

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

204017Orig1s000

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)

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

Date of This Review:	July 22, 2019
Application Type and Number:	NDA 204017
Product Name and Strength:	Twirla (Levonorgestrel and Ethinyl Estradiol) transdermal system, 120 mcg/30 mcg/day
Product Type:	Combination Product (Drug-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Agile Therapeutics, Inc. (Agile)
Panorama #:	2019-32058071
DMEPA Safety Evaluator:	Chad Morris, PharmD, MPH
DMEPA Team Leader (Acting):	Briana Rider, PharmD

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Twirla, 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. Agile submitted an external name study, conducted by [REDACTED]^{(b) (4)}, for this proposed proprietary name.

1.1 REGULATORY HISTORY

Agile previously submitted the proposed proprietary name, Twirla, on April 19, 2012. We found the name, Twirla, conditionally acceptable on July 3, 2012^a. A Complete Response (CR) was issued for NDA 204017 on February 13, 2013.

NDA 204017 was resubmitted on June 26, 2017. As part of the Class II resubmission, Agile resubmitted the name, Twirla, for our review on June 26, 2017. We found the name, Twirla, conditionally acceptable on September 8, 2017^b. A CR was issued for NDA 204017 on December 21, 2017.

NDA 204017 was resubmitted on May 16, 2019. Thus, Agile resubmitted the name, Twirla, for review on May 29, 2019.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on May 29, 2019.

- Intended Pronunciation: TWER-la
- Active Ingredient: Levonorgestrel and Ethinyl Estradiol
- Indication of Use: prevention of pregnancy
- Route of Administration: transdermal
- Dosage Form: transdermal system
- Strength: 120 mcg/30 mcg/day
- Dose and Frequency: Apply 1 patch once weekly for 3 weeks, followed by no patch for one week.
- How Supplied: carton containing 3 patches
- Storage: Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F). [REDACTED]^{(b) (4)}

^a Park, A. Proprietary Name Review for Twirla NDA 204017. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2012 JUL 03. Panorama No. 2012-969.

^b Morris, C. Proprietary Name Review for Twirla NDA 204017. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 SEP 08. Panorama No. 2017-16401702.

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Twirla would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Bone, Reproductive and Urologic Products (DBRUP) concurred with the findings of OPDP's assessment for Twirla.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proposed proprietary name^c.

2.2.2 Components of the Proposed Proprietary Name

Agile did not provide a derivation or intended meaning for the proposed proprietary name, Twirla, 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 Comments from Other Review Disciplines at Initial Review

In response to the OSE, June 13, 2019 e-mail, the Division of Bone, Reproductive and Urologic Products (DBRUP) did not forward any comments or concerns relating to Twirla at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Ninety-four practitioners participated in DMEPA's prescription (Rx) studies for Twirla. One participant in the inpatient Rx study misinterpreted the proposed name, Twirla, as Twista, which is a close variation to the currently marketed product, Twynsta. We note, the name Twynsta was identified in the previous external study and evaluated in our previous review (OSE RCM# 2017-16401702). However, in light of this response in our Rx study, we re-evaluated the name pair, Twirla and Twynsta, and maintain that there are sufficient orthographic, phonetic, and product characteristic differences.

Orthographically, the infixes and suffixes of this name pair are sufficiently different. Twynsta contains the downstroke letter 'y' in the infix whereas, Twirla does not contain any downstroke letters, which gives the names different shapes when scripted. Additionally, Twirla contains the upstroke letter 'l' in the suffix whereas, Twynsta contains the crossed letter 't' in the suffix.

^c USAN stem search conducted on June 6, 2019.

Phonetically, the ending of the first syllables (TWER vs TWIN) and second syllables (la vs stah) sound different.

Our assessment is further supported by the FDA Phonetic and Orthographic Computer Analysis (POCA) software, which calculates a combined phonetic and orthographic score of 43% for this name pair, which suggests that the names have low similarity.

Furthermore, there is no direct overlap in strength (120 mcg/30 mcg/day vs 40 mg/5 mg, 40 mg/10 mg, 80 mg/5 mg, and 80 mg/10 mg), dosage form (transdermal system vs. tablet), or route of administration (transdermal vs. oral) which further mitigates the risk for confusion when this information is included on a prescription. See Appendix E.

Appendix B contains the results from the verbal and written prescription studies.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search^d identified 29 names with the combined score of $\geq 55\%$ or individual orthographic or phonetic score of $\geq 70\%$. We had identified and evaluated some of the names in our previous proprietary name reviews. We re-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 name. We note that none of the product characteristics have changed and we agree with the findings from our previous review for the names evaluated previously. Therefore, we identified 2 names not previously analyzed. These names are included in Table 1 below.

2.2.6 Names Retrieved for Review Organized by Name Pair Similarity

Table 1 lists the number of names retrieved from our POCA search and the FDA Prescription Simulation Study. These name pairs are organized as highly similar, moderately similar or low similarity for further evaluation.

Table 1. Names Retrieved for Review Organized by Name Pair Similarity	
Similarity Category	Number of Names
Highly similar name pair: combined match percentage score $\geq 70\%$	0
Moderately similar name pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$	2
Low similarity name pair: combined match percentage score $\leq 54\%$	1

^d POCA search conducted on June 6, 2019 in version 4.3.

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

Our analysis of the 3 names contained in Table 1 determined none of the names will pose a risk for confusion with Twirla as described in Appendices C through H.

2.2.8 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Bone, Reproductive and Urologic Products (DBRUP) via e-mail on July 22, 2019. At that time, we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Bone, Reproductive and Urologic Products (DBRUP) on July 22, 2019, they stated no additional concerns with the proposed proprietary name, Twirla.

3 CONCLUSION

The proposed proprietary name, Twirla, is acceptable.

If you have any questions or need clarifications, please contact Mammah Borbor, OSE project manager, at 301-796-7731.

3.1 COMMENTS TO AGILE THERAPEUTICS, INC.

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

If any of the proposed product characteristics as stated in your submission, received on May 29, 2019, 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. ^e

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

***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 $\geq 70\%$.
 - Moderately similar pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$.
 - Low similarity: combined match percentage score $\leq 54\%$.

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

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

- 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 $\geq 70\%$).

<p>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.</p>			
<u>Orthographic Checklist</u>		<u>Phonetic Checklist</u>	
Y/N	<p>Do the names begin with different first letters?</p> <p><i>Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.</i></p>	Y/N	<p>Do the names have different number of syllables?</p>
Y/N	<p>Are the lengths of the names dissimilar* when scripted?</p> <p><i>*FDA considers the length of names different if the names differ by two or more letters.</i></p>	Y/N	<p>Do the names have different syllabic stresses?</p>
Y/N	<p>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?</p>	Y/N	<p>Do the syllables have different phonologic processes, such as vowel reduction, assimilation, or deletion?</p>
Y/N	<p>Is there different number or placement of cross-stroke or dotted letters present in the names?</p>	Y/N	<p>Across a range of dialects, are the names consistently pronounced differently?</p>
Y/N	<p>Do the infixes of the name appear dissimilar when scripted?</p>		
Y/N	<p>Do the suffixes of the names appear dissimilar when scripted?</p>		

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is $\geq 55\%$ to $\leq 69\%$).

