CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

211302Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME MEMORANDUM

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:	April 16, 2020
Application Type and Number:	NDA 211302
Product Name and Strength:	Cystadrops (cysteamine hydrochloride) ophthalmic solution, 0.37%
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Recordati Rare Diseases, Inc.
Panorama #:	2020-38232691
DMEPA Safety Evaluator:	Nasim Roosta, PharmD
DMEPA Team Leader:	Otto L. Townsend, PharmD

1 INTRODUCTION

This memorandum is to reassess the proposed proprietary name, Cystadrops, which was found conditionally acceptable under NDA 211302 on June 18, 2019[a]. We note that all product characteristics remain the same.

1.1 REGULATORY HISTORY

We initiated an internal review of the proposed proprietary name, Cystadrops, to capture additional names not identified in our previous review. Our re-assessment did not identify any names that represented a potential source for confusion.[b] Recordati received a complete response (CR) letter on January 28, 2020 citing deficiencies in the methods, facilities and controls used for the manufacture, processing, packing and holding of the drug product. Recordati addressed these deficiencies and resubmitted the application and the name, Cystadrops, under NDA 211302 for re-evaluation on February 28, 2020.

2 METHODS AND DISCUSSION

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Cystadrops would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Ophthalmology (DO) concurred with the findings of OPDP's assessment for Cystadrops.

2.2 SAFETY ASSESSMENT

To re-assess the proposed proprietary name, we conducted a gap analysis and searched the Phonetic and Orthographic Computer Analysis (POCA) database to identify names with orthographic and phonetic similarity to the proposed name that have been approved since the previous OSE proprietary name reviews. Additionally, we re-evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the proposed proprietary name. Our POCA search[c] identified 121 names with the combined score of ≥55% or individual orthographic or phonetic score of ≥70%. We had identified and evaluated some of the names in our previous proprietary name reviews. We note that none of the product characteristics have changed and we agree with the findings from our previous reviews for the names evaluated previously. Therefore, we identified seven (7) names not previously analyzed. These names do not represent a potential source of drug name confusion (see Appendices).

Additionally, we searched the United States Adopted Name (USAN) stem list to determine if the proposed proprietary name contains any USAN stems as of the last USAN updates. The March

[a] Fanari, M. Proprietary Name Review for Cystadrops (NDA 211302). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 Jun 18. Panorama No.: 2019-30888897.
[b] Fanari, M. Proprietary Name Review Memo for Cystadrops (NDA 211302). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 DEC 17. Panorama No.: 2019-30888897-1.

[c] POCA search conducted on March 18, 2020 in version 4.3.

16, 2020 search of USAN stems did not find any USAN stems in the proposed proprietary name, Cystadrops.

2.3 COMMUNICATION OF DMEPA'S ANALYSIS AT MIDPOINT OF REVIEW

We communicated our findings to the Division of Ophthalmology (DO) via e-mail on April 9, 2020. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Ophthalmology (DO) on April 14, 2020, they stated no additional concerns with the proposed proprietary name, Cystadrops.

3 CONCLUSION

Our re-assessment did not identify any names that represent a potential source of drug name confusion. Therefore, we maintain that the proposed proprietary name, Cystadrops, is acceptable.

If you have any questions or need clarifications, please contact Mammah Borbor, OSE project manager, at 301-796-7731.

3.1 COMMENTS TO RECORDATI RARE DISEASES, INC.

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

If any of the proposed product characteristics as stated in your submission, received on February 28, 2020, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCE

1. **USAN Stems (**https://www.ama-assn.org/about/united-states-adopted-names-approved-stems**)**

   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.

