CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

200740Orig1s000

PROPRIETARY NAME REVIEW(S)

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

Proprietary Name Review

Date:	June 27, 2012
Reviewer:	Jung Lee, RPh Division of Medication Error Prevention and Analysis
Acting Team Leader:	Chi-Ming (Alice) Tu, PharmD Division of Medication Error Prevention and Analysis
Division Director:	Carol Holquist, RPh Division of Medication Error Prevention and Analysis
Drug Name and Strength:	Cystaran (Cysteamine Hydrochloride Ophthalmic Solution), 0.44%
Application Type/Number:	NDA 200740
Applicant:	Sigma-Tau Pharmaceuticals, Inc
OSE RCM #:	2012-952

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

CONTENTS

1 INTRODUCTION

This review evaluates the proposed proprietary name, Cystaran, from a safety and promotional perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively.

1.1 REGULATORY HISTORY

On March 26, 2010, the Applicant submitted a request for a proprietary name review for the proposed proprietary name, Cystoran, for this product. The name was found unacceptable (b) (4) The name was subsequently withdrawn and on May 14, 2010, the Applicant submitted a request for the proprietary name, Cystaran. The name was found conditionally acceptable. On September 3, 2010, the application received a Complete Response due to deficiencies regarding non-cGMP compliance of the manufacturing facilities. Due to the amount of time that has elapsed since the previous proprietary name evaluation, the Applicant submitted a Request for Proprietary Name Review for Cystaran on April 13, 2012.

1.2 PRODUCT INFORMATION

The following product information is provided in the April 13, 2012 proprietary name submission.

- Active Ingredient: Cysteamine Hydrochloride
- Indication of Use: A cystine-depleting agent indicated for the treatment of corneal cystine crystal accumulation in patients with cystinosis
- Route of Administration: Ophthalmic
- Dosage Form: Ophthalmic Solution
- Strength: 0.44% (as free base)
- Dose and Frequency: Instill one drop in each eye, every waking hour
- How Supplied: 15 mL LDPE bottle with an LDPE controlled dropper tip
- Storage: Store in freezer -25°C to -15°C (-13°F to 5°F). Thaw for approximately 24 hrs before use. Thawed bottle can be stored at 2°C to 25°C (36°F to 77°F) for up to 1 week. Do not refreeze. Discard after 1 week of use.
- Container and Closure Systems: 15 mL, round, white, LDPE bottle with a 15 mm, white, LDPE dropper tip and a white polypropylene screw-cap

2 RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion OPDP determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Transplant and Ophthalmology concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) SEARCH

The May 2, 2012 search of the United States Adopted Name (USAN) stems did not identify that a USAN stem is present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The Applicant indicated in their submission that the proposed name, Cystaran, 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 FDA Name Simulation Studies

Thirty-one practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with or appear or sound similar to any currently marketed products. Seventeen participants correctly interpreted the name, Cystaran. Of those participants who misinterpreted the name, most of the verbal participants misinterpreted the 1st letter 'C' in Cystaran for 'S', the 2nd letter 'y' for 'i' and the 7th letter 'a' for 'e'. Of the inpatient participants, the letter 'n' in the last position of the name Cystaran was misinterpreted with the letter 'm' while the outpatient partcipants misinterpreted the 6th letter 'r' with the letter 'l' and the 'n' in the last position with the letter 'm'. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines

In response to the OSE, May 8, 2012 e-mail, the Division of Transplant and Ophthalmology (DTOP) did not forward any comments or concerns relating to the proposed name at the initial phase of the proprietary name review.

2.2.5 Failure Mode and Effects Analysis of Similar Names

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in the proposed proprietary name, Cystaran. Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Cystaran identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines. Table 1 also includes the names identified from the FDA Prescription Simulation, not identified by DMEPA, and require further evaluation.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, Other Disciplines, FDA Name Simulation Studies, and External Name Study)

Look Similar		Look Similar		Look Similar	
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Antara	EPD	Cystamin	EPD	Glycerin	EPD
Aplenzin	EPD	Cystogen	EPD	Glycerine	EPD
Aptivus	EPD	Cystografin	EPD	Lysodren	EPD
Azactam	EPD	Cystospaz	EPD	Lysteda	EPD
Azasan	EPD	Cysview	EPD	(b) (4)	EPD
Cayston	EPD	Cytarabine	EPD	Synalar	EPD
Cefotaxime	EPD	Cytosar-U	EPD	Zyban	EPD
Cisatracurium Besylate	EPD	Cytotec	EPD	Zyclara	EPD
Cyclafem	EPD	Cytovene	EPD	Zydone	EPD
Cyclessa	EPD	Cytoxan	EPD		
Cydonal	EPD	(b) (4)	EPD		
Look & Sound Similar		**Look & Sound Similar**		**Look & Sound Similar**	
Cisplatin	EPD	Cysteamine	EPD/Primary Reviewer	Sylatron	EPD
Cystadane	EPD/Primary Reviewer	Cystine	EPD	Systane	EPD
Cystagon	EPD/Primary Reviewer	Cytadren	EPD		
Cysteine	EPD/Primary Reviewer	Cytogam	EPD		

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

Our analysis of the 41 names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics. We determined 41 names will not pose a risk for confusion as described in Appendix D through E.

2.2.6 Communication of DMEPA's Final Decision to Other Disciplines

DMEPA communicated our findings to the Division of Transplant and Ophthalmology via e-mail on May 16, 2012. 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 on May 22, 2012, they stated no additional concerns with the proposed proprietary name, Cystaran.

3 CONCLUSIONS

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

If you have further questions or need clarifications, please contact Karen Townsend, OSE project manager, at 301-796-5413.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Cystaran, and have concluded that this name is acceptable. However, if any of the proposed product characteristics as stated in your April 13, 2012 submission are altered, DMEPA rescinds this finding and the name must be resubmitted for review.

Additionally, the proposed proprietary name must be re-reviewed 90 days prior to approval of the NDA. The conclusions upon re-review are subject to change.

4 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. This database also lists the orphan drugs.

4. ***FDA Document Archiving, Reporting & Regulatory Tracking System [DARRTS]***

   DARRTS is a government database used to organize Applicant and Sponsor submissions as well as to store and organize assignments, reviews, and communications from the 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. ***U.S. Patent and Trademark Office (http://www.uspto.gov)***

   USPTO provides information regarding patent and trademarks.

8. ***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.

9. ***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.

10. ***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.

11. ***Access Medicine (www.accessmedicine.com)***

    Access Medicine® from McGraw-Hill contains full-text information from approximately 60 titles; it includes tables and references. Among the titles are: Harrison's Principles of Internal Medicine, Basic & Clinical Pharmacology, and Goodman and Gilman's The Pharmacologic Basis of Therapeutics.

12. ***USAN Stems (http://www.ama-assn.org/ama/pub/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml)***

    USAN Stems List contains all the recognized USAN stems.

13. ***Red Book (www.thomsonhc.com/home/dispatch)***

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

14. ***Lexi-Comp (www.lexi.com)***

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

15. ***Medical Abbreviations (www.medilexicon.com)***

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

16. ***CVS/Pharmacy (www.CVS.com)***

    This database contains commonly used over the counter products not usually identified in other databases.

17. ***Walgreens (www.walgreens.com)***

    This database contains commonly used over the counter products not usually identified in other databases.

18. ***Rx List (www.rxlist.com)***

    RxList is an online medical resource dedicated to offering detailed and current pharmaceutical information on brand and generic drugs.

