

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

125370

PROPRIETARY NAME REVIEW(S)

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

Date: February 25, 2011

Application Type/Number: BLA 125370

Through: Carlos Mena-Grillasca, RPh, Team Leader *CMena 2/25/2011*
Carol A. Holquist, RPh, Director *CHolquist 2/28/11*
Division of Medication Error Prevention and Analysis (DMEPA)

From: Lissa C. Owens, PharmD, Safety Evaluator *LO 2/25/11*
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name: Benlysta (Belimumab) for Injection
120 mg/vial and 400 mg/vial

Applicant: Human Genome Sciences

OSE RCM# 2010-2551

*****Note: This review contains proprietary and confidential information that should not be released to the public*****

1 INTRODUCTION

This re-assessment of the proposed proprietary name, Benlysta, is written in response to the anticipated approval of this BLA within 90 days from the date of this review. DMEPA found the proposed name Benlysta, acceptable in OSE Review # 2008-1164, dated March 26, 2009 and OSE Review # 2010-1311, dated August 13, 2010.

2 METHODS AND MATERIALS

For this proposed proprietary name, DMEPA staff searched a standard set of databases and information sources (see section 4) to identify names with orthographic and phonetic similarity to the proposed name that have been approved since the previous OSE proprietary name reviews. We used the same search criteria that was used in OSE Review # 2010-1311 for the proposed proprietary name, Benlysta. Since none of the proposed product characteristics were altered we did not re-evaluate previous names of concern. Additionally, DMEPA searched the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates.

The search of the databases yielded no new names thought to look similar to Benlysta and represent a potential source of drug name confusion. DMEPA staff also did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name Benlysta, as of February 25, 2011.

3 CONCLUSIONS

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

DMEPA considers this a final review; however, if approval of the BLA is delayed beyond 90 days from the date of this review, the Division of Pulmonary, Allergy, and Rheumatology should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

4 REFERENCES

- 1. OSE review #2008-1164 Proprietary Name Review of Benlysta; Holmes, Loretta**
- 2. OSE review #2010-1311 Proprietary Name Review of Benlysta; Park, Judy**
- 3. 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.
- 4. USANStems (<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
- 5. Division of Medication Error Prevention and Analysis proprietary name 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.

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 13, 2010
Application Type/Number:	BLA 125370
Through:	Carlos Mena-Grillasca, RPh, Team Leader <i>C. Mena 8/13/2010</i> Denise Toyer, PharmD, Deputy Director <i>D.P. Toyer 8/13/2010</i> Carol Holquist, RPh, Director <i>Carol Holquist 8/13/2010</i> Division of Medication Error Prevention and Analysis (DMEPA)
From:	Judy Park, PharmD, Safety Evaluator <i>Judy Park 8/13/2010</i> Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Benlysta (Belimumab) Lyophilized Powder for Intravenous Infusion 120 mg/vial and 400 mg/vial
Applicant/sponsor:	Human Genome Sciences
OSE RCM #:	2010-1311

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

CONTENTS

EXECUTIVE SUMMARY	3
1 BACKGROUND	3
1.1 Introduction	3
1.2 Product Information	3
2 METHODS AND MATERIALS	3
2.1 Search Criteria	3
2.2 FDA Prescription Analysis Studies	4
2.3 External Proprietary name Risk Assessment	4
3 RESULTS	5
3.1 Database and Information Sources	5
3.2 CDER Expert Panel Discussion	5
3.3 FDA Prescription Analysis Studies	5
3.4 External Name Study	5
3.5 Safety Evaluator Risk Assessment	5
3.6 Comments from the Division of Pulmonary, Allergy and Rheumatology (DPARP)	6
4 DISCUSSION	6
4.1 Promotional Assessment	6
4.2 Safety Risk Assessment	6
5 CONCLUSIONS AND RECOMMENDATIONS	7
5.1 Comments To The Applicant	7
6 REFERENCES	8
APPENDICES	10

EXECUTIVE SUMMARY

This review summarizes DMEPA's evaluation of the proposed proprietary name, Benlysta, for belimumab lyophilized powder for intravenous infusion. Our evaluation did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of this review. Thus, DMEPA finds the proposed proprietary name, Benlysta, acceptable for this product.