Step 1	<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 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.</p> <p>For single strength products, also consider circumstances where the strength may not be expressed.</p> <p>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.</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
Step 2	<p>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.</p>

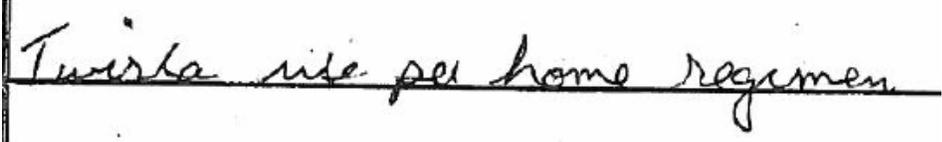
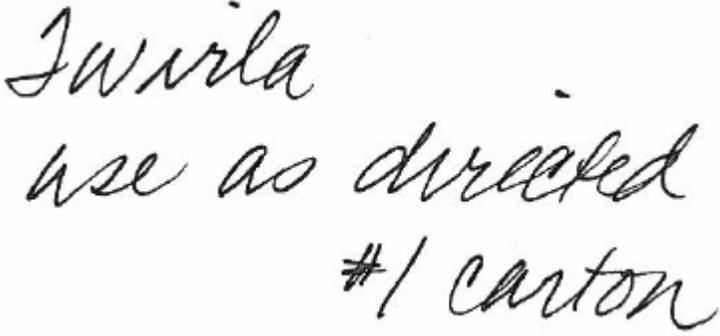
	<p>Orthographic Checklist (Y/N to each question)</p> <ul style="list-style-type: none"> • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* 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 <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 $\leq 54\%$).

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 B: Prescription Simulation Samples and Results

Figure 1. Twirla Study (Conducted on June 7, 2019)

Handwritten Medication Order/Prescription	Verbal Prescription
<p><u>Medication Order:</u></p> 	<p>Twirla Use as directed #1 carton</p>
<p><u>Outpatient Prescription:</u></p> 	

FDA Prescription Simulation Responses (Aggregate Report)

Study Name: Twirla

As of Date 6/27/2019

220 People Received Study

94 People Responded

Study Name: Twirla

	Total	54	15	25	94
INTERPRETATION	OUTPATIENT	VOICE	INPATIENT	TOTAL	
IWIRLA	3	0	0	3	
JUVERLA	1	0	0	1	
JWIRLA	3	0	0	3	
LWIRLA	1	0	0	1	
SWIRLA	2	0	0	2	
TIVERLA	0	0	1	1	
TORLA	0	5	0	5	
TORLOFF	0	1	0	1	
TOURLA	0	1	0	1	
TUEILA	0	0	1	1	
TWARIDA	1	0	0	1	
TWERLA	0	2	0	2	
TWIRLA	41	6	20	67	
TWISLA	0	0	2	2	
TWISTA	0	0	1	1	
ZWIRLA	2	0	0	2	

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

No.	Proposed name: Established name: Levonorgestrel and Ethinyl Estradiol Dosage form: transdermal system Strength(s): 120 mcg/30 mcg/day Usual Dose: 1 patch weekly for 3 weeks, then 1 week off	POCA Score (%)	Orthographic and/or phonetic differences in the names sufficient to prevent confusion Other prevention of failure mode expected to minimize the risk of confusion between these two names.
N/A			

Appendix D: Moderately Similar Names (e.g., combined POCA score is $\geq 55\%$ to $\leq 69\%$) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
1.	Turalio***	58

Appendix E: Moderately Similar Names (e.g., combined POCA score is $\geq 55\%$ to $\leq 69\%$) with overlap or numerical similarity in Strength and/or Dose

No.	Proposed name: Established name: Levonorgestrel and Ethinyl Estradiol Dosage form: transdermal system Strength(s): 120 mcg/30 mcg/day Usual Dose: 1 patch weekly for 3 weeks, then 1 week off	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
2.	(b) (4)***	55	This name pair has sufficient orthographic and phonetic differences. Orthographically, the lengths of the names (b) (4) Phonetically, the name pair contains a different number of syllables (b) (4) sound

No.	Proposed name: Twirla Established name: Levonorgestrel and Ethinyl Estradiol Dosage form: transdermal system Strength(s): 120 mcg/30 mcg/day Usual Dose: 1 patch weekly for 3 weeks, then 1 week off	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
3.	Twynsta	43	<p>different.</p> <p>This name pair has sufficient orthographic and phonetic differences.</p> <p>Orthographically, the infixes and suffixes of this name pair are sufficiently different. Twynsta contains the downstroke letter ‘y’ in the infix whereas, Twirla does not contain any downstroke letters, which gives the names different shapes when scripted. Additionally, Twirla contains the upstroke letter ‘l’ in the suffix whereas, Twynsta contains the crossed letter ‘t’ in the suffix.</p> <p>Phonetically, the ending of the first syllables (TWER vs TWIN) and second syllables (la vs stah) sound different.</p> <p>Furthermore, there is no direct overlap in strength (120 mcg/30 mcg/day vs 40 mg/5 mg, 40 mg/10 mg, 80 mg/5 mg, and 80 mg/10 mg), dosage form (transdermal system vs. tablet), or route of administration (transdermal vs. oral).</p>

Appendix F: Low Similarity Names (e.g., combined POCA score is $\leq 54\%$)

No.	Name	POCA Score (%)
N/A		

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
N/A			

Appendix H: Names not likely to be confused due to absence of attributes that are known to cause name confusion^g.

No.	Name	POCA Score (%)
N/A		

^g Shah, M, Merchant, L, Chan, I, and Taylor, K. Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

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PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
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***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	September 8, 2017
Application Type and Number:	NDA 204017
Product Name and Strength:	Twirla (ethinyl estradiol / levonorgestrel transdermal system) 120 mcg / 30 mcg
Product Type:	Combination Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Agile Therapeutics
Panorama #:	2017-16401702
DMEPA Primary Reviewer:	Chad Morris, PharmD, MPH
DMEPA Team Leader:	Lolita White, PharmD

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Twirla, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively. The Applicant submitted an external name study, conducted by [REDACTED]^{(b) (4)}, for this product.

1.1 REGULATORY HISTORY

Agile previously submitted the proposed proprietary name, Twirla on April 19, 2012. The Division of Medication Error Prevention and Analysis (DMEPA) found the name, Twirla, conditionally acceptable in OSE Review #2012-969^a, dated July 3, 2012. A Complete Response (CR) was issued for the application on February 13, 2013^b. The NDA was resubmitted (Class II resubmission) on June 26, 2017.

Thus, as part of the Class II resubmission the Applicant submitted the name, Twirla, for our review on June 26, 2017.

1.2 PRODUCT INFORMATION

The following product information is provided in the June 26, 2017 proprietary name submission.