APPENDICES

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

No.	**Proposed name:** Cystadrops **Established name:** cysteamine hydrochloride **Dosage form:** ophthalmic solution **Strength(s):** 0.37% **Usual Dose:** 1 drop per eye 4 times per day during waking 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**
	N/A		

Appendix B: Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
1.	Cytosar-U	56
2.	Astramorph PF	55

Appendix C: Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with overlap or numerical similarity in Strength and/or Dose

No.	**Proposed name:** Cystadrops **Established name:** cysteamine hydrochloride **Dosage form:** ophthalmic solution **Strength(s):** 0.37% **Usual Dose:** 1 drop per eye 4 times per day during waking 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**
3.	Septra Grape	58	This name pair has sufficient orthographic and phonetic differences
4.	Cisapride	55	This name pair has sufficient orthographic and phonetic differences

Appendix D: Low Similarity Names (e.g., combined POCA score is ≤54%)

No.	Name	POCA Score (%)
	N/A	

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

No.	Name	POCA Score (%)	Failure preventions
5.	Cysteine, Dl-	58	Product is not a drug. It is a semi-essential proteinogenic amino acid.
6.	Cystemms-V	56	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.
7.	Testoderm	56	Brand discontinued with no generic equivalent available. NDA 19762 withdrawn FR Effective 6/18/2009.

Appendix F: Names not likely to be confused due to absence of attributes that are known to cause name confusion[d].

No.	Name	POCA Score (%)
	N/A	

[d] Shah, M, Merchant, L, Chan, I, and Taylor, K. Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

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/s/

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OTTO L TOWNSEND
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PROPRIETARY NAME MEMORANDUM

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

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Date of This Review:	December 17, 2019
Application Type and Number:	NDA 211302
Product Name and Strength:	Cystadrops (cysteamine hydrochloride) ophthalmic solution, 0.37 %
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Recordati Rare Diseases, Inc. (Recordati)
Panorama #:	2019-30888897-1
DMEPA Safety Evaluator:	Melina Fanari, R.Ph.
DMEPA Team Leader:	Otto L. Townsend, PharmD

1 INTRODUCTION

This memorandum is to reassess the proposed proprietary name, Cystadrops, which was found conditionally acceptable under NDA 211302 on June 18, 2019.[a] We internally initiated this review to capture additional names not previously identified in our previous review. We note that all product characteristics remain the same.

2 METHODS AND DISCUSSION

2.1 SAFETY ASSESSMENT

2.1.1 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search[b] identified 99 names with the combined score of ≥55% or individual orthographic or phonetic score of ≥70%. We had identified and evaluated some of the names in our previous proprietary name review. We re-evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the name. We note that none of the product characteristics have changed and we agree with the findings from our previous review for the names evaluated previously. Therefore, we identified 15 names not previously analyzed. These names are included in Table 1 below.

2.1.2 Names Retrieved for Review Organized by Name Pair Similarity

Table 1 lists the number of names retrieved from our POCA search. These name pairs are organized as highly similar, moderately similar or low similarity for further evaluation.

Table 1. Names Retrieved for Review Organized by Name Pair Similarity

Similarity Category	Number of Names
Highly similar name pair: combined match percentage score ≥70%	0
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	15
Low similarity name pair: combined match percentage score ≤54%	0

[a] Fanari, M. Proprietary Name Review for Cystadrops (NDA 211302). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 Jun 18. Panorama No.: 2019-30888897.

[b] POCA search conducted on December 4, 2019 in version 4.3.

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

Our analysis of the 15 names contained in Table 1 determined none of the names will pose a risk for confusion with Cystadrops as described in Appendices C through H.

3 CONCLUSION

Our re-assessment did not identify any names that represent a potential source of drug name confusion. Therefore, we maintain that the proposed proprietary name, Cystadrops, is acceptable.

4 REFERENCE

1. ***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.

APPENDICES

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

Appendix D: Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
1.	Astagraf	56
2.	Vistacot	56

Appendix E: Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with overlap or numerical similarity in Strength and/or Dose

No.	**Proposed name:** Cystadrops **Established name:** cysteamine hydrochloride **Dosage form:** ophthalmic solution **Strength(s):** 0.37 % **Usual Dose:** one drop in each eye 4 ties daily while awake	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**
3.	Irofol Drops	56	This name pair has sufficient orthographic and phonetic differences
4.	Refresh drops	58	This name pair has sufficient orthographic and phonetic differences

Appendix F: Low Similarity Names (e.g., combined POCA score is ≤54%)- N/A

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
5.	Nystamont	55	International product formally marketed in Greece and the UK

Appendix H: Names not likely to be confused due to absence of attributes that are known to cause name confusion[c].

