CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

217660Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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

Date of This Review:	February 15, 2023
Application Type and Number:	NDA 217660
Product Name and Strength:	Trikafta (elexacaftor, tezacaftor, and ivacaftor; ivacaftor) oral granules, 80 mg/40 mg/60 mg and 59.5 mg of ivacaftor 100 mg/50 mg/75 mg and 75 mg of ivacaftor
Product Type:	Multiple Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Vertex Pharmaceuticals Incorporated (Vertex)
PNR ID #:	2022-1044724850
DMEPA 1 Safety Evaluator:	Lissa C. Owens, PharmD
DMEPA 1 Team Leader:	Idalia E. Rychlik, PharmD
DMEPA 1 Director:	Mishale Mistry, PharmD, MPH

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Trikafta, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed proprietary name are outlined in the reference section and Appendix A, respectively. Vertex did not submit a current external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

Vertex previously submitted the proposed proprietary name, Trikafta on May 16, 2018[a] under IND 134285 for the oral tablets. We found the name acceptable under the IND. On July 19, 2019[b], Vertex submitted the proposed proprietary name, Trikafta under NDA 212273 for the oral tablets, and we re-assessed the name and maintained that the proposed name was acceptable. Trikafta oral tablets were approved under NDA 212273 on October 21, 2019.

On November 18, 2022, Vertex submitted the proposed proprietary name Trikafta, under NDA 217660, for the oral granule dosage form for use in patients aged 2 years and older.

1.2 PRODUCT INFORMATION

The following product information is provided in the labeling submission received on October 28, 2022. Product information for Trikafta oral tablets is also provided in Table 1 below.[c]

Table 1. Relevant Product Information for Trikafta NDA 217660 and Trikafta 212273

NDA	**217660**	**212273**
Product Name	**Trikafta** tri-KAF-tuh	**Trikafta** tri-KAF-tuh
Initial Approval Date	N/A	October 21, 2019
Active Ingredient	elexacaftor, tezacaftor, and ivacaftor oral granules; ivacaftor oral granules	elexacaftor, tezacaftor, and ivacaftor tablets; ivacaftor tablets
Indication	the treatment of cystic fibrosis (CF) in patients aged 2 years and older who have at least one F508del mutation in the CFTR gene or a mutation in the CFTR gene that is responsive based on in vitro data	
Route of Administration	Oral	
Dosage Form	*Oral granules*	*Oral tablets*

[a] Abraham, S. Proprietary Name Review for Trikafta (IND 134285). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 Nov 01. PNR ID No. 2018- 23096373.

[b] Owens, L. Proprietary Name Review for Trikafta (NDA 212273). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 AUG 22. PNR ID No. 2019-33248911

[c] Trikafta [Prescribing Information] DailyMed. U.S. National Library of Medicine. [cited 2023 Jan 09]. Available from: DailyMed - FDA Resources: SPL, Other Prescription Drug Labeling Resources, and Guidances (nih.gov).

<table>
<tr><td>Strength</td><td>100 mg/50 mg/75 mg and 75 mg of ivacaftor
80 mg/40 mg/60 mg and 59.5 mg of ivacaftor</td><td>50 mg/25 mg/37.5 mg and 75 mg of ivacaftor
100 mg/50 mg/75 mg and 150 mg of ivacaftor</td></tr>
<tr><td>Dose and Frequency</td><td><u>Ages 2 to less than 6 years old:</u><table><tr><th>Weight</th><th>Morning Dose</th><th>Evening Dose</th></tr><tr><td>Less than 14 kg</td><td>One packet containing elexacaftor 80 mg/tezacaftor 40 mg/ivacaftor 60 mg oral granules</td><td>One packet containing ivacaftor 59.5 mg oral granules</td></tr><tr><td>14 kg or more</td><td>One packet containing elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg oral granules</td><td>One packet containing ivacaftor 75 mg oral granules</td></tr></table></td><td><u>Ages 6 to 12 years old:</u><table><tr><th>Weight</th><th>Morning Dose</th><th>Evening Dose</th></tr><tr><td>Less than 30 kg</td><td>Two tablets, each containing elexacaftor 50 mg/tezacaftor 25 mg/ivacaftor 37.5 mg</td><td>One tablet of ivacaftor 75 mg</td></tr><tr><td>30 kg or more</td><td>Two tablets, each containing elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg</td><td>One tablet of ivacaftor 150 mg</td></tr></table><u>12 years and older:</u><table><tr><th>Morning Dose</th><th>Evening Dose</th></tr><tr><td>Two tablets, each containing elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg</td><td>One tablet of ivacaftor 150 mg</td></tr></table></td></tr>
<tr><td>How Supplied</td><td>Oral granules are supplied in morning and evening unit-dose packets containing a fixed dose. The packets are placed into a printed wallet. Four wallets are placed in a printed outer carton.</td><td>Tablets are supplied in a co-packaged blister pack sealed into a printed wallet containing a fixed-dose. Four such wallets are placed in a printed outer caron.</td></tr>
<tr><td>Storage</td><td colspan="2">Store at 68ºF - 77ºF (20ºC - 25ºC); excursions permitted to 59ºF - 86ºF (15ºC - 30ºC)</td></tr>
</table>