- Intended Pronunciation: TWER-luh
- Active Ingredient: ethinyl estradiol / levonorgestrel
- Indication of Use: Prevention of pregnancy
- Route of Administration: Transdermal
- Dosage Form: Patch
- Strength: 120 mcg levonorgestrel /30 mcg ethinyl estradiol
- Dose and Frequency: 120 mcg levonorgestrel/30 mcg ethinyl estradiol per day. Apply 1 patch once weekly for 3 weeks, followed by no patch for one week.
- How Supplied: 3 patches per carton
- Storage: Room temperature
- Container and Closure Systems: [REDACTED]^{(b) (4)}

2 RESULTS

^a Park, A. Proprietary Name Review for Twirla NDA 204017. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2012 JUL 03. RCM No.: 2012-969. Available from:

<http://darrts.fda.gov:9602/darrts/ViewDocument?documentId=090140af802867ec>

^b CR available from: <http://darrts.fda.gov:9602/darrts/ViewDocument?documentId=090140af802b94a4>

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that the proposed name would not misbrand the proposed product. DMEPA and the Division of Bone, Reproductive, and Urologic Products concurred with the findings of OPDP's 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 name^c.

2.2.2 Components of the Proposed Proprietary Name

The Applicant did not provide a derivation or intended meaning for the proposed name, Twirla, 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 Comments from Other Review Disciplines at Initial Review

In response to the OSE, July 28, 2017 e-mail, the Division of Bone, Reproductive, and Urologic Products (DBRUP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Seventy-four (74) practitioners participated in DMEPA's prescription studies. 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 the verbal and written prescription studies.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search^d identified 27 names with a combined phonetic and orthographic score of $\geq 55\%$ or an individual phonetic or orthographic score ≥ 70 . These names are included in Table 1 below.

2.2.6 Names Retrieved for Review Organized by Name Pair Similarity

Table 1 lists the number of names retrieved from our POCA search and the (b) (4) external study. These name pairs are organized as highly similar, moderately similar, or low similarity for further evaluation.

^c USAN stem search conducted on July 19, 2017.

^d POCA search conducted on July 25, 2017 in version 4.0.

Table 1. Similarity Category	Number of Names
Highly similar name pair: combined match percentage score $\geq 70\%$	2
Moderately similar name pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$	27
Low similarity name pair: combined match percentage score $\leq 54\%$	14

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

We determined none of the 43 names would pose a risk for confusion as described in Appendices C through H.

2.2.8 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Bone, Reproductive, and Urologic Products (DBRUP) via e-mail on August 31, 2017. At that time, we also requested additional information or concerns that could inform our review. Per e-mail correspondence from DBRUP on September 5, 2017, they stated no additional concerns with the proposed proprietary name, Twirla.

3 CONCLUSIONS

The proposed proprietary name is acceptable.

If you have any questions or need clarifications, please contact Mammah Borbor, OSE project manager, at 301-796-7731.

3.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your June 26, 2017 submission are altered prior to approval of the marketing application, 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.

3. Electronic Drug Registration and Listing System (eDRLS) database

The electronic Drug Registration and Listing System (eDRLS) was established to support the FDA's Center for Drug Evaluation and Research (CDER) goal to establish a common Structured Product Labeling (SPL) repository for all facilities that manufacture regulated drugs. The system is a reliable, up-to-date inventory of FDA-regulated, drugs and establishments that produce drugs and their associated information.

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. ^c

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

***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 $\geq 70\%$.
 - Moderately similar pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$.
 - Low similarity: combined match percentage score $\leq 54\%$.

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^f. 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.,

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

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 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.

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 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.			
<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 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 $\geq 55\%$ to $\leq 69\%$).

Step 1	<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 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.</p> <p>For single strength products, also consider circumstances where the strength may not be expressed.</p> <p>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.</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
--------	--

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.	
	<p>Orthographic Checklist (Y/N to each question)</p> <ul style="list-style-type: none"> • 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 <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?

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

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 B: Prescription Simulation Samples and Results

Figure 1. Twirla Study (Conducted on 07/21/2017)

Handwritten Medication Order/Prescription	Verbal Prescription
<p>Medication Order:</p>  <p>Outpatient Prescription:</p> 	<p>Twirla Use as directed #1 carton</p>

FDA Prescription Simulation Responses (Aggregate 2 Rx Studies Report)

Study Name: Twirla

As of Date 8/7/2017

291 People Received Study
74 People Responded

Study Name: Twirla

OUTPATIENT	VOICE	INPATIENT
TIVERLA (1)	TORALA (1)	TIVERLA (2)
TWIRLA (32)	TORDERLA (1)	TWERLA (5)
	TORLA (11)	TWIRLA (12)
	TOROLA (1)	TWISLA (2)
	TOURLA (1)	
	TUERLA (1)	
	TWERLA (1)	
	TWIRLA (3)	

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

No.	Proposed name: Twirla Established name: Levonorgestrel/ethinyl estradiol transdermal system Dosage form: Patch Strength(s): 120 mcg levonorgestrel /30 mcg ethinyl estradiol Usual Dose: as directed, 1 patch weekly x3 weeks then 1 week off	POCA Score (%)	Orthographic and/or phonetic differences in the names sufficient to prevent confusion Other prevention of failure mode expected to minimize the risk of confusion between these two names.
1.	Twirla	100	This is the name under review
2.	(b) (4) ***	75	Proposed proprietary name for IND 105004 found unacceptable by DMEPA (OSE# 2016-7853541). BLA 761061 approved under the proprietary name Tremfya.

Appendix D: Moderately Similar Names (e.g., combined POCA score is $\geq 55\%$ to $\leq 69\%$) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
3.	Thiola	55

Appendix E: Moderately Similar Names (e.g., combined POCA score is $\geq 55\%$ to $\leq 69\%$) with overlap or numerical similarity in Strength and/or Dose

No.	Proposed name: Twirla Established name: Levonorgestrel/ethinyl estradiol transdermal system Dosage form Patch Strength(s): 120 mcg levonorgestrel /30 mcg ethinyl estradiol Usual Dose: as directed, 1 patch weekly x3 weeks then 1 week off	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
4.	Titralac	63	This name pair has sufficient orthographic and phonetic differences.
5.	Teril	61	This name pair has sufficient orthographic and phonetic differences.

No.	Proposed name: Twirla Established name: Levonorgestrel/ethinyl estradiol transdermal system Dosage form Patch Strength(s): 120 mcg levonorgestrel /30 mcg ethinyl estradiol Usual Dose: as directed, 1 patch weekly x3 weeks then 1 week off	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
6.	Utira	60	This name pair has sufficient orthographic and phonetic differences.
7.	Atripla	58	This name pair has sufficient orthographic and phonetic differences.
8.	Twilite	56	This name pair has sufficient orthographic and phonetic differences.
9.	Tara-8	56	This name pair has sufficient orthographic and phonetic differences.
10.	Terrell	56	This name pair has sufficient orthographic and phonetic differences.
11.	Trivora	54	This name pair has sufficient orthographic and phonetic differences.
12.	Wilate	49 (75 O)	This name pair has sufficient orthographic and phonetic differences.
13.	Ritalin La	49 (70 O)	This name pair has sufficient orthographic and phonetic differences.

Appendix F: Low Similarity Names (e.g., combined POCA score is $\leq 54\%$)

No.	Name	POCA Score (%)
14.	Jublia	36
15.	Luride	18
16.	Skyla	38
17.	Talwin	48
18.	Tamsulosin	24
19.	Tessalon	35
20.	Toradol	44
21.	Toujeo	24
22.	Transderm Scop	20
23.	Tresiba	42
24.	Truvada	41
25.	Tums	22

No.	Name	POCA Score (%)
26.	Tussionex	18
27.	Twynsta	43

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
28.	Teviral	61	Name identified in external study. Unable to find product characteristics in commonly used drug databases.
29.	Tilarin	52	International product marketed in Czech Republic, Finland, New Zealand, Switzerland, United Kingdom, Austria, Italy.
30.	Tirilazad	56	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
31.	Topilar	56	International product marketed in United Kingdom, Australia and France
32.	Touro La	62	Discontinued per Redbook and no generics available.
33.	Tral	56	Discontinued per Drugs@FDA and no generics available. International drug with different ingredients marketed in the Phillipines.

