CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022424Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

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

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

Date of This Review:	March 9, 2015
Application Type and Number:	NDA 022424
Product Name and Strength:	Flowtuss (Hydrocodone Bitartrate/Guaifenesin) Oral Solution 2.5 mg/200 mg per 5 mL
Product Type:	Single Ingredient Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Mikart, Inc.
Panorama #:	2015-46934
DMEPA Primary Reviewer:	Teresa McMillan, PharmD
DMEPA Team Leader:	Kendra Worthy, PharmD
DMEPA Associate Director:	Lubna Merchant, MS, PharmD

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Flowtuss, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively. The Applicant submitted an external name study, conducted (b) (4) for this product.

1.1 REGULATORY HISTORY

The Applicant previously submitted the proposed proprietary name, Flowtuss on May 16, 2011. The Division of Medication Error Prevention and Analysis (DMEPA) found the name, Flowtuss acceptable in OSE Review #2011-2070, 2001-31, dated August 8, 2011. However, the application received a Complete Response on November 29, 2011.

Thus, the Applicant resubmitted the name, Flowtuss, for review on January 13, 2015. In addition, the proposed proprietary name, Flowtuss has the same product characteristics (i.e. active ingredients, indication of use, route of administration, dosage form, strength, dose and frequency) as the marketed product Obredon (hydrocodone and guaifenesin).

1.2 PRODUCT INFORMATION

The following product information is provided in the January 13, 2015 proprietary name submission.

- Intended Pronunciation: flow-tuss
- Schedule: C-II
- Active Ingredient: hydrocodone and guaifenesin
- Indication of Use: Symptomatic relief of cough and to loosen mucus associated with the common cold.
- Route of Administration: Oral
- Dosage Form: Solution
- Strength: 2.5 mg/200 mg per 5 mL
- Dose and Frequency: Adults and adolescents 18 years of age and older: 10 mL every 4 to 6 hours, not to exceed 6 doses (60 mL) in 24 hours
- How Supplied:
- Storage: 20° to 25°C (68° to 77°F)
- Container and Closure Systems:

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that the proposed name would not misbrand the proposed product. DMEPA and the Division of Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) concurred with the findings of OPDP's assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proprietary name[1].

2.2.2 Components of the Proposed Proprietary Name

The Applicant indicated in their submission that the proposed name, Flowtuss, is derived from the indication proposed based on the primary action of the active ingredients included in the product formulation (Hydrocodone Bitartrate and Guaifenesin). This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.4 FDA Name Simulation Studies

Eighty seven practitioners participated in DMEPA's prescription studies. Two responses from the voice study, Lotel and Clopress, look similar to currently marketed products, Lotrel and Clopres (names evaluated in appendices C through H). Forty-nine participants interpreted the name correctly as "Flowtuss". The remaining participants provided incorrect responses. The remaining misinterpretations occurred with the letter 'F' being misinterpreted for the letters 'C', 'S', or L, the letter 'l' for the letter 'o' or was omitted, the letter 'w' for the letter 'u' and the letter strings 'ru', 'ven', 've', and 'or', the letter 't' for the letter 'p', the letter 'u' for the letters 'e', 'c', or the letter string 're', the letter 's' for the letters 'l', 'c', and the letter 's' for the letter 'h' or was omitted. Appendix B contains the results from the verbal and written prescription studies.

2.2.5 Comments from Other Review Disciplines at Initial Review

In response to the OSE, January 21, 2015 e-mail, the Division of Medication Error Prevention and Analysis (DMEPA) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.6 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Table 1 lists the number of names with the combined orthographic and phonetic score of ≥50% retrieved from our POCA search[2] organized as highly similar, moderately similar

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[1]USAN stem search conducted on 2/4/15.

[2] POCA search conducted on 2/4/15.

or low similarity for further evaluation. Table 1 also includes names identified from the external name study (b) (4)

Table 1. POCA Search Results	Number of Names
Highly similar name pair: combined match percentage score ≥70%	6
Moderately similar name pair: combined match percentage score ≥50% to ≤ 69%	95
Low similarity name pair: combined match percentage score ≤49%	6

2.2.7 Safety Analysis of Names with Potential Orthographic, Spelling, and Phonetic Similarities

Our analysis of the 107 names contained in Table 1 determined none of the names will pose a risk for confusion as described in Appendices C through H.

2.2.8 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Medication Error Prevention and Analysis (DPARP) via e-mail on March 2, 2015. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DPARP on March 2, 2015, they stated no additional concerns with the proposed proprietary name, Flowtuss.

3 CONCLUSIONS

The proposed proprietary name is acceptable.

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

3.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your January 13, 2015 submission are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

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

   USAN Stems List contains all the recognized USAN stems.

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

POCA is a system that FDA designed. As part of the name similarity assessment, POCA is used to evaluate proposed names via a phonetic and orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists that operates in a similar fashion. POCA is publicly accessible.

Drugs@FDA

Drugs@FDA is an FDA Web site that contains most of the drug products approved in the United States 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*; *therapeutic biological products*, *prescription* and *over-the-counter* human drugs; and *discontinued drugs* (see Drugs @ FDA Glossary of Terms, available at http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther_biological).

RxNorm

RxNorm contains the names of prescription and many OTC drugs available in the United States. RxNorm includes generic and branded:

- Clinical drugs – pharmaceutical products given to (or taken by) a patient with therapeutic or diagnostic intent
- Drug packs – packs that contain multiple drugs, or drugs designed to be administered in a specified sequence

Radiopharmaceuticals, contrast media, food, dietary supplements, and medical devices, such as bandages and crutches, are all out of scope for RxNorm (http://www.nlm.nih.gov/research/umls/rxnorm/overview.html#).

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.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment evaluates proposed proprietary names for misbranding and safety concerns.

1. **Misbranding Assessment**: For prescription drug products, OPDP assesses the name for misbranding concerns. . For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNCE. OPDP or DNCE evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNCE provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment**: The safety assessment is conducted by DMEPA, and includes the following:

a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [3]

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

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

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
Y/N	**Is the proposed name obviously similar in spelling and pronunciation to other names?**
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	**Are there medical and/or coined abbreviations in the proprietary name?**
	Proprietary names should not incorporate medical abbreviations (e.g., QD, BID, or others commonly used for prescription communication) or coined abbreviations that have no established meaning.
Y/N	**Are there inert or inactive ingredients referenced in the proprietary name?**
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
Y/N	**Does the proprietary name include combinations of active ingredients?**
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
Y/N	**Is there a United States Adopted Name (USAN) stem in the proprietary name?**
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
Y/N	**Is this proprietary name used for another product that does not share at least one common active ingredient?**
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	**Is this a proprietary name of a discontinued product?**
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

b. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@fda, CernerRxNorm, and names in the review pipeline using a 50% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:

- Highly similar pair: combined match percentage score ≥70%.
- Moderately similar pair: combined match percentage score ≥50% to ≤ 69%.
- Low similarity: combined match percentage score ≤49%.

Using the criteria outlined in the check list (Table 3-5) that corresponds to each of the three categories (highly similar pair, moderately similar pair, and low similarity), DMEPA evaluates the name pairs to determine the acceptability or non-acceptability of a proposed proprietary name. The intent of these checklists is to increase the transparency and predictability of the safety determination of whether a proposed name is vulnerable to confusion from a look-alike or sound-alike perspective. Each bullet below corresponds to the name similarity category cross-references the respective table that addresses criteria that DMEPA uses to determine whether a name presents a safety concern from a look-alike or sound-alike perspective.

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 3).
- Moderately similar names with overlapping or similar strengths or doses represent an area for concern for FDA. The dosage and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and it can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form, etc.) may be limited when the strength or dose overlaps. We review such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).
- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

c. FDA Prescription Simulation Studies: DMEPA staff also conducts a prescription simulation studies using FDA health care professionals.

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

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

d. Comments from Other Review Disciplines: DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

   The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

   Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name.

Table 3. Highly Similar Name Pair Checklist (i.e., combined Orthographic and Phonetic score is ≥ 70%).

Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion, provided that the pair do not share a common strength or dose.			
Orthographic Checklist		Phonetic Checklist	
Y/N	Do the names begin with different first letters? *Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.*	**Y/N**	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar* when scripted? **FDA considers the length of names different if the names differ by two or more letters.*	**Y/N**	Do the names have different syllabic stresses?
Y/N	Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names?	**Y/N**	Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?
Y/N	Is there different number or placement of cross-stroke or dotted letters present in the names?	**Y/N**	Across a range of dialects, are the names consistently pronounced differently?
Y/N	Do the infixes of the name appear dissimilar when scripted?		
Y/N	Do the suffixes of the names appear dissimilar when scripted?		

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is ≥50% to ≤69%).

Step 1	Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation. For single strength products, also consider circumstances where the strength may not be expressed. For any i.e. drug products comprised of more than one active ingredient, consider whether the strength or dose may be expressed using only one of the components. To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion: o Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa. o Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. o Similar sounding doses: 15 mg is similar in sound to 50 mg
Step 2	Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names **with** overlapping or similar strengths or doses.