No.	Name	POCA Score (%)
6.	Soothe Caplets	58
7.	Stratagraft	56
8.	Sustachron Er	56
9.	Trac Tabs 2X	56
10.	Dinoprost	56
11.	Sektayos	55
12.	Sitosterols	55
13.	Spectrobid	55
14.	Vistogard	55
15.	Diet Caplets	55

[c] Shah, M, Merchant, L, Chan, I, and Taylor, K. Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

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/s/

MELINA N FANARI
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PROPRIETARY NAME REVIEW

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

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

Date of This Review:	June 18, 2019
Application Type and Number:	NDA 211302
Product Name and Strength:	Cystadrops (cysteamine hydrochloride) ophthalmic solution, 0.37%
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Recordati Rare Diseases, Inc. (Recordati)
Panorama #:	2019-30888897
DMEPA Safety Evaluator:	Melina Fanari, R.Ph.
DMEPA Team Leader:	Otto L. Townsend, PharmD

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Cystadrops, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed proprietary name are outlined in the reference section and Appendix A respectively. Recordati submitted their results from an internally conducted evaluation for this proposed proprietary name.

1.1 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on April 17, 2019.

- Intended Pronunciation: sys-tah-drops
- Active Ingredient: cysteamine hydrochloride
- Indication of Use: For the treatment of corneal cycstine crystal deposits in adults and children with cycstinosis.
- Route of Administration: ophthalmic
- Dosage Form: ophthalmic solution
- Strength: 0.37%
- Dose and Frequency: one drop in each eye 4 times daily during waking hours
- How Supplied: 5 mL sterile solution in a 10 mL amber glass vial closed by a stopper and sealed with aluminum tear-off cap. Each carton is packaged with a PVC dropper applicator.
- Storage:

  Before First Opening: Store in refrigerator 2°C to 8°C (36°F to 46°F). Keep the vial in the outer carton in order to protect from light.

  After First Opening: Store at (b) (4) 25°C (77°F). Do not refrigerate. Keep the dropper bottle tightly closed in the outer carton in order to protect from light. Discard 7 days after first opening.

- Reference Listed Drug/Reference Product: Cystaon; NDA 20392

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Cystadrops would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Transplant and Ophthalmology Products (DTOP) concurred with the findings of OPDP's assessment for Cystadrops.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the proposed proprietary name, Cystadrops.

2.2.1 United States Adopted Names (USAN) Search

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

2.2.2 Components of the Proposed Proprietary Name

Recordati indicated in their submission that the proposed proprietary name, Cystadrops, is derived from "cysteamine", the established name for the product's active ingredient as well as "Cystagon" the listed drug. 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.

2.2.3 Comments from Other Review Disciplines at Initial Review

In response to the OSE, April 30, 2019 e-mail, the Division of Transplant and Ophthalmology Products (DTOP) did not forward any comments or concerns relating to Cystadrops at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Eighty-eight practitioners participated in DMEPA's prescription studies for Cystadrops. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline. Appendix B contains the results from the verbal and written prescription studies.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search[b] identified 99 names with a combined phonetic and orthographic score of ≥55% or an individual phonetic or orthographic score ≥70%. These names are included in Table 1 below.

2.2.6 Names Retrieved for Review Organized by Name Pair Similarity

Table 1 lists the number of names retrieved from our POCA search and Applicant's evaluation. These name pairs are organized as highly similar, moderately similar or low similarity for further evaluation.