19. Dogpile (www.dogpile.com)

Dogpile is a Metasearch engine that searches multiple search engines including Google, Yahoo! and Bing, and returns the most relevant results to the search.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment considers the promotional and safety aspects of a proposed proprietary name. The promotional review of the proposed name is conducted by OPDP. OPDP evaluates proposed proprietary names to determine if they are overly fanciful, so as to misleadingly imply unique effectiveness or composition, as well as to assess whether they contribute to overstatement of product efficacy, minimization of risk, broadening of product indications, or making of unsubstantiated superiority claims. OPDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, 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.). 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. [1]

Following the preliminary screening of the proposed proprietary name, DMEPA gathers to discuss their professional opinions on the safety of the proposed proprietary name. This meeting is commonly referred to the Center for Drug Evaluation and Research (CDER) Expert Panel discussion. DMEPA also considers other aspects of the name that may be misleading from a safety perspective. DMEPA staff conducts a prescription simulation studies using FDA health care professionals. 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. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name and misleading nature of the proposed proprietary name with a focus on the avoidance of medication errors.

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. DMEPA considers the product characteristics associated with the proposed product 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.

---

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

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. DMEPA considers how these product characteristics may or may not be present in communicating a product name throughout the medication use system. Because drug name confusion can occur at any point in the medication use process, DMEPA considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.[2]

The DMEPA considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA compares the proposed proprietary name with the proprietary and established name of existing and proposed drug products and names currently under review at the FDA. DMEPA 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. DMEPA examines the phonetic similarity using patterns of speech. 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. The orthographic appearance of the proposed name is evaluated using a number of different handwriting samples. DMEPA applies expertise gained from root-cause analysis of postmarketing 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).

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

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/Similar shape Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, DMEPA 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 searches 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. A standard description of the databases used in the searches is provided in the reference section of this review. To complement the process, the DMEPA uses a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, DMEPA reviews 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. DMEPA also evaluates if there are characteristics included in the composition that may render the name unacceptable from a safety perspective (abbreviation, dosing interval, etc.).

2. Expert Panel Discussion

DMEPA gathers gather CDER professional opinions on the safety of the proposed product and discussed the proposed proprietary name (Expert Panel Discussion). The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Office of Prescription Drug Promotion (OPDP). We also consider input from other review disciplines (OND, ONDQA/OBP). 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 database and information searches to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend additional 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 Simulation 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 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.

4. 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.

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, considers all aspects of the name that may be misleading or confusing, conducts a Failure Mode and Effects Analysis, and provides an overall decision on acceptability dependent on their 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.[3] When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product

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

characteristics listed in Section 1.2 of this review. 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? And are there any components of the name that may function as a source of error beyond sound/look-alike?"***

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 or because of some other component of the name. 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.

Moreover, 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 Overall Risk Assessment:

a. OPDP finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with OPDP'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 but involve a naming characteristic that when incorporated into a proprietary name, may be confusing, misleading, cause or contribute to medication errors.

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 generally recommends that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. 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 Applicant/Sponsor. However, the safety concerns set forth in criteria a through e above 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, confusing, or misleading 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 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.

Appendix B: Letters with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Cystaran	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'C'	A, G, L, O, S, Z	'Z', 'K', 'S'
Lower Case 'c'	a, e, i, l	'z', 'k', 's'
Lower Case 'y'	f, p, u, v, x, Z	'e', 'i', 'u'
Lower Case 's'	5, G, g, n	'x'
Lower Case 't'	A, f, x	'd'
Lower Case 'a'	el, ci, cl, d, o, u	Any vowel
Lower Case 'r'	e, i, l, n, s, v	l
Lower Case 'a'	el, ci, cl, d, o, u	Any vowel
Lower Case 'n'	h, m, r, s, u, v, x	'dn', 'gn', 'kn', 'mn', 'pn'

Appendix C: Prescription Simulation Samples and Results

Figure 1. Cystaran Study (Conducted on April 27, 2012)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order: Cystaran 1 drop in each eye q1h while awake	Cystaran Instill 1 drop in both eyes every hour while awake #15 mL bottle
Outpatient Prescription: Cystaran 15 mL Instill 1 drop OU every hour while awake	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

Study Name: Cystaran

As of Date 5/11/2012

84 People Received Study

31 People Responded

Study Name: Cystaran

Total	**12**	**9**	**10**	**31**
INTERPRETATION	**INPATIENT**	**VOICE**	**OUTPATIENT**	**TOTAL**
CISTARIN	0	1	0	1
CISTARTIN	0	1	0	1
CYSTALAN	0	0	2	2
CYSTALAN 15ML	0	0	1	1
CYSTARAM	1	0	1	2
CYSTARAN	11	0	6	17
CYSTAREN	0	1	0	1
CYSTARIN	0	4	0	4
SISTARIN	0	1	0	1
SYSTAREN	0	1	0	1

Appendix D: Proprietary names not likely to be confused or not used in usual practice settings for the reasons described. (n=22)

No.	Proprietary Name	Active Ingredient	Similarity to Cystaran	Failure preventions
1	Antara	Fenofibrate	Look Alike	The pair have sufficient orthographic differences
2	Azasan	Azathioprine	Look Alike	The pair have sufficient orthographic differences
3	Cefotaxime	Cefotaxime	Look Alike	The pair have sufficient orthographic differences
4	Cisatracurium Besylate	Cisatracurium Besylate	Look Alike	The pair have sufficient orthographic differences
5	Cisplatin	Cisplatin	Look & Sound Alike	The pair have sufficient orthographic and phonetic differences
6	Cydonol	Multi Ingredient Lotion	Look Alike	The pair have sufficient orthographic differences
7	Cystamin	Methanamine	Look Alike	Unable to find product characteristics in commonly used drug databases. This is one of the chemical names for methanamine, used for urinary tract infections, malaria, prevention of ticks, lice, and mites.
8	Cystine	Cystine-Amino Acid	Look & Sound Alike	Unable to find product characteristics in commonly used drug databases. This is a compounding powder ingredient.
9	Cystogen	Methanamine	Look Alike	Unable to find product characteristics in commonly used drug databases. This is one of the chemical names for methanamine, used for urinary tract infections, malaria, prevention of ticks, lice, and mites.
10	Cystografin	Diatrizoate Meglumine	Look Alike	The pair have sufficient orthographic differences
11	Cystospaz	Hyoscyamine Sulfate	Look Alike	The pair have sufficient orthographic differences
12	Cysview	Hexaminolevulinate Hydrochloride	Look Alike	The pair have sufficient orthographic differences
13	Cytadren	Aminoglutethimide	Look & Sound Alike	The pair have sufficient orthographic and phonetic differences
14	Cytarabine	Cytarabine	Look Alike	The pair have sufficient orthographic differences

No.	Proprietary Name	Active Ingredient	Similarity to Cystaran	Failure preventions
15	Cytogam	Cytomegalovirus Immune Globulin	Look & Sound Alike	The pair have sufficient orthographic and phonetic differences
16	Cytotec	Misoprostol	Look Alike	The pair have sufficient orthographic differences
17	Glycerin	Glycerin	Look Alike	The pair have sufficient orthographic differences
18	Glycerine	Glycerin	Look Alike	The pair have sufficient orthographic differences
				(b) (4)
20	Sylatron	Peginterferon Alfa-2b	Look & Sound Alike	The pair have sufficient orthographic and phonetic differences
21	Synalar	Fluocinolone Acetonide	Look Alike	The pair have sufficient orthographic differences
22	Zyban	Buproprion Hydrochloride	Look Alike	The pair have sufficient orthographic differences

