CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

206843Orig1s000

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 Memorandum

Date:	April 10, 2015
Reviewer:	Mónica Calderón, PharmD, BCPS Division of Medication Error Prevention and Analysis
Team Leader:	Vicky Borders-Hemphill, PharmD Division of Medication Error Prevention and Analysis
Drug Name and Strength:	Daklinza (daclatasvir) Tablets, 30 mg and 60 mg
Application Type/Number:	NDA 206843
Applicant/Sponsor:	Bristol-Myers Squibb
OSE RCM #:	2015-49526

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

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1 INTRODUCTION

This memorandum is to re-assess the proposed proprietary name, Daklinza, under NDA 206843. DMEPA previously found the name Daklinza, acceptable for this product in OSE Review# 2014-17178 dated April 29, 2014; however, the Application received a Complete Response November 25, 2014. Thus, the Applicant re-submitted the name, Daklinza, for review on February 13, 2015. All product characteristics remain the same.

2 METHODS AND DISCUSSION

For re-assessments of the proposed proprietary name, DMEPA conducted a gap analysis and searched the POCA database (see Appendix A) to identify names with high orthographic and phonetic similarity to the proposed name that have been approved since the previous OSE proprietary name review #2014-17178. Additionally, we evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the proposed proprietary name. Our evaluation has not altered our previous conclusion regarding the acceptability of the proposed proprietary name. Additionally, our POCA search did not identify any new names that represent a potential source of drug name confusion. One new name was further evaluated and can be found in Appendix A.

Since the proposed product, Daklinza will be available in strength of 30 mg and 60 mg and these are not typical strengths, we searched the Pragmatic® Regulated Product Labeling Listing and Registration System (PR°PLLR™) database to identify any names with potential orthographic, spelling, and phonetic similarities with Daklinza that were not identified in POCA, and found to have an overlap in strength with Daklinza (Table 1). As a result, we maintain that the name is acceptable.

Table 1. (PR°PLLR™) **Search Results**	**POCA score**
Duet DHA	35
Dexmethylphenidate Hydrochloride extended-release	12

Additionally, DMEPA searched the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. The March 13, 2015 search of USAN stems did not find any USAN stems in the proposed proprietary name.

The Office of Prescription Drug Promotion OPDP determined the proposed name is acceptable from a promotional perspective. The Division of Antiviral Products (DAVP) concurred with OPDP's assessment in an email dated March 9, 2015.

3 CONCLUSIONS

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

If you have further questions or need clarifications, please contact Sarah Harris, OSE Project Manager, Danyal Chaudhry, at 301-796-3813

3.1 COMMENTS TO THE APPLICANT/SPONSOR

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

If any of the proposed product characteristics as stated in your February 13, 2015 re-submission are altered, the name must be resubmitted for review.

4 REFERENCES

1. Calderon M. Proprietary Name Review for Daklinza (NDA 206843). Silver Spring (MD): Food and Drug Administration, Center for Drug Evaluation and Research, Office of Surveillance and Epidemiology, Division of Medication Error Prevention and Analysis (US); 2014 Apr 29. OSE RCM No.: 2014-17178.

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

USAN Stems List contains all the recognized USAN stems.

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

APPENDICES

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

No.	**Proposed name: Daklinza** **Established name: daclatasvir** **Dosage form: tablets** **Strength(s): 30 mg and 60 mg** **Usual Dose: 1 tablet once daily**	**Combined POCA Score (%)**	**Orthographic and/or phonetic differences in the names sufficient to prevent confusion** **Other prevention of failure mode expected to minimize the risk of confusion between these two names.**
1.	EPI-CLENZ	56 (Phonetic only: 72)	The prefixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sounds different.
2.	SAXENDA	58 (Phonetic only: 71)	The prefixes and suffixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sounds different.
3.	BETAlin S	60 (Phonetic only: 70)	The prefixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sounds different. Betalin S has an extra syllable.
4.	PURKLENZ	60 (Phonetic only: 70)	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sounds different.
5.	ZUPLENZ	56 (Phonetic only: 70)	The prefixes and infixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sounds different. Daklinza has an extra syllable.