Table 1. Names Retrieved for Review Organized by Name Pair Similarity

Similarity Category	Number of Names
Highly similar name pair: combined match percentage score ≥70%	5

[a] USAN stem search conducted on May 8, 2019.

[b] POCA search conducted on May 8, 2019 in version 4.3.

Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	90
Low similarity name pair: combined match percentage score ≤54%	8

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

Our analysis of the 103 names contained in Table 1 determined none of the names will pose a risk for confusion with Cystadrops 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 Transplant and Ophthalmology Products (DTOP) via e-mail on June 10, 2019. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Transplant and Ophthalmology Products (DTOP) on June 18, 2019, they stated no additional concerns with the proposed proprietary name, Cystadrops.

3 CONCLUSION

The proposed proprietary name, Cystadrops, is acceptable.

If you have any questions or need clarifications, please contact Danyal Chaudhry, OSE project manager, at 301-796-3813.

3.1 COMMENTS TO RECORDATI RARE DISEASES, INC.

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

If any of the proposed product characteristics as stated in your submission, received on April 17, 2019, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

1. USAN Stems (https://www.ama-assn.org/about/united-states-adopted-names-approved-stems)

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 DNDP. OPDP or DNDP 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 DNDP 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. [c]

[c] 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 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 55% 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 ≥55% to ≤ 69%.

- Low similarity: combined match percentage score ≤54%.

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 are further evaluated to identify the presence of attributes that are known to cause name confusion.
    - Name attributes: We note that the beginning of the drug name plays a significant role in contributing to confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are major contributing factor in the confusion of drug names[d]. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.
    - Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information 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) may be limited when the strength or dose overlaps. DMEPA reviews 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

[d] Shah, M, Merchant, L, Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

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 does 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 ≥55% 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: • 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. • Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. • 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 ≤54%).

Names with low similarity are generally acceptable 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.

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Appendix B: Prescription Simulation Samples and Results

Figure 1. Cystadrops Study (Conducted on April 29, 2019)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order: Cystadrops One drop into each eye 4 times per day Outpatient Prescription: Cystadrops 1 gtt into each eye QID while awake #1 box Dr. Ose	Cystadrops Instill one drop in each eye 4 times a day while awake

FDA Prescription Simulation Responses (Aggregate Report)

219 People Received Study
88 People Responded

Study Name: Cystadrops

Total	46	16	26	88
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
CRYSTADROP	0	0	1	1
CRYSTADROPS	0	0	1	1
CYSTA DROPS	1	2	0	3
CYSTADROPA	0	0	1	1
CYSTADROPS	44	0	22	66
CYSTAROPS	0	0	1	1

CYSTDROPS	1	0	0	1
SISDADROPS	0	1	0	1
SISTA DROPS	0	3	0	3
SISTADROPS	0	3	0	3
SYSTA DROPS	0	2	0	2
SYSTADROP	0	1	0	1
SYSTADROPS	0	4	0	4

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

No.	**Proposed name:** Cystadrops **Established name:** cysteamine hydrochloride **Dosage form:** ophthalmic solution **Strength(s):** 0.37% **Usual Dose:** one drop in each eye 4 times daily while awake	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.	Cystadrops	100	Name subject of this review
2.	Nasadrops	74	Orthographically, the prefixes of this name pair ('Nasa" vs 'Cysta') differ due to the presence of the downstroke "y" and upstoke "t" in Cystadrops. Nasadrops has neither a downstroke or upstroke in the prefix.. Phonetically, the first syllables ('Na' vs 'Cys') of the names sound different.
3.	Nutradrops	72	Orthographically, the prefixes of this name pair ('Nutra" vs 'Cysta') differ due to the presence of the downstroke "y" in Cystadrops. Nutradrops has no downstroke in the prefix. Phonetically, the first syllables ('Nu' vs 'Cys') of the names sound different.
4.	Cardec Drops	70	Product was an unapproved prescription cough, cold, and allergy product that included chlorpheniramine and phenylephrine for use in pediatric patients. Product is deactivated and no generic equivalents are available.
5.	Viva-Drops	70	Orthographically, the prefixes of this name pair ('Viva" vs 'Cysta') differ. Phonetically, the first syllables ('Vi' vs 'Cys') of the names sound different.

