal Reflux Disease:</u> 10 mg to 15 mg by mouth up to four times a day at least 30 minutes before each meal and at bedtime.
Midazolam	<p>Phonetic similarity ('Mid-' vs. 'Met-' may sound similar when spoken and the letter combinations 'azol' vs. 'ozol' may sound similar when spoken)</p> <p>Orthographic similarity (both names contain the same number of upstrokes, 3, if the modifier ODT is omitted from Metozolv ODT, both names contain the same numbers of downstrokes (1) located in the same position (fifth letter), 'Mi' and 'Me' may look similar when scripted, the letters 'a' and 'o' may look similar when scripted, and both names contain the letter combination 'zol' in same positions (fifth, sixth, and seventh letters)</p> <p>Similar dose (5 mg)</p>	<p>Phonetic and orthographic differences in the names and product characteristics minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>The risk for medication error is minimized by the phonetic differences in the names. Midazolam has a different number of syllables (4 vs. 3 if the modifier is omitted or 6 if the modifier 'ODT' is included with Metozolv ODT). Additionally the ending of each (-'am' vs. '-v' if the modifier 'ODT' is omitted or '-v ODT' if the modifier 'ODT' is included with Metozolv ODT) name sounds different when spoken.</p> <p>The risk for medication error is also minimized by the orthographic differences in the names. The names are different lengths (9 letters vs. 8 letters if the modifier 'ODT' is omitted and 11 letters if the modifier 'ODT' is included with Metozolv ODT), contain a different number of dotted letters (1 'i' vs. none), and contain a different number of crosstrokes (none vs. 1 if the modifier 'ODT' is omitted and 2 if the modifier 'ODT' is included with Metozolv ODT). Additionally the ending of each name (-'am' vs. '-v' if the modifier 'ODT' is omitted or '-v ODT' if the modifier 'ODT' is included with Metozolv ODT) name appears different when scripted.</p> <p>Although Midazolam and Metozolv ODT do have an overlapping dose (5 mg); frequency (once vs. once to four times daily), directions for use (give intramuscularly up to one hour prior to surgery vs. take one to four times daily by mouth at least 30 minutes before meal and bedtime), and formulation (solution for injection and oral syrup vs. orally disintegrating tablets) are different. Since the frequency, directions for use, and formulation will most likely be included on a prescription the possibility of a medication error is minimized.</p> <p>Despite an overlapping dose; the phonetic, orthographic, and product characteristic differences minimizes the potential for confusion between Midazolam and Metozolv ODT.</p>

<p>Metoprolol</p>	<p>Phonetic similarity (both contain 'Meto-' and the letter combination '-ol' in similar positions)</p> <p>Orthographic similarity (both contain the beginning 'Meto-', the same number of downstrokes (1) located in the same position (fifth letter), and the same letter combination '-ol-' in similar positions (seventh and eighth letter vs. sixth and seventh letter))</p> <p>Similar numerical strength (50 mg and 100 mg vs. 5 mg and 10 mg if a trailing zero is included. For example 5.0 mg)</p> <p>Overlapping dosage form (tablet), route of administration (oral), and frequency (twice daily)</p>	<p>Phonetic and orthographic differences in the names and the unlikelihood of the inclusion of a trailing zero minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>The risk for medication error is minimized by the phonetic differences in the names. Metoprolol has a different number of syllables (4 vs. 3 if the modifier 'ODT' is omitted or 6 if the modifier 'ODT' is included with Metozolv ODT). Additionally the middle portion of each name sounds different when spoken ('-pr-' vs. '-z-'). Furthermore the endings of each name ('-ol' vs. '-v' if the modifier 'ODT' is omitted or '-v ODT' if the modifier 'ODT' is included with Metozolv ODT) sound different when spoken.</p> <p>The risk for medication error is also minimized by the orthographic differences in the names. Both names contain a different numbers of letters (10 letters vs. 8 letters if the modifier 'ODT' is omitted or 11 if the modifier 'ODT' is included with Metozolv ODT), contain a different number of up strokes (4 vs. 3 if the modifier 'ODT' is omitted or 6 if the modifier 'ODT' is included. Additionally the middle portion of each name appears different when scripted ('-pr-' vs. '-z-'). Furthermore the endings of each name ('-ol' vs. '-v' if the modifier 'ODT' is omitted or '-v ODT' if the modifier 'ODT' is included with Metozolv ODT) appear different when scripted.