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/s/

MONICA M CALDERON
04/10/2015

BRENDA V BORDERS-HEMPHILL
04/10/2015

PROPRIETARY NAME REVIEW MEMORANDUM

Division of Medication Error Prevention and Analysis (DMEPA)

Office of Medication Error Prevention and Risk Management (OMEPRM)

Office of Surveillance and Epidemiology (OSE)

Center for Drug Evaluation and Research (CDER)

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Date of This Review:	April 29, 2014
Application Type and Number:	NDA 206843
Product Name and Strength:	Daklinza (daclatasvir) Tablets, 30 mg and 60 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Bristol-Myers Squibb
Submission Date:	April 4, 2014
Panorama #:	2014-17178
DMEPA Primary Reviewer:	Mónica Calderón, PharmD, BCPS
DMEPA Team Leader:	Irene Chan, PharmD, BCPS

Contents

1 INTRODUCTION

The proposed proprietary name, Daklinza, was found acceptable in OSE Review# 2013-2602, dated March 13, 2014 under IND 079599. This memorandum is to communicate that DMEPA maintains the proposed proprietary name, Daklinza, is acceptable from both a promotional and safety perspective under the NDA 206843.

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

1.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your April 4, 2014 submission are altered, the name must be resubmitted for review.

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2 REFERENCES

OSE Review# 2013-2602: Proprietary Name Review for Daklinza (daclatasvir), March 13, 2014.

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/s/

MONICA M CALDERON
04/29/2014

IRENE Z CHAN
04/29/2014

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:	March 13, 2014
Reviewer:	Rachna Kapoor, PharmD Division of Medication Error Prevention and Analysis
Team Leader:	Yelena Maslov, PharmD Division of Medication Error Prevention and Analysis
Drug Name and Strength(s):	Daklinza (Daclatasvir) 30 mg and 60 mg
Application Type/Number:	IND 079599
Applicant/Sponsor:	Bristol-Myers Squibb
OSE RCM #:	2013-2602

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CONTENTS

1 INTRODUCTION

This review evaluates the proposed proprietary name, Daklinza, 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

The Applicant submitted a request for proprietary name on November 11, 2013. Additionally, the Applicant submitted an external Proprietary Name Safety Summary conducted by Addison Whitney.

1.2 PRODUCT INFORMATION

The following product information is provided in the November 11, 2013 proprietary name submission.

- Intended Pronunciation: dak LIN zuh
- Active Ingredient: daclatasvir
- Indication of Use: treatment of hepatitis C
- Route of Administration: oral
- Dosage Form: tablet
- Strength: 30 mg and 60 mg
- Dose and Frequency: 60 – 90 mg by mouth once daily
- How Supplied: in bottle
- Storage: store at 25ºC (77°F); excursions permitted between 15°C and 30°C (59°F and 86°F)

2 RESULTS

The following sections provide 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 Antiviral Drug Products concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) SEARCH

The December 20, 2013 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, Daklinza, has no derivation or intended meaning. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 FDA Name Simulation Studies

Fifty-six practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with any currently marketed products nor did the misinterpretations sound or look similar to any currently marketed products or any products in the pipeline.

In the written outpatient study, 2 of 18 participants correctly interpreted the prescription. Common misinterpretations in the written outpatient study were substitution of 'm' for 'nz' and 'lz' for 'k'. In the written inpatient study, 10 of 18 participants correctly interpreted the prescription. Common misinterpretations in the written inpatient study were substitution of 'b' for 'k'. In the voice study, none of the 20 participants correctly interpreted the prescription. Common misinterpretations in the voice study include: 'p', 'vp', and 's' for 'k'; and 'y' for 'a'.

We have considered these variations in our look-alike and sound-alike searches and analysis (see Appendix B). See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines at Initial Review

In response to the OSE, November 21, 2013 e-mail, the Division of Antiviral Drug Products (DAVP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the 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, Daklinza. Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Daklinza 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 or by (b) (4) not identified by DMEPA and require further evaluation.