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Trikafta would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis 1 (DMEPA 1) concurred with the findings of OPDP's assessment for Trikafta. The Division of Pulmonology, Allergy, and Critical Care (DPACC) concurred with the findings of OPDP's assessment for Trikafta.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

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

[d] USAN stem search conducted on December 13, 2022.

2.2.2 Components of the Proposed Proprietary Name

Vertex did not provide a derivation or intended meaning for the proposed proprietary name, Trikafta, in their submission. This proprietary name is comprised of a single word. We note that the proposed name Trikafta contains the letter string '-af-' which is an abbreviation for the direction 'augmented formula, atrial fibrillation/atrial flutter', which may be used on prescription. We note that the product is an oral granule given by mouth for the treatment of cystic fibrosis and therefore it is unlikely that this could lead to any confusion or errors. Although we typically discourage the inclusion of medical abbreviations in proprietary names, we determined that the location of the letter string embedded in the middle of the name is unlikely to be separated from the surrounding letters in a manner that could lead to confusion in this case.

Additionally, Trikafta contains the letters 'Tr' at the beginning of the name, which is the abbreviation for time release. We evaluated the potential risk of misinterpreting the proposed proprietary name ('ikafta') and did not identify any concern. A POCA search of the name "ikafta" did not identify any names that would pose a risk of confusion.[e] Thus, we do not object to the inclusion of the letters 'Tr' in this case. Beyond these abbreviations, we note that Trikafta does not contain any additional components (i.e., a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 Comments from Other Review Disciplines at Initial Review

On December 8, 2022, the Division of Pulmonology, Allergy, and Critical Care (DPACC) did not forward any comments or concerns relating to Trikafta at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

In our November 28, 2022, study, one hundred and two (n=102) practitioners participated in DMEPA's prescription studies for Trikafta. We note that this study listed the dosage form incorrectly as 'tablet'.

In the inpatient written prescription simulation study, one participant misinterpreted the proposed proprietary name as 'Trileptal', a currently marketed product used to treat partial-onset seizures. We evaluated the name pair, Trikafta and Trileptal, further and found that there are sufficient orthographic, phonetic and product characteristic differences. Orthographically, the upstroke from the letter 'l' in the ninth position of Trileptal provide some differences not seen in Trikafta. Phonetically, the second (kaf vs. lep) and third syllables (ta vs. tal) sound different. Furthermore, we note that the proprietary name Trikafta is currently marketed for the oral tablet formulation under NDA 212273 and a search of the FDA Adverse Event Reporting System (FAERS) search (see Section 2.2.8) was conducted between Trikafta and Trileptal did not identify any reports of name confusion between the name pair.