</p> <p>Although Metoprolol and Metozolv ODT share a similar numerical strength (50 mg and 100 mg vs. 5 mg and 10 mg if a trailing zero is included), usual practice would not typically involve the inclusion of a trailing zero, though medication errors have been linked to this dangerous habit. Numerous campaigns (Joint Commission, Institute of Safe Medication Practices, and Food and Drug Administration) to eliminate use of trailing zeros when communicating drug information should help to further reduce risk of medication error.</p> <p>Despite some overlapping product characteristics, the phonetic and orthographic differences and the unlikelihood of the inclusion of a trailing zero minimizes the potential for confusion between Metoprolol and Metozolv ODT.</p>
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<p>Mintezol</p>	<p>Phonetic similarity (both contain the same number of syllables, 3, when the modifier ‘ODT’ is omitted from Metozolv ODT and ‘-tezol’ vs. ‘-tozolv’ may sound similar when spoken)</p> <p>Orthographic similarity (both contain 8 letters, the same number of upstrokes (3), if the modifier ODT is omitted from Metozolv ODT, both contain the same number of downstrokes (1), ‘Mi’ and ‘Me’ may look similar when scripted both have the letter ‘t’ in similar positions (fourth letter vs. third letter), and both contain the letter combination ‘zol’ in similar positions (sixth through eighth letter vs. fifth through seventh letter))</p> <p>Similar numerical strength (500 mg vs. 5 mg if two trailing zeros are included. For example 5.00 mg)</p> <p>Overlapping dosage form (tablet), route of administration (oral), and frequency (twice daily).</p>	<p>Phonetic and orthographic differences in the names, the unlikelihood of the inclusion of trailing zeros, and the duration of treatment minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>The risk for medication error is minimized by the phonetic differences in the names. The beginning of the names ‘Min-’ vs. ‘Met-’ sound different when spoken.</p> <p>The risk for medication error is also minimized by the orthographic differences in the names. Both names contain a different number of letters (9 letters vs. 8 letters if the modifier ‘ODT’ is omitted and 11 letters if the modifier ‘ODT’ is included with Metozolv ODT) and contain a different number of dotted letters (1 ‘i’ vs. none). Additionally the middle portion of each name appears different when scripted (‘-nte-’ vs. ‘-eto-’).</p> <p>Additionally Mintezol would be written in either grams or mL. While it is possible to write for Mintezol in mg and have a similar numerical strength with Metozolv ODT (500 mg vs. 5 mg if two trailing zeros are included), usual practice would not typically involve the inclusion of two trailing zeros, though medication errors have been linked to this dangerous habit. Numerous campaigns (Joint Commission, Institute of Safe Medication Practices, and Food and Drug Administration) to eliminate use of trailing zeros when communicating drug information should help to further reduce risk of medication error.</p> <p>Furthermore, the duration of treatment helps to differentiate Mintezol and Metozolv ODT. The duration for treatment for Mintezol is two to four days while the duration of treatment for Metozolv ODT would be chronic treatment. Most likely a prescriber would include a duration of treatment for Mintezol and likely would not include a duration of treatment for Metozolv ODT.</p> <p>Despite some overlapping product characteristics and the phonetic and orthographic similarities, the unlikelihood of the inclusion of trailing zeros, and the difference in the duration of treatment minimizes the potential for confusion between Mintezol and Metozolv ODT.</p>