Appendix H: Names not likely to be confused due to absence of attributes that are known to cause name confusion^g.

No.	Name	POCA Score (%)
34.	300 Pro La	56
35.	Citral	57
36.	Detrol La	57
37.	(b) (4) ***	56
38.	Otezla	55
39.	Petrola	58
40.	Pirmella 1/35	59
41.	Pirmella 7/7/7	59

^g Shah, M, Merchant, L, Chan, I, and Taylor, K. Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

No.	Name	POCA Score (%)
42.	Ulr-La	56
43.	Viril Lam	55

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/s/

JOHN C MORRIS
09/08/2017

LOLITA G WHITE
09/08/2017

**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: July 3, 2012

Reviewer(s): Alison Park, PharmD, Safety Evaluator
Division of Medication Error Prevention and Analysis

Team Leader Zachary Oleszczuk, PharmD, Team Leader
Division of Medication Error Prevention and Analysis

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

Drug Name(s) and Strength(s): Twirla (Levonorgestrel and Ethinyl Estradiol
Transdermal Delivery System)
2.6 mg/2.3 mg

Application Type/Number: NDA 204017

Applicant: Agile Therapeutics, Inc.

OSE RCM #: 2012-969

*** 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, Twirla, 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

This application is a 505(b)(2) application with reference being made to the published scientific literature.

1.2 PRODUCT INFORMATION

The following product information is provided in the April 19, 2012 proprietary name submission.

- Active Ingredient: Levonorgestrel and Ethinyl Estradiol
- Indication of Use: [REDACTED] (b) (4)
[REDACTED] contraception
- Route of Administration: Transdermal Patch
- Dosage Form: Transdermal System
- Strength: 2.6 mg Levonorgestrel and 2.3 Ethinyl Estradiol per patch which is equivalent to an oral dose of 120 mcg Levonorgestrel and 30 mcg Ethinyl Estradiol daily.
- Dose and Frequency: Apply one patch to the abdomen, buttock, or upper torso on the same day every week for three weeks. Week four is patch free.
- How Supplied: 1) One folding carton of 1 cycle each, each cycle contains 3 patches; 2) One folding carton containing a single patch, intended for use as a replacement in the event that a patch is inadvertently lost or destroyed; 3) One folding carton of 1 cycle each, each cycle contains 3 patches for clinic usage. Each patch packaged in a protective pouch.
- Storage: Store at 25°C (77°F); excursions permitted to 15°-30°C (59°-86°F)
- Container and Closure Systems: [REDACTED] (b) (4)
[REDACTED]

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 Reproductive and Urologic Products concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 *United States Adopted Names (USAN) SEARCH*

On May 2, 2012, the United States Adopted Name (USAN) stem search identified that a USAN stem is not present in the proposed proprietary name.

2.2.2 *Components of the Proposed Proprietary Name*

The Applicant indicated in their submission that the proposed name, Twirla, has no derivation or inherent meaning. The intended pronunciation provided by the Applicant is “TWER-luh.” 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*

Thirty-one practitioners participated in DMEPA’s prescription studies. The interpretations did not overlap with or appear or sound similar to any currently marketed products. Eighteen (82%) of the 22 practitioners in the written prescription studies interpreted the name correctly as “Twirla.” The remainder of the written responses misinterpreted the drug name. Misinterpretations included the letter strings ‘-ui-’, ‘-irv-’, and ‘-iv-’ versus the letter ‘w’ and the letter ‘d’ versus the letter ‘l.’ In the verbal study, only one (11%) of the nine practitioners interpreted the name correctly. The most common misinterpretation was “Torla” (n=5). See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.4 *Comments from Other Review Disciplines*

In response to the OSE May 3, 2012 e-mail, the Division of Reproductive and Urologic Products (DRUP) 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, Twirla. Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Twirla, identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines. Table 1 also includes the names identified from the FDA Prescription Simulation or by ^{(b) (4)} not identified by DMEPA and require further evaluation.

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

		Look Similar			
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
Luride	External	Talwin	External	Tamsulosin	External
Tessalon	External	Toradol	External	Transderm Scop	External
Tussionex	External	Femilax	FDA	(b) (4)***	FDA
Levitra	FDA	Levora	FDA	Livalo	FDA
Lunesta	FDA	Tarka	FDA	Thiola	FDA
Thyrel	FDA	Treanda	FDA	Truvada	FDA/External
(b) (4)***	FDA	Tween 80	FDA	Twice-A-Day	FDA
Twinject	FDA	Twin-K	FDA	Twisthaler	FDA
Vi-Twel	FDA				
Sound Similar					
Tora	FDA				
Look and Sound Similar					
Twynsta	FDA/External	Twilite	FDA	TwinLab	FDA
Twinrix	FDA	Twirla***	FDA		

Our analysis of the 31 names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics. We determined 31 names will not pose a risk for confusion as described in Appendix D through E.

2.2.6 Communication of DMEPA’s Final Decision to Other Disciplines

DMEPA communicated our findings to the Division of Reproductive and Urologic Products via e-mail on May 30, 2012. At that time we also requested additional information or concerns that could inform our review. Per correspondence from the Division of Reproductive and Urologic Products on May 31, 2012, they stated no additional concerns with the proposed proprietary name, Twirla.

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 Maria Wasilik, OSE project manager, at 301-796-0567.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Twirla, and have concluded that this name is acceptable. However, if any of the proposed product characteristics as stated in your April 19, 2012 submission are altered, DMEPA rescinds this finding and the name must be resubmitted for review.

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

4 REFERENCES

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

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

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

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

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

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

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

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

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

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

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

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

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

USPTO provides information regarding patent and trademarks.

8. *Clinical Pharmacology Online* (www.clinicalpharmacology-ip.com)

Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common,

combination, nutraceutical and nutritional products. It also provides a keyword search engine.

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

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

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

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

11. Access Medicine (www.accessmedicine.com)

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

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

USAN Stems List contains all the recognized USAN stems.

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

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

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

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

15. Medical Abbreviations (www.medilexicon.com)

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

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

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

17. Walgreens (www.walgreens.com)

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

18. Rx List (www.rxlist.com)

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

19. Dogpile (www.dogpile.com)

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

APPENDICES

Appendix A

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

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, we consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.). DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.¹

Following the preliminary screening of the proposed proprietary name, DMEPA gathers to discuss their professional opinions on the safety of the proposed proprietary name. This meeting is commonly referred to the Center for Drug Evaluation and Research (CDER) Expert Panel discussion. DMEPA also considers other aspects of the name that may be misleading from a safety perspective. DMEPA staff conducts a prescription simulation studies using FDA health care professionals. When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name and misleading nature of the proposed proprietary name with a focus on the avoidance of medication errors.

DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product. DMEPA considers the product characteristics associated with the proposed product throughout the risk assessment because the product characteristics of the

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, Twirla	Scripted May Appear as	Spoken May Be Interpreted as
Capital ‘T’	F, Z, J, L	D
Lower case ‘t’	r, f, x, A	d
Lower case ‘w’	eu, ui, ivi, irv	
Lower case ‘i’	e	Any vowel
Lower case ‘r’	s, n, e, v	
Lower case ‘l’	b, e, s, A, P, d	
Lower case ‘a’	el, ci, cl, d, o, u	Any vowel
Letter string ‘la’	k	

Appendix C: Prescription Simulation Samples and Results

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

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Medication Order:</u></p> <p>Twirla Apply 1 patch weekly x3, then off</p>	<p>Twirla</p> <p>Apply one patch weekly for 3 weeks then off for 1 week.</p>
<p><u>Outpatient Prescription:</u></p> <p>Twirla</p> <p>Apply 1 patch weekly</p> <p>x 3 weeks then off</p> <p>x 1 week</p>	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

84 People Received Study

31 People Responded

Study Name: Twirla

	Total	12	9	10
INTERPRETATION	INPATIENT	VOICE	OUTPATIENT	TOTAL
ATWORLA	0	1	0	1
FUTURLA	0	1	0	1
TIRVIRLA	0	0	1	1
TIVIRLA	0	0	1	1
TORLA	0	5	0	5
TUIRLA	1	0	0	1
TWIRDA	0	0	1	1
TWIRLA	11	1	7	19
TWORLA	0	1	0	1

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 Twirla	Failure preventions
Talwin	Pentazocine	Look alike	The pair have sufficient orthographic and/or phonetic differences.
Tamsulosin	Tamsulosin Hydrochloride	Look alike	The pair have sufficient orthographic and/or phonetic differences.
Tessalon	Benzonatate	Look alike	The pair have sufficient orthographic and/or phonetic differences.
Toradol	Ketoralac Tromethamine	Look alike	The pair have sufficient orthographic and/or phonetic differences.
Tansderm Scop	Scopolamine Transdermal	Look alike	The pair have sufficient orthographic and/or phonetic differences.
Tussionex	Hydrocodone Bitartrate and Chlorpheniramine Maleate	Look alike	The pair have sufficient orthographic and/or phonetic differences.
Twice-A-Day	Oxymetazoline	Look alike	The pair have sufficient orthographic and/or phonetic differences.
Twinject	Epinephrine	Look alike	The pair have sufficient orthographic and/or phonetic differences.
Twisthaler	Mometasone Furoate	Look alike	Twisthaler is the modifier for the drug product, Asmanex Twisthaler. The pair have sufficient orthographic and/or phonetic differences.
Vi-Twel	Cyanocobalamin	Look alike	The pair have sufficient orthographic and/or phonetic differences.
(b) (4) ***	Bupropion Hydrobromide extended release	Look alike	Proprietary name submission for NDA 22108 (OSE 2007-1565, July 25, 2007). Name denied due to DDMAC objection. NDA 22108 approved April 23, 2008 with the name Aplenzin.
(b) (4) ***	NDA 22424 (Hydrocodone Bitartrate and Guaifenesin) NDA 22279 (Hydrocodone Bitartrate, Pseudoephedrine, and Guaifenesin)	Look alike	NDA 22424, OSE 2011-2070-This is the alternate name in submission. The proposed proprietary name, Flowtuss, was found acceptable in OSE review 2011-2070, dated August 8, 2011. However, this application is currently pending with a CR as of September 28, 2011. NDA 22279, OSE 2011-4480-This name was withdrawn by the Applicant on February 9, 2012.

Proprietary Name	Active Ingredient	Similarity to Twirla	Failure preventions
Tween 80	Polysorbate 80	Look alike	Product is a chemical often used in food and other products as an emulsifier and not a drug. Name identified in Red Book with a deactivated date of April 15, 1997. Unable to find product characteristics in commonly used drug databases. Polysorbate 80 is.
Twirla***	Levonorgestrel and Ethinyl Estradiol	Look and Sound alike	Subject of this review

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

PROPOSED NAME: Twirla (Levonorgestrel and Ethinyl Estradiol Transdermal Patch)		STRENGTH: 2.6 mg Levonorgestrel/ 2.3 mg Ethinyl Estradiol	USUAL DOSE: Apply one patch weekly for three weeks then off for one week OR Use as directed
FAILURE MODE: Name Confusion		CAUSES: (Potential reasons for name confusion that could lead to medication error)	PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)
1	<p>Luride (Sodium Fluoride) 0.25 mg, 0.5 mg, 1 mg Chewable Tablet; 0.5 mg/mL Oral drops/solution; (Sodium Fluoride and Hydrogen Fluoride) 1.2% Gel</p> <p><u>Usual Dosage</u> <i>Tablets and drops:</i> 0.25 to 3.8 mg by mouth daily. <i>Gel:</i> Brush teeth thoroughly, preferably after each meal or at least twice a day.</p>	<p><u>Orthographic</u> Both names contain 6 letters and contain 2 upstrokes in the 1st and 5th positions. Additionally, the beginning letter string ‘Luri-’ and the ending letter string ‘-de’ in Luride may appear similar to the beginning letter string ‘Twi-’ and the ending letter string ‘-la’, respectively, in Twirla when scripted.</p> <p><u>Product Strength</u> Both available in a single strength (for drops/solution and gel) or fixed-combination strength products</p> <p><u>Directions for Use</u> Use as directed (for gel)</p>	<p><u>Dosage Form and Strength</u> Single dosage form vs. chewable tablet, oral drops/solution, or gel. Either the dosage form or the strength of the Luride product would have to be specified.</p>

<p>PROPOSED NAME:</p> <p>Twirla (Levonorgestrel and Ethinyl Estradiol Transdermal Patch)</p>	<p>STRENGTH:</p> <p>2.6 mg Levonorgestrel/ 2.3 mg Ethinyl Estradiol</p>	<p>USUAL DOSE:</p> <p>Apply one patch weekly for three weeks then off for one week OR Use as directed</p>	
<p>FAILURE MODE:</p> <p>Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>	
<p>2</p>	<p>Femilax (Bisacodyl) Tablets 5 mg</p> <p><u>Usual Dosage</u> 5 to 15 mg by mouth given in the evening or before breakfast.</p> <p>*OTC</p>	<p><u>Orthographic</u> Both names consist of similar number of letters (7 vs. 6), contain 2 upstrokes in the 1st and 5th position, and contain the letter string '-la'. Additionally, the beginning letter 'F' in Femilax may appear similar to the letter 'T' in Twirla when scripted.</p> <p><u>Product Strength</u> Both available as single strength or fixed-combination strength products</p> <p><u>Dosage Form</u> Both available in a single dosage form</p> <p><u>Directions for Use</u> Use as directed</p>	<p><u>Orthographic</u> The name Femilax ends in a cross-stroke 'x' vs. Twirla which elongates the ending after the upstroke 'l' when scripted.</p>