We also note that the following product characteristics would aid in the mitigation of name confusion between the two products:

[e] POCA search for "ikafta" conducted on February 13, 2023, in version 5.2

The two products are presented in multiple strength formulations, which would require the strength to be transcribed on a medication order/prescription. Trikafta oral granules are proposed as a fixed dose combination in two strengths: elexacaftor 80 mg, tezacaftor 40 mg, and ivacaftor 60 mg and 59.5 mg of ivacaftor; and elexacaftor 100 mg, tezacaftor 50 mg, and ivacaftor 75 mg and 75 mg of ivacaftor. We also note that Trikafta tablets are available as a fixed-dose combination containing elexacaftor 50 mg, tezacaftor 25 mg and ivacaftor 37.5 mg co-packaged with ivacaftor 75 mg; and fixed-dose combination containing elexacaftor 100 mg, tezacaftor 50 mg, and ivacaftor 75 mg co-packaged with ivacaftor 150 mg. Trileptal is available in 150 mg, 300 mg, and 600 mg tablets; and 300 mg/5 mL (60 mg/mL) oral suspension. We acknowledge there is a numerical overlap in the ivacaftor component of one of the strengths of the proposed Trikafta granules and the Trileptal dosages forms (60 mg *versus* 60 mg/mL). However, given the unique fixed-dose strength presentation of Trikafta, further strength and dose differentiation would be required for a prescription/medication order.

When all of the aforementioned mitigations are considered in totality, we find the risk of name confusion is minimal. We also note that we evaluated the name pair in our previous review[f] with Trikafta oral tablets and found the pair acceptable. We agree with our previous decision.

The remaining responses in this study did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline.

In our January 27, 2023, prescription studies for Trikafta, we corrected the dosage form (from tablet to packet). Ninety-one (n=91) practitioners participated in this study. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline.

Appendix B contains the results from both prescription simulation studies.

2.2.5 Multiple Dosage Forms under a Single Proprietary Name

Under NDA 217660, the Applicant proposes a new dosage form of oral granules which will be available in two strengths: 100 mg/50 mg/75 mg and 75 mg of ivacaftor and 80 mg/40 mg/60 mg and 59.5 mg of ivacaftor oral granules. The Applicant proposes to market the dosage form of oral granules to facilitate administration in pediatric patients aged 2 years to less than 6 years. We note that Trikafta is currently available as oral tablets in strengths of 100 mg/50 mg/75 mg and 150 mg of ivacaftor; and 50 mg/25 mg/37.5 mg and 75 mg of ivacaftor. The oral tablets are intended for patients aged 6 years and older. We note that proposed oral granules share the same active ingredients, indication, route of administration, and frequency of administration as that of the currently approved tablets. We note that the proposed oral granules differ from the currently marketed Trikafta oral tablets with respect to the indicated age range, dosage form, and dose (see Section 1.1 Product Information, Table 1). Notably, both products are available in multiple fixed-dose strengths[g], which when prescribed, the unique fixed strength combination would need

[f] Abraham, S. Proprietary Name Review for Trikafta (IND 134285). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 Nov 01. PNR ID No. 2018- 23096373

[g] Oral granules: 100 mg/50 mg/75 mg and 75 mg of ivacaftor; 80 mg/40 mg/60 mg and 59.5 mg of ivacaftor

to be indicated on the prescription or medication order. However, we do acknowledge that the 'morning' dose for one of the strengths of the oral granules overlaps with the one of the strengths of the oral tablets (100 mg/50 mg/75 mg of ivacaftor); however, the 'evening' dose differs (75 mg of ivacaftor *versus* 150 mg of ivacaftor). Given the portion of overlapping strengths (100 mg/50 mg/75 mg), we consulted DPACC for input regarding the risk if the wrong formulation were dispensed and the wrong dose were to be administered. In the instance that a pediatric patient under the age of 6 and over 14 kg were prescribed the 100 mg/50 mg/75 mg and 75 mg of ivacaftor oral granule but inadvertently received the 100 mg/50 mg/75 mg and 150 mg of ivacaftor oral tablets, and was able to swallow the oral tablets, the clinical team stated that the "ivacaftor is well tolerated and an isolated higher dose would not likely have a lot of clinical implications". The Office of Pharmaceutical Quality (OPQ) stated that the granule formulation is not "exactly bioequivalent" to the tablet formulation but "does not expect these differences are clinically meaningful".

We note that in the instance that a healthcare provider includes only "100 mg/50 mg/75 mg of ivacaftor" on a prescription/medication order, the pharmacist would need to seek clarification from the healthcare provider to determine which product was intended, given that the oral granules and oral tablets differ with respect to the evening strength of ivacaftor.