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<p>Metronidazole</p>	<p>Phonetic similarity (both contain 'Met-' and both contain an 'o' in similar positions (the 8<sup>th</sup> letter vs. the 7<sup>th</sup> letter))</p> <p>Orthographic similarity (both contain 'Met-', contain the letter 'o' in similar positions (8<sup>th</sup> letter vs. 7<sup>th</sup> letter), contain the same number of downstrokes (1), and the same letter combination '-zol-').</p> <p>Similar numerical strength (500 mg vs. 5 mg two trailing zeros are included. For example 5.00 mg)</p> <p>Overlapping dosage form (tablet), route of administration (oral), and frequency (three times per day).</p>	<p>Phonetic and orthographic differences in the names and the unlikelihood of the inclusion of two trailing zeros minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>The risk for medication error is minimized by the phonetic differences in the names. Metronidazole has a different number of syllables (5 vs. 3 if the modifier 'ODT' is omitted or 6 if the modifier 'ODT' is included with Metozolv ODT) Additionally the middle portion of each name sounds different when spoken ('-ronida-' vs. '-o-').</p> <p>The risk for medication error is also minimized by the orthographic differences in the names. Both names contain a different numbers of letters (13 letters vs. 8 letters if the modifier 'ODT' is omitted or 11 letters if the modifier 'ODT' is included with Metozolv ODT), contain a different number of up strokes (4 vs. 3 if the modifier 'ODT' is omitted or 6 if the modifier 'ODT' is included), and contain a different number of dotted letters (1 'i' vs. none). Additionally the ending of each name appears different when scripted ('-ronidazole' vs. 'ozolv ODT').</p> <p>Although Metronidazole and Metozolv ODT share a similar numerical strength (500 vs. 5 mg if two trailing zeros are included), usual practice would not typically involve the inclusion of trailing zeros, though medication errors have been linked to the use of trailing zeros. Numerous campaigns (Joint Commission, Institute of Safe Medication Practices, and Food and Drug Administration) to eliminate use of trailing zeros when communicating drug information should help to further reduce risk of medication error.</p> <p>Despite some overlapping product characteristics, the phonetic and orthographic differences and the unlikelihood of the inclusion of two trailing zeros minimizes the potential for confusion between Metronidazole and Metozolv ODT.</p>
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<p>Nefazodone</p>	<p>Orthographic similarity (both names contain the same number of upstrokes (3), crosstrokes (1) if the modifier 'ODT' is omitted from Metozolv ODT, the letters 'N' and 'M' can look similar when scripted, both names contain the letter 'e' as the second letter of each name, both names contain an upstroke and crosstroke as the third letter ('f' vs. 't'), the letters 'a' and 'o' may appear similar when scripted, both names contain the letter combination '-zo-' as the fifth and sixth letter of the name and the seventh letter is an upstroke for each name ('d' vs. 'l'))</p> <p>Similar numerical strength and dose (50 mg, 100 mg, and 150 mg, and vs. 5 mg, 10 mg, and 15 mg, if a trailing zero is included. For example 5.0 mg)</p> <p>Overlapping dosage form (tablet), route of administration (oral), and frequency (two times per day).</p>	<p>Orthographic differences in the names and the unlikelihood of the inclusion of a trailing zero minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>The risk for medication error is minimized by the orthographic differences in the names. Both names have a different number of letters (10 letters vs. 8 letters if the modifier 'ODT' is omitted or 11 letters if the modifier 'ODT' is included with Metozolv ODT), contain a different number of downstrokes (2 vs. 1). Additionally the ending of each name appears different when scripted ('-done' vs. 'lv' if the modifier 'ODT' is omitted or '-vl ODT' if the modifier is included from Metozolv ODT).</p> <p>Although Nefazodone and Metozolv ODT share a similar numerical strength and dose (50 mg, 100 mg, and 150 mg, and vs. 5 mg, 10 mg, and 15 mg, if a trailing zero is included. For example 5.0 mg), usual practice would not typically involve the inclusion of trailing zeros, though medication errors have been linked to this dangerous habit. Numerous campaigns (Joint Commission, Institute of Safe Medication Practices, and Food and Drug Administration) to eliminate use of trailing zeros when communicating drug information should help to further reduce risk of medication error.</p> <p>Despite some overlapping product characteristics, the orthographic differences and the unlikelihood of the inclusion of a trailing zero minimizes the potential for confusion between Nefazodone and Metozolv ODT.</p>
