

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

203094Orig1s000

203094Orig2s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

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

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Date of This Review:	June 11, 2014
Application Type and Number:	NDA 203094
Product Name and Strength:	Tybost (cobicistat) Tablets, 150 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Gilead Sciences
Submission Date:	April 9, 2014
Panorama #:	2014-17201
DMEPA Primary Reviewer:	Mónica Calderón, PharmD, BCPS
DMEPA Team Leader:	Irene Chan, PharmD, BCPS

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Tybost, 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. The Applicant re-submitted a previously evaluated external name study conducted by (b) (4).

1.1 REGULATORY HISTORY

The sponsor previously submitted the proposed proprietary name, Tybost on June 28, 2012. The Division of Medication Error Prevention and Analysis (DMEPA) found the name, Tybost acceptable in OSE Reviews #2012-1481 and #2012-2228, dated September 20, 2012 and March 11, 2013 respectively.

NDA 203094 was given a Complete Response on April 26, 2013, due to issues with the facility inspections and product quality deficiencies. Thus, the sponsor re-submitted the name, Tybost, under NDA 203094 as part of the Class 2 resubmission for review on April 9, 2014.

1.2 PRODUCT INFORMATION

The following product information is provided in the April 9, 2014 proprietary name submission.

- Intended Pronunciation: TYE-bost
- Active Ingredient: cobicistat
- Indication of Use: The proposed indication is for use as a pharmacoenhancer of (b) (4) atazanavir and darunavir in the treatment of HIV-1 infection.
- Route of Administration: Oral
- Dosage Form: Tablet
- Strength: 150 mg
- Dose and Frequency: 150 mg once daily with darunavir, atazanavir, or (b) (4)
- How Supplied: 30 count bottles
- Storage: Controlled room temperature of 25°C (77°F); excursions are permitted between 15°C and 30°C (b) (4)°F and 86°F, respectively).

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 Products (DAVP) 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

There is no USAN stem present in the proprietary name¹.

2.2.2 Components of the Proposed Proprietary Name

The Applicant did not provide a derivation or intended meaning for the proposed name, Tybost, in their submission. 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

One hundred and twenty one 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. Eighty participants interpreted the name correctly (outpatient n= 28, voice n= 15, inpatient n= 37). Twenty two participants misinterpreted the 'y': eight for 'g' (outpatient n=8) and fourteen for 'i' (voice n=14). Nine participants misinterpreted the 'b': two for 'v' (voice n=2), two for 'p' (voice n=4), and three for 'l' (outpatient n=3). Twelve participants misinterpreted 'bost': nine for 'boast' (voice n=9) and three for 'boste' (voice n=3). Appendix B contains the results from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines at Initial Review

In response to the OSE, April 27, 2014 e-mail, the Division of Antiviral 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 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Table 1 lists the number of names with the combined orthographic and phonetic score of $\geq 50\%$ retrieved from our POCA search organized as highly similar, moderately similar or low similarity for further evaluation. Sixty two names were initially identified; however, 10 names were excluded as they were previously identified and evaluated in prior reviews (OSE Review ##2011-2499, #2012-148, and #2012-2228).

¹USAN stem search conducted on May 13, 2014.

Table 1. POCA Search Results	Number of Names
Highly similar name pair: combined match percentage score $\geq 70\%$	2
Moderately similar name pair: combined match percentage score $\geq 50\%$ to $\leq 69\%$	50
Low similarity name pair: combined match percentage score $\leq 49\%$	0

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

Our analysis of the 52 names contained in Table 1 determined none of the names will pose a risk for confusion as described in Appendices C through G.

2.2.7 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Antiviral Products (DAVP) via e-mail on May 23, 2014. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DAVP on June 6, 2014, they stated no additional concerns with the proposed proprietary name, Tybost.

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.

3.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your April 9, 2014 submission are altered, the name must be resubmitted for review.

4 REFERENCES

1. **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.

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 considers the promotional and safety aspects of a proposed proprietary name.