If the approval of this BLA is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

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 Human Genome Sciences (HGS) on May 28, 2010 for an assessment of the proposed proprietary name, Benlysta, regarding potential name confusion with other proprietary or established drug names in the usual practice settings. DMEPA reviewed the proposed name under IND phase (IND 9970) in OSE RCM #2008-1164 dated March 26, 2009. Additionally, the Applicant re-submitted an independent name analysis conducted by (b) (4) for the name Benlysta which is a duplicate of the report reviewed in OSE RCM #2008-1164.

The Applicant also submitted container labels which will be reviewed under separate cover (OSE RCM #2010-1312).

1.2 PRODUCT INFORMATION

Benlysta (Belimumab) lyophilized powder for intravenous infusion is a B-lymphocyte stimulator (BLyS)-specific inhibitor indicated for (b) (4) in adult patients with active, autoantibody-positive, systemic lupus erythematosus who are receiving standard therapy. The recommended dose is 10 mg/kg administered as an intravenous infusion over 1 hour at 2 week intervals for the first 3 doses and at 4-week intervals thereafter. Benlysta will be available in single use vials of 120 mg and 400 mg.

2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment for all proprietary names. Sections 2.1, 2.2, and 2.3 identify specific information associated with the methodology for the proposed proprietary name, Benlysta.

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter 'B' 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}

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

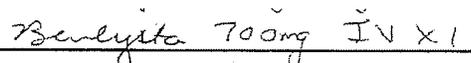
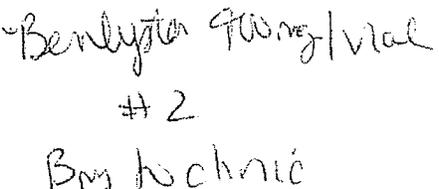
To identify drug names that may look similar to Benlysta, the DMEPA safety evaluators also consider the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (8 letters), upstrokes (three, capital letter 'B', lowercase letter 'l' and 't'), down strokes (one, lower case letter 'y'), cross strokes (one, lower case letter 't'), and dotted letters (none). Additionally, several letters in Benlysta may be vulnerable to ambiguity when scripted (See Appendix B). As a result, the DMEPA safety evaluators also consider these alternate appearances when identifying drug names that may look or sound similar to Benlysta.

When searching to identify potential names that may sound similar to Benlysta, the DMEPA safety evaluators search for names with similar number of syllables (3), stresses (BEN-lys-ta, ben-LYS-ta, ben-lys-TA), and placement of vowel and consonant sounds. Additionally, the DMEPA safety evaluators consider that pronunciation of parts of the name can be misinterpreted (See Appendix B). The Applicant's intended pronunciation is *\ben-LIST-uh* was also taken into consideration. However, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

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 and outpatient medication orders and verbal prescription was communicated during the FDA prescription studies.

Figure 1. Benlysta Prescription Study (conducted on June 25, 2010)

HANDWRITTEN MEDICATION ORDER	VERBAL PRESCRIPTION
<p><u>Inpatient Medication Order:</u></p> 	<p>Benlysta 400 mg Dispense 2 vials Bring to clinic</p>
<p><u>Outpatient Medication Order:</u></p> 	

2.3 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

For this product the Applicant submitted an external evaluation of the proposed proprietary name. The Division of Medication Error Prevention and Analysis conducts an independent analysis and evaluation of the data provided, and responds to the overall findings of the assessment.² 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

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

analyzed independently by the Safety Evaluator to determine if the potentially confusing name could lead to medication errors in the usual practice settings.

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

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The DMEPA Safety Evaluators' database searches yielded a total of 15 names as having some similarity to the name, Benlysta.

Seven names were thought to look like Benlysta by the DMEPA Safety Evaluators. These include: BanzaClin, Benadryl, Butisol, Carlesta, Kinlytic, Lunesta, and Prezista. Two additional names, (b) (4), and Relistor, were thought to sound like Benlysta. The remaining six names, Benahist, Benahist 10, Benahist 50, Bentyl, Benylin, and Benylsta, were thought to look and sound like Benlysta.

Additionally, DMEPA Safety Evaluators did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of July 19, 2010.

3.2 CDER EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMEPA Safety Evaluators (see Section 3.1 above) and noted one additional name, Linjeta^{***}, thought to have orthographic similarity to Benlysta.