We note that it is a common and accepted practice to have a product line with multiple formulations/dosage forms and strengths managed under one proprietary name. In this case, the residual risk of confusion between the oral granule and tablet formulations of the product may be mitigated through labels and labeling intervention and the different age indications for the products. Moreover, we have not identified any relevant medication errors involving name confusion with the proprietary name Trikafta. Therefore, given the precedent for using this naming convention and the considerations discussed above, we do not object to the Applicant's proposal to market the proposed product with the proprietary name, Trikafta.

2.2.6 Medication Error Data Selection of Cases

On January 24, 2023, we searched the FDA Adverse Event Reporting System (FAERS) database using the strategy listed in Table 2 (see Appendix A1 for a description of FAERS database) for name confusion errors involving ***Trikafta and Trileptal*** that would be relevant for this review.

Table 2. FAERS Search Strategy	
FAERS Field	Drug name confusion, Drug name look-alike, Drug name sound-alike, Product name confusion
Initial FDA Receive Dates	No date limitation
Product Name	Trikafta, Trileptal
Verbatim Name(s)	Trikafta, Trileptal
Event	DMEPA Official PNR Name Confusion Search Terms

Oral tablets: 100 mg/50 mg/75 mg and 150 mg of ivacaftor; 50 mg/25 mg/37.5 mg and 75 mg of ivacaftor

Country (derived)	USA

There were no reports retrieved.

2.2.7 Communication of DMEPA's Determination

On February 15, 2023, DMEPA 1 communicated our determination to the Division of Pulmonology, Allergy, and Critical Care (DPACC).

3 CONCLUSION

The proposed proprietary name, Trikafta, is conditionally acceptable.

If you have any questions or need clarifications, please contact Cristina Attinello, OSE project manager, at 301-796-3986.

3.1 COMMENTS TO VERTEX PHARMACEUTICALS INCORPORATED

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

If any of the proposed product characteristics as stated in your submission, received on November 18, 2022, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

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

USAN Stems List contains all the recognized USAN stems.

2. Phonetic and Orthographic Computer Analysis (POCA)

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

Drugs@FDA

Drugs@FDA is an FDA Web site that contains most of the drug products approved in the United States since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA-approved *brand name* and *generic drugs*; *therapeutic biological products*, *prescription* and *over-the-counter* human drugs; and *discontinued drugs* (see Drugs @ FDA Glossary of Terms, available at http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther_biological).

RxNorm

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

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

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

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

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

APPENDICES

Appendix A

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

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

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

[h] National Coordinating Council for Medication Error Reporting and Prevention. https://www nccmerp.org/about-medication-errors Last accessed 10/05/2020.

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

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
Y/N	**Is the proposed name obviously similar in spelling and pronunciation to other names?**
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	**Are there inert or inactive ingredients referenced in the proprietary name?**
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
Y/N	**Does the proprietary name include combinations of active ingredients?**
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
Y/N	**Is there a United States Adopted Name (USAN) stem in the proprietary name?**
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
Y/N	**Is this proprietary name used for another product that does not share at least one common active ingredient?**
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	**Is this a proprietary name of a discontinued product?**
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

b. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@fda, CernerRxNorm, and names in the review pipeline using a 55% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:

- Highly similar pair: combined match percentage score ≥70%.
- Moderately similar pair: combined match percentage score ≥55% to ≤ 69%.

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

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

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 3).
- Moderately similar names are further evaluated to identify the presence of attributes that are known to cause name confusion.
    - Name attributes: We note that the beginning of the drug name plays a significant role in contributing to confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are major contributing factor in the confusion of drug names[i]. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.
    - Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).

- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign

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

a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

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

   Four 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, verbal pronunciation of the drug name or during computerized provider order entry. 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 vulnerability of the proposed name to be misinterpreted by healthcare practitioners during written, verbal, or electronic prescribing.

   In order to evaluate the potential for misinterpretation of the proposed proprietary name during written, verbal, or electronic prescribing of the name, written inpatient medication orders, written outpatient prescriptions, verbal orders, and electronic orders are simulated, each consisting of a combination of marketed and unapproved drug products, including the proposed name.

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

   The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name.

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

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

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

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

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

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is ≥55% to ≤69%).

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

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

Table 5: Low Similarity Name Pair Checklist (i.e., combined score is ≤54%).