1. **Promotional Assessment:** For prescription drug products, the promotional review of the proposed name is conducted by OPDP. For over-the-counter (OTC) drug products, the promotional review of the proposed name is conducted by DNCE. OPDP or DNCE 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 or DNCE 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.²

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

	Affirmative answers to these questions indicate a potential area of concern.
Y/N	Does the name have obvious Similarities in Spelling and Pronunciation to other Names?
Y/N	Are there Manufacturing Characteristics in the Proprietary Name?
Y/N	Are there Medical and/or Coined Abbreviations in the Proprietary Name?
Y/N	Are there Inert or Inactive Ingredients referenced in the Proprietary Name?
Y/N	Does the Proprietary Name include combinations of Active Ingredients?
Y/N	Is there a United States Adopted Name (USAN) Stem in the Proprietary Name?
Y/N	Is this the same Proprietary Name for Products containing Different Active Ingredients?
Y/N	Is this a Proprietary Name of a discontinued product?

² National Coordinating Council for Medication Error Reporting and Prevention.
<http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

- 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 50% 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 $\geq 70\%$.
 - Moderately similar pair: combined match percentage score $\geq 50\%$ to $\leq 69\%$.
 - Low similarity: combined match percentage score $\leq 49\%$.

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. Based on our root cause analysis of post marketing experience errors, we find the expression of strength and dose, which is often located in close proximity to the drug name itself on prescriptions and medication orders, is an important factor in mitigating or potentiating confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion is limited (e.g., route, frequency, dosage form, etc.).

- For highly similar names, there is little that can mitigate a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are likely to be rejected by FDA. (See Table 3)
- Moderately similar names with overlapping or similar strengths or doses represent an area for concern for FDA. The dosage and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, 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 (e.g., route, frequency, dosage form, etc.) to mitigate confusion may be limited when the strength or dose overlaps. FDA will review these 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 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 (See Table 5).

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

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

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

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

The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

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

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

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

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

Answer the questions in the checklist below. Affirmative answers to 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 do not share a common strength or dose (see Step 1 of the Moderately Similar Checklist).			
<u>Orthographic Checklist</u>		<u>Phonetic Checklist</u>	
Y/N	Do the names begin with different first letters? <i>Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.</i>	Y/N	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar* when scripted? <i>*FDA considers the length of names different if the names differ by two or more letters.</i>	Y/N	Do the names have different syllabic stresses?
Y/N	Considering variations in scripting of some letters (such as <i>z</i> and <i>f</i>), 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 as 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 $\geq 50\%$ to $\leq 69\%$).

<p>Step 1</p>	<p>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 have a higher potential for confusion and should be evaluated further (see Step 2).</p> <p>For single strength products, also consider circumstances where the strength may not be expressed.</p> <p>For any combination drug products, consider whether the strength or dose may be expressed using only one of the components.</p> <p>To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion:</p> <ul style="list-style-type: none"> ○ 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
<p>Step 2</p>	<p>Answer the questions in the checklist below. Affirmative answers to these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion between moderately similar names with overlapping or similar strengths or doses.</p>

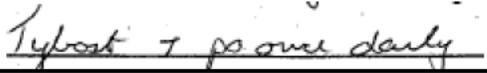
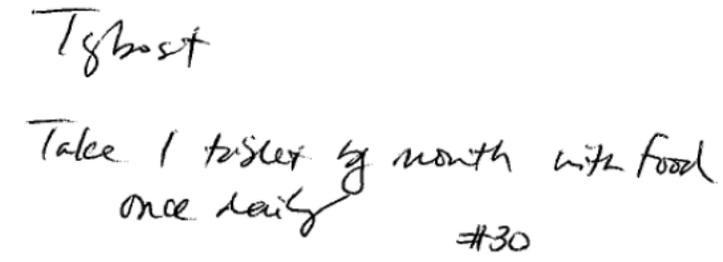
<p>Orthographic Checklist (Y/N to each question)</p> <ul style="list-style-type: none"> • Do the names begin with different first letters? <p>Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.</p> <ul style="list-style-type: none"> • Are the lengths of the names dissimilar* when scripted? <p>*FDA considers the length of names different if the names differ by two or more letters.</p> <ul style="list-style-type: none"> • Considering variations in scripting of some letters (such as <i>z</i> and <i>f</i>), 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? 	<p>Phonetic Checklist (Y/N to each question)</p> <ul style="list-style-type: none"> • Do the names have different number of syllables? • Do the names have different syllabic stresses? • Do the syllables have different phonologic processes, such as vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?
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Table 5: Low Similarity Name Pair Checklist (i.e., combined score is $\leq 49\%$).