<p>PROPOSED NAME:</p> <p>Twirla (Levonorgestrel and Ethinyl Estradiol Transdermal Patch)</p>	<p>STRENGTH:</p> <p>2.6 mg Levonorgestrel/ 2.3 mg Ethinyl Estradiol</p>	<p>USUAL DOSE:</p> <p>Apply one patch weekly for three weeks then off for one week</p> <p>OR</p> <p>Use as directed</p>	
<p>FAILURE MODE:</p> <p>Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>	
<p>3</p>	<p>Levitra (Vardenafil) Tablets 2.5 mg, 5 mg, 10 mg, 20 mg</p> <p><u>Usual Dosage</u> 2.5 to 20 mg, taken approximately 60 minutes before sexual activity.</p>	<p><u>Orthographic</u> Both names consist of similar number of letters (7 vs. 6), contain 2 upstrokes in the 1st and 5th position, and end in the letter 'a'. Additionally, the letter string 'Lev-' in Levitra may appear similar to the letter string 'Tw' in Twirla when scripted.</p> <p><u>Dosage Form</u> Both available in a single dosage form</p> <p><u>Directions for Use</u> Use as directed</p>	<p><u>Orthographic</u> The name Levitra contains an additional letter 'r' between the upstroke 't' and the ending letter 'a' which elongates the ending of the name vs. Twirla.</p> <p><u>Product Strength</u> Single strength (fixed-combination strength product) vs. multiple strength which must be specified</p>

<p>PROPOSED NAME:</p> <p>Twirla (Levonorgestrel and Ethinyl Estradiol Transdermal Patch)</p>	<p>STRENGTH:</p> <p>2.6 mg Levonorgestrel/ 2.3 mg Ethinyl Estradiol</p>	<p>USUAL DOSE:</p> <p>Apply one patch weekly for three weeks then off for one week</p> <p>OR</p> <p>Use as directed</p>	
<p>FAILURE MODE:</p> <p>Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>	
<p>4</p>	<p>Levora (Levonorgestrel and Ethinyl Estradiol) Tablets 0.15 mg/0.03 mg</p> <p><u>Usual Dosage</u> One tablet by mouth daily</p>	<p><u>Orthographic</u> Both names contain 6 letters and end in the letter ‘a’. Additionally, the letter string ‘Lev-’ in Levora may appear similar to the letter string ‘Tw-’ in Twirla when scripted.</p> <p><u>Product Strength</u> Both available as single fixed-combination strength products</p> <p><u>Dosage Form</u> Both available in a single dosage form</p> <p><u>Directions for Use</u> Use as directed</p>	<p><u>Orthographic</u> The name Twirla contains an upstroke in the 5th position vs. no upstroke in Levora.</p>
<p>5</p>	<p>Livalo (Pitavastatin) Tablets 1 mg, 2 mg, 4 mg</p> <p><u>Usual Dosage</u> 1 to 4 mg by mouth once daily</p>	<p><u>Orthographic</u> Both names contain 6 letters and contain 2 upstrokes in the 1st and 5th position. Additionally, the letter string ‘Liv-’ and the ending letter ‘o’ in Livalo may appear similar to the letter string ‘Tw-’ and the ending letter ‘a’, respectively, in Twirla when scripted.</p> <p><u>Dosage Form</u> Both available in a single dosage form</p>	<p><u>Orthographic</u> The letter string ‘-ir-’ in Twirla does not appear similar to the more rounded letter ‘a’ in Livalo when scripted which helps differentiates the two names.</p> <p><u>Product Strength</u> Single fixed-combination strength vs. multiple strengths which must be specified</p> <p><u>Frequency of Use</u> Q weekly or UAD vs. once daily</p>

<p>PROPOSED NAME:</p> <p>Twirla (Levonorgestrel and Ethinyl Estradiol Transdermal Patch)</p>	<p>STRENGTH:</p> <p>2.6 mg Levonorgestrel/ 2.3 mg Ethinyl Estradiol</p>	<p>USUAL DOSE:</p> <p>Apply one patch weekly for three weeks then off for one week</p> <p>OR</p> <p>Use as directed</p>	
<p>FAILURE MODE:</p> <p>Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>	
<p>6</p>	<p>Lunesta (Eszopiclone) Tablets 1 mg, 2 mg, 3 mg</p> <p><u>Usual Dosage</u> 1 to 3 mg by mouth immediately before bedtime</p>	<p><u>Orthographic</u> Both names consist of similar number of letters (7 vs. 6), contain 2 upstrokes in similar positions, and end in the letter ‘a’. Additionally, the letter string ‘Lun-’ in Lunesta may appear similar to the letter string ‘Twir-’ when scripted.</p> <p><u>Dosage Form</u> Both available in a single dosage form</p>	<p><u>Orthographic</u> The name Lunesta contains the letter string ‘-es-’ between the letter string ‘Lun-’ and the 2nd upstroke ‘t’ which elongates the middle portion vs. no extra letters after the beginning letter string “Twir-” in the name Twirla which gives both names a different shape when scripted.</p> <p><u>Product Strength</u> Single fixed-combination strength vs. multiple strengths which must be specified</p>
<p>7</p>	<p>Tarka (Trandolapril/Verapamil Hydrochloride) Tablets 1 mg/240 mg; 2 mg/180 mg; 2 mg/240 mg; 4 mg/240 mg</p> <p><u>Usual Dosage</u> Trandolapril 1 to 4 mg/day and Verapamil 120 to 480 mg/day in a single dose or 2 divided doses</p>	<p><u>Orthographic</u> Both names consist of similar number of letters (5 vs. 6), begin with the letter ‘T’, contain 2 upstrokes in similar positions, and end in the letter ‘a’.</p> <p><u>Dosage Form</u> Both available in a single dosage form</p>	<p><u>Orthographic</u> The letter string ‘-ar-’ in Tarka appear shorter than the letter string ‘-wir-’ in Twirla when scripted. Additionally, while both names end in the letter ‘a’, the name Tarka contains an upstroke ‘k’ which appears similar to the letter string ‘-la-’, thus elongating the ending after the upstroke vs. the name Twirla which gives both names a different shape when scripted.</p> <p><u>Product Strength</u> Single fixed-combination strength vs. multiple fixed-combination strengths which must be specified</p> <p><u>Frequency of Use</u> Q weekly or UAD vs. once or twice daily</p>

<p>PROPOSED NAME:</p> <p>Twirla (Levonorgestrel and Ethinyl Estradiol Transdermal Patch)</p>	<p>STRENGTH:</p> <p>2.6 mg Levonorgestrel/ 2.3 mg Ethinyl Estradiol</p>	<p>USUAL DOSE:</p> <p>Apply one patch weekly for three weeks then off for one week</p> <p>OR</p> <p>Use as directed</p>
<p>FAILURE MODE:</p> <p>Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>
<p>8 Thiola (Tiopronin) Tablets 100 mg</p> <p><u>Usual Dosage</u> <i>Adults:</i> Initial dose 800 mg orally three times a day, then readjusted depending on the urinary cystine value. <i>9 years of age and older:</i> Initial dose 15 mg/kg/day, then dosage readjusted depending on the urinary cystine value.</p>	<p><u>Orthographic</u> Both names contain 6 letters, begin with the letter 'T', contain an 'i' in the 3rd position, and end in the letter string '-la'.</p> <p><u>Product Strength</u> Both available as single strength or fixed-combination strength products</p> <p><u>Dosage Form</u> Both available in a single dosage form</p>	<p><u>Orthographic</u> The name Thiola contains an extra upstroke in the 2nd position vs. no upstroke in Twirla. Additionally, the name Thiola contains a rounded letter 'o' before the upstroke 'l' which does not appear similar to the letter 'r' in Twirla.</p> <p><u>Frequency of Use</u> Once weekly or UAD vs. three times a day</p>