Table 1: Collective List of Potentially Similar Names (DMEPA, Expert Panel Discussion (EPD), Other Disciplines, and External Name Study)					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Look Similar					
Dixlanta	FDA	(b) (4)	FDA	Anakinra	FDA
Diclegis	FDA	Dakrina	FDA	Dallergy	FDA
Diltzac	FDA	Oaklide	FDA	Diclofenac	AW
Danazol	FDA	Salkera	FDA	Diltiazem	AW
Zolinza	FDA	Simbrinza	FDA		
Declomycin	FDA	Tekturna	FDA		
Sound Similar					
Clindamycin	AW				
Look and Sound Similar					
Dakin's Solution	FDA/AW	Relenza	FDA/AW	Onglyza	AW
Avinza	FDA/AW	Lovaza	AW		
Daclizumab	FDA/AW	Dexilant	AW		

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

2.2.6 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Antiviral Drug Products via e-mail on March 7, 2014. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Antiviral Drug Products on March 11, 2014, they stated no additional concerns with the proposed proprietary name, Daklinza.

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 Danyal Chaudhry, OSE project manager, at 301-796-3813.

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3.1 COMMENTS TO THE APPLICANT

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

Additionally, the proposed proprietary name must be submitted at the time of NDA submission. If any of the proposed product characteristics as stated in your November 11, 2013 submission are altered, the name must be resubmitted for review.

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. ***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.

10. ***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.

11. ***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.

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

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

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

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

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

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

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

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

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

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

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

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

18. 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.

19. Natural Standard (http://www.naturalstandard.com)

Natural Standard is a resource that aggregates and synthesizes data on complementary and alternative medicine.

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.

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[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 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 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 and Letter Strings with Possible Orthographic or Phonetic Misinterpretation

Letters in Name Daklinza	**Scripted May Appear as**	**Spoken May Be Interpreted as**
Capital 'D'	O, T, block B, P, Z, S	B, T
Lower case 'd'	cl, ci	b, t
Lower case 'a'	el, ci, cl, d, o, u	any vowel, y
Lower case 'k'	x, h, la, lc, b, lz	c. g, p, vp, s
Lower case 'l'	b, e, s, A, P, i	--
Lower case 'i'	e, l	any vowel, y
Lower case 'n'	m, u, x, r, h, s	dn, gn, kn, mn, pn
Lower case 'z'	c, e, g, n, m, q, r, s, v, y	c, s, x
Letter strings in Name Daklinza	**Scripted May Appear as**	**Spoken May Be Interpreted as**
li	b, w, u	--
nz	m	--

Appendix C: Prescription Simulation Samples and Results

Figure 1. Daklinza Study (Conducted on December 23, 2013)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order: Daklinza 60 mg po once daily	Daklinza 60 mg by mouth once daily Dispense: #30
Outpatient Prescription: Daklinza Sig: 60 mg PO qd Disp: #30	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

Study Name: Daklinza

As of Date 2/25/2014

198 People Received Study

56 People Responded

Total	18	20	18	
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
DABLINZA	0	0	1	1
DACLENZA	0	1	0	1
DAKINRA	1	0	0	1
DAKLIMA	2	0	0	2
DAKLINDRA	1	0	0	1
DAKLINNA	1	0	0	1
DAKLINRA	10	0	0	10
DAKLINZA	2	0	10	12
DALZLIMA	1	0	0	1
DEGLENZA	0	3	0	3
DEGLENZIA	0	1	0	1
DEGLINZA	0	3	0	3
DEKLINGER	0	0	1	1
DEKLINZA	0	0	1	1
DEPLENZA	0	1	0	1
DEVPLANZA	0	1	0	1
DICLENZA	0	1	0	1
DICLINZA	0	1	0	1
DIGLENZA	0	2	0	2
DIGLINZA	0	1	0	1