In most circumstances, these names are viewed as sufficiently different to minimize confusion. Exceptions to this would occur in circumstances where there are data that suggest a name with low similarity might be vulnerable to confusion with your proposed name (for example, misinterpretation of the proposed name as a marketed product in a prescription simulation study). In such instances, FDA would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

Appendix B: Prescription Simulation Samples and Results

Figure 1. Proposed Name Study (Conducted on date of study)

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Medication Order:</u> </p> <p><u>Outpatient Prescription:</u> </p>	<p>Tybost 1 tablet by mouth once daily with food #30</p>

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

<p>Study Name: Tybost</p>					274 People Received Study
					121 People Responded
Total	36	44	41		
INTERPRETATION	OUTPATIENT	VOICE	INPATIENT	TOTAL	
TAIPOST	0	1	0	1	
TGBOST	7	0	0	7	
TGBUST	1	0	0	1	

TIBOAST	0	4	0	4
TIBOSE	0	1	0	1
TIBOST	0	7	0	7
TIBOSTE	0	1	0	1
TIPOST	0	1	0	1
TYBO	0	1	0	1
TYBOAST	0	5	0	5
TYBOS	0	1	0	1
TYBOSE	0	1	0	1
TYBOST	28	15	37	80
TYBOSTE	0	2	0	2
TYLBOST	0	0	1	1
TYLOST	0	0	3	3
TYPOST	0	2	0	2
TYVOST	0	2	0	2

Appendix C: Highly Similar Names (i.e., combined POCA score is $\geq 70\%$)

No.	Proposed name: Tybost Strength(s): 150 mg Usual Dose: 150 mg once daily with darunavir, atazanavir (b) (4)	POCA Score (%)	Orthographic and/or phonetic differences in the names sufficient to prevent confusion
1.	Tybost***	100	<ul style="list-style-type: none"> Proposed proprietary name of this review.
2.	Tavist-1	70	<ul style="list-style-type: none"> The names do not appear orthographically similar due to the downstroke 'y' and upstroke 'b' in Tybost that is not present in Tavist, which gives the names a different shape when scripted. The first syllables in the names sound different when spoken.

Appendix D: Moderately Similar Names (i.e., combined POCA score is $\geq 50\%$ to $\leq 69\%$)
with no overlap or numerical similarity in Strength and/or Dose

No.	Proposed Name	POCA Score (%)
3.	Tylox-325	60
4.	Adipost	58
5.	Totect	58
6.	Tavist-D	56
7.	Syntest	55
8.	Binosto	54
9.	Tatum-T	54
10.	Tovalt***	54
11.	Tencet	54
12.	Tusstat	53
13.	Depocyt	52
14.	Dymista	52
15.	Tirosint	52

16.	Cosopt	51
17.	Triostat	51
18.	Menest	50
19.	Timoptic	50
20.	Degest	50
21.	Degest 2	50
22.	Triposed	50
23.	(b) (4)	50

Appendix E: Moderately Similar Names (i.e., combined POCA score is $\geq 50\%$ to $\leq 69\%$) with overlap or numerical similarity in Strength and/or Dose

No.	Proposed name: Tybost Strength(s): 150 mg Usual Dose: 150 mg once daily with darunavir, atazanavir ^{(b) (4)}	POCA Score (%)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
24.	Bidhist	54	<ul style="list-style-type: none"> • The prefixes of the names have sufficient orthographic differences. • Tybost has a downstroke letter, which is absent in Bidhist. • Bidhist has an additional upstroke letter, which is absent in Tybost. • The first and second syllables in the names sound different when spoken.
25.	Stamoist	54	<ul style="list-style-type: none"> • The prefixes of the names have sufficient orthographic differences. • Tybost has a downstroke letter, which is absent in Stamoist. • The first and second syllables in the names sound different when spoken.
26.	Tri-kort	53	<ul style="list-style-type: none"> • The suffixes of the names have sufficient orthographic differences. • Tybost has a downstroke letter, which is absent in Tri-kort. • The second syllables in the names sound different when spoken.
27.	Dibent	52	<ul style="list-style-type: none"> • The prefixes and suffixes of the names have sufficient orthographic differences. • Tybost has a downstroke letter, which is absent in Dibent. • The second syllables in the names sound different when spoken.