<p>PROPOSED NAME:</p> <p>Twirla (Levonorgestrel and Ethinyl Estradiol Transdermal Patch)</p>	<p>STRENGTH:</p> <p>2.6 mg Levonorgestrel/ 2.3 mg Ethinyl Estradiol</p>	<p>USUAL DOSE:</p> <p>Apply one patch weekly for three weeks then off for one week</p> <p>OR</p> <p>Use as directed</p>
<p>FAILURE MODE:</p> <p>Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>
<p>9 Thyrel TRH (Protirelin) Injection 500 mcg in 1 mL ampules*</p> <p><u>Usual Dosage*</u> <i>Adults:</i> 200 to 500 mcg intravenous bolus over a period of 15 to 30 seconds with the patient in the supine position. <i>Children:</i> 7 mcg/kg body weight up to dose of 500 mcg.</p> <p>*Discontinued product (Clinical Pharmacology) in 2003. Relefact TRH is currently only available <i>outside</i> the US in injectable and nasal formulations.</p>	<p><u>Orthographic</u> Both root names contain 6 letters and begin with the letter 'T'.</p> <p><u>Product Strength*</u> Both available as single strength or fixed-combination strength products</p> <p><u>Dosage Form*</u> Both available in a single dosage form</p>	<p><u>Orthographic</u> The root name Thyrel contains an extra upstroke in the 2nd position and a down stroke in the 3rd position vs. no upstroke or down stroke in similar positions in Twirla. Additionally, the name Twirla ends in a letter 'a' after the upstroke 'l' vs. no ending letter after the upstroke 'l' in Thyrel which gives both names a different shape when scripted.</p> <p><u>Frequency of Administration</u> Once weekly or UAD vs. one time dose</p>

<p>PROPOSED NAME:</p> <p>Twirla (Levonorgestrel and Ethinyl Estradiol Transdermal Patch)</p>	<p>STRENGTH:</p> <p>2.6 mg Levonorgestrel/ 2.3 mg Ethinyl Estradiol</p>	<p>USUAL DOSE:</p> <p>Apply one patch weekly for three weeks then off for one week</p> <p>OR</p> <p>Use as directed</p>
<p>FAILURE MODE:</p> <p>Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>
<p>10 Treanda (Bendamustine Hydrochloride) Solution 25 mg, 100 mg</p> <p><u>Usual Dosage</u> <i>For Chronic lymphocytic leukemia:</i> 25 mg/m² to 100 mg/m² intravenously over 30 minutes on days 1 and 2 of a 28-day cycle for up to 6 cycles. <i>For Non-Hodgkin lymphoma:</i> 60 mg/m² to 120 mg/m² administered IV over 60 minutes on days 1 and 2 of a 21-day cycle for up to 8 cycles.</p>	<p><u>Orthographic</u> Both names consist of similar number of letters (7 vs. 6), begin with the letter 'T', contain 2 upstrokes in similar positions, and end with the letter 'a'. Additionally, the upstroke 'd' in Treanda may appear similar to the upstroke 'l' in Twirla when scripted.</p> <p><u>Dosage Form</u> Both available in a single dosage form</p>	<p><u>Orthographic</u> The name Twirla contains only 3 letters between upstrokes vs. 4 letters between the upstrokes plus the rounded part of the upstroke 'd' in Treanda which elongates the middle portion of the name and helps differentiate the two names.</p> <p><u>Product Strength</u> Single fixed-combination strength vs. multiple strengths which must be specified</p> <p><u>Frequency of Administration</u> Once weekly or UAD vs. once daily on days 1 and 2 of a 28 day cycle up to 6 to 8 cycles</p> <p><u>Usual Dose</u> One patch vs. XX mg/m²</p>

<p>PROPOSED NAME:</p> <p>Twirla (Levonorgestrel and Ethinyl Estradiol Transdermal Patch)</p>	<p>STRENGTH:</p> <p>2.6 mg Levonorgestrel/ 2.3 mg Ethinyl Estradiol</p>	<p>USUAL DOSE:</p> <p>Apply one patch weekly for three weeks then off for one week</p> <p>OR</p> <p>Use as directed</p>	
<p>FAILURE MODE:</p> <p>Name Confusion</p>	<p>CAUSES:</p> <p>(Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE</p> <p>(Reasons why the risk of medication error is minimized)</p>	
<p>11</p>	<p>Truvada (Emtricitabine and Tenofovir Disoproxil Fumarate) Tablets 200 mg/300 mg</p> <p><u>Usual Dosage</u> One tablet once daily. <i>Dose adjustment if CrCl 30mL/min to 49 mL/min:</i> One tablet once every 48 hours.</p>	<p><u>Orthographic</u> Both names consist of similar number of letters (7 vs. 6), begin with the letter 'T', contain 2 upstrokes in similar positions, and end with the letter 'a'. Additionally, the upstroke 'd' in Truvada may appear similar to the upstroke 'l' in Twirla when scripted.</p> <p><u>Product Strength</u> Both available as single fixed-combination strength products</p> <p><u>Dosage Form</u> Both available in a single dosage form</p>	<p><u>Orthographic</u> The name Twirla contains only 3 letters between upstrokes vs. 4 letters between the upstrokes plus the rounded part of the upstroke 'd' in Truvada which elongates the middle portion of the name and helps differentiate the two names.</p> <p><u>Frequency of Administration</u> Once weekly or UAD vs. once daily or every other day</p>

<p>PROPOSED NAME:</p> <p>Twirla (Levonorgestrel and Ethinyl Estradiol Transdermal Patch)</p>	<p>STRENGTH:</p> <p>2.6 mg Levonorgestrel/ 2.3 mg Ethinyl Estradiol</p>	<p>USUAL DOSE:</p> <p>Apply one patch weekly for three weeks then off for one week</p> <p>OR</p> <p>Use as directed</p>	
<p>FAILURE MODE:</p> <p>Name Confusion</p>	<p>CAUSES:</p> <p>(Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE</p> <p>(Reasons why the risk of medication error is minimized)</p>	
<p>12</p>	<p>Twin-K (Potassium Citrate and Potassium Gluconate) Solution 20 mEq/15 mL</p> <p><u>Usual Dosage*</u> <i>Adults:</i> 20 mEq orally daily in 1-2 divided doses. <i>Children:</i> 1 to 2 mEq/kg/day given in 1-2 divided doses.</p> <p>*General dosing for oral potassium salt products. Twin-K dosing not available. Deactivated per Red Book 6/29/97. No equivalent products containing Potassium Citrate and Gluconate available despite Twin-K showing up on Facts & Comparisons and Clinical Pharmacology databases (as Monograph).</p>	<p><u>Orthographic</u> Both names consist of similar number of letters (5 vs. 6), begin with the letter string 'Twi-', and contain 2 upstrokes in similar positions. Additionally, the letter 'K' may appear similar to the letter string '-la' when scripted.</p> <p><u>Product Strength</u> Both available as single strength or fixed-combination strength products</p> <p><u>Dosage Form</u> Both available in a single dosage form</p>	<p><u>Frequency of Administration</u> Once weekly or UAD vs. once or twice daily</p> <p><u>Usual Dose</u> 1 patch vs. 1 Tsp or 1 Tbsp or XX mEq (e.g. 10 mEq or 20 mEq)</p>