DIPLENZA	0	2	0	2
DUPLENZA	0	1	0	1
DYSLENZA	0	1	0	1
PAKLINZA	0	0	5	5
TAGLINZA	0	1	0	1

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

No.	Proprietary Name	Active Ingredient	Similarity to Daklinza	Failure preventions
1	Diclegis	Doxylamine succinate and pyridoxine hydrochloride	Look	The pair has sufficient orthographic differences
2	N/A	Danazol	Look	The pair has sufficient orthographic differences
3	Declomycin	Demeclocycline hydrochloride	Look	The pair has sufficient orthographic differences
4	Tekturna	Aliskiren	Look	The pair has sufficient orthographic differences
5	N/A	Diclofenac	Look	The pair has sufficient orthographic differences
6	N/A	Diltiazem hydrochloride	Look	The pair has sufficient orthographic differences
7	N/A	Clindamycin	Sound	The pair has sufficient phonetic differences
8	Lovaza	Omega-3-acid ethyl esters	Look and sound	The pair has sufficient orthographic and phonetic differences
9	Onglyza	Saxagliptin hydrochloride	Look and sound	The pair has sufficient orthographic and phonetic differences
10	N/A	Daclizumab	Look and sound	The pair has sufficient orthographic and phonetic differences
11	Salkera	Salicylic acid	Look	The pair has sufficient orthographic differences
12	Dallergy	Chlorpheniramine maleate and methscopolamine nitrate and phenylephrine hydrochloride	Look	The pair has sufficient orthographic differences
13	Oaklide	Leuprolide	Look	The pair has sufficient orthographic differences

No.	Proprietary Name	Active Ingredient	Similarity to Daklinza	Failure preventions
14	Diltzac	Diltiazem hydrochloride	Look	The pair has sufficient orthographic differences
(b) (4)			Look	(b) (4)
16	Dexilant	Dexlansoprazole	Look and sound	The pair has sufficient orthographic and phonetic differences

*** This document contains proprietary and confidential 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.

	Proposed name: ***Daklinza*** (Daclatasvir) **Dosage form and Strength(s):** Oral tablet: 30 mg and 60 mg **Usual dose:** 60 – 90 mg by mouth once daily	**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	**Dixlanta** (Aluminum hydroxide and magnesium hydroxide and simethicone) **Dosage form and Strength:** Oral suspension: aluminum hydroxide 200 mg, magnesium hydroxide 200 mg, simethicone 20 mg / 5 mL **Usual dose:** 10 – 20 mL by mouth between meals and at bedtime	**Orthographic similarities:** Both names have a similar length. Both names begin with the letter 'D', have the letter 'l' in the fourth position, have the letter 'n' in the 6th position and end with the letter 'a'.	**Orthographic differences:** The infix 'ix' in Dixlanta looks orthographically different than the infix 'ak' in Daklinza. The fifth and seventh letters in both names look orthographically different ('a' vs. 'i' and 't' vs. 'z') when scripted. The 't' has an upstroke and the 'z' has a downstroke when scripted. **Product characteristics differences:** Strength: the strengths do not overlap Dose: the doses do not overlap

	Proposed name: ***Daklinza*** (Daclatasvir) **Dosage form and Strength(s):** Oral tablet: 30 mg and 60 mg **Usual dose:** 60 – 90 mg by mouth once daily	**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**
2	**Dakrina** (Polyvinyl alcohols and povidone) **Dosage form and Strength:** Ophthalmic solution: polyvinyl alcohols 2.7% and povidone 2% **Usual dose:** Instill one drop in the affected eye(s) as needed	**Orthographic similarities:** Both names have a similar length and begin with the same prefix 'Dak'.	**Orthographic differences:** The ending 'rina' in Dakrina looks orthographically different than the ending 'linza' in Daklinza when scripted. **Product characteristics differences:** Strength: the strengths do not overlap Dose: the doses do not overlap This ophthalmic product is no longer being produced. It was discontinued in 2001.
3	**Zolinza** (Vorinostat) **Dosage form and Strength:** Oral capsule: 100 mg **Usual dose:** 400 mg by mouth once daily with food	**Orthographic similarities:** Both names have a similar shape and length. The prefix 'Zo' in Zolinza appears similar to the prefix 'Dak' in Daklinza when scripted. Both names have the same ending 'linza'.	**Product characteristics differences:** Strength: the strengths do not overlap Dose: the doses do not overlap