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<p>Hetrazan</p>	<p>Orthographic similarity (both names contain the same number of downstrokes (1), dotted letters (none) and crosstrokes (1) if the modifier 'ODT' is omitted from Metozolv ODT, the letters 'H' and 'M' may appear similar when scripted, both names have the same letter combination '-et-' in the same positions (second and third letters), the letters 'a' and 'o' can look similar when scripted and both names contain the letter 'z' in similar positions of the name (sixth letter vs. fifth letter))</p> <p>Similar numerical strength (50 mg vs. 5 mg if a trailing zero is included. For example 5.0 mg)</p> <p>Overlapping dosage form (tablet), and route of administration (oral)</p>	<p>Orthographic differences in the names, the unlikelihood of the inclusion of a trailing zero, and the difference in dosing regimens minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>The risk for medication error is minimized by the orthographic differences in the names. The ending of each name appears different when scripted ('n' vs. 'lv' if the modifier 'ODT' is omitted or '-vl ODT' if the modifier is included from Metozolv ODT).</p> <p>Although Hetrazan and Metozolv ODT share a similar numerical strength and dose (50 mg and vs. 5 mg if a trailing zero is included. For example 5.0 mg), usual practice would not typically involve the inclusion of trailing zeros, though medication errors have been linked to this dangerous habit. Numerous campaigns (Joint Commission, Institute of Safe Medication Practices, and Food and Drug Administration) to eliminate use of trailing zeros when communicating drug information should help to further reduce risk of medication error.</p> <p>Additionally the dosing regimen is different for the Hetrazan and Metozolv ODT. Hetrazan is dosed based on weight (2 mg/kg/dose) given orally three times a day immediately after meals. Metozolv ODT can be given orally, three times a day however, Metozolv ODT is given 30 minutes prior to meals.</p> <p>Despite some overlapping product characteristics, the orthographic differences, the unlikelihood of the inclusion of a trailing zero, and the difference in dosing regimens minimizes the potential for confusion between Hetrazan and Metozolv ODT.</p>
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<p>Neptazane</p>	<p>Orthographic similarity (the letters 'N' and 'M' can look similar when scripted, both names contain the letter 'e' as the second letter of each name, the letters 'a' and 'o' may appear similar when scripted and both names contain the letter 'z' in similar positions (sixth letter vs. seventh letter))</p> <p>Similar numerical strength and dose (50 mg vs. 5 mg if a trailing zero is included. For example 5.0 mg)</p> <p>Overlapping dosage form (tablet), route of administration (oral), and frequency (two to three times per day).</p>	<p>Orthographic differences in the names and the unlikelihood of the inclusion of a trailing zero minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>The risk for medication error is minimized by the orthographic differences in the names. Both names contain a different number of letters (9 letters vs. 8 letters if the modifier 'ODT' is omitted or 11 letters if the modifier 'ODT' is included with Metozolv ODT), contain a different number of upstrokes (2 vs. 3 if the modifier 'ODT' is omitted or 6 if the modifier 'ODT' is included with Metozolv ODT), and contain a different number of downstrokes (2 vs. 1). Additionally the ending of each name appears different when scripted ('-ne' vs. 'lv' if the modifier 'ODT' is omitted or '-vl ODT' if the modifier is included from Metozolv ODT).</p> <p>Although Neptazane and Metozolv ODT share a similar numerical strength and dose (50 vs. 5 mg if a trailing zero is included. For example 5.0 mg), usual practice would not typically involve the inclusion of trailing zeros, though medication errors have been linked to this dangerous habit. Numerous campaigns (Joint Commission, Institute of Safe Medication Practices, and Food and Drug Administration) to eliminate use of trailing zeros when communicating drug information should help to further reduce risk of medication error.</p> <p>Despite some overlapping product characteristics, the orthographic differences and the unlikelihood of the inclusion of a trailing zero minimizes the potential for confusion between Neptazane and Metozolv ODT.</p>