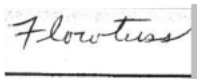
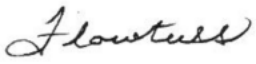
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length of names different if the names differ by two or more letters. • Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names? • Is there different number or placement of cross-stroke or dotted letters present in the names? • Do the infixes of the name appear dissimilar when scripted? • Do the suffixes of the names appear dissimilar when scripted?	Phonetic Checklist (Y/N to each question) • Do the names have different number of syllables? • Do the names have different syllabic stresses? • Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?

Table 5: Low Similarity Name Pair Checklist (i.e., combined score is ≤49%).

In most circumstances, these names are viewed as sufficiently different to minimize confusion. Exceptions to this would occur in circumstances where, for example, there are data that suggest a name with low similarity is nonetheless misinterpreted as a marketed product name in a prescription simulation study. In such instances, FDA would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

Appendix B: Prescription Simulation Samples and Results

Figure 1. Flowtuss Study (Conducted on 1/23/15)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order:  (b) (4)	Flowtuss (b) (4) (b) (4)
Outpatient Prescription:  (b) (4)	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

252 People Received Study

87 People Responded

Study Name: Flowtuss

Total	31	24	32	-
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
CLOPRESS	0	1	0	1
FLORUTUSS	0	0	1	1
FLOTASH	0	1	0	1
FLOTOSH	0	2	0	2
FLOTOUCH	0	2	0	2
FLOTUS	0	1	0	1
FLOTUSH	0	2	0	2
FLOTUSS	1	5	0	6
FLO-TUSS	0	1	0	1
FLOUTUSS	1	0	0	1
FLOVENTUSS	0	0	1	1
FLOVETUSS	1	0	0	1
FLOW TUSS	1	0	0	1
FLOWTESS	0	0	1	1

FLOWTRESS	**0**	**0**	**1**	**1**
FLOWTUSS	**25**	**1**	**28**	**54**
FLOWTUSS TAKE 10ML PO Q4H	**1**	**0**	**0**	**1**
FLUORTUSS	**1**	**0**	**0**	**1**
FOLTUS	**0**	**1**	**0**	**1**
LOTEL	**0**	**1**	**0**	**1**
SLO-PRESS	**0**	**1**	**0**	**1**
SLOTOUCH	**0**	**1**	**0**	**1**
SLOTUSH	**0**	**1**	**0**	**1**
SLOTUSS	**0**	**1**	**0**	**1**
SLOWTUSH	**0**	**1**	**0**	**1**
SLOWTUSS	**0**	**1**	**0**	**1**

Appendix C: Highly Similar Names (e.g., combined POCA score is ≥70%)

No.	**Proposed name:** Flowtuss **Established name:** Hydrocodone Bitartrate/Guaifenesin **Dosage form:** Oral Solution **Strength(s):** 2.5 mg/200 mg per 5 mL **Usual Dose:** 10 mL every 4 to 6 hours, not to exceed 6 doses (60 mL) in 24 hours	**POCA Score (%)**	**Orthographic and/or phonetic differences in the names sufficient to prevent confusion** **Other prevention of failure mode expected to minimize the risk of confusion between these two names.**
1.	Flowtuss	100	This name is the subject of this review.
2.	Chlo Tuss	73 combined/ 79- phonetic only	In this particular situation, we determined the differences in scheduling (CII vs OTC), along with minor differences in the prefix sound should sufficiently reduce the potential for confusion between these products. In addition, per ISMP there is no reported name confusion between "F" and "C" names.
3.	Solotuss	73 combined / 79- phonetic only	In this particular situation, we determined the orthographic differences in the prefix and the phonetic differences of the first syllable of this name pair should sufficiently reduce the potential for confusion between these products. This product has also been discontinued.
4.	(b) (4) ***	70 combined /81- orthographic only	Name found unacceptable in OSE Review (b) (4) The application is still pending and another name hasn't been submitted to date.
5.	(b) (4) ***	70 combined /81- orthographic only	IND 076365 found unacceptable in OSE Review (b) (4) The application is still pending and another name hasn't been submitted to date.

6.	(b) (4) ***	70 combined /73- phonetic only	Proposed proprietary name found unacceptable by DMEPA (OSE Review (b) (4)).Application was withdrawn (b) (4)

Appendix D: Moderately Similar Names (e.g., combined POCA score is ≥50% to ≤69%) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
1.	Flovent	57
2.	Fluonid	52
3.	Zortress	52
4.	Flagyl S	51
5.	Floxin	50
6.	Fluotrex	50
7.	Fluxid	50
8.	Hycotuss	50

Appendix E: Moderately Similar Names (e.g., combined POCA score is ≥50% to ≤69%) with overlap or numerical similarity in Strength and/or Dose

No.	**Proposed name:** Flowtuss **Established name:** Hydrocodone Bitartrate/Guaifenesin **Dosage form:** Oral Solution **Strength(s):** 2.5 mg/200 mg per 5 mL **Usual Dose:** 10 mL every 4 to 6 hours, not to exceed 6 doses (60 mL) in 24 hours	**POCA Score (%)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
1.	Fluocet	62/77-phonetic	The suffixes of this name pair have sufficient orthographic differences The third syllables of this name pair sound different and contain an extra syllable.
2.	Fluex	55/70	The suffixes of this name pair have sufficient orthographic differences. The third syllables of this name pair sound different.
3.	Protuss	68	The prefixes of this name pair have sufficient orthographic differences The first syllables of this name pair sound different.
4.	Pro Tuss	68	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
5.	Glytuss	64	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
6.	Trituss	61	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.

7.	Zonatuss	61	The prefixes and infixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different and contain an extra syllable.
8.	Fentuss	60	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
9.	Protuss D	60	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
10.	Codotuss	58	The prefixes and infixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different and contain an extra syllable.
11.	Flonase	58	The suffixes of this name pair have sufficient orthographic differences. The second syllables of this name pair sound different.
12.	Lortuss HC	58	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
13.	Lotussin	58	The suffixes of this name pair have sufficient orthographic differences. The third syllables of this name pair sound different contain an extra syllable.
14.	Lortuss DM	57	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
15.	Lortuss LQ	57	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.

16.	Certuss	56	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
17.	Coldtuss	56	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
18.	Exo-Tuss	56	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
19.	Liquituss	56	The prefixes and infixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different and contain an extra syllable.
20.	flomax	55	The suffixes of this name pair have sufficient orthographic differences. The second syllables of this name pair sound different.
21.	Phanatuss	55	The prefixes and infixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different and contain an extra syllable.
22.	(b) (4)	55	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
23.	Foltabs	54	The prefixes and suffixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different.
24.	Fortabs	54	The prefixes and suffixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different.

25.	Sudatuss 2	54	The prefixes and infixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different and contain an extra syllable.
26.	Trituss A	54	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
27.	Flatulex	52	The infixes and suffixes of this name pair have sufficient orthographic differences. The second and third syllables of this name pair sound different and contain an extra syllable.
28.	Lortuss EX	52	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
29.	Protuss DM	52	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
30.	(b) (4) ***	52	The prefixes and infixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different and contain an extra syllable.
31.	Ru-Tuss	52	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
32.	Poly-Tussin	51	The prefixes and infixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different and contain two extra syllables.

33.	Quartuss	51	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
34.	Cotuss-V	50	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
35.	Duratuss	50	The prefixes and infixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different and contain an extra syllable.
36.	Dytuss	50	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
37.	Exetuss	50	The prefixes and infixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different and contain an extra syllable.
38.	Flector	50	The prefixes and suffixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different.
39.	flo-Pred	50	The suffixes of this name pair have sufficient orthographic differences. The second syllables of this name pair sound different.

Appendix F: Low Similarity Names (e.g., combined POCA score is ≤49%)

No.	Name	POCA Score (%)
1.	Guiatuss	48
2.	Flowaway	46
3.	Clopres	46
4.	Robitussin	40
5.	Lotrel	40
6.	Fentora	28

Appendix G: Names not likely to be confused or not used in usual practice settings for the reasons described.

No.	Name	POCA Score (%)	Failure preventions
1.	Mallotuss	68/71-orthographic	Name found in RxNorm. No product characteristics available in common drug references.
2.	FluTuss HC	68	Discontinued product with no generic equivalents.
3.	Flutuss XP	60	Discontinued product with no generic equivalents.
4.	Rolatuss	60	Discontinued product with no generic equivalents
5.	Brontuss	59	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
6.	Bron-Tuss	59	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
7.	Contuss	56	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.

8.	P Tuss	56/70-orthograhic only	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
9.	Penntuss	56	Product was withdrawn Federal Register effective August 5,1996.
10.	Vicotuss	56	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
11.	Z Tuss	56/70-orthograhic only	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
12.	ZTuss	56/70-orthograhic only	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
13.	Sorbutuss	55	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
14.	Neotuss	54	Discontinued with no generic equivalents.
15.	Panatuss	54	Discontinued with no generic equivalents.
16.	Pedituss	54	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.