	Proposed name: ***Daklinza*** (Daclatasvir) **Dosage form and Strength(s):** Oral tablet: 30 mg and 60 mg **Usual dose:** 60 – 90 mg by mouth once daily	**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**
4	**Simbrinza** (Brinzolamide and brimonidine tartrate) **Dosage form and Strength:** Ophthalmic suspension: brinzolamide 1% - brimonidine 0.2% **Usual dose:** Instill one drop into the affected eyes(s) three times daily	**Orthographic similarities:** Both names have a similar length and shape. The first letter 'S' in Simbrinza appears similar to the first letter 'D' in Daklinza when scripted. Both names have an upstroke letter in the 4th position ('b' vs. 'l'). Both names have the same ending 'inza'.	**Orthographic differences:** The infix 'imbr' in Simbrinza looks orthographically different than the infix 'akl' in Daklinza when scripted. **Product characteristics differences:** Strength: brinzolamide 1% and brimonidine tartrate 0.2% can be expressed as a single strength product with no strength noted. Daclatasvir is available as 30 mg and 60 mg. The strengths do not overlap Dose: the doses do not overlap
5	(Anakinra) **Dosage form and Strength:** Solution for injection: 100 mg/0.67 mL **Usual dose:** 100 mg subcutaneously once daily	**Orthographic similarities:** Both names have a similar length. The ending 'inra' in Anakinra appears similar to the ending 'inza' in Daklinza when scripted.	**Orthographic differences:** The prefix 'Anak' in Anakinra looks orthographically different than the prefix 'Dakl' in Daklinza when scripted. **Product characteristics differences:** Strength: the strengths do not overlap Dose: the doses do not overlap

	Proposed name: ***Daklinza*** (Daclatasvir) **Dosage form and Strength(s):** Oral tablet: 30 mg and 60 mg **Usual dose:** 60 – 90 mg by mouth once daily	**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**
6	**Dakin's Solution** (Sodium hypochloride) **Dosage form and Strength(s):** Topical solution: 0.25% and 0.5% **Usual dose:** Apply to affected area once or twice daily	**Orthographic similarities:** Both names have the same beginning 'Dak'. **Phonetic similarities:** The first syllable of both names is the same ('dak').	**Orthographic differences:** Dakin's is shorter in length vs. Daklinza. The ending 'ins' in Dakin's looks orthographically different than the ending 'linza' in Daklinza. **Phonetic differences:** Dakin's has two syllables and Daklinza has three syllables. The second syllable gives the names a distinctly different sound when spoken ('ins' vs. 'lin'). Also, Daklinza has a third syllable 'zuh'. **Product characteristics differences:** Strength: the strengths do not overlap Dose: the doses do not overlap

	Proposed name: ***Daklinza*** (Daclatasvir) **Dosage form and Strength(s):** Oral tablet: 30 mg and 60 mg **Usual dose:** 60 – 90 mg by mouth once daily	**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	**Avinza** (Morphine sulfate) **Dosage form and Strength(s):** Extended-release capsule: 30 mg, 45 mg, 60 mg, 75 mg, 90 mg, and 120 mg **Usual dose:** 30 – 120 mg by mouth once daily	**Orthographic similarities:** Both names have the same ending 'inza'. **Phonetic similarities:** Both names contain 3 syllables. The third syllable of both names is the same ('zuh'). **Product characteristics similarities:** Strength: there is overlap in strength – morphine sulfate 30 mg and 60 mg vs. daclatasvir 30 mg and 60 mg	**Orthographic differences:** Avinza is shorter in length vs. Daklinza. The prefix 'Av' in Avinza looks orthographically different than the prefix 'Dakl' in Daklinza when scripted. **Phonetic differences:** The first and second syllables in both names give the names a distinctly different sound when spoken ('uh' vs. 'dak' and 'vin' vs. 'lin').

	Proposed name: ***Daklinza*** (Daclatasvir) **Dosage form and Strength(s):** Oral tablet: 30 mg and 60 mg **Usual dose:** 60 – 90 mg by mouth once daily	**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**
8	**Relenza** (Zanamivir) **Dosage form and Strength:** Powder for inhalation: 5 mg **Usual dose:** 10 mg inhaled once or twice daily	**Orthographic similarities:** Both names have a similar shape and length. Both names have the same ending 'nza'. The infix 'le' in Relenza appears similar to the infix 'li' in Daklinza when scripted. **Phonetic similarities:** Both names contain 3 syllables. The third syllable of both names is the same ('zuh'). The second syllable of both names sound similar when spoken ('len' vs. 'lin').	**Orthographic differences:** The prefix 'Re' in Relenza looks orthographically different than the prefix 'Dak' in Daklinza when scripted. **Phonetic differences:** The first syllable in both names gives the names a distinctly different sound when spoken ('ruh' vs. 'dak'). **Product characteristics differences:** Strength: the strengths do not overlap Dose: the doses do not overlap

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/s/

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03/13/2014

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03/19/2014