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**Appendix G: Adverse Event Reporting System (AERS) Summary**

ISR # FDA Receipt Date	Products Involved and Outcome	Narrative
4979227-6 04/20/2006	Oral Metoclopramide  And Oral Dexamethasone  Delay in treatment	<p>A nurse called pharmacist A from the Emergency Center, and said “ I am going to be sending down a STAT order for an infant for metoclopramide for an infant, please be sure and get the medication tube back to me ASAP’.</p> <p>Pharmacist A asked the nurse for the infant’s weight (5.2 kg) so that she could begin gathering dose-range checking information per the hospitals protocol. The pharmacist looked up the drug in NeoFax and waited for the order to arrive. Shortly after the order arrived form the ED. The pharmacist checked the dose printed on the order sheet and entered the order into the HMM pharmacy system for `metoclopramide 3 mg/3 mL orally stay.</p> <p>The pharmacist documented the information on the dosage range and calculations on the computer and printed this out for another pharmacist to double check.</p> <p>Pharmacist A took the labels and printed information from the HMM screen and brought this over to the extemporaneous compounding area and began preparing the oral syringe. The oral syringe was drawn up, labeled, and checked by pharmacist A and placed on the counter. Pharmacist B was called over to double check the oral syringe before sending to the ETC. Pharmacist B looked at the bottle, the syringe, and the printed computer sheet to verify dosage, drug, volume, and patient. All appeared correct, and Pharmacist B signed off on the compound. Pharmacist A took the syringe and tube up to the ED.</p> <p>A few minutes later, Pharmacist B receives a call from a nurse in the ED. The nurse says that “I have an oral syringe here for my patient and I am not sure, but I think it is mislabeled. I am looking for dexamethasone, not metoclopramide; I am going to send the medication back down to you with the original order.” The oral syringe arrives at the pharmacy with the original order from that read `dexamethasone 3 mg/3 mL orally STAT’ and is for the same patient. The metoclopramide order is cancelled on the HMM system, and the correct order for dexamethasone is entered for the patient. Pharmacist A checks dosage, and re-prepares the correct oral syringe. Pharmacist B verifies, and signs off.</p>
4995398-X 05/03/2006	Metoclopramide tablets and  Metoprolol Tablets  The error may have contributed to or resulted in temporary harm to the patient and required intervention.	<p>A pharmacist reported a pharmacy error that occurred at a community pharmacy. The error may have contributed to or resulted in temporary harm to the patient and required intervention. The products involved were Mylan’s Metoprolol tablets, 25mg and Pliva’s metoclopramide tablets, 5mg. The pharmacist reported that the error occurred because the tablets had similar names. The product (not specified which product) was reportedly taken by the patient, but no event was noted. The pharmacy error was discovered by poison control. The patient was a 53-year-old male with a history of diabetes and hypertension.</p>

<p>5196640-5 12/29/2006</p>	<p>Metoclopramide injection and Methylprednisolone injection</p> <p>Error never reached a patient</p>	<p>We are writing to express concern about a potential error. The vials for metoclopramide for injection (NDC #0703-4502-01; 10 mg/2L) and methylprednisolone for injection (NDC #0703-0051-01; 80 mg/1 mL) both look extremely similar. Not only do the drug names look similar at a glance but the packaging for both is the same shade of lavender and white. This could easily lead to the incorrect drug being dispensed. At our facility, both were placed in the same stock bag before this was discovered by a dispensing pharmacist. Fortunately, no incident resulted.</p> <p>No patient was affected.</p> <p>Not only do the drug names look similar at a glance but the packaging for both is the same shade of lavender and white. This could easily lead to the incorrect drug being dispensed.</p>