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

Appendix E: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described. (n=19)

No.	**Proposed name: Cystaran** **Dosage Form: Ophthalmic Solution** **Strength: 0.44%** **Usual Dose: Instill one drop in each eye, every waking hour**	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion** **Causes (could be multiple)**	**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	Aplenzin (Buproprion Hydrobromide) Extended Release Tablets **Strength:** 174 mg, 348 mg, 522 mg **Usual Dose:** Begin with 174 mg to 522 mg by mouth once daily in the morning **Hepatic Dose:** 174 mg by mouth every other day	**Orthographic Similarity:** Both names contain 8 letters, contain a similar letter string (Ap vs. Cys) when scripted, and end with the letter 'n'. **Dose:** Both can be written as one dose without specifying the dosage form (tablet vs. drop).	**Orthographic Difference:** Aplenzin contains an upstroke 'l' in the 3rd position while Cystaran contains a cross-stroke 't' in the 4th position. **Differentiating Product Characteristics:** Strength: No strength overlap. Aplenzin is available in multiple strengths; thus a strength would need to be specified on the prescription for dispensing. Frequency: once daily vs. every waking hour
2	Aptivus (Tipranavir) Capsules, Solution **Strength:** Capsule: 250 mg Solution: 100 mg/mL **Usual Dose:** 500 mg (two 250 mg capsules or 5 mL oral solution) by mouth coadministered with ritonavir 200 mg twice daily	**Orthographic Similarity:** Both names contain a similar letter string (Ap vs. Cys) when scripted followed by a cross-stroke 't'.	**Orthographic Difference:** Aptivus contains the letter string 'ivus' which when scripted appears different than the letter string 'aran' in Cystaran. **Differentiating Product Characteristics:** Dosage Form and Strength: Aptivus is available in multiple dosage forms (capsule and solution); therefore, a dosage form or the strength specific to that dosage form would need to be specified when prescribed on an order. Coadministration and Dose: No dose overlap. Aptivus is dosed as 2 capsules or 1 teaspoonful coadministered with ritonavir 200 mg vs. Cystaran is dosed as one drop. Frequency: twice daily vs. every waking hour

No.	Proposed name: Cystaran Dosage Form: Ophthalmic Solution Strength: 0.44% Usual Dose: Instill one drop in each eye, every waking hour	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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	Azactam (Aztreonam) Injection Solution **Strength:** 1 gm, 2 gm **Usual Dose:** Adults: 500 mg to 2 gm intravenously or intramuscularly every 6 to 12 hours based on severity and type of infection Children: 30 mg/kg/day to 120 mg/kg/day intravenously every 6 to 8 hours	**Orthographic Similarity:** Both names contain similar letter string (Az vs. Cy) when scripted.	**Orthographic Difference:** Azactam contains the cross-stroke 't' in the 5th position while Cystaran contains the same letter in the 4th position. In addition, the suffix 'aran' in Cystaran appears longer than the suffix 'am' in Azactam giving the names a different appearance. **Differentiating Product Characteristics:** Strength: No strength overlap. Azactam is available in multiple strengths; thus a strength would need to be specified on the prescription for dispensing. Frequency: every 6 to 12 hours vs. every waking hour
4	Cayston (Aztreonam Lysine) Inhalation Solution **Strength:** 75 mg **Usual Dose:** 75 mg 3 times a day via inhalation using an Altera Nebulizer System. Doses should be taken at least 4 hours apart. 28 days on, 28 days off	**Orthographic Similarity:** Both names begin with the letter 'C', contain the same letter string (yst), and ends with the letter 'n'. **Strength:** Both products are available in a single strength. **Dose:** Both can be written as one dose without specifying the dosage form (one dose vs. one drop).	**Orthographic Difference:** Cayston contains an extra letter 'a' in the 2nd position which is not seen in Cystaran. Also, the letter string 'on' and 'aran' appear different when scripted. **Differentiating Product Characteristics:** Frequency: three times a day vs. every waking hour

No.	Proposed name: Cystaran Dosage Form: Ophthalmic Solution Strength: 0.44% Usual Dose: Instill one drop in each eye, every waking hour	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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
5	Cyclafem 1/35 (Norethindrone/Ethinyl Estradiol) Tablets **Strength:** 1 mg/0.035 mg **Usual Dose:** One tablet by mouth once daily Cyclafem 7/7/7 (Norethindrone/Ethinyl Estradiol) Tablets **Strength:** 0.5 mg, 0.075 mg, 1 mg/0.035 mg, 0.035 mg, 0.035 mg **Usual Dose:** One tablet by mouth once daily	**Orthographic Similarity:** Both names contain 8 letters, begin with the letters 'Cy' and contain an upstroke in the 4th position. **Dose:** Both can be written as one dose without specifying the dosage form (tablet vs. drop).	**Orthographic Difference:** Cyclafem contains an upstroke 'f' in the 6th position which is not seen in Cystaran giving the names a different shape and appearance. Modifier: Cyclafem contains the modifiers 1/35 or 7/7/7 which makes the name orthographically different than Cystaran. A modifier would need to be specified on the prescription in order to dispense Cyclafem. **Differentiating Product Characteristics:** Frequency: once daily vs. every waking hour
6	Cyclessa (Desogestrel/Ethinyl Estradiol) Tablets **Strength:** 0.125 mg, 0.15 mg, 0.1 mg/0.025 mg, 0.025 mg, 0.025 mg **Usual Dose:** 1 tablet by mouth once daily for 21 days, followed by a period of 7 days without drug (Triphasic regimen)	**Orthographic Similarity:** Both names contain 8 letters and begin with the letters 'Cy'. **Strength:** Both products are available in a single strength. **Dose:** Both can be written as one dose without specifying the dosage form (tablet vs. drops).	**Orthographic Difference:** Cyclessa contains the letter string 'essa' which when scripted appears different than the letter string 'aran' in Cystaran.. **Differentiating Product Characteristics:** Frequency: once daily vs. every waking hour

No.	Proposed name: Cystaran Dosage Form: Ophthalmic Solution Strength: 0.44% Usual Dose: Instill one drop in each eye, every waking hour	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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
7	Cystadane (Betaine, Anhydrous) Powder for Solution **Strength:** 1 g/Scoop **Usual Dose:** Children & Adults greater than or equal to 3 years of age: 3 g (3 scoops) by mouth twice daily Children less than 3 years of age: 100 mg/kg/day by mouth twice daily	**Orthographic Similarity:** Both names begin with the letters 'Cysta'. **Strength:** Both products are available in a single strength.	**Orthographic Difference:** Cystadane contains an upstroke 'd' in the 6th position which is not seen in Cystaran giving the names a different shape and appearance. **Differentiating Product Characteristics:** Frequency: twice daily vs. every waking hour Unit of Measure: scoop vs. drop
8	Cystagon (Cysteamine Bitartrate) Capsules **Strength:** 50 mg, 150 mg **Usual Dose:** Adults & Children 12 years and older: 500 mg by mouth every 6 hours Children under 12 years of age: 1.3 g/m^2/day by mouth every 6 hours	**Orthographic and Phonetic Similarities:** Both names begin with the letters 'Cysta' and end with the letter 'n'. Both names contain 3 syllables in which the first 2 syllables sound similar when spoken.	**Orthographic and Phonetic Differences:** Cystagon contains a downstroke 'g' in the 6th position which is not seen in Cystaran giving the names a different shape and appearance. When spoken, the 3rd syllable in Cystagon and Cystaran sound distinctly different. **Differentiating Product Characteristics:** Strength: No strength overlap. Cystagon is available in multiple strengths; thus a strength would need to be specified on the prescription for dispensing. Frequency: every 6 hours vs. every waking hour