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

3.3 FDA PRESCRIPTION ANALYSIS STUDIES

A total of 34 practitioners responded. Seventeen practitioners interpreted the name correctly as 'Benlysta', with correct interpretations all occurring in the written studies. The most common misinterpretation occurred with the letters 'l,' 'n,' and 'a' in the written studies. Practitioners misinterpreted the letter 'l' as 's' (n=1), the letter 'n' as 'v' (n=1), and the letter 'a' as 'er' (n=3), 'an' (n=1), 'en' (n=1), or 'on' (n=1). In the voice study, all the practitioners misinterpreted the letter 'y' as 'i' (n = 10). None of the responses in any of the studies identified a currently marketed drug name.

3.4 EXTERNAL NAME STUDY

The Applicant submitted a proprietary name risk assessment conducted by (b) (4) which is the same analysis submitted and reviewed in the IND phase (OSE RCM #2008-1164). Therefore, this report was not re-evaluated in this review.

3.5 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator identified no additional names thought to look or sound similar to Benlysta and represent a potential source of drug name confusion.

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

During the IND phase (OSE RCM #2008-1164), 22 names were evaluated for potential similarity to Benlysta. These 22 names were: Balziva, Bellergal, Benadryl, Benahist 10, Benahist 50, Benicar, Benlate, Bently, Benylin, BenzaClin, Benzotropine, Biohist LA, Byetta, Evista, Kinlytic, Lunesta, Neulasta, Pentasa, Phenytoin, Restanza^{***}, Vinblastine, and (b) (4). These 22 names were not re-evaluated since none of the product characteristics have changed from the IND phase except for the finalization of the dose which is now 10 mg/kg. The proposed dose in the IND phase was (b) (4). Both doses were considered during evaluation of the names in the IND phase, independently (b) (4).

Upon evaluation of the 16 names found in this review, 8 names (BenzaClin, Benadryl, Bently, Benylin, Benahist 10, Benahist 50, Kinlytic, and Lunesta) were previously reviewed in the IND phase. As noted above, we will not re-evaluate these 8 names.

As such, 8 new names were evaluated for their potential similarity to Benlysta.

3.6 COMMENTS FROM THE DIVISION OF PULMONARY, ALLERGY AND RHEUMATOLOGY (DPARP)

3.6.1 Midpoint of Review

On July 27, 2010, DMEPA notified DPARP via e-mail that we had no objections to the proposed proprietary name, Benlysta. Per e-mail correspondence from DPARP on August 13, 2010 they indicated that the review team does not have any issues with the proposed proprietary name, Benlysta.

4 DISCUSSION

Benlysta is the proposed proprietary name for Belimumab. This proposed name, Benlysta, was evaluated from a promotional and safety 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 had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name. DMEPA and DPARP concurred with this assessment.

4.2 SAFETY RISK ASSESSMENT

4.2.1 Proprietary Name Risk Assessment

DMEPA identified a total of 8 new names as having some similarity to the proposed name, Benlysta. We did not identify other aspects of the proprietary name that could function as a source of error.

The following names were not evaluated further for the following reasons: one name, Benlysta, is the proprietary name of the proposed product; one name, Benahist, is the root name of previously evaluated names in the IND phase (Benahist 10 and Benahist 50), one name (b) (4), was approved under the established name (see Appendix D), and the last name, Carlesta, has been discontinued (see Appendix E).

Failure Mode and Effects Analysis was then applied to determine if the proposed name, Benlysta, could potentially be confused with any of the remaining four names and lead to medication errors. This analysis

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

determined that the name similarity between Benlysta and all of the identified names was unlikely to result in medication errors for the reasons presented in Appendices F.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment indicates that the proposed name, Benlysta, is acceptable.

If any of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMEPA rescinds this Risk Assessment finding and the name must be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. If the approval of this BLA is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation. If you have further questions or need clarifications, please contact Carolyn Volpe, OSE Project Manager, at 301-796-5204.

5.1 COMMENTS TO THE APPLICANT

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

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

If any of the proposed product characteristics as stated in your May 28, 2010 submission are altered prior to approval of the marketing application, the proprietary name should be re-submitted 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. ***AMF Decision Support System [DSS]***

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

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

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

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

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

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

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 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

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

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.

because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examines the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly and 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 Applicant’s intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Applicant has little control over how the name will be spoken in clinical practice.