<p>5219055-X 01/24/2007</p>	<p>Metoclopramide injection and Methylprednisolone injection</p> <p>No outcome reported</p>	<p>Similar appearance of vial size and coloring contributing to stocking/dispensing error.</p>
<p>5263654-6 03/12/2007</p>	<p>Metoclopramide injection and Methylprednisolone injection</p> <p>No outcome reported</p>	<p>Look-alike label on packaging</p> <p>N/A</p> <p>Look-alike drug packaging</p>
<p>5313789-4 04/30/2007</p>	<p>Metoclopramide tablets and Prograf capsules</p> <p>Patients Prograf blood level was less than 1.5</p>	<p>A 63 year-old male patient started Prograf (tacrolimus) 2 mg BID on MAYXX, 2003. On NOVXX, 2006, Prograf dosage was decreased to 1 mg BID.</p> <p>On DECXX, 2006, the patient's Prograf blood level was below 1.5. Blood test was repeated ~DECXX, 2006 and it was still below 1.5. The patient went to his nephrologist who recommended him to go to the transplant clinic.</p> <p>On DECXX, 2006, the patient went to the transplant clinic. The medical assistant noticed the patient had incorrect medication in his Prograf 1 mg bottle. The medicine had markings of Pliva430, identified as metoclopramide 10 mg. The patient had been taking the incorrect medication for a month. That same day ( DECXX, 2006) the patient was given Prograf 3 mg to be taken twice daily.</p> <p>Patient's Prograf level was below 1.5.</p>
<p>5334112-5 05/23/2007</p>	<p>Metoclopramide injection and Methylprednisolone injection</p> <p>No outcome reported</p>	<p>Look alike drug NDC: 00703005101 methylprednisolone 80mg/ml NDC: 00703450201 metoclopramide 5mg/ml Vials are same size, both have white caps and pink labels. Bottles look extremely similar and have similar names. Please rectify this problem by changing the labeling on one of the medications in order to prevent medication errors. Manufacturer: Sicor Pharmaceuticals, Irvine, CA 92618</p>

<p>5355667-0 06/12/2007</p>	<p>Metoclopramide injection and Methylprednisolone injection</p> <p>Error never reached the patient</p>	<p>I work in a hospital pharmacy. We have in stock Methylprednisolone 80 mg/mL vials (from Sicor) and Metoclopramide 10 mg/2 mL vials (from Sicor). The vials were inadvertently mixed up in our inventory.</p> <p>The Methylprednisolone (which is for IM or soft tissue Inj only) was ALMOST sent up to the floor to be given as Reglan IV. The vials are from the same manufacturer and look very similar.</p> <p>The Methylprednisolone vials have a pinkish label and the Metoclopramide have a light purple label (very similar shades!) This was a potential error which could have had serious consequences. The pharmacist, upon checking meds the technician pulled, found the error.</p> <p>To prevent further errors, the pharmacy department (all staff) was educated on the similarities of the vials, and large caution stickers were placed on the bins of both meds.</p> <p>The vials are from the same manufacturer and look very similar. The Methylprednisolone vials have a pinkish label and the metoclopramide have a light purple label (very similar shades!)</p>
<p>5467088-0 09/21/2007</p>	<p>Metoclopramide injection and Fosphenytoin injection</p> <p>No outcome reported</p>	<p>Fosphenytoin and metoclopramide vials made by Hospira look alike with the same green color tops. The only difference is the color of lettering of fosphenytoin –drug name-</p>
<p>5519065-9 11/14/2007</p>	<p>Metoclopramide injection and Methylprednisolone injection</p> <p>Error never reached the patient</p>	<p>Look-alike products. Methylprednisolone acetate 40 mg (Sicor) &amp; Metoclopramide 10 mg injection (Baxter) - both are white labels with purple boxes on the labels - even though one solution is clear and the other white, a few found their way into med bins.</p>
<p>5523434-0 11/19/2007</p>	<p>Metoclopramide injection and Fosphenytoin injection</p> <p>Error never reached the patient</p>	<p>Generic Fosphenytoin 2 mL. (Hospira) looks identical to Metoclopramide (Hospira) 2 mL. Cap colors, vial, etc. 2 vials of Fosphenytoin mixed with Metoclopramide stock.</p>