17.	Primatuss 4	54	Discontinued with no generic equivalents.
18.	Ventuss	54	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
19.	Ferro DSS	53	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
20.	Notuss	53	Discontinued product with no generic equivalents.
21.	Ricotuss	53	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
22.	XiraTuss	53	Discontinued product with no generic equivalents.
23.	Bronkotuss	52	Discontinued product with no generic equivalents.
24.	Endotuss	52	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
25.	Nasotuss	52	Discontinued product with no generic equivalents.
26.	Nucotuss	52	Discontinued product with no generic equivalents.
27.	Oratuss	52	International drug not marketed in the US

28.	Oratuss 12	52	International drug not marketed in the US
29.	Rutuss	52	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
30.	Coughtuss	51	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
31.	Vistuss	51	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
32.	Dia-Tuss	50	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
33.	Ferrous DS	50	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
34.	Fluidil	50	Product was withdrawn Federal Register effective 2/9/1987.
35.	Fluothane	50	Product was withdrawn Federal Register effective 9/17/03.
36.	Ry-Tuss	50	Discontinued product with no generic equivalents

37.	Spec-tuss	50	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
38.	Vi Q Tuss	50	Discontinued product with no generic equivalents
39.	Z-Tuss E	50	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.

Appendix H: Names not likely to be confused due to notable spelling, orthographic and phonetic differences.

No.	Name	POCA Score (%)
1.	Pelodis	57
2.	Lantus	56
3.	Klorvess	54
4.	(b) (4)***	54
5.	Latisse	52
6.	Pluset	51
7.	1 Plus 1 F	50
8.	(b) (4)	50
9.	Selenos	50

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

/s/

TERESA S MCMILLAN
03/09/2015

KENDRA C WORTHY
03/09/2015

LUBNA A MERCHANT
03/09/2015

PROPRIETARY NAME REVIEW

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

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

Date of This Review:	March 9, 2015
Application Type and Number:	NDA 022424
Product Name and Strength:	Flowtuss (Hydrocodone Bitartrate/Guaifenesin) Oral Solution 2.5 mg/200 mg per 5 mL
Product Type:	Single Ingredient Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Mikart, Inc.
Panorama #:	2015-46934
DMEPA Primary Reviewer:	Teresa McMillan, PharmD
DMEPA Team Leader:	Kendra Worthy, PharmD
DMEPA Associate Director:	Lubna Merchant, MS, PharmD

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Flowtuss, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively. The Applicant submitted an external name study, conducted [redacted] (b) (4) for this product.

1.1 REGULATORY HISTORY

The Applicant previously submitted the proposed proprietary name, Flowtuss on May 16, 2011. The Division of Medication Error Prevention and Analysis (DMEPA) found the name, Flowtuss acceptable in OSE Review #2011-2070, 2001-31, dated August 8, 2011. However, the application received a Complete Response on November 29, 2011.

Thus, the Applicant resubmitted the name, Flowtuss, for review on January 13, 2015. In addition, the proposed proprietary name, Flowtuss has the same product characteristics (i.e. active ingredients, indication of use, route of administration, dosage form, strength, dose and frequency) as the marketed product Obredon (hydrocodone and guaifenesin).

1.2 PRODUCT INFORMATION

The following product information is provided in the January 13, 2015 proprietary name submission.

- Intended Pronunciation: flow-tuss
- Schedule: C-II
- Active Ingredient: hydrocodone and guaifenesin
- Indication of Use: Symptomatic relief of cough and to loosen mucus associated with the common cold.
- Route of Administration: Oral
- Dosage Form: Solution
- Strength: 2.5 mg/200 mg per 5 mL
- Dose and Frequency: Adults and adolescents 18 years of age and older: 10 mL every 4 to 6 hours, not to exceed 6 doses (60 mL) in 24 hours
- How Supplied:
- Storage: 20° to 25°C (68° to 77°F)
- Container and Closure Systems:

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that the proposed name would not misbrand the proposed product. DMEPA and the Division of Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) concurred with the findings of OPDP's assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proprietary name[1].

2.2.2 Components of the Proposed Proprietary Name

The Applicant indicated in their submission that the proposed name, Flowtuss, is derived from the indication proposed based on the primary action of the active ingredients included in the product formulation (Hydrocodone Bitartrate and Guaifenesin). This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.4 FDA Name Simulation Studies

Eighty seven practitioners participated in DMEPA's prescription studies. Two responses from the voice study, Lotel and Clopress, look similar to currently marketed products, Lotrel and Clopres (names evaluated in appendices C through H). Forty-nine participants interpreted the name correctly as "Flowtuss". The remaining participants provided incorrect responses. The remaining misinterpretations occurred with the letter 'F' being misinterpreted for the letters 'C', 'S', or L, the letter 'l' for the letter 'o' or was omitted, the letter 'w' for the letter 'u' and the letter strings 'ru', 'ven', 've', and 'or', the letter 't' for the letter 'p', the letter 'u' for the letters 'e', 'c', or the letter string 're', the letter 's' for the letters 'l', 'c', and the letter 's' for the letter 'h' or was omitted. Appendix B contains the results from the verbal and written prescription studies.

2.2.5 Comments from Other Review Disciplines at Initial Review

In response to the OSE, January 21, 2015 e-mail, the Division of Medication Error Prevention and Analysis (DMEPA) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.6 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Table 1 lists the number of names with the combined orthographic and phonetic score of ≥50% retrieved from our POCA search[2] organized as highly similar, moderately similar

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[1]USAN stem search conducted on 2/4/15.

[2] POCA search conducted on 2/4/15.

or low similarity for further evaluation. Table 1 also includes names identified from the external name study [redacted] (b) (4)

Table 1. POCA Search Results	Number of Names
Highly similar name pair: combined match percentage score ≥70%	6
Moderately similar name pair: combined match percentage score ≥50% to ≤ 69%	95
Low similarity name pair: combined match percentage score ≤49%	6

2.2.7 Safety Analysis of Names with Potential Orthographic, Spelling, and Phonetic Similarities

Our analysis of the 107 names contained in Table 1 determined none of the names will pose a risk for confusion as described in Appendices C through H.

2.2.8 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Medication Error Prevention and Analysis (DPARP) via e-mail on March 2, 2015. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DPARP on March 2, 2015, they stated no additional concerns with the proposed proprietary name, Flowtuss.

3 CONCLUSIONS

The proposed proprietary name is acceptable.

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

3.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your January 13, 2015 submission are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

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

   USAN Stems List contains all the recognized USAN stems.

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

POCA is a system that FDA designed. As part of the name similarity assessment, POCA is used to evaluate proposed names via a phonetic and orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists that operates in a similar fashion. POCA is publicly accessible.

Drugs@FDA

Drugs@FDA is an FDA Web site that contains most of the drug products approved in the United States 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*; *therapeutic biological products*, *prescription* and *over-the-counter* human drugs; and *discontinued drugs* (see Drugs @ FDA Glossary of Terms, available at http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther_biological).

RxNorm

RxNorm contains the names of prescription and many OTC drugs available in the United States. RxNorm includes generic and branded:

- Clinical drugs – pharmaceutical products given to (or taken by) a patient with therapeutic or diagnostic intent
- Drug packs – packs that contain multiple drugs, or drugs designed to be administered in a specified sequence

Radiopharmaceuticals, contrast media, food, dietary supplements, and medical devices, such as bandages and crutches, are all out of scope for RxNorm (http://www.nlm.nih.gov/research/umls/rxnorm/overview.html#).

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.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment evaluates proposed proprietary names for misbranding and safety concerns.

1. **Misbranding Assessment**: For prescription drug products, OPDP assesses the name for misbranding concerns. . For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNCE. OPDP or DNCE evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNCE provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment**: The safety assessment is conducted by DMEPA, and includes the following:

a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [3]

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

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

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
Y/N	**Is the proposed name obviously similar in spelling and pronunciation to other names?**
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	**Are there medical and/or coined abbreviations in the proprietary name?**
	Proprietary names should not incorporate medical abbreviations (e.g., QD, BID, or others commonly used for prescription communication) or coined abbreviations that have no established meaning.
Y/N	**Are there inert or inactive ingredients referenced in the proprietary name?**
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
Y/N	**Does the proprietary name include combinations of active ingredients?**
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
Y/N	**Is there a United States Adopted Name (USAN) stem in the proprietary name?**
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
Y/N	**Is this proprietary name used for another product that does not share at least one common active ingredient?**
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	**Is this a proprietary name of a discontinued product?**
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

b. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@fda, CernerRxNorm, and names in the review pipeline using a 50% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:

- Highly similar pair: combined match percentage score ≥70%.
- Moderately similar pair: combined match percentage score ≥50% to ≤ 69%.
- Low similarity: combined match percentage score ≤49%.

Using the criteria outlined in the check list (Table 3-5) that corresponds to each of the three categories (highly similar pair, moderately similar pair, and low similarity), DMEPA evaluates the name pairs to determine the acceptability or non-acceptability of a proposed proprietary name. The intent of these checklists is to increase the transparency and predictability of the safety determination of whether a proposed name is vulnerable to confusion from a look-alike or sound-alike perspective. Each bullet below corresponds to the name similarity category cross-references the respective table that addresses criteria that DMEPA uses to determine whether a name presents a safety concern from a look-alike or sound-alike perspective.