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

Type of similarity	Considerations when searching the databases		
	<i>Potential causes of drug name similarity</i>	<i>Attributes examined to identify similar drug names</i>	<i>Potential Effects</i>
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, the DMEPA staff also considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a

variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

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

2. CDER Expert Panel Discussion

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

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

3. FDA Prescription Analysis Studies

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

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

4. Comments from the OND review Division or Generic drugs

DMEPA requests the Office of New Drugs (OND) or Office of Generic Drugs (OGD) Regulatory Division responsible for the application for their comments or concerns with the proposed proprietary name and any

clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with DDMAC's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

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

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.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 possess 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

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

the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend the use of an alternate proprietary name.

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

- a. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].
- b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
- c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
- d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
- e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Applicant 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. 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), Joint Commission on Accreditation of Hospitals (JCOAH), 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 Applicant 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. Applicants have undertaken higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Applicant and at the expense of the public welfare, not to mention the Agency's

credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Applicants' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval. (See Section 4 for limitations of the process).

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in name, Benlysta	Scripted may appear as	Spoken may be interpreted as
Capital 'B'	'P,' 'V,' 'F,' 'f,' 'R'	V, P
Lower case 'n'	'm,' 'r,' 'u,' or 'v'	m
Lower case 'e' or 'a'	any vowel	any vowel
Lower case 'l'	'i,' 't,' 'e,' 'b,' or 's'	--
Lower case 'y'	'z,' 'p,' 'g'	i, ee
Lower case 's'	'e,' 'i,' 'n,' 'r,' or 'u'	z
Lower case 't'	'l,' 'f,' 'b'	d, t

Appendix C: FDA Prescription Study Responses for Benlysta.

Inpatient Medication Order	Outpatient Medication Order	Voice Prescription
Benlysta	Benlystan	Benlista
Bevlysta	Benlysta	Benlista
Benlysta	Benlyster	Benlista
Benlysta	Benlyston	Benlista
Benlysta	Benlysta	Benlista
Benlysta	Bensystem	Benlista
Benlyster	Benlysta	Benlista
Benlysta	Benlysta	
	Benlysta	
	Benlyster	

Appendix D: Proprietary name approved under the established name

Proprietary Name	Similarity to Benlysta	Status	Alternate proposed name
(b) (4)			

Appendix E: Proprietary name of a discontinued OTC product

Proprietary Name	Similarity to Benlysta	Status	Source
Carlesta (Zinc Oxide 26%) Over-the-counter	Look	Discontinued	Clinical Pharmacology Online

Appendix F: Proprietary names with differentiating product characteristics

Product name with potential for confusion	Similarity to Benlysta	Dosage Form/ Strength	Usual Dose	Differentiating product characteristics (Product vs. Benlysta)
Benlysta (Belimumab)	NA	Lyophilized Powder for Intravenous Infusion: 120 mg, 400 mg	10 mg/kg administered as an intravenous infusion over 1 hour at 2 week intervals for the first 3 doses and at 4-week intervals thereafter	NA
Prezista (Darunavir Ethanolate)	Look	Tablet: 75 mg, 150 mg, 300 mg, 400 mg, 600 mg	600 mg twice daily or 800 mg once daily with Ritonavir 100 mg and food	Frequency: once or twice daily vs. every 2 or 4 weeks Dosage form: tablet vs. injectable Route: oral vs. intravenous infusion
Butisol (Butabarbital Sodium)	Look	Tablet: 30 mg, 50 mg Elixir: 30 mg/5 mL	Depends on indication of use: 15 mg to 30 mg three to four times daily; or 50 mg to 100 mg at bedtime	Frequency: once, three or four times daily vs. every 2 or 4 weeks Dosage form: tablet or elixir vs. injectable Strength: 30 mg, 50 mg, 30 mg/5 mL vs. 120 mg, 400 mg Dose: 15 mg to 100 mg vs. 10 mg/kg

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

Relistor (Methylnaltrexone Bromide)	Sound	Injectable: 12 mg/0.6 mL	8 mg, 12 mg or 0.15 mg/kg every other day via subcutaneous injection	Frequency: every other day vs. every 2 or 4 weeks Strength: 12 mg/0.6 mL vs. 120 mg, 400 mg Dose: 8 mg, 12 mg or 0.15 mg/kg vs. 10 mg/kg Route: subcutaneous vs. intravenous infusion
Linjeta ^{***} ((b) (4)) Recombinant Human Insulin)	Look			

(b) (4)

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