Names with low similarity are generally acceptable unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

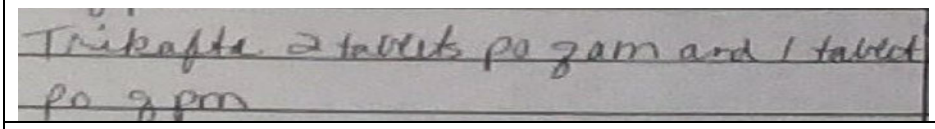
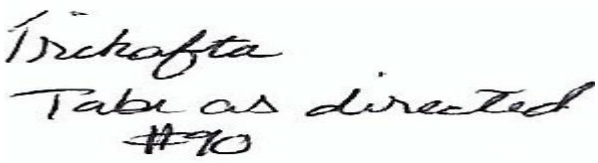
Appendix A1: Description of FAERS

The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support the FDA's postmarket safety surveillance program for drug and therapeutic biologic products. The informatic structure of the FAERS database adheres to the international safety reporting guidance issued by the International Conference on Harmonisation. FDA's Office of Surveillance and Epidemiology codes adverse events and medication errors to terms in the Medical Dictionary for Regulatory Activities (MedDRA) terminology. Product names are coded using the FAERS Product Dictionary. More information about FAERS can be found at:

http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm.

Appendix B: Prescription Simulation Samples and Results

Figure 1. Trikafta Study (Conducted on November 28, 2022)

Handwritten Medication Order/Prescription	**Verbal Prescription**
Medication Order:  	Trikafta Take as directed #90
Outpatient Prescription:  	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Trikafta	

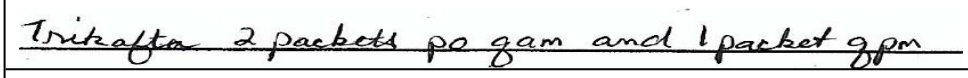
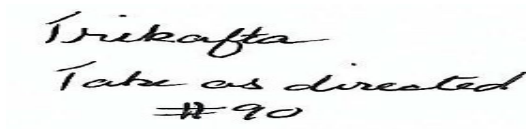
Study Name: Trikafta
As of Date 1/17/2023

262 People Received Study
102 People Responded

Study Name: Trikafta

Total	26	23	25	28	
INTERPRETATION	INPATIENT	CPOE	VOICE	OUTPATIENT	TOTAL
CRYKAFTA	0	0	1	0	1
FRIKEPTA	0	0	1	0	1
FRYCAFTA	0	0	1	0	1
PRIPATHTA	0	0	1	0	1
PRYCAFTA	0	0	1	0	1
RYKAPHTA	0	0	1	0	1
TRICAFTA	0	0	11	0	11
TRICALFTA	0	0	1	0	1
TRICASTA	0	0	1	0	1
TRICHAFTA	0	0	0	3	3
TRICKAFTA	0	0	0	1	1
TRIHAFTA	0	0	0	17	17
TRIHOFTA	0	0	0	3	3
TRIKAFTA	24	23	5	4	56
TRIKAFTE	1	0	0	0	1
TRILEPTAL	1	0	0	0	1
TRKAFTA	0	0	1	0	1

Figure 1. Trikafta Study (Conducted on January 27, 2023)

Handwritten Medication Order/Prescription	**Verbal Prescription**
Medication Order:  	Trikafta Take as directed #90
Outpatient Prescription:  	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Trikafta	

FDA Prescription Simulation Responses (<u>Aggregate Report)</u>

Study Name: Trikafta
As of Date 2/10/2023

258 People Received Study
91 People Responded

Study Name: Trikafta

Total	27	23	22	19	
INTERPRETATION	**INPATIENT**	**CPOE**	**VOICE**	**OUTPATIENT**	**TOTAL**
TIKAFTA	1	0	0	0	1
TRICAFTA	0	0	12	0	12
TRICALFTA	0	0	1	0	1
TRICAPTA	0	0	1	0	1
TRICASTA	0	0	1	0	1
TRIKAFTA	24	23	6	19	72
TRIKALFTA	1	0	0	0	1
TRIKALTA	1	0	0	0	1
TRYKEFTA	0	0	1	0	1

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/s/

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