No.	Proposed name: Cystaran Dosage Form: Ophthalmic Solution Strength: 0.44% Usual Dose: Instill one drop in each eye, every waking hour	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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
9	Cysteamine (Cysteamine Bitartrate) Capsules **Strength:** 50 mg, 150 mg **Usual Dose:** Children & Adults greater than or equal to 50 kg: Initial dose is $1/4^{th}$ to $1/6^{th}$ the final maintenance dose. The recommended maintenance dose is 2 g/day by mouth cysteamine free base, given in 4 equal daily doses. Children less than 50 kg: Initial dose is $1/4^{th}$ to $1/6^{th}$ the final maintenance dose. The recommended maintenance dose is 1.3 g/m^2/day by mouth cysteamine free base, given in 4 equal daily doses.	**Orthographic Similarity:** Both names begin with the letters 'Cyst'. **Dose:** Both can be written as one dose without specifying the dosage form (capsule vs. drop).	**Orthographic Difference:** Cysteamine contains 10 letters while Cystaran contains 8 letters giving the name Cysteamine a longer appearance. **Differentiating Product Characteristics:** Strength: No strength overlap. Cysteamine is available in multiple strengths; thus, a strength would need to be specified on the prescription for dispensing. Frequency: four times daily vs. every waking hour
10	Cysteine (Cysteine Hydrochloride) Solution for Injection **Strength:** 50 mg/mL **Usual Dose:** Administration of 30 mg to 40 mg of L-cysteine per every gram of amino acids in the individual daily Parenteral Nutrition (PN) formula. For example: for every 250 ml of a 5% amino acid solution (12.5 g protein) in the infusate, add 0.5 g of L-cysteine to the PN.	**Orthographic Similarity:** Both names contain 8 letters and begin with the letters 'Cyst'. **Strength:** Both products are available in a single strength.	**Orthographic Difference:** Cysteine contains the letter string 'eine' vs 'aran' in Cystaran which appears orthographically different when scripted. **Differentiating Product Characteristics:** Dose: No dose overlap. Cysteine is dosed based on the patient's individual daily Parenteral Nutrition (PN) formula (mg or mL) vs. Cystaran is dosed as one drop.

No.	Proposed name: Cystaran Dosage Form: Ophthalmic Solution Strength: 0.44% Usual Dose: Instill one drop in each eye, every waking hour	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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
11	Cytosar-U (Cytarabine) Powder for Injection **Strength:** 100 mg, 500 mg, 1 g, 2 g **Usual Dose:** *Subcutaneous Dosage:* For Acute Myelogenous Leukemia (AML): 100 mg/m^2/day for 5 days For Chronic Myelogenous Leukemia (CML): 15 mg/m^2/day to 20 mg/m^2/day for 10 to 21 days *Intravenous (IV) Dosage:* For AML: During induction--100 mg/m^2/day to 200 mg/m^2/day continuous IV infusion for 7 days During intensification--1 g/m^2 to 3 g/m^2 every 12 hours for 8 to 12 doses For Acute Lymphocytic Leukemia (ALL): 1 g/m^2 to 3 g/m^2 IV every 12 hours for 8 to 12 doses For CML: 200 mg/m^2/day continuous IV infusion for 9 days; 500 mg/m^2 every 12 hours for 3 days; 3 g/m^2/day for 5 days *Intrathecal Dosage:* For Carcinomatous meningitis: Children: 20 mg to 70 mg	**Orthographic Similarity:** Both names begin with the letters 'Cy' and contain a cross-stroke 't' in the middle of their names.	**Orthographic Difference:** Cystaran contains an extra letter 's' between the downstroke 'y' and the cross-stroke 't' which is not seen in Cytosar-U. **Differentiating Product Characteristics:** Strength: No strength overlap. Cytosar-U is available in multiple strengths; thus, a strength would need to be specified on the prescription for dispensing. Dose: Cytosar-U is dosed based on the patient's body surface area (mg or g) vs. Cystaran is dosed as one drop. Frequency: continuous IV infusion every 12 hours vs. every waking hour

No.	Proposed name: Cystaran Dosage Form: Ophthalmic Solution Strength: 0.44% Usual Dose: Instill one drop in each eye, every waking hour	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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
	Adults: 5 mg/m^2 to 7 mg/m^2 prepared in 5 mL to 10 mL of preservative free diluent or Ringer's lactate		
12	Cytovene (Ganciclovir) Capsules, Powder for Injection **Strength:** Capsule: 250 mg, 500 mg **Usual Dose:** 1000 mg 3 times a day or 500 mg 6 times a day with food Renal Dose: 500 mg by mouth 3 times per week to once daily to 1500 mg once daily or 500 mg 3 times per day **Strength:** Powder for Injection: 500 mg **Usual Dose:** Initial Dose: 5 mg/kg intravenously at a constant rate over 1 hour every 12 hours for 7 to 14 days. Maintenance Dose: 5 mg/kg intravenously at a constant rate over 1 hour once daily 7 days per week, or 6 mg/kg once daily 5 days per week **Renal Dose:** Initial Dose: 1.25 mg/kg	**Orthographic Similarity:** Both names contain 8 letters, begin with the letters 'Cy', and contains a cross-stroke 't' in the middle of their names. **Dose:** Both can be written as one dose without specifying the dosage form (capsule vs. drop).	**Orthographic Difference:** Cystaran contains an extra letter 's' between the downstroke 'y' and the cross-stroke 't' which is not seen in Cytovene. **Differentiating Product Characteristics:** Dosage Form and Strength: Cytovene is available in multiple dosage forms (capsule and injection solution); therefore, a dosage form or the strength specific to that dosage form would need to be specified when prescribed on an order. Frequency: Capsules: three to six times daily vs. every waking hour Injection Solution: intravenously at a constant rate over 1 hour every 12 hours or once daily vs. every waking hour

No.	Proposed name: Cystaran Dosage Form: Ophthalmic Solution Strength: 0.44% Usual Dose: Instill one drop in each eye, every waking hour	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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
	intravenously 3 times per week to once daily; 2.5 mg/kg once daily to 5 mg/kg every 12 hours Maintenanace Dose: 0.625 mg/kg 3 times per week to 0.625 mg/kg to 5 mg/kg once daily		
13	Cytoxan (Cyclophosphamide) Tablets, Powder for Injection **Strength:** Tablet: 25 mg, 50 mg Powder for Injection: 500 mg, 1 g, 2 g **Usual Dose:** Dosed in mg/kg or mg/m^2 for some indications. 1 mg/kg/day to 5 mg/kg/day **Renal Dose:** Up to 75% of the usual dosage in severe renal failure	**Orthographic Similarity:** Both names begin with the letters 'Cy', contain a cross-stroke 't' in the middle of their names, and end with the letters 'an'.	**Orthographic Difference:** Cystaran contains an extra letter 's' between the downstroke 'y' and the cross-stroke 't' which is not seen in Cytoxan. Also, Cytoxan contains a cross-stroke 'x' in the 5^{th} position not seen in Cystaran. **Differentiating Product Characteristics:** Strength: No strength overlap. Cytoxan is available in multiple strengths; thus, a strength would need to be specified on the prescription for dispensing. Dose: No dose overlap. Cytoxan is dosed based on the patient's body surface area or weight (mg or g) vs. Cystaran is dosed as one drop.