28.	MyDocs	52	<ul style="list-style-type: none"> The prefixes and suffixes of the names have sufficient orthographic differences. The second syllables in the names sound different when spoken.
29.	Time-Hist	52	<ul style="list-style-type: none"> The lengths of the names differ by two letters. Tyboost has a downstroke letter, which is absent in Time-Hist. The second syllables in the names sound different when spoken.
30.	(b) (4)		
31.	Tripohist	51	<ul style="list-style-type: none"> The lengths of the names differ by three letters. The position of the downstroke letter in Tyboost is placed in the prefix, whereas the downstroke letter in Tripohist is in the infix. Tyboost has two syllables whereas Tripohist has three syllables.
32.	Bar-Test	50	<ul style="list-style-type: none"> The prefixes of the names have sufficient orthographic differences. Tyboost has a downstroke letter, which is absent in Bar-Test. The first and second syllables in the names sound different when spoken.

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

No.	Name	POCA Score (%)	Failure preventions
33.	Trest	60	NDA 13420 was withdrawn FR effective 09/04/1991. There are no generic equivalents available.
34.	Tisept	58	Name identified in RxNorm database.

			Unable to find product characteristics in commonly used drug databases.
35.	Tylosin	58	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
36.	(b) (4)		
37.			
38.			
39.			
40.			
41.	Ketaset	54	Name identified in RxNorm database. Unable to find product

			characteristics in commonly used drug databases.
42.	Tenoret	54	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
43.	Femtest	53	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
44.	(b) (4)		
45.			
46.			
47.			
48.			
49.	P Tuss D	50	Name identified in RxNorm database.

			Unable to find product characteristics in commonly used drug databases.
50.	Tabcin	50	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
51.	Timoptol	50	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
52.	Tustan	50	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.

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/s/

MONICA M CALDERON
06/11/2014

LUBNA A MERCHANT on behalf of IRENE Z CHAN
06/11/2014

**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--Final

Date: March 11, 2013

Reviewer: Morgan Walker, Pharm.D., MBA
Division of Medication Error Prevention and Analysis

Team Leader: Jamie Wilkins Parker, Pharm.D.
Division of Medication Error Prevention and Analysis

Drug Name and Strength: Tybost (Cobicistat) Tablets, 150 mg

Application Type/Number: NDA 203094

Applicant/sponsor: Gilead Sciences

OSE RCM #: 2012-2228

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

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1 INTRODUCTION

This re-assessment of the proposed proprietary name, Tybost (Cobicistat) Tablets, 150 mg is written in response to the anticipated approval of this NDA within 90 days from the date of this review. DMEPA found the proposed name, *Tybost*, acceptable in OSE Review # 2012-1481 dated September 20, 2012.

2 METHODS AND DISCUSSION

For re-assessments of proposed proprietary names, DMEPA searches 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 review. For this review we used the same search criteria described in OSE Review # 2012-1481. We note that none of the proposed product characteristics were altered. However, 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. The searches of the databases yielded no new names thought to look or sound similar to Tybost and represent a potential source of drug name confusion.

Additionally, DMEPA searched the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. The Safety Evaluator did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of March 1, 2013. The Office of Prescription Drug Promotion OPDP re-reviewed the proposed name on November 8, 2012 and had no concerns regarding the proposed name from a promotional perspective.

3 CONCLUSIONS

The re-evaluation of the proposed proprietary name, Tybost, did not identify any vulnerabilities that would result in medication errors with any additional name(s) noted in this review. Thus, DMEPA has no objection to the proprietary name, Tybost, for this product at this time.

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Anti-Viral Products (DAVP) should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

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

4 REFERENCES

1. **OSE Reviews: 2012-1481 (NDA 203094); 2011-2499 (IND 101283)**

2. ***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.

3. ***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.