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 3).
- Moderately similar names with overlapping or similar strengths or doses represent an area for concern for FDA. The dosage and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and it can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form, etc.) may be limited when the strength or dose overlaps. We review such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).
- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

c. FDA Prescription Simulation Studies: DMEPA staff also conducts a prescription simulation studies using FDA health care professionals.

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

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

d. Comments from Other Review Disciplines: DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

   The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

   Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name.

Table 3. Highly Similar Name Pair Checklist (i.e., combined Orthographic and Phonetic score is ≥ 70%).

Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion, provided that the pair do not share a common strength or dose.			
Orthographic Checklist		Phonetic Checklist	
Y/N	Do the names begin with different first letters? *Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.*	Y/N	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar* when scripted? **FDA considers the length of names different if the names differ by two or more letters.*	Y/N	Do the names have different syllabic stresses?
Y/N	Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names?	Y/N	Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?
Y/N	Is there different number or placement of cross-stroke or dotted letters present in the names?	Y/N	Across a range of dialects, are the names consistently pronounced differently?
Y/N	Do the infixes of the name appear dissimilar when scripted?		
Y/N	Do the suffixes of the names appear dissimilar when scripted?		

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is ≥50% to ≤69%).

Step 1	Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation. For single strength products, also consider circumstances where the strength may not be expressed. For any i.e. drug products comprised of more than one active ingredient, consider whether the strength or dose may be expressed using only one of the components. To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion: o Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa. o Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. o Similar sounding doses: 15 mg is similar in sound to 50 mg
Step 2	Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names **with** overlapping or similar strengths or doses.

	Orthographic Checklist (Y/N to each question)	Phonetic Checklist (Y/N to each question)
	• Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length of names different if the names differ by two or more letters. • Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names? • Is there different number or placement of cross-stroke or dotted letters present in the names? • Do the infixes of the name appear dissimilar when scripted? • Do the suffixes of the names appear dissimilar when scripted?	• Do the names have different number of syllables? • Do the names have different syllabic stresses? • Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?

Table 5: Low Similarity Name Pair Checklist (i.e., combined score is ≤49%).

In most circumstances, these names are viewed as sufficiently different to minimize confusion. Exceptions to this would occur in circumstances where, for example, there are data that suggest a name with low similarity is nonetheless misinterpreted as a marketed product name in a prescription simulation study. In such instances, FDA would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

Appendix B: Prescription Simulation Samples and Results

Figure 1. Flowtuss Study (Conducted on 1/23/15)

Handwritten Requisition Medication Order	**Verbal Prescription**
Medication Order: Flowtuss (b) (4)	Flowtuss (b) (4)
Outpatient Prescription: Flowtuss (b) (4)	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

252 People Received Study

87 People Responded

Study Name: Flowtuss

Total	31	24	32	-
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
CLOPRESS	0	1	0	1
FLORUTUSS	0	0	1	1
FLOTASH	0	1	0	1
FLOTOSH	0	2	0	2
FLOTOUCH	0	2	0	2
FLOTUS	0	1	0	1
FLOTUSH	0	2	0	2
FLOTUSS	1	5	0	6
FLO-TUSS	0	1	0	1
FLOUTUSS	1	0	0	1
FLOVENTUSS	0	0	1	1
FLOVETUSS	1	0	0	1
FLOW TUSS	1	0	0	1
FLOWTESS	0	0	1	1

FLOWTRESS	0	0	1	1
FLOWTUSS	25	1	28	54
FLOWTUSS TAKE 10ML PO Q4H	1	0	0	1
FLUORTUSS	1	0	0	1
FOLTUS	0	1	0	1
LOTEL	0	1	0	1
SLO-PRESS	0	1	0	1
SLOTOUCH	0	1	0	1
SLOTUSH	0	1	0	1
SLOTUSS	0	1	0	1
SLOWTUSH	0	1	0	1
SLOWTUSS	0	1	0	1

Appendix C: Highly Similar Names (e.g., combined POCA score is ≥70%)

No.	**Proposed name:** Flowtuss **Established name:** Hydrocodone Bitartrate/Guaifenesin **Dosage form:** Oral Solution **Strength(s):** 2.5 mg/200 mg per 5 mL **Usual Dose:** 10 mL every 4 to 6 hours, not to exceed 6 doses (60 mL) in 24 hours	**POCA Score (%)**	**Orthographic and/or phonetic differences in the names sufficient to prevent confusion** **Other prevention of failure mode expected to minimize the risk of confusion between these two names.**
1.	Flowtuss	100	This name is the subject of this review.
2.	Chlo Tuss	73 combined/ 79-phonetic only	In this particular situation, we determined the differences in scheduling (CII vs OTC), along with minor differences in the prefix sound should sufficiently reduce the potential for confusion between these products. In addition, per ISMP there is no reported name confusion between "F" and "C" names.
3.	Solotuss	73 combined / 79-phonetic only	In this particular situation, we determined the orthographic differences in the prefix and the phonetic differences of the first syllable of this name pair should sufficiently reduce the potential for confusion between these products. This product has also been discontinued.
4.	(b) (4) ***	70 combined /81-orthographic only	Name found unacceptable in OSE Review (b) (4) (b) (4) The application is still pending and another name hasn't been submitted to date.
5.	(b) (4) ***	70 combined /81-orthographic only	IND 076365 found unacceptable in OSE Review (b) (4) (b) (4) The application is still pending and another name hasn't been submitted to date.

6.	(b) (4) ***	70 combined /73- phonetic only	Proposed proprietary name found unacceptable by DMEPA (OSE Review (b) (4) (b) (4)). Application was withdrawn (b) (4)

Appendix D: Moderately Similar Names (e.g., combined POCA score is ≥50% to ≤69%) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
1.	Flovent	57
2.	Fluonid	52
3.	Zortress	52
4.	Flagyl S	51
5.	Floxin	50
6.	Fluotrex	50
7.	Fluxid	50
8.	Hycotuss	50

Appendix E: Moderately Similar Names (e.g., combined POCA score is ≥50% to ≤69%) with overlap or numerical similarity in Strength and/or Dose

No.	**Proposed name:** Flowtuss **Established name:** Hydrocodone Bitartrate/Guaifenesin **Dosage form:** Oral Solution **Strength(s):** 2.5 mg/200 mg per 5 mL **Usual Dose:** 10 mL every 4 to 6 hours, not to exceed 6 doses (60 mL) in 24 hours	POCA Score (%)	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
1.	Fluocet	62/77-phonetic	The suffixes of this name pair have sufficient orthographic differences The third syllables of this name pair sound different and contain an extra syllable.
2.	Fluex	55/70	The suffixes of this name pair have sufficient orthographic differences. The third syllables of this name pair sound different.
3.	Protuss	68	The prefixes of this name pair have sufficient orthographic differences The first syllables of this name pair sound different.
4.	Pro Tuss	68	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
5.	Glytuss	64	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
6.	Trituss	61	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.

7.	Zonatuss	61	The prefixes and infixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different and contain an extra syllable.
8.	Fentuss	60	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
9.	Protuss D	60	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
10.	Codotuss	58	The prefixes and infixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different and contain an extra syllable.
11.	Flonase	58	The suffixes of this name pair have sufficient orthographic differences. The second syllables of this name pair sound different.
12.	Lortuss HC	58	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
13.	Lotussin	58	The suffixes of this name pair have sufficient orthographic differences. The third syllables of this name pair sound different contain an extra syllable.
14.	Lortuss DM	57	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
15.	Lortuss LQ	57	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.

16.	Certuss	56	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
17.	Coldtuss	56	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
18.	Exo-Tuss	56	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
19.	Liquituss	56	The prefixes and infixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different and contain an extra syllable.
20.	flomax	55	The suffixes of this name pair have sufficient orthographic differences. The second syllables of this name pair sound different.
21.	Phanatuss	55	The prefixes and infixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different and contain an extra syllable.
22.	(b) (4)	55	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
23.	Foltabs	54	The prefixes and suffixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different.
24.	Fortabs	54	The prefixes and suffixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different.

25.	Sudatuss 2	54	The prefixes and infixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different and contain an extra syllable.
26.	Trituss A	54	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
27.	Flatulex	52	The infixes and suffixes of this name pair have sufficient orthographic differences. The second and third syllables of this name pair sound different and contain an extra syllable.
28.	Lortuss EX	52	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
29.	Protuss DM	52	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
30.	(b) (4) ***	52	The prefixes and infixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different and contain an extra syllable.
31.	Ru-Tuss	52	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
32.	Poly-Tussin	51	The prefixes and infixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different and contain two extra syllables.

33.	Quartuss	51	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
34.	Cotuss-V	50	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
35.	Duratuss	50	The prefixes and infixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different and contain an extra syllable.
36.	Dytuss	50	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
37.	Exetuss	50	The prefixes and infixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different and contain an extra syllable.
38.	Flector	50	The prefixes and suffixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different.
39.	flo-Pred	50	The suffixes of this name pair have sufficient orthographic differences. The second syllables of this name pair sound different.