No.	Proposed name: Cystaran Dosage Form: Ophthalmic Solution Strength: 0.44% Usual Dose: Instill one drop in each eye, every waking hour	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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
			(b) (4)
15	Lysodren (Mitotane) Tablet **Strength:** 500 mg **Usual Dose:** 1 g to 19 g/day by mouth given in 3 to 4 divided doses	**Orthographic Similarity:** Both names contain 8 letters, begin with a similar letter string (Lys vs. Cys) when scripted, and ends with the letter 'n'. **Strength:** Both products are available in a single strength.	**Orthographic Difference:** Lysodren contains an upstroke 'd' in the 5th position while Cystaran contains a cross-stroke 't' in the 4th position giving the names a different appearance. **Differentiating Product Characteristics:** Frequency: three to four times a day vs. every waking hour

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

No.	Proposed name: Cystaran Dosage Form: Ophthalmic Solution Strength: 0.44% Usual Dose: Instill one drop in each eye, every waking hour	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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
16	Lysteda (Tranexamic Acid) Tablet **Strength:** 650 mg **Usual Dose:** Two 650 mg tablets by mouth 3 times daily for a maximum of 5 days during monthly menstruation **Renal Dose:** 650 mg once daily to 1300 mg once to twice daily for a maximum of 5 days during menstruation	**Orthographic Similarity:** Both names begin the similar letter string (Lyst vs. Cyst) when scripted. **Strength:** Both products are available in a single strength. **Dose:** Both can be written as one dose without specifying the dosage form (tablet vs. drop).	**Orthographic Difference:** Lysteda contains an upstroke 'd' in the 6th position not seen in Cystaran giving the names a different shape and appearance. **Differentiating Product Characteristics:** Frequency: once to three times a day vs. every waking hour
17	Systane (Polylene Glycol/PEG-400) Ophthalmic Solution **Strength:** 0.3%/0.4% **Usual Dose:** Instill 1 to 2 drops into eye(s) 3 to 4 times a day, as needed	**Orthographic and Phonetic Similarities:** Both names contain the similar letter string 'ysta' and when spoken, the first syllable in both names sound identical. **Strength:** Both products are available in a single strength. **Dose:** Both can be written as one dose without specifying the dosage form (drop vs. drop). **Route of Administration:** Both are given ophthalmically.	**Orthographic and Phonetic Differences:** When scripted, the first letters of the name pair, 'S' and 'C', appear orthographically different. Also, the name Systane consists of 2 syllables vs. 3 syllables in Cystaran in which the 2nd syllable in Systane sounds distinctly different. **Differentiating Product Characteristics:** Frequency: three to four times a day as needed vs. every waking hour

No.	Proposed name: Cystaran Dosage Form: Ophthalmic Solution Strength: 0.44% Usual Dose: Instill one drop in each eye, every waking hour	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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
18	Zyclara (Imiquimod) Cream **Strength:** 3.75% **Usual Dose:** Apply 1 to 2 packets before bedtime to the skin of the affected area; leave on for 8 hours, then remove with mild soap and water.	**Orthographic Similarity:** Both names begin with a similar letter string (Zy vs. Cy) when scripted and contain an upstroke in the 4th position. **Strength:** Both products are available in a single strength. **Dose:** Both can be written as one dose without specifying the dosage form (packet vs. drop).	**Differentiating Product Characteristics:** Frequency: once a day before bedtime, leave on for 8 hours then remove vs. every waking hour
19	Zydone (Hydrocodone Bitartrate/Acetaminophen) Tablet **Strength:** 5 mg/400 mg, 7.5 mg/400 mg, 10 mg/400 mg **Usual Dose:** 1 or 2 tablets every 4 to 6 hours up to 6 to 8 tablets per day	**Orthographic Similarity:** Both names begin with a similar letter (Zy vs. Cy) when scripted and contain an upstroke in the middle of the name. **Dose:** Both can be written as one dose without specifying the dosage form (tablet vs. drop).	**Orthographic Difference:** Cystaran contains an extra letter 's' between the downstroke 'y' and the upstroke 'd' which is not seen in Zydone. **Differentiating Product Characteristics:** Strength: No strength overlap. Zydone is available in multiple strengths; thus, a strength would need to be specified on the prescription for dispensing.

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

/s/

JUNG E LEE
06/27/2012

TODD D BRIDGES on behalf of CHI-MING TU
06/27/2012

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

Date:	August 10, 2010
Application Type/Number:	NDA 200740
Through:	Todd Bridges, RPh, Team Leader Denise Toyer, PharmD, Deputy Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis
From:	Deveonne Hamilton-Stokes, RN, BSN, Safety Evaluator Division of Medication Error Prevention and Analysis
Subject:	Proprietary Name Review
Drug Name(s):	Cystaran (Cysteamine HCl) Ophthalmic Solution 0.65%
Applicant:	Sigma-Tau Pharmaceuticals, Inc.
OSE RCM #:	2010-1021

CONTENTS

EXECUTIVE SUMMARY

This review summarizes the proprietary name evaluation of Cystaran (Cysteamine Hydrochloride) Ophthalmic Solution. Our evaluation finds that the proposed proprietary name, Cystaran acceptable.

The proposed proprietary name must be re-reviewed 90 days before approval of the NDA.

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

1 BACKGROUND

1.1 INTRODUCTION

This review responds to a request from Sigma-Tau Pharmaceuticals, Inc., for an assessment of the proposed proprietary name, Cystaran, regarding potential name confusion with other proprietary or established drug names in the usual practice settings.

Additionally, container labels and carton labeling were submitted and will be reviewed in a separate review.

1.2 REGULATORY HISTORY

On March 26, 2010, the Applicant submitted a request for the review of the proposed proprietary name, Cystoran. DMEPA found the name unacceptable (b) (4) The Applicant was notified via teleconference of DMEPA's findings and the name Cystoran was withdrawn by the Applicant.

1.3 PRODUCT INFORMATION

Cystaran ophthalmic solution is a cystine-depleting agent indicated for (b) (4) treatment of corneal cystine crystal accumulation in children and adults with cystinosis. The recommended dose is 1 drop instilled in both eyes every waking hour. It is available in a strength of 0.65 % and will be supplied in a 15 mL bottle. Cystaran should be stored in the freezer -25˚ to -15˚ C (-13˚ to 5˚F) prior to use. Cystaran must be thawed for approximately 24 hours before use. During waking hours Cystaran should be stored at (b) (4) or below for up to 1 week.

Cystaran is an orphan drug and will be used to treat a population of only 250-300 patients. Due to the small number of patients that Cystaran will be used to treat, Cystaran will only be dispensed by a single specialty pharmacy.

2 METHODS AND MATERIALS

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

2.1 SEARCH CRITERIA

The DMEPA safety evaluator considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Table 1.

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

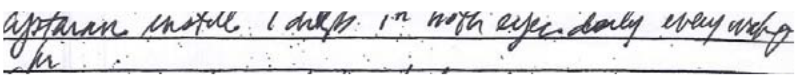
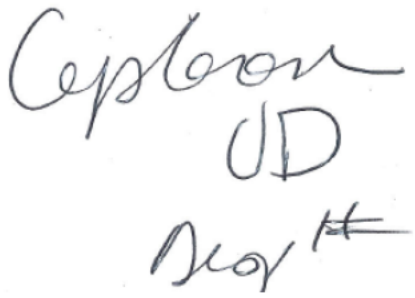
To identify drug names that may look similar to 'Cystaran', the DMEPA safety evaluator also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (eight letters), upstrokes (2, capital letter 'C', lower case letter 't'), downstrokes (one, lower case letter 'y'), dotted letters (none) and cross-strokes (one, lower case letter 't') . Additionally, several letters in Cystaran may be vulnerable to ambiguity when scripted (see Appendix B). As a result, the DMEPA safety evaluator also considers these alternate appearances when identifying drug names that may look similar to Cystaran.