Appendix D: Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
6.	Cystagon	63
7.	Catapres-TTS-1	62

No.	Name	POCA Score (%)
8.	Catapres-TTS-2	62
9.	Catapres-TTS-3	62
10.	Catapres	58
11.	Somatropin	57
12.	Cytosar	56

Appendix E: Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with overlap or numerical similarity in Strength and/or Dose

No.	**Proposed name:** Cystadrops **Established name:** cysteamine hydrochloride **Dosage form:** ophthalmic solution **Strength(s):** 0.37% **Usual Dose:** one drop in each eye 4 times daily while awake	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**
13.	Accuhist Drops	69	This name pair has sufficient orthographic and phonetic differences.
14.	Sildec Drops	69	This name pair has sufficient orthographic and phonetic differences
15.	Ceron Drops	69	This name pair has sufficient orthographic and phonetic differences
16.	Cystospaz	66	This name pair has sufficient orthographic and phonetic differences
17.	Sundrops 77	66	This name pair has sufficient orthographic and phonetic differences
18.	Vicks Vapodrops	66	This name pair has sufficient orthographic and phonetic differences
19.	Zoto-Hc Drops	66	This name pair has sufficient orthographic and phonetic differences
20.	Colic Drops	66	This name pair has sufficient orthographic and phonetic differences
21.	Sastid Soap	65	This name pair has sufficient orthographic and phonetic differences
22.	Flura-Drops	65	This name pair has sufficient orthographic and phonetic differences
23.	Carbopost	64	This name pair has sufficient orthographic and phonetic differences
24.	Colidrops	64	This name pair has sufficient orthographic and phonetic differences
25.	Cystaran	64	This name pair has sufficient orthographic and phonetic differences

No.	**Proposed name:** Cystadrops **Established name:** cysteamine hydrochloride **Dosage form:** ophthalmic solution **Strength(s):** 0.37% **Usual Dose:** one drop in each eye 4 times daily while awake	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**
26.	Rondec Drops	64	This name pair has sufficient orthographic and phonetic differences
27.	Septra DS	64	This name pair has sufficient orthographic and phonetic differences
28.	Cystografin	62	This name pair has sufficient orthographic and phonetic differences
29.	Cystospaz-M	62	This name pair has sufficient orthographic and phonetic differences
30.	Kid Kare Drops	62	This name pair has sufficient orthographic and phonetic differences
31.	Uni-Hist Drops	62	This name pair has sufficient orthographic and phonetic differences
32.	(b) (4) ***	60	This name pair has sufficient orthographic and phonetic differences
33.	Ceron-DM Drops	60	This name pair has sufficient orthographic and phonetic differences
34.	Charcocaps	60	This name pair has sufficient orthographic and phonetic differences
35.	Pediacare Drops	60	This name pair has sufficient orthographic and phonetic differences
36.	Cystadane	60	Orthographically, the suffixes of this name pair (‘ane’ vs ‘rops’) differ due to the presence of the downstoke “p” in Cystadrops. Cystadane has no downstroke in the suffix. Phonetically, the last syllables of the names (‘dane’ vs. ‘drops’) differ.
37.	Neo DM Drops	59	This name pair has sufficient orthographic and phonetic differences
38.	Histatrol	59	This name pair has sufficient orthographic and phonetic differences
39.	Sterapred DS	59	This name pair has sufficient orthographic and phonetic differences
40.	Calmodrox	58	This name pair has sufficient orthographic and phonetic differences
41.	Luden’s Drops	58	This name pair has sufficient orthographic and phonetic differences