Appendix F: Low Similarity Names (e.g., combined POCA score is ≤49%)

No.	Name	POCA Score (%)
1.	Guiatuss	48
2.	Flowaway	46
3.	Clopres	46
4.	Robitussin	40
5.	Lotrel	40
6.	Fentora	28

Appendix G: Names not likely to be confused or not used in usual practice settings for the reasons described.

No.	Name	POCA Score (%)	Failure preventions
1.	Mallotuss	68/71-orthographic	Name found in RxNorm. No product characteristics available in common drug references.
2.	FluTuss HC	68	Discontinued product with no generic equivalents.
3.	Flutuss XP	60	Discontinued product with no generic equivalents.
4.	Rolatuss	60	Discontinued product with no generic equivalents
5.	Brontuss	59	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
6.	Bron-Tuss	59	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
7.	Contuss	56	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.

8.	P Tuss	56/70-orthograhic only	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
9.	Penntuss	56	Product was withdrawn Federal Register effective August 5,1996.
10.	Vicotuss	56	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
11.	Z Tuss	56/70-orthograhic only	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
12.	ZTuss	56/70-orthograhic only	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
13.	Sorbutuss	55	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
14.	Neotuss	54	Discontinued with no generic equivalents.
15.	Panatuss	54	Discontinued with no generic equivalents.
16.	Pedituss	54	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.

17.	Primatuss 4	54	Discontinued with no generic equivalents.
18.	Ventuss	54	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
19.	Ferro DSS	53	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
20.	Notuss	53	Discontinued product with no generic equivalents.
21.	Ricotuss	53	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
22.	XiraTuss	53	Discontinued product with no generic equivalents.
23.	Bronkotuss	52	Discontinued product with no generic equivalents.
24.	Endotuss	52	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
25.	Nasotuss	52	Discontinued product with no generic equivalents.
26.	Nucotuss	52	Discontinued product with no generic equivalents.
27.	Oratuss	52	International drug not marketed in the US

28.	Oratuss 12	52	International drug not marketed in the US
29.	Rutuss	52	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
30.	Coughtuss	51	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
31.	Vistuss	51	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
32.	Dia-Tuss	50	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
33.	Ferrous DS	50	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
34.	Fluidil	50	Product was withdrawn Federal Register effective 2/9/1987.
35.	Fluothane	50	Product was withdrawn Federal Register effective 9/17/03.
36.	Ry-Tuss	50	Discontinued product with no generic equivalents

37.	Spec-tuss	50	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
38.	Vi Q Tuss	50	Discontinued product with no generic equivalents
39.	Z-Tuss E	50	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.

Appendix H: Names not likely to be confused due to notable spelling, orthographic and phonetic differences.

No.	Name	POCA Score (%)
1.	Pelodis	57
2.	Lantus	56
3.	Klorvess	54
4.	(b) (4) ***	54
5.	Latisse	52
6.	Pluset	51
7.	1 Plus 1 F	50
8.	(b) (4)	50
9.	Selenos	50

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

Date:	August 8, 2011
Application Type/Number:	NDA 022424
To:	Badrul Chowdhury, MD, Director Division of Pulmonary, Allergy, and Rheumatology
Through:	Zachary Oleszczuk, PharmD, Team Leader Carol Holquist, RPh., Division Director Division of Medication Error Prevention and Analysis
From:	Teresa McMillan, PharmD, Safety Evaluator
Subject:	Proprietary Name, Label, and Labeling Review
Drug Name(s): & Strength	Flowtuss (Hydrocodone Bitartrate/Guaifenesin Oral Solution) 2.5 mg/200 mg per 5 mL
Applicant/sponsor:	Tiber Laboratories, LLC
OSE RCM #:	2011-2070, 2011-31

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

CONTENTS

EXECUTIVE SUMMARY

This review summarizes DMEPA's evaluation of the proposed proprietary name, Flowtuss, the labels and labeling of NDA 02242. Our evaluation of the proposed proprietary name did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of this review. Thus, DMEPA finds the proposed proprietary name Flowtuss acceptable for this product. The proposed proprietary name must be re-reviewed 90 days before approval of the NDA. If any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change. DMEPA will notify the Applicant of these findings via letter.

Additionally, our evaluation of the labels and labeling for this product noted areas of needed improvement in order to minimize the potential for medication errors. We provided our recommendations regarding the labels and labeling in Section 5.

1 BACKGROUND

1.1 INTRODUCTION

This review responds to requests from Tiber Laboratories, LLC, dated May 16, 2011, for an assessment of the proposed proprietary name, Flowtuss regarding potential name confusion with other proprietary or established drug names in the usual practice setting. The Applicant also included an external name review of the proposed proprietary name, Flowtuss, conducted by (b) (4)

Additionally, this review evaluates container labels, carton, and package insert labeling for Flowtuss submitted to the FDA on May 16, 2011.

1.2 REGULATORY HISTORY

On May 16, 2011, Mikart, Inc, on behalf of Tiber Laboratories, LLC, submitted a request for an assessment of the proposed proprietary name (b) (4) *** (b) (4) This proposed proprietary name will be evaluated in a separate review (see OSE RCM # 2011-1804).

1.3 PRODUCT INFORMATION

Flowtuss (Hydrocodone and Guaifenesin Oral Solution) 2.5 mg/200 mg per 5 mL is a combination product which contains an opiod antitussive and (b) (4) an expectorant. Flowtuss is indicated (b) (4)

The recommended dosage (b) (4)

Flowtuss will be supplied as a clear, violet-colored, black raspberry-flavored solution available in (b) (4) mL or 473 mL bottles. The product should be dispensed in a tight, light-resistant container, as defined in the USP, with a child-resistant closure and stored at USP Controlled Room Temperature (20 -25 degrees Celsius or 68-77 degrees Fahrenheit). Flowtuss is available by prescription only.

2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment for all proprietary names. Sections 2.1, 2.2, and 2.3 identify specific information associated with the methodology for the proposed proprietary names, Flowtuss. Additionally, Section 2.4 identifies specific methodology and materials we use to evaluate the label and labeling.

2.1 SEARCH CRITERIA

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

To identify drug names that may look or sound similar to Flowtuss, DMEPA considers the orthographic appearance of the shared root name and the modifiers on lined and unlined orders.

Specific attributes taken into consideration to identify drug names that may look similar to Flowtuss include the length of the root name Flowtuss (eight letters), upstrokes in the root name (three, the first Capital or lower case letter 'F', one lower case letter 'l', and one lower case 't'), down strokes (none), cross strokes (one, the lower case letter 't'), and dotted letters (none). Additionally, several letters in the proposed root name Flowtuss may be vulnerable to ambiguity when scripted (See Appendix B).

When searching to identify potential names that may sound similar to Flowtuss, DMEPA safety evaluators search for names with similar number of syllables (two), stresses (FLOW-tuss or flow-TUSS), and placement of vowel and consonant sounds in the root name. Similar considerations are also given to the modifiers. Additionally, DMEPA safety evaluators consider that pronunciation of the part of the name can vary (See Appendix B). The Applicant's intended pronunciation [flow-tuss] was also taken into consideration, as it was included in the Proprietary Name Review Request. Moreover, names are often mispronounced or spoken with regional accents and dialects, so other pronunciations of the names are considered.

2.2 FDA PRESCRIPTION ANALYSIS STUDIES

In order to evaluate the potential for misinterpretation of the proposed proprietary names in handwriting and verbal communication of the name, the following inpatient and verbal orders were communicated during FDA prescription studies conducted on June 10, 2011.

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

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

Figure 1: Flowtuss study samples

Handwritten Requisition Medication Order	Verbal Prescription from 06/10/2011
Medication Order from 06/10/2011  (b) (4)	
Outpatient Prescription from 6/10/2011  (b) (4)	Flowtuss (b) (4)

2.3 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

For this product, the Applicant submitted an external evaluation of the proposed proprietary name. The Division of Medication Error Prevention and Analysis conducts an independent analysis and evaluation of the data provided, and responds to the overall findings of the assessment. When the external proprietary name risk assessment identifies potentially confusing names that were not captured in DMEPA's database searches or in the Expert Panel Discussion, these names are included in the Safety Evaluator's Risk Assessment and analyzed independently by the Safety Evaluator to determine if the potentially confusing name could lead to medication errors in usual practice settings.

After the Safety Evaluator has determined the overall risk associated with proposed name, the Safety Evaluator compares the findings of their overall risk assessment with the findings of the proprietary name risk assessment submitted by the Applicant. The Safety Evaluator then determines whether the Division's risk assessment concurs or differs with the findings. When the proprietary name risk assessment differs, the Division of Medication Error Prevention and Analysis provides a detailed explanation of these differences.

2.4 LABELS AND LABELING RISK ASSESSMENT

We use Failure Mode and Effects Analysis[3] (FMEA), the principles of human factors, and errors learned from the post marking experience to identify potential sources of error with the proposed product labels and insert labeling. Thereafter, we provide recommendations that aim at reducing the risk of medication errors.

[3] Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006. p275.