When searching to identify potential names that may sound similar to Cystaran, DMEPA staff searches for names with similar number of syllables (three), stresses (CYST a ran, cys TAR an, or cyst tar AN), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary (See Appendix B). Moreover, names are often mispronounced or spoken with regional accents and dialects, so other potential pronunciations of the name are considered. The Applicant's intended pronunciation of the proprietary name was not provided.

2.2 FDA Prescription Analysis Studies

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, the following inpatient medication order, outpatient and verbal prescription was communicated during the FDA prescription studies.

Figure 1. Cystaran Rx Study (conducted on June 8, 2010)

HANDWRITTEN MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order : 	Cystaran As directed # 1
Outpatient Prescription: 	

[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)

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The DMEPA safety evaluator searches yielded a total of 19 names as having some similarity to the name, Cystaran.

Thirteen of the 19 names (Azactam, Azasan, Cistacurium, Lystodren, Cyclessa, Lysteda, Cytosar/Cytosar-U, Cysteine, Cayston, Cystine, Aptivus, Cystografin, and Cytoxan) were thought to look like Cystaran. Five names (Cytadren, Systane, Cystadane, Cytogam, and Cystagon) were thought to look and sound like Cystaran. The remaining name (Lysodren) was thought to sound similar to Cystaran.

A search of the United States Adopted Names (USAN) stems list on July 15, 2010 did not identify any USAN stems in the proposed proprietary name, Cystaran.

3.2 EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMEPA safety evaluator (See Section 3.1 above) and noted one additional name (b) (4) which was thought to have orthographic similarity to Cystaran.

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

3.3 FDA PRESCRIPTION ANALYSIS STUDIES

A total of 40 practitioners responded to the prescription analysis studies, but none of the responses overlapped with any existing or proposed drug names. None of the respondents interpreted the name correctly as Cystaran. Common misinterpretations included the first letter 'C' mistaken for: 'S' in the voice study and as the letter 'A' in the inpatient written study. The letter 'y' was misinterpreted as: the letter 'i' in the voice study and as the letter 'p' in the written studies. The first vowel 'a' was misinterpreted as the vowel 'e' in the voice study and the outpatient written study. The second vowel 'a' was misinterpreted as the vowels 'i', 'e' and 'o' in the written studies. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 COMMENTS FROM THE REVIEW DIVISIONS

3.4.1 Initial Phase of Review

In response to the OSE May 26, 2010 e-mail, the Division of Anti-Infective and Ophthalmology Products (DAIOP) stated that they had no preliminary concerns with the proposed proprietary name, Cystaran.

3.4.2 Midpoint of Review

On July 20, 2010, DMEPA notified DAIOP via e-mail that we had no objections to the proposed proprietary name, Cystaran. Per e-mail correspondence from DAIOP on July 29, 2010, they indicated that they concur with our assessment of the proposed proprietary name, Cystaran.

3.5 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator resulted in two additional names (Cytovene and Cefotaxime) thought to look similar to Cystaran and represent a potential source of drug name confusion.

Thus, we evaluated a total of 22 names for their similarity to the proposed name.

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

4 DISCUSSION

Cystaran is the proposed proprietary name for Cysteamine Hydrochloride Ophthalmic solution. This proposed name was 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

DDMAC did not have promotional concerns with the proposed name, Cystaran. The Division of Anti-Infective and Ophthalmology Products and DMEPA concurred with DDMAC's assessment.

4.2 LOOK-ALIKE AND SOUND ALIKE ANALYSIS

DMEPA identified and evaluated 22 names for their potential similarity to the proposed name, Cystaran. No other aspects of the name were identified as a source of potential confusion and error.

One name was withdrawn by the Applicant and was not evaluated further (see Appendix D). Failure mode and effect analysis (FMEA) was then applied to determine if the proposed proprietary name could potentially be confused with the remaining 21 names and lead to medication errors. This analysis determined that the name similarity between Cystaran was unlikely to result in medication errors with the remaining 21 names for the reasons presented in Appendices E and F. Thus, DMEPA has no objection to the proprietary name, Cystaran.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Cystaran, is not vulnerable to name confusion that could lead to medication errors, nor is it considered promotional. Thus the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Cystaran, for this product at this time.

The proposed proprietary name must be re-reviewed 90 days before approval of the NDA.

We are willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Brantley Dorch, OSE Project Manager, at 301-796-0150.

5.1 COMMENTS TO THE APPLICANT

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

The proposed proprietary name, Cystaran, will be re-reviewed 90 days prior to 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 are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

6 REFERENCES

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

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. FDA Document Archiving, Reporting & Regulatory Tracking System [DARRTS]

DARRTS is a government database used to organize Applicant and Sponsor submissions as well as to store and organize assignments, reviews, and communications from the review divisions.

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

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

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

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

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

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

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

USPTO provides information regarding patent and trademarks.

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

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

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

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

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

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

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

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

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

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

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

APPENDICES

Appendix A:

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

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

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

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

the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and focuses on the avoidance of medication errors.

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

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

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

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

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

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

Table 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 Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

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

1. Database and Information Sources

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

2. CDER Expert Panel Discussion

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

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

3. FDA Prescription Analysis Studies

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

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/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

DMEPA requests the Office of New Drugs (OND) responsible for the application for its 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 is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys its decision to accept or reject the name. OND is requested to concur/not concur with DMEPA's final decision.

5. External Proprietary Name Risk Assessment

DMEPA 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 assessment of the proposed name, the Safety Evaluator compares the findings of the overall risk assessment to the findings of the proprietary name risk

assessment submitted by the Applicant. The Safety Evaluator then determines whether the DMEPA staff's risk assessment concurs or differs with the findings. When the proprietary name risk assessments differ, the DMEPA staff provides a detailed explanation of these differences.

6. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

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

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

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

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

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

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

> ***"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:

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

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.

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in Name, Cystaran	Scripted may appear as	Spoken may be interpreted as
Capital 'C'	'A', 'E', 'O', 'G', 'L'	"S"
Lower case 'y'	'g', 'j', 'p',	"i"
Lower case 's'	'r',	
Lower case 't'	'f', 'l'	"D"
Lower case 'a'	'e', 'i', 'o', 'u'	any vowel
Lower case 'r'	'n', 'l'	
Lower case 'n'	'r', 's', 'm'	

Appendix C:

CDER Prescription Study Responses

Inpatient Medication Order	Voice Prescription	Outpatient Prescription
Aptarian	Sisteran	Cepleron
Aptaran	Sisteran	Cepheron
Aptarin	Sisteran	Cepleron
Aptaran	Cisteran	Cepteron
Apraran	Systeran	Cepleron
Cystarin	Cysteran	Cepleron
Aptaran	Cysteran	Cepbron OD
Aptarin	Cysteran	Cepteron
Aptaran	Cysteran	Cephalon
Aptaren	Systeran	Cepteon
Eptaran	Cistoran	Cepleon
Aptaran	Sisteran	Cepleon
Aptaran		Cepleren
		Cepleon
		Cepbon

Appendix D: Product withdrawn from market

Proprietary Name	Similarity to Cystoran	Comment
Cytadren (Aminoglutethimide)	Look and Sound	Withdrawn by Applicant 2008, no generics available

Appendix E: Drug names with differentiating product characteristics which minimize the risk of medication errors