No.	**Proposed name:** Cystadrops **Established name:** cysteamine hydrochloride **Dosage form:** ophthalmic solution **Strength(s):** 0.37% **Usual Dose:** one drop in each eye 4 times daily while awake	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**
42.	Minidrops	58	This name pair has sufficient orthographic and phonetic differences
43.	Star-Otic	58	This name pair has sufficient orthographic and phonetic differences
44.	Syndros	58	This name pair has sufficient orthographic and phonetic differences
45.	Cosyntropin	58	This name pair has sufficient orthographic and phonetic differences
46.	Cysto-Conray	57	This name pair has sufficient orthographic and phonetic differences
47.	Neutrahist Drops	57	This name pair has sufficient orthographic and phonetic differences
48.	Cystex	57	This name pair has sufficient orthographic and phonetic differences
49.	Dihydro-CP	56	This name pair has sufficient orthographic and phonetic differences
50.	Hista-Tabs	56	This name pair has sufficient orthographic and phonetic differences
51.	Dallergy Drops	56	This name pair has sufficient orthographic and phonetic differences
52.	Hydron Pcs	56	This name pair has sufficient orthographic and phonetic differences
53.	Statrol	56	This name pair has sufficient orthographic and phonetic differences
54.	Dimetapp Cold Drops	56	This name pair has sufficient orthographic and phonetic differences
55.	Sulfatrim-SS	56	This name pair has sufficient orthographic and phonetic differences
56.	Cefadroxil	56	This name pair has sufficient orthographic and phonetic differences
57.	Donatussin Drops	55	This name pair has sufficient orthographic and phonetic differences
58.	Histatab PH	55	This name pair has sufficient orthographic and phonetic differences
59.	Oticin HC Ear Drops	55	This name pair has sufficient orthographic and phonetic differences

Appendix F: Low Similarity Names (e.g., combined POCA score is ≤54%)

No.	Name	POCA Score (%)
60.	Cytosar	54
61.	Nystaform	53
62.	Capstar	52
63.	Stadol	50
64.	Cysteine hydrochloride	48
65.	Ceftiflex	46
66.	Westadone	46
67.	Procysbi	36

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
68.	Infadrops	68	International product marketed in the UK
69.	Aspidrox	65	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
70.	Testotop TTS	65	International product marketed in Germany and formally marketed in the UK and Austria
71.	Clindrops	62	Veterinary product
72.	Cytadren	62	Discontinued product with no available generics. NDA 18202 withdrawn FR effective 06/18/209.
73.	Cyprostat	60	International product marketed in Australia and the UK
74.	Postprophy	60	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases
75.	Cardec DM Drops	60	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.
76.	Crystapen V	59	International product marketed in numerous foreign countries
77.	Beta-D-Ribose	58	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases
78.	Spectogard	56	Veterinary product
79.	Syntaris	56	International product marketed in Italy and Germany

No.	Name	POCA Score (%)	Failure preventions
80.	Strong Caps	56	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.
81.	Crystacide	56	International product marketed in numerous foreign countries.
82.	Soy Sterol	56	Name identified in RxNorm and is an ingredient in a multi-ingredient dietary supplement named Sanchol.
83.	Carbofed DM	55	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.
84.	Crystapen	55	International product marketed in numerous foreign countries.

Appendix H: Names not likely to be confused due to absence of attributes that are known to cause name confusion[e].

No.	Name	POCA Score (%)
85.	Testoderm TTS	62
86.	Tafluprost	60
87.	Estraderm TTS 100	59
88.	Estraderm TTS25	59
89.	Estraderm TTS50	59
90.	Pepcid Rpd	58
91.	Phytosterols	58
92.	Travoprost	58
93.	Estro-Cyp	57
94.	Ferra T.D. Caps	57
95.	Vincasar PFS	57
96.	Acetadrink	56
97.	Doxy-Caps	56
98.	Latanoprost	56
99.	Testradiol	56
100.	Vasostrict	56
101.	(b) (4) ***	56
102.	Dispermox	55
103.	Oasis Tears	55

[e] Shah, M, Merchant, L, Chan, I, and Taylor, K. Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

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