For Flowtuss the Applicant submitted the following container label and package insert labeling on May 16, 2011. (See Appendix N for all images):

3 RESULTS

The following sections describe the findings of database and information sources searches, FDA prescription studies, expert panel discussions, external study, labels and labeling evaluation.

3.1 DATABASE AND INFORMATION SOURCES

The DMEPA Safety Evaluators search yielded a total of forty-two names (n=42) as having some similarity to the name Flowtuss.

Twenty-two (n=22) of the forty-two names were thought to look like Flowtuss. These names are Fentora, Fentuss, Fentuss expectorant, Flomax, Flonase, Floranex, Flolan, Flovent, Flovent HFA, Flow-eze-vented, Fluotrex, Gani-Tuss, Glycotuss, Halotussin DAC, Lortuss EX, Nocotuss, Penntuss, Pluratuss, Protuss, Relatuss HC, Ricotuss, and Vazotuss. Eighteen (n=18) names were thought to look and sound like Flowtuss. They were Biotuss, ChloTuss, Duratuss, Drotuss, Flowtuss, (b) (4) Flutuss, Flutuss HC, Flutuss XP, Flutex, Focalin, Foltx, Lortuss, Notuss, Notuss AC, Notuss DC, Notuss PD, and Solotuss.

The remaining two (n=2) names were thought to sound like Flowtuss. They were Aerotuss and Lotussin.

Additionally, DMEPA safety evaluators did not identify any United States Adopted Names (USAN) stems in the proposed proprietary names, as of June 9, 2011.

3.2 EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMEPA safety evaluators (See Section 3.1 above) and noted no additional names thought to have orthographic or phonetic similarity to the names Flowtuss.

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

3.3 FDA PRESCRIPTION STUDIES

A total of 35 practitioners responded to the three FDA Prescription Analysis studies. Nine respondents interpreted the proposed name correctly as 'Flowtuss', with correct interpretation occurring with inpatient (n=4), outpatient prescriptions (n=4), and voice prescriptions (n=1). The remaining twenty-six participants misinterpreted the name Flowtuss with the majority of misinterpretations occurring with the first letter 'F' misinterpreted as 'A' and 'H', the letter 'l' was omitted, the letter 'o' misinterpreted as the letters 'a' and 'u', the 'w' misinterpreted as the letters 'r', 's', and 'v', the letter 't' misinterpreted as the letter 's', the letter 'u' misinterpreted as the letters 'a' and 'u' and the letter 's' misinterpreted as 'a', 'c', and 'e'. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 EXTERNAL STUDY

The proposed name risk assessment submitted by the Sponsor, (b) (4) concluded the name acceptable (b) (4) identified and evaluated seventeen names (Codotuss, Coldtuss, Fentora, Fentuss, Flomax, Flovent, Flowaway, Fluidil, Fluocet, Fluothane, Fluotrex, Flutabs, Flutex, Guiatuss, Protuss, Robitussin, and Solotuss) that were thought to have some look-alike and/or sound-alike qualities and potential for confusion with Flowtuss. Nine of the names (Fentora, Fentuss, Flomax, Flovent, Fluotrex, Flutex, Flutabs, Protuss, and Solotuss) were

also identified by DMEPA during the database searches. The remaining eight names were included in DMEPA's assessment.

3.5 COMMENTS FROM THE DIVISION OF PULMONARY, ALLERGY, AND RHEUMATOLOGY

3.5.1 Initial Phase of Review

In response to an OSE email on June 9, 2011, the Division of Pulmonary, Allergy, and Rhematology did not have any comments or concerns regarding the proposed proprietary name, Flowtuss at the initial point of review.

3.5.2 Midpoint of Review

DMEPA notified DRARP via email on June 29, 2011 that the proprietary name, Flowtuss, is not vulnerable to confusion that could lead to medication errors. Per email correspondence on July 25, 2011, DPARP stated that they have no objections to DMEPA's assessment.

3.6 SAFETY EVALUATOR SEARCH

The primary Safety Evaluator identified fifteen (n=15) additional names. Six names, Amerituss AD, Anextuss, Antituss AC, Exe-tuss, Exo-tuss, and Trituss, were thought to look and sound similar to Flowtuss, 8 names, Flatulex, Fluress, Flutabs, Histussin D, Hycotuss, Panatuss, Phen-Tuss AD, and Zonatuss were thought to look similar and one name, Flophed, was thought to sound similar to Flowtuss and represent a potential source of drug name confusion.

Thus, a total of sixty-five names (n=65) were identified for the potential similarity to the proposed name, Flowtuss: 42 names from EPD, 15 names from primary safety evaluator, and 8 names from the independent search.

3.7 LABEL AND LABELING RISK ASSESSMENT

Our evaluation of the proposed container label as well as the package insert labeling noted areas of needed improvement in order to minimize the potential for medication errors. Specifically, the product's labels and labeling do not follow the United States Pharmacopeia (USP) recommendation for the expression of the established name. Additionally, the usual dose directions should be revised to provide better clarity.

4 DISCUSSION

The proposed name, Flowtuss is evaluated from a safety and promotional perspective based on the product characteristics provided by the Applicant. We sought input from pertinent disciplines involved with the review of this application and considered it accordingly.

4.1 PROMOTIONAL ASSESSMENT

On June 9, 2011, DDMAC did not find the name, Flowtuss promotional. DMEPA and DPRAP concurred with this finding.

4.2 SAFETY ASSESSMENT

A total of 65 names were identified for their potential similarity to the proposed name Flowtuss. No other aspects of the name were identified as a potential source of confusion. Forty (n=40) of the sixty-five names were eliminated from further analysis for the reasons listed in Appendices D through F.

Failure Mode and Effect Analysis (FMEA) was applied to determine if the proposed proprietary name could potentially be confused with the remaining 25 names. This analysis determined that

the name similarity between Flowtuss and the remaining 25 names were unlikely to result in medication errors for the reasons presented in Appendices G through H.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Flowtuss, is not vulnerable to name confusion that could lead to medication errors, nor is the name considered promotional. Thus, DMEPA has no objection to the proposed name, Flowtuss, for NDA 022424. DMEPA will notify the Applicant of this finding via letter (See Section 5.1 below).

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

Additionally, our evaluation of the proposed labels and labeling identified areas of needed improvement in order to minimize the potential for medication errors. We provide recommendations to the Division concerning the Prescribing Information in Section 5.2. and provide recommendations for the applicant in Section 5.3. We request that these recommendations be forwarded to the Applicant prior to approval. Please copy the Division of Medication Error Prevention and Analysis on any communication to the Applicant with regard to this review.

If you have any further questions or need clarification, please contact Nichelle Rashid, Regulatory Project Manager, at 301-796-3904.

5.1 COMMENTS TO THE APPLICANT REGARDING PROPRIETARY NAME

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

The proposed proprietary name, Flowtuss, 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 May 16, 2011, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

5.2 COMMENTS TO THE DIVISION OF PULMONARY, ALLERGY, AND RHEUMATOLOGY

A. **Full Prescribing Information: Dosage and Administration-Section 2**

(b) (4)

B. We note that the container Label for Flowtuss contains the following statement: (b) (4) Please refer to CMC for accuracy of this statement.

5.3 COMMENTS TO THE APPLICANT REGARDING LABELS AND LABELING

We have completed evaluation of the labels and labeling Flowtuss and we have the following recommendations:

A. Container Label

1. We note that the established name is not half the size of the proprietary name, and lacks prominence commensurate with the proprietary name. Increase the prominence of the established name and strength of each ingredient taking into account all pertinent factors, including typography, layout, contrast, and other printing features in accordance with 21 CFR 201.10(g)(2). Relocate the established names to appear immediately following the proprietary name.

2. Currently, there is an intervening matter between the proprietary name and established name. Relocate the (b) (4) symbol to another area on the label.

3. Revise the statement (b) (4) to state the following:

(b) (4)

4. To enhance the readability and increase clarity to the directions, we recommend the usual dosage section on the side panel be revised as follows:

USUAL DOSAGE:

(b) (4)

5. (b) (4)

(b) (4)

6 REFERENCES

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

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

2. Phonetic and Orthographic Computer Analysis (POCA)

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

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

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

4. The Document Archiving, Reporting, and Regulatory Tracking System (DARRTS)

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

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

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

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

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

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

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

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

USPTO provides information regarding patent and trademarks.

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

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

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

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

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

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

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

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

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

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

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

APPENDICES

Appendix A:

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [4]

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

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

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail. [5] DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

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

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

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

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

monitoring the impact of the medication.[6] DMEPA provides the product characteristics considered for this review in section one.

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

Table 1. Criteria used to identify drug names that look- or sound-similar to a proposed proprietary name.

Type of similarity	**Considerations when searching the databases**		
	Potential causes of drug name similarity	*Attributes examined to identify similar drug names*	*Potential Effects*
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstrokes Down strokes Cross-strokes	• Names may look similar when scripted, and lead to drug name confusion in written communication

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

		Dotted letters Ambiguity introduced by 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	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, the DMEPA staff also considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

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

2. CDER Expert Panel Discussion

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

The primary Safety Evaluator presents the pooled results of the DMEPA staff to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of names, additional searches by the primary

Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

3. FDA Prescription Analysis Studies

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

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

4. Comments from the OND review Division or Generic drugs

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

The OND or OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to concur/not concur with DMEPA's final decision.