Product name with potential for confusion	Similarity to Product Name	Dosage Form/ Strength	Usual Dose	Differentiating Product Characteristics Cystaran vs. product
Cystaran (Cysteamine Hydrochloride)		Ophthalmic solution: 0.65%	Instill one drop in both eyes every waking hour	
Cystine	Look	Powder: 1 gram	Not found	**Dosage form:** Ophthalmic solution vs. Powder **Route of administration:** Ophthalmically vs. Orally **Frequency of administration:** Every waking hour vs. Not found **Dose:** 1 drop vs. Not found Cystaran will only be dispensed from a single specialty pharmacy. Limited product characteristics found in Redbook 2009. Although the usual dose and frequency of administration of Cystine could not be found, the remaining product characteristics differ and will help to distinguish the product from Cystaran.
Cystagon (Cysteamine Bitartrate)	Look and Sound	Capsule: 50 mg, 150 mg	500 mg by mouth every 6 hours	**Dosage form:** Ophthalmic solution vs. Capsule **Route of administration:** Ophthalmically vs. Orally **Frequency of administration:** Every waking hour vs. Every 6 hours **Dose:** 1 drop vs. 500 mg Since Cystaran will only be used in a limited patient population (250-300 patients), Cystaran will only be dispensed from one specialty pharmacy.

Cytosar/Cystosar-U (Cytarabine)	Look	Injection: 100 mg/vial, 500 mg/vial, 1 gram/vial, 2 gram/vial	Non-lymphocytic Leukemia: 100 mg/m^2/day by continuous intravenous infusion (days 1 to 7) or 100 mg/m^2 intravenously ever 12 hours (days 1 to 7) Meningeal Leukemia: 5 mg/m^2 to 75 mg/m^2 intrathecally from once a day for 4 days to once every 4 days	**Dosage form:** Ophthalmic solution vs. Injection **Route of administration:** Ophthalmically vs. Intravenously or Intrathecally **Frequency of administration:** Every waking hour vs. every 12 hours or once daily for 7 days or once a day for 4 days **Dose:** 1 drop vs. 5 mg/m^2 to 75 mg/m^2 or 100 mg/m^2 Since Cystaran will only be used in a limited patient population (250-300 patients), Cystaran will only be dispensed from one specialty pharmacy.
Cytotec (Misoprostol)	Look	Tablet: 100 mcg, 200 mcg	200 mcg four times a day with food; (100 mcg can be given if 200 mcg is not tolerated)	**Dosage form:** Ophthalmic solution vs. Tablet **Route of administration:** Ophthalmically vs. Orally **Frequency of administration:** Every waking hour vs. 4 times a day **Dose:** 1 drop vs. 100 mcg or 200 mcg Since Cystaran will only be used in a limited patient population (250-300 patients), Cystaran will only be dispensed from one specialty pharmacy.
Azactam (Aztreonam)	Look	Injection: 500 mg/vial, 1 gram/vial, 2 gram/vial	500 mg to 2 grams intravenously ever 6 to 12 hours depending on severity and type of infection	**Dosage form:** Ophthalmic solution vs. Injection **Route of administration:** Ophthalmically vs. Intravenously **Frequency of administration:** Every waking hour vs. Every 6 hours to 12 hours **Dose:** 1 drop vs. 500 mg to 2 grams Since Cystaran will only be used in a limited patient population (250-300 patients), Cystaran will only be dispensed from one specialty pharmacy.
Azasan (Azathioprine)	Look	Tablets: 25 mg, 50 mg, 75 mg, 100 mg Injection: 100 mg/vial	Renal Homotransplantation: Initial dose: 3 mg/kg to 5 mg/kg daily Maintenance dose: 1 mg/kg to	**Dosage form:** Ophthalmic solution vs. Tablets and Injection **Route of administration:** Ophthalmically vs. Orally and Intravenously

			3 mg/kg daily Rheumatoid arthritis: 1 mg/kg (50 to 100 mg) given as a single dose or on a twice-daily schedule; Dose increments should be 0.5 mg/kg daily, up to a maximum dose of 2.5 mg/kg per day	**Frequency of administration:** Every waking hour vs. daily **Dose:** 1 drop vs. 1 mg/kg (50 mg to 100 mg) to 5 mg/kg daily Since Cystaran will only be used in a limited patient population (250-300 patients), Cystaran will only be dispensed from one specialty pharmacy.
Aptivus (Tipranavir)	Look	Capsules: 250 mg Solution: 100 mg/mL	500 mg by mouth twice daily (co-administered with ritonavir)	**Dosage form:** Ophthalmic solution vs. Tablet and Solution **Route of administration:** Ophthalmically vs. Orally **Frequency of administration:** Every waking hour vs. Twice daily **Dose:** 1 drop vs. 500 mg Since Cystaran will only be used in a limited patient population (250-300 patients), Cystaran will only be dispensed from one specialty pharmacy.
Cisatracurium Besylate (Nimbex)	Look	Injection : 2 mg/vial, 10 mg/vial	Tracheal intubation: 0.15 mg/kg or 0.20 mg/kg one time Maintenance of neuromuscular block: 0.03 mg/kg one time	**Dosage form:** Ophthalmic solution vs. Injection **Route of administration:** Ophthalmically vs. Intravenously **Frequency of administration:** Every waking hour vs. One time **Dose:** 1 drop vs. 0.03mg/kg, 0.15 mg/kg, or 0.20 mg/kg Since Cystaran will only be used in a limited patient population (250-300 patients), Cystaran will only be dispensed from one specialty pharmacy.
Cefotaxime	Look	Injection : 500 mg, 1 gram, 2 grams	Intramuscularly or Intravenously 0.5 gram to 2 grams as a single dose or every 4 to 12 hours depending on diagnosis	**Dosage form:** Ophthalmic solution vs. Injection **Route of administration:** Ophthalmically vs. Intravenously **Frequency of administration:** Every waking hour vs. Single dose or every 4 to 12 hours depending on diagnosis **Dose:** 1 drop vs. 0.5 gram to 2 grams Since Cystaran will only be used in a

				limited patient population (250-300 patients), Cystaran will only be dispensed from one specialty pharmacy.
Cytoxan (Cyclo-phosphamide)	Look	Tablet: 25 mg, 50 mg	1 mg/kg to 5 mg/kg/day (dosage must be adjusted in accord with evidence of antitumor activity)	**Dosage form:** Ophthalmic solution vs. Tablets and Injection **Route of administration:** Ophthalmically vs. Orally and Intravenously **Frequency of administration:** Every waking hour vs. daily or divided dose over a period of 2 to 5 days **Dose:** 1 drop vs. 1 mg/kg to 5 mg/kg or 40 mg to 50 mg/kg Since Cystaran will only be used in a limited patient population (250-300 patients), Cystaran will only be dispensed from one specialty pharmacy.
		Injection: 500 mg/vial, 1 gram/vial, 2 gram/vial	40 mg to 50 mg/kg intravenously in divided doses over a period of 2 to 5 days	
Cysteine (Cysteine Hydrochloride)	Look	Injection: 0.5 gram/10 mL vial	For use only after dilution in Aminosyn (a crystalline amino acid solution). Combine 10 mL of Cysteine aseptically with 12.5 grams of amino acids. The admixture is then diluted with 250 mL of dextrose 50%. Final solution should be infused within one hour of mixing	**Dosage form:** Ophthalmic solution vs. Injection **Route of administration:** Ophthalmically vs. Intravenously by central venous infusion **Frequency of administration:** Every waking hour vs. One time **Dose:** 1 drop vs. 0.5 gram Since Cystaran will only be used in a limited patient population (250-300 patients), Cystaran will only be dispensed from one specialty pharmacy.
Cyclessa (Desogestrel and Ethinyl Estradiol)	Look	Tablet: 0.1 mg, 0.125 mg, 0.15 mg; 0.025 mg	Take 1 tablet by mouth daily	**Dosage form:** Ophthalmic solution vs. Tablet **Route of administration:** Ophthalmically vs. Orally **Frequency of administration:** Every waking hour vs. Daily Since Cystaran will only be used in a limited patient population (250-300 patients), Cystaran will only be dispensed from one specialty pharmacy.