<p>5546334-9 12/06/2007</p>	<p>Metoclopramide injection and Methylprednisolone injection</p> <p>Error never reached the patient</p>	<p>We are a medium-sizes community hospital located in XXX. Two vials look-alike. Both are manufactured by Sikor. Both have a pinkish gray and white label. One is for Methylprednisolone acetate 80 mg/mL and the other is for Metoclopramide 10 mg/2 mL. The metoclopramide vials were accidentally returned to the Depo-Medrol bin in the pharmacy.</p> <p>When filling PYXIS a tech bagged 8 Depo-Medrol in with 2 metoclopramide and this was not detected by the pharmacist checking nor by the technician filling the PYXIS station. Error was determined only when a nurse withdrew from PYXIS what she thought was Depo-Medrol, drew it up in a syringe then questioned by the solution was clear.</p> <p>The medication was never administered to the patient. This was the lesser of the two mix-up errors that could occur with this labeling. The more serious error would have been Depo-Medrol in with metoclopramide then given inadvertently IV to a patient. Sikor should change their labeling to prevent further Look-Alike mixups.</p> <p>Please see my follow up e-mail with an attached photo of the two vials.</p>
<p>5546238-1 12/06/2007</p>	<p>Metoclopramide injection and Enalaprilat injection</p> <p>Error never reached the patient</p>	<p>Metoclopramide injection 5 mg/mL 2 mL single dose vial manufactured by Hospira and Enalaprilat injection 1.25 mg/mL 1 mL single dose vial manufactured by Bedford Labs. Flip tops are both green, almost identical in color.</p> <p>Enalaprilat vial is visually smaller than Metoclopramide vial. Enalaprilat vial has orange lines above and below the drug name as the concentration highlighted in orange. The Metoclopramide vial had black lettering on a white background.</p> <p>Submitted via ISMP</p> <p>Neither error reached a patient.</p>
<p>5545443-8 12/06/2007</p>	<p>Metoclopramide injection and Methylprednisolone injection</p> <p>Error never reached the patient</p>	<p>Attached are excerpts of a medication error filed at our facility. "Tonight we got a call from an ICU nurse that there were generic Depo-Medrol 80 mg vials (NDC 00703-0051-01) mixed in with the generic Reglan injectables (NDC 00703-4502-04) in the Pyxis.</p> <p>Regardless, both vials look remarkably alike and are stored 2 shelves apart, one on top of the other. Another issue is the box that the medications listed above come in. Both are white with pink on them. In our case, the methylprednisolone vials were put away wrong and missed by the tech that pulled, the pharmacist that checked the refill and the tech that stocked the Pyxis.</p> <p>Submitted via ISMP</p> <p>Unknown. There were generic Depo-Medrol 80 mg vials (NDC 00703-0051-01) mixed in with the generic Reglan injectables (NDC 00703-4502-04) in the Pyxis.</p> <p>Regardless, both vials look remarkably alike and are stored 2 shelves apart, one on top of the other. Another issue is the box that the medications listed above come in. Both are white with pink on them.</p>

<p>5585602-1 01/08/2008</p>	<p>Metoclopramide injection and Fosphenytoin injection</p> <p>No reported outcome</p>	<p>Generic fosphenytoin vials were used to prepare dilutions instead of metoclopramide vials. Generic fosphenytoin vials look very similar to metoclopramide.</p>
<p>5610687-3 01/31/2008</p>	<p>Metoclopramide injection and Fosphenytoin injection</p> <p>No reported outcome</p>	<p>I work at a level one trauma center affiliated with a medical college. I received a phone call this AM from a RN in our L&amp;D department. It appears a Fosphenytoin 100 mg. PE vial made it into the Metoclopramide 10 mg injection bin. After further review we have determined that these two vials are nearly identical.</p> <p>The Metoclopramide (Hospira, NDC 0409-3414-01) and Fosphenytoin (Hospira, NDC 0409-4857-02) are the same size, have the same color lid, and have black and green writing.</p> <p>Forwarded via ISMP</p> <p>It appears that the Fosphenytoin was inadvertently placed in the wrong bin in our pick station and was missed during the fill and check process. After further review we have determined that these two vials are nearly identical.</p> <p>The Metoclopramide (Hospira, NDC 0409-3414-01) and Fosphenytoin (Hospira, NDC 0409-4857-02) are the same size, have the same color lid, and have black and green writing.</p>

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DRUG SAFETY OFFICE REVIEWER

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