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[7] When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

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

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

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

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

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names posses similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

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

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

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

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

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

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

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

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

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

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

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

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

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Sponsors have undertaken higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Sponsors' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval. . (See Section 4 for 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 primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Sponsor with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

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

Appendix B:

Table 1: Letters with possible orthographic or phonetic misinterpretation

Letters in Name-Flowtuss	Scripted may appear as	Spoken may be interpreted as
Capital 'F'	'L', 'T'	'Ph', 'Pf'
Capital 'Fl'	'H', 'A'	
Lower case 'l'	'b', 'e', 'i', 's'	
Lower case 'o'	'a', 'c', 'e', 'u'	'Oh', any vowel
Lower case 'w'	'eu'	
Lower case 't'	'f', 'r', 'x'	'd'
Lower case 'u'	'n', 'v', 'w', 'y', any vowel	Any vowel
Lower case 's'	'g', 'n'	
Lower case 'ss'	'm'	

Appendix C: FDA Prescription study for Flowtuss

Figure 1: Flowtuss study samples

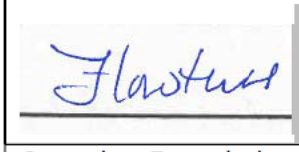
Handwritten Requisition Medication Order	Verbal Prescription from 06/10/2011
Medication Order from 06/10/2011 (b) (4)  (b) (4)	Flowtuss
Outpatient Prescription from 06/10/2011  (b) (4)	(b) (4)

Table 1: **Responses to prescription study for Flowtuss**

Inpatient Medication Order 06/10/2011	Outpatient Prescription Order 06/10/2011	Voice Prescription 06/10/2011
FLASTUCE	FLOROTUSS	FLOSAS
FLAVTUSE	FLOROTUSS	FLOSESS
FLAVTUSS	FLORUTUSS	FLOTA
FLOROTUSE	FLOWTRUSS	FLOTUS
FLOWTUSE	FLOWTUSS	FLOTUS
FLOWTUSS	FLOWTUSS	FLOTUSS
FLOWTUSS	FLOWTUSS	FLOTUSS
FLOWTUSS	FLOWTUSS	FLOTUSS
FLOWTUSS	HORUTUSS	FLOTUSS
FLUTUSS	HOWTUSS	FLOTUSS
		FLOTUSS
		FLOTUSS
		FLOTUSS
		FLOWTUSS
		SLOW-TUSS

Appendix D: **Names of products that lack convincing orthographic and/or phonetic similarity**

	PROPRIETARY NAME	SIMILARITY TO FLOWTUSS
1	Aerotuss	Sound alike
2	Amerituss AD	Look & Sound alike
3	Anextuss	Look & Sound alike
4	Antituss AC	Look & Sound alike
5	Biotuss	Look & Sound alike
6	Drotuss	Look & Sound alike
7	ExeTuss	Look & Sound alike
8	Exo-Tuss	Look & Sound alike
9	Flomax	Look alike
10	Flonase	Look alike
11	Floranex	Look alike
12	Flo-pred	Sound alike
13	Flolan	Look alike
14	Flovent	Look alike
15	Flovent HFA	Look alike
16	Flow-eze vented	Look alike
17	Flutex	Look & Sound alike
18	Focalin	Look & Sound alike
19	Foltx	Look & Sound alike
20	Hycotuss	Look alike
21	Gani-Tuss	Look alike
22	Glycotuss	Look alike
23	Lotussin	Look alike
24	Relatuss HC	Look alike
25	Ricotuss	Look alike
26	Solotuss	Look & Sound alike
27	VazoTuss	Look alike
28	Codotuss	Look & Sound alike
29	Coldtuss	Look & Sound alike

30	Flowaway	Look & Sound alike
31	Fluidil	Look & Sound alike
32	Fluocet	Look & Sound alike
33	Guiatuss	Look & Sound alike
34	Robitussin	Look & Sound alike
35	Zonatuss	Look alike

Appendix E: Names only found in the United States Patent and Trademark Office and in POCA

Name	Similarity to Flowtuss	Patent Status
Flowtuss	Look & sound alike	Active-currently owned by Tiber Lab, LLC
(b) (4)	Look & sound alike	Active-currently owned by Tiber Lab, LLC

Appendix F: Names identified that are parts of proprietary names

Name	Similarity to Flowtuss	Actual Product Name
Fentuss	Look alike	Fentuss expectorant
Flutuss	Look & sound alike	Flutuss HC & Flutuss XP
Lortuss	Look & sound alike	Lortuss EX

Appendix G: Names of products with no overlap in strength

Proprietary Name/ Established Name/ Dosage Form	Similarity to Flowtuss	Dosage Form and Strength	Usual Dose (if applicable)
Flowtuss **(Hydrocodone Bitatrate and Guaifenesin , USP)** **Oral Solution**	**N/A**	**Oral Solution:** **2.5 mg/200 mg per 5mL**	(b) (4)
Chlotuss (Chlophedianol Hydrochloride / Dexbrompheniramine Maleate / Phenylephrine Hydrochloride) (Discontinued-no generic equivalents available)	Sound alike	Oral Solution: 12.5 mg/1 mg/5 mg per 5 mL	Take 2 teaspoonfuls every 6 to 8 hours, not to exceed 8 teaspoonfuls in a 24 hour period
Fentora (Fentanyl citrate)	Look alike	Buccal Tablet: 100 mcg 200 mcg 400 mcg 600 mcg	Place 100 mcg tablet above a rear molar between the upper cheek and gum. Do not suck, chew, or split the tablets
Fentuss expectorant (hydrocodone bitartrate /guaifenesin) (Discontinued - no generic equivalents)	Look alike	Oral Solution: 5 mg/100 mg per 5 mL	Take 1-2 teaspoonfuls by mouth every 4-6 hours as needed

Fluotrex (fluocinolone acetate) (Discontinued–no generic equivalents)	Look alike	Solution/Ointment/Cream: 0.01% & 0.025%	Apply sparingly to the affected area two to four times per day
Flutuss HC (Brompheniramine Maleate/Hydrocodone Bitartrate/Phenylephrine Hydrochloride) (Discontinued –no generic equivalents)	Look and sound	Oral solution: 2 mg/2.5 mg/7.5 mg per 5 mL	Take 5—10 mL PO every 4—6 hours. Do not exceed 30 ml in 24 hours
Flutuss XP (Hydrocodone Bitartrate/Guaifenesin) (Discontinued–no generic equivalents)	Look and sound	Oral Solution: 5 mg/150 mg per 5 mL	Take 1-2 teaspoonfuls by mouth every 4-6 hours as needed
Notuss PD (Hydrocodone Bitartrate, Dexchlorpheniramine Maleate, Phenylephrine Hydrochloride) (Discontinued-no generic equivalents)	Look and sound	Oral Solution: 10 mg/30 mg per 5 mL	Take 5 mL by mouth every 6 hours
Penntuss (Chlorpheniramine Polisitrex:Codeine Polistirex) (Discontinued-no generic equivalents)	Look alike	Oral Extended Release Suspension 4 mg/10 mg per 5 mL	No usual dose information available
Protuss (Hydrocodone Bitartrate, Potassium Guaiacolsulfonate) (Discontinued-no generic equivalents)	Look	Oral Solution: 5mg/300 mg per 5 mL	Take 5—7.5 mL by mouth 4 times daily, given every 4—6 hours, as needed
Flutabs (Acetaminophen, Dextromethorphan Hydrobromide, Guaifenesin, Pseudoephedrine Hydrochloride)	Look	Oral Tablet: 500 mg, 20 mg, 200 mg, 60 mg	Take 2 tablets by mouth every 4 hours, not to exceed 12 tablets, in 24 hours

Fluothane (Halothane) (Discontinued-no generic equivalents)	Look Alike	Liquid inhalation: 99.99%	No usual dose information available

Appendix H: Potentially confusing names, but analysis indicates low potential for confusion

Failure Mode: Name confusion	Causes (can be multiple)	Rationale for Failure Mode Prevention
Flowtuss **(Hydrocodone Bitatrate and Guaifenesin , USP)** **Oral Solution:** **2.5 mg/200 mg per 5mL**	**N/A**	(b) (4)
Duratuss (Guaifenesin/Phenylephrine Hydrochloride) Oral tablet, extended release: 900mg-25mg Usual Dose Take one tablet by mouth every 12 hours. Do not exceed 2 tablets in 24 hours	Orthographic Both names contain the letter sting 'tuss' Both names contain the same cross stoke 't' in a similar position Route of Administration Oral Strength Single Strength Products	Orthographic Letter 'F' does not appear similar to letter 'D' when scripted Three upstokes ('F', 'l', 't')vs. Two upstrokes ('D', 't') Usual Dose (b) (4) (10 mL) vs. 1 tablet Frequency of Administration (b) (4) vs. twice daily