4. ***Division of Medication Error Prevention and Analysis Proprietary Name Consultation Request***

Compiled list of proposed proprietary names submitted to the Division of Medication Error Prevention and Analysis for review. The list is generated on a weekly basis from the Access database/tracking system.

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

/s/

MORGAN A WALKER
03/11/2013

JAMIE C WILKINS PARKER
03/12/2013

**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: September 20, 2012

Reviewer: Morgan Walker, Pharm.D., M.B.A.
Division of Medication Error Prevention and Analysis

Acting Team Leader: Jamie Wilkins Parker, Pharm.D.
Division of Medication Error Prevention and Analysis

Division Director: Carol Holquist, RPh.
Division of Medication Error Prevention and Analysis

Drug Name and Strength: Tybost (Cobicistat) Tablets, 150 mg

Application Type/Number: NDA 203094

Applicant: Gilead Sciences

OSE RCM #: 2012-1481

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

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Tybost, 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

DMEPA completed a proprietary name review in OSE Review # 2011-2499 for Tybost (Cobicistat) IND 101283. The name was found acceptable at that time.

1.2 PRODUCT INFORMATION

The following product information is provided in the June 28, 2012 proprietary name submission.

- Proprietary Name: Tybost
- Established Name: Cobicistat
- Indication of Use: Pharmacokinetic enhancer of the HIV-1 protease inhibitors atazanavir and darunavir in adults
- Route of Administration: Oral
- Dosage Form: Tablets
- Strength: 150 mg
- Dose: One tablet once daily with food with either atazanavir 300 mg once daily or darunavir 800 mg once daily
- How Supplied: 30-count bottles
- Storage: Store at 25°C (77°F), excursions permitted to 15-30°C (59-86°F) (see USP Controlled Room Temperature).

2. RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion OPDP determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Anti-Viral 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 July 12, 2012 search of the United States Adopted Name (USAN) stems did not identify that a USAN stem is present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

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. The Applicant did not submit a derivation of the name with this submission.

2.2.3 FDA Name Simulation Studies

Twenty-eight practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with or appear or sound similar to any currently marketed products. Eight participants interpreted the inpatient prescription correctly. All of the outpatient study participants (n=11) misinterpreted the proposed name. The most common misinterpretation was replacing the 'o' in Tybost with the letter 'u'. The misinterpretations did not overlap with or appear or sound similar to any currently marketed products. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines

In response to the OSE, August 28, 2012 e-mail, the Division of Anti-Viral Products (DAVP) did not forward any comments or concerns relating to the proposed name at the initial phase of the proprietary name review.

2.2.5 Failure Mode and Effects Analysis of Similar Names

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in the proposed proprietary name, Tybost. Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Tybost identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines, which were not initially identified and evaluated in OSE Review #2011-2499.

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

Look Similar	
<i>Name</i>	<i>Source</i>
Azilect	FDA
Tyros 1	FDA
Tiject-20	FDA

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

2.2.6 Communication of DMEPA's Final Decision to Other Disciplines

DMEPA communicated our findings to the Division of Anti-Viral Products via e-mail on August 28, 2012. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Anti-Viral Products on September 5, 2012, they stated no additional concerns with the proposed proprietary name, Tybost.

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.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Tybost, and have concluded that this name is acceptable. However, if any of the proposed product characteristics as stated in your June 28, 2012 submission are altered, name must be resubmitted for review.

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

4 REFERENCES

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

Micromedex contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.

2. ***Phonetic and Orthographic Computer Analysis (POCA)***

POCA is a database which was created for the Division of Medication Error Prevention and Analysis, FDA. As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion.

3. ***Drug Facts and Comparisons, online version, St. Louis, MO***
(<http://factsandcomparisons.com>)

Drug Facts and Comparisons is a compendium organized by therapeutic course; it contains monographs on prescription and OTC drugs, with charts comparing similar products. This database also lists the orphan drugs.

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

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

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

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

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

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

7. ***U.S. Patent and Trademark Office*** (<http://www.uspto.gov>)

USPTO provides information regarding patent and trademarks.