Lysteda (Tranexamic Acid)	Look	Tablets: 650 mg	Two 650 mg by mouth three times daily for a maximum of 5 days during monthly menstruation	**Dosage form:** Ophthalmic solution vs. Tablet **Route of administration:** Ophthalmically vs. Orally **Frequency of administration:** Every waking hour vs. Three times daily for a maximum of 5 days **Dose:** 1 drop vs. 1300 mg Since Cystaran will only be used in a limited patient population (250-300 patients), Cystaran will only be dispensed from one specialty pharmacy.
Cystografin (Diatrizoate Meglumine)	Look	Urethral Solution: 30 %	25 mL to 300 mL (depending on the age and degree of bladder irritability) via bladder instillation depending on the age and degree of bladder irritability	**Dosage form:** Ophthalmic solution vs. Urethral Solution **Route of administration:** Ophthalmically vs. Intravesical **Frequency of administration:** Every waking hour vs. one time **Dose:** 1 drop vs. 25 mL to 300 mL Since Cystaran will only be used in a limited patient population (250-300 patients), Cystaran will only be dispensed from one specialty pharmacy.
Cytogam (Cytomegalovirus Immune Globulin)	Look and Sound	Injection: 50 mg/mL	15 mg/kg/hr via intravenous infusion; Infusion should be complete within 12 hours	**Dosage form:** Ophthalmic solution vs. Injection **Route of administration:** Ophthalmically vs. Intravenously **Frequency of administration:** Every waking hour vs. One time within 72 hours of transplant and 2, 4, 6, 8, 12 and 16 weeks post transplant **Dose:** 1 drop vs. 15 mg/kg/hr Cytogam is dosed on patient's body weight. Since Cystaran will only be used in a limited patient population (250-300 patients), Cystaran will only be dispensed from one specialty pharmacy.
Cayston (Aztreonam)	Look	Inhalation solution: 75 mg	75 mg via nebulizer three times a day for 28 days with the Altera Nebulizer system	**Dosage form:** Ophthalmic solution vs. Inhalation solution **Route of administration:** Ophthalmically vs. Inhalation

				Frequency of administration: Every waking hour vs. Three times a day for 28 days **Dose:** 1 drop vs. 75 mg Since Cystaran will only be used in a limited patient population (250-300 patients), Cystaran will only be dispensed from one specialty pharmacy.
Lysodren (Mitotane)	Look	Tablet: 500 mg	2 grams to 16 grams per day in divided doses by mouth either 3 or 4 times a day	**Dosage form:** Ophthalmic solution vs. Tablet **Route of administration:** Ophthalmically vs. Orally **Frequency of administration:** Every waking hour vs. Three times or four times a day **Dose:** 1 drop vs. 2 grams to 16 grams Since Cystaran will only be used in a limited patient population (250-300 patients), Cystaran will only be dispensed from one specialty pharmacy.
Cytovene (Ganciclovir)	Look	Injection: 500 mg/10 mg vial	CMV Retinitis Treatment: 5 mg/kg intravenously over 1 hour every 12 hours for 14 to 21 days Prevention of CMV disease in Transplant Recipients: 5 mg/kg intravenously over 1 hours every 12 hours for 7 days to 14 days, followed by 5 mg/kg once daily, 7 days per week or 6 mg/kg once daily, 5 days per week	**Dosage form:** Ophthalmic solution vs. Injection **Route of administration:** Ophthalmically vs. Intravenously **Frequency of administration:** Every waking hour vs. every 12 hours to 24 hours for 7 to 21 days **Dose:** 1 drop vs. 5 mg/kg/hr Additionally, Cytovene is dosed on patient's body weight. Since Cystaran will only be used in a limited patient population (250-300 patients), Cystaran will only be dispensed from one specialty pharmacy.

(b) (4)

				Frequency of administration: Every waking hour vs. one **Dose:** 1 drop vs. up to 5 mL (600 mg) Since Cystaran will only be used in a limited patient population (250-300 patients), Cystaran will only be dispensed from one specialty pharmacy.

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

Appendix F: Potential confusing names with numerical overlap in strength or dose; however, risk of confusion with Cystaran minimized because of other differentiating product characteristics

Proposed name: Cystaran (Cysteamine Hydrochloride) Ophthalmic solution	**Strength:** 0.65%	**Usual Dose:** **Instill one drop in both eyes every waking hour**
Failure Mode: Name confusion	**Causes (could be multiple)**	**Effects**
Cystadane (Betaine Anhydrous) for oral solution powder 180 grams Usual dose: 6 grams per day by mouth in divided doses of 3 grams two times a day Indicated for the treatment of homocystinuria to decrease elevated homocysteine blood levels	Orthographic similarities: Both begin with 'Cyst-'; share the letters 'an' in similar positions near the end of the name Both products will be available as a single strength	Medication errors unlikely to occur in usual practice setting. *Rationale:* Although Cystaran and Cystadane are orthographically and phonetically similar, the differing product characteristics will help provide differentiation. Cystoran and Cystadane differ in regards to route of administration (ophthalmic vs. oral), frequency of administration (every hour while awake vs. twice daily) and usual dose (1 drop vs. 6 grams). Although the products are both single strength products and may be written without the strength, Cystaran may include a descriptor such as "instill" or "apply". Additionally, since Cystaran will only be used in a limited patient population (250-300 patients), Cystaran will only be dispensed from one specialty pharmacy.
Systane and Systane Ultra (OTC) (Polyethylene Glycol 400 0.4 % and Propylene Glycol 0.3 %) Apply 1 or 2 drops in the affected eye(s) as needed Systane Nightime Ointment (OTC) (Mineral Oil 3 % and White Petrolatum 94 %) Apply a small amount (one-fourth inch) of ointment of the inside of the eyelid	Orthographic similarities: Both share the letters 'ysta' in the same position; both contain the letter 'n' in similar positions Phonetic similarities: Both share the same beginning syllable (Cyst vs. Syst) Same route of administration: Ophthalmically Overlapping dosage form: Ophthalmic solution	Medication errors unlikely to occur in usual practice setting. *Rationale:* Cystaran and Systane are orthographically similar. However their endings differ phonetically ('ta ran' vs. 'tane'). Although the products share the same route of administration (ophthalmically), an overlapping dosage form (ophthalmic solution), and usual dose (1 drop) Cystaran and Systane differ with regards to frequency of administration (every hour while awake vs. as needed) and prescription status (RX vs. OTC) Additionally, since Cystaran will only be used in a limited patient population (250-300 patients), Cystaran will only be dispensed from one specialty pharmacy.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200740	ORIG-1	SIGMA TAU PHARMACEUTICALS INC	(Cysteamine hydrochloride ophthalmic solution) 0.65% Sterile

---

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

/s/

DEVEONNE G HAMILTON-STOKES
08/10/2010

DENISE P TOYER
08/11/2010

CAROL A HOLQUIST
08/12/2010