Flatulex (Charcoal; Simethicone) Oral Tablet: 250 mg/80 mg Usual Dose Take 1 tablet PO three times per day and at bedtime	Orthographic Both names begin with the letters 'Fl' Both names contain the cross-stroke letter 't' in a similar position Route of Administration Oral Strength Single strength products	Orthographic Letter 'F' does not appear similar to letter 'D' when scripted Three upstokes ('F', 'l', 't') vs. Four upstrokes ('F', 'two l's','t') Usual Dose (b) (4) (10 mL) vs. 1 tablet Frequency of Administration (b) (4) vs. three times daily
Fluress (Benoxinate HCl/Fluorescein Sodium) Ophthalmic drops, solution: 4%-0.25% Usual Dose Instill 1 or 2 drops into eye(s) prior to procedure	Orthographic Both names begin with the letters 'Fl' Both names contain the same letter string 'ss' at the end of the names Strength Single Strength Products	Orthographic Three upstokes ('F', 'l', 't') vs. Two upstokes ('F', 'l',) One cross-stroke ('t') vs. none Usual Dose (b) (4) (10 mL) vs. 1-2 drops Route of Administration Oral vs. Opthalmic Frequency of Administration (b) (4) vs. once daily

Halotussin DAC **(**Codeine/Guaifenesin/ Pseudoephedrine) Oral Syrup: 10mg-100mg-30mg/5ml Usual Dose Take 10 mL by mouth every 4—6 hours	Orthographic Letters 'Fl' may be scripted to appear similar to letter 'H' Both names contain the letter sting 'tuss' Both names contain the same cross stoke 't' in similar position Both names contain 3 upstrokes if modifier is omitted Route of Administration Oral Usual Dose (b) (4) (10 mL) (b) (4) Strength Single Strength Products Dosage Form Oral Solution	Orthographic No Modifier vs. Modifier DAC. If modifier is omitted the letters 'in' in halotussin help to differentiate the names
Histussin D (Hydrocodone Bitartrate, Pseudoephedrine Hydrochloride) Oral Solution: 5 mg/60 mg per 5 mL Usual dose Take 5 mL PO every 6 hours as needed. (discontinued-Rezira approved with same active ingredients)	Orthographic Letter 'F' may be scripted to appear similar to letter 'H' Both names contain the letter string 'tuss' Route of Administration Oral Strength Single Strength Products Dosage Form Oral Solution	Orthographic If modifier is omitted-Three upstokes ('F', 'l', 't') vs. Two upstrokes ('H', 't') No Modifier vs. Modifier D. If modifier is omitted the letters 'in' in histussin help to differentiate the names.

Lortuss EX (Codeine Phosphate/Guaifenesin/ Pseudoephedrine Hydrochloride) Oral Solution: 10 mg/100 mg/22.5 mg per 5 mL Usual Dose Take 2 teaspoonfuls every 6 to 8 hours, not to exceed 8 teaspoonfuls in 24 hours	Orthographic Letter 'F' may be scripted to appear similar to letter 'L' Both names contain the letter sting 'tuss' Both names contain the same cross stoke 't' Route of Administration Oral Usual Dose (b) (4) (10 mL) Strength Single Strength Products Dosage Form Oral Solution	Orthographic If modifier is omitted-Three upstokes ('F', 'l', 't') vs. Two upstrokes ('L', 't') If modifier is included- Three upstokes ('F', 'l', 't') vs. Four upstrokes ('L', 't', 'E', 'X') No Modifier vs. Modifier EX
Nucotuss (Codeine Phosphate/ Guaifenesin/ Pseudoephedrine Hydrochloride) Oral Solution: 20 mg/200 mg/60 mg per 5 mL Usual Dose: Take 5 mL by mouth every 6 hours. (discontinued- with generic equivalents)	Orthographic Both names contain the letter sting 'tuss' Both names contain the same cross stoke 't' in a similar position Route of Administration Oral Strength Single Strength Products Dosage Form Oral Solution	Orthographic Letter 'F' does not appear similar to letter 'N' when scripted Three upstokes ('F', 'l', 't') vs. Two upstrokes ('N', 't')

Notuss (Hydrocodone Bitartrate, Chlorpheniramine Maleate, Pseudoephedrine Hydrochloride) Oral Solution: 2 mg/ 5 mg/30 mg per 5 mL Usual Dose Take 1 teaspoonful (5 mL) every 4 hours, not to exceed 6 teaspoonfuls in a 24 hour period. (discontinued-generic equivalent-Zutripro)	Orthographic Both names contain the letter sting 'tuss' Both names contain the same cross stoke 't' in a similar position Route of Administration Oral Strength Single Strength Products (b) (4) Dosage Form Oral Solution	Orthographic Letter 'F' does not appear similar to letter 'N' when scripted Three upstokes ('F', 'l', 't') vs. Two upstrokes ('N', 't'
Notuss AC (Chlorpheniramine Maleate, Codeine Phosphate) Oral Solution: 10 mg/2 mg per 5 mL Usual Dose Take 10 mL PO every 12 hours, not to exceed 20 ml in 24 hours	Orthographic Both names contain the letter sting 'tuss' Both names contain the same cross stoke 't' in a similar position Route of Administration Oral Strength Single Strength Products Dosage Form Oral Solution	Orthographic Letter 'F' does not appear similar to letter 'N' when scripted If modifier is omitted-Three upstokes ('F', 'l', 't') vs. Two upstrokes ('N', 't') If modifier is included- Three upstokes ('F', 'l', 't') vs. Four upstrokes ('N', 't', 'A', 'C') No Modifier vs. Modifier AC

Notuss DC (Codeine Phosphate, Pseudoephedrine Hydrochloride) Oral Solution: 10mg/30mg per 5mL Usual Dose Take 5 mL by mouth every 6 hours	Orthographic Both names contain the letter sting 'tuss' Both names contain the same cross stoke 't' in a similar position Route of Administration Oral Strength Single Strength Products Dosage Form Oral Solution	Orthographic Letter 'F' does not appear similar to letter 'N' when scripted If modifier is omitted-Three upstokes ('F', 'l', 't') vs. Two upstrokes ('N', 't') If modifier is included- Three upstokes ('F', 'l', 't') vs. Four upstrokes ('N', 't', 'D', 'C') No Modifier vs. Modifier DC
Panatuss (Chlorpheniramine; Dextromethorphan; Guaifenesin; Phenylephrine) Oral Solution: 4 mg/ 30 mg/ 200 mg/10mg per 10 mL Usual Dose Take 10 mL by mouth every 4—6 hours	Orthographic Both names contain the letter sting 'tuss' Both names contain the same cross stoke 't' in a similar position Route of Administration Oral Strength Single Strength Products (b) (4) Usual Dose (b) (4) (10 mL) Dosage Form Oral Solution	Orthographic Three upstokes ('F', 'l', 't') vs. Two upstrokes ('P', 't')

Phen-tuss AD (Phenylephrine; Promethazine) Oral Syrup: 5 mg/ 6.25 mg per 5 mL Usual dose Take 5 mL by mouth every 4—6 hours as needed. Do not exceed 30 mL in 24 hours (Discontinued but generic equivalents available)	Orthographic Letter string 'Fl' can be scripted to appear similar to letter sting 'Ph' Both names contain one cross stoke letter 't' in similar position Both names end with the same letter string 'tuss' Route of Administration Oral (b) (4) Strength Single Strength Product	Orthographic No Modifier vs. Modifier AD If modifier included- Three upstokes ('F', 'l', 't') vs. Four upstrokes ('P', 't', 'A', 'D') Discontinued product. Additionally, no usage data identified for this product.
Pluratuss (Brompheniramine Maleate / Codeine Phosphate / Phenylephrine Hydrochloride) Oral Solution: 4 mg/10 mg/ 7.5 mg per 5 mL Usual Dose Take 1 teaspoonful (5 mL) every 4 to 6 hours, not to exceed 6 teaspoonfuls in a 24 hour period (Discontinued but generic equivalents available)	Orthographic Letter 'Fl' can be scripted to appear similar to letter sting 'Pl' Both names end with letter string 'tuss' Both names have three upstrokes Both names contain the same cross stoke 't' Route of Administration Oral (b) (4) Strength Single Strength Product Dosage Form Oral Solution	Discontinued product. Additionally, no usage data identified for this product.

Trituss (Dextromethorphan Hydrobromide, Guaifenesin, Phenylephrine Hydrochloride) Oral Syrup: 25 mg/175 mg/12.5 mg per 5 mL Usual dose Take 10 mL by mouth every 4 hours as needed, not to exceed 6 doses per day	Orthographic Letter 'F' can be scripted to appear similar to letter 'F' Both names end with the same letter string 'tuss' Both names contain the cross stroke letter 't' in a similar position Route of Administration Oral Usual Dose (b) (4) (10 mL) (b) (4) Strength Single Strength Product	Orthographic Three upstokes ('F', 'l', 't') vs. Two upstrokes ('T', 't')

Appendix N: Labels and Labeling for Flowtuss

Container Label for Flowtuss

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

/s/

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08/09/2011

ZACHARY A OLESZCZUK
08/09/2011

CAROL A HOLQUIST
08/09/2011