8. ***Clinical Pharmacology Online*** (www.clinicalpharmacology-ip.com)
Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. It also provides a keyword search engine.
9. ***Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at*** (www.thomson-thomson.com)
The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and trade names that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.
10. ***Natural Medicines Comprehensive Databases*** (www.naturaldatabase.com)
Natural Medicines contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.
11. ***Access Medicine*** (www.accessmedicine.com)
Access Medicine® from McGraw-Hill contains full-text information from approximately 60 titles; it includes tables and references. Among the titles are: Harrison's Principles of Internal Medicine, Basic & Clinical Pharmacology, and Goodman and Gilman's The Pharmacologic Basis of Therapeutics.
12. ***USAN Stems*** (<http://www.ama-assn.org/ama/pub/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml>)
USAN Stems List contains all the recognized USAN stems.
13. ***Red Book*** (www.thomsonhc.com/home/dispatch)
Red Book contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.
14. ***Lexi-Comp*** (www.lexi.com)
Lexi-Comp is a web-based searchable version of the Drug Information Handbook.
15. ***Medical Abbreviations*** (www.medilexicon.com)
Medical Abbreviations dictionary contains commonly used medical abbreviations and their definitions.
16. ***CVS/Pharmacy*** (www.CVS.com)
This database contains commonly used over the counter products not usually identified in other databases.

17. Walgreens (www.walgreens.com)

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

18. Rx List (www.rxlist.com)

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

19. Dogpile (www.dogpile.com)

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

20. 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

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

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. 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		
	<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/Similar shape 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, 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 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

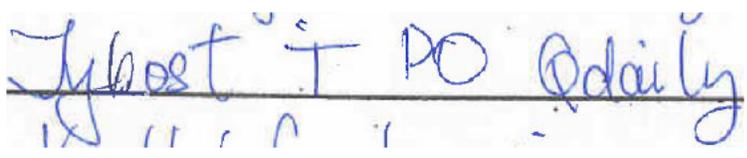
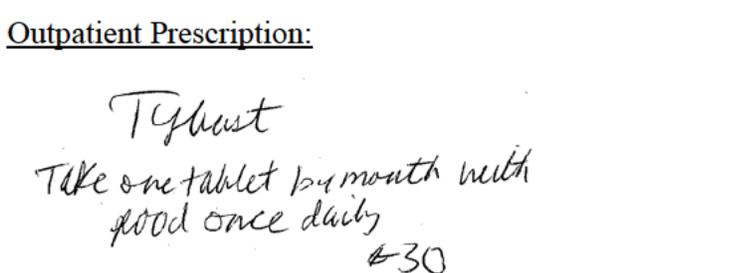
past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Sponsors' have changed a product's proprietary name in the post-approval 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 with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Tybost	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'T'	F, Z, J	D
Lower case 't'	r, f, x, A	d
Lower case 'y'	f, p, u, v, x, Z	e, i, u
Lower case 'b'	l, h, k	p, v, d
Lower case 'o'	a, c, e, u	N/A
Lower case 's'	G, 5, g, n,	x
Lower case 't'	r, f, x, A	d

Appendix C: Prescription Simulation Samples and Results

Figure 1. Tybost Study (Conducted on July 13, 2012)

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Medication Order:</u></p> 	<p>Tybost Take one by mouth with food once daily. Disp. # 30</p>
<p><u>Outpatient Prescription:</u></p> 	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

					88 People Received Study
					28 People Responded
Study Name: Tybost					
Total	9	8	11		
INTERPRETATION	INPATIENT	VOICE	OUTPATIENT	TOTAL	
HYBOATH	0	1	0	1	
HYVOST	0	1	0	1	
JYBOST	1	0	0	1	
TIBOST	0	2	0	2	
TYBAST	0	0	5	5	
TYBO TYPOS	0	1	0	1	
TYBOST	8	2	0	10	
TYBOT	0	1	0	1	
TYBUST	0	0	6	6	

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

Proprietary Name	Active Ingredient	Similarity to Tybost	Failure preventions
Azilect	Rasagiline Mesylate	Look Alike	The pair has sufficient orthographic differences.
Tyros 1	N/A	Look Alike	This is not a drug product, therefore, a prescription would not be written for this.
Tiject-20	N/A	Look Alike	This is not a drug product, therefore, a prescription would not be written for this.

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/s/

MORGAN A WALKER
09/20/2012

CAROL A HOLQUIST
09/21/2012