<p>PROPOSED NAME:</p> <p>Twirla (Levonorgestrel and Ethinyl Estradiol Transdermal Patch)</p>	<p>STRENGTH:</p> <p>2.6 mg Levonorgestrel/ 2.3 mg Ethinyl Estradiol</p>	<p>USUAL DOSE:</p> <p>Apply one patch weekly for three weeks then off for one week</p> <p>OR</p> <p>Use as directed</p>
<p>FAILURE MODE:</p> <p>Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>
<p>13 Tora (Phentermine Hydrochloride) Tablet 8 mg</p> <p><u>Usual Dosage*</u> One tablet daily, administered before breakfast or 1 to 2 hours after breakfast.</p> <p>*General dosing for Phentermine products. Tora dosing not available. Withdrawn FR effective 5/12/94 with no therapeutic equivalents in the same strength.</p>	<p><u>Phonetic</u> Both names contain 2 syllables, begin with the ‘T’ sound, and end in an ‘ah’ sound.</p> <p><u>Product Strength</u> Both available as single strength or fixed-combination strength products</p> <p><u>Dosage Form</u> Both available in a single dosage form</p>	<p><u>Phonetic</u> The name Twirla contains a lateral alveolar ‘l’ in the 2nd syllable which combines with the letter ‘a’ making a ‘-la’ sound vs. only the ‘ah’ sound in the name Tora.</p> <p><u>Frequency of Use</u> Once weekly or UAD vs. once daily</p>

<p>PROPOSED NAME:</p> <p>Twirla (Levonorgestrel and Ethinyl Estradiol Transdermal Patch)</p>	<p>STRENGTH:</p> <p>2.6 mg Levonorgestrel/ 2.3 mg Ethinyl Estradiol</p>	<p>USUAL DOSE:</p> <p>Apply one patch weekly for three weeks then off for one week</p> <p>OR</p> <p>Use as directed</p>	
<p>FAILURE MODE:</p> <p>Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>	
<p>14</p>	<p>Twynsta (Telmisartan and Amlodipine) Tablets 40 mg/5 mg; 40 mg/10 mg; 80 mg/5 mg; 80 mg/10 mg</p> <p><u>Usual Dosage</u> One tablet by mouth daily</p>	<p><u>Orthographic</u> Both names consist of similar number of letters (7 vs. 6), begin with the letter string ‘Tw-’, contain 2 upstrokes in similar positions, and end in the letter ‘a’. Additionally, the upstroke ‘t’ in the 6th position of the name Twynsta may appear similar to the upstroke ‘l’ in Twirla when scripted.</p> <p><u>Phonetic</u> Both names contain 2 syllables, begin with the ‘Tw’ sound and end in an ‘ah’ sound when spoken.</p> <p><u>Dosage Form</u> Both available in a single dosage form</p>	<p><u>Orthographic</u> The name Twynsta contains a down stroke in the 3rd position vs. no down stroke in the name Twirla which gives both names a different shape when scripted.</p> <p><u>Phonetic</u> The middle and ending before the ‘ah’ sound of both names (‘-ynsta’ vs. ‘-irla’) sound distinct when spoken.</p> <p><u>Product Strength</u> Single fixed-combination strength vs. multiple fixed-combination strengths which must be specified</p> <p><u>Frequency of Use</u> Q weekly or UAD vs. once daily</p>

<p>PROPOSED NAME:</p> <p>Twirla (Levonorgestrel and Ethinyl Estradiol Transdermal Patch)</p>	<p>STRENGTH:</p> <p>2.6 mg Levonorgestrel/ 2.3 mg Ethinyl Estradiol</p>	<p>USUAL DOSE:</p> <p>Apply one patch weekly for three weeks then off for one week</p> <p>OR</p> <p>Use as directed</p>	
<p>FAILURE MODE:</p> <p>Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>	
<p>15</p>	<p>Twilite (Diphenhydramine Hydrochloride) Tablet 50 mg</p> <p><u>Usual Dosage</u> 12.5 to 50 mg by mouth every 4 to 6 hours; do not exceed 300 mg/day.</p> <p>*OTC</p>	<p><u>Orthographic</u> Both names consist of similar number of letters (7 vs. 6) and begin with the letter string 'Twi-'. Additionally, the ending letter 'e' in Twilite may appear similar to the letter 'a' in Twirla when scripted.</p> <p><u>Phonetic</u> Both names contain 2 syllables and begin with the 'Tw' sound.</p> <p><u>Product Strength</u> Both available as single strength or fixed-combination strength products</p> <p><u>Dosage Form</u> Both available in a single dosage form</p>	<p><u>Orthographic</u> The name Twilite contains 3 upstrokes vs. 2 upstrokes in the name Twirla giving both names a different shape when scripted.</p> <p><u>Phonetic</u> The name Twilite ends in a plosive alveolar consonant 't' sound vs. the name Twirla which ends in an 'ah' sound giving both names a distinct sound when spoken.</p> <p><u>Frequency of Use</u> Once weekly or UAD vs. every 4 to 6 hours</p>

<p>PROPOSED NAME:</p> <p>Twirla (Levonorgestrel and Ethinyl Estradiol Transdermal Patch)</p>	<p>STRENGTH:</p> <p>2.6 mg Levonorgestrel/ 2.3 mg Ethinyl Estradiol</p>	<p>USUAL DOSE:</p> <p>Apply one patch weekly for three weeks then off for one week</p> <p>OR</p> <p>Use as directed</p>
<p>FAILURE MODE:</p> <p>Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>
<p>16 TwinLab Ultra GLA (Gamma-linolenic acid, GLA) Capsules GLA 300 mg (from borage seed oil)/oleic acid 187.5 mg/cis-linoleic acid 475 mg NOTE: dosage is expressed as GLA</p> <p><u>Usual Dosage</u> 40 mg GLA to 2.8 g of GLA orally per day, administered in divided doses.</p> <p>*OTC nutraceutical marketed under the Dietary Supplement and Health Education Act of 1994 (Clinical Pharmacology)</p>	<p><u>Orthographic</u> Both root names consist of similar number of letters (7 vs. 6), begin with the letter string “Twi-”, and contain the letter string ‘-la-’. Additionally, the letter ‘n’ in TwinLab may appear similar to the letter ‘r’ in Twirla when scripted.</p> <p><u>Phonetic</u> Both root names consist of 2 syllables, begin with the ‘Tw’ sound, and contain a ‘la’ sound when spoken.</p> <p><u>Product Strength</u> Both available as single strength or fixed-combination strength products</p> <p><u>Dosage Form</u> Both available in a single dosage form</p>	<p><u>Orthographic</u> The root name TwinLab ends in an upstroke ‘b’ vs. no ending upstroke in the name Twirla which gives both names a different shape when scripted.</p> <p><u>Phonetic</u> The middle and ending (‘-inlab’ vs. ‘-irla’) of both names sound distinct when spoken.</p> <p><u>Frequency of Use</u> Once weekly or UAD vs. divided daily doses</p>

<p>PROPOSED NAME:</p> <p>Twirla (Levonorgestrel and Ethinyl Estradiol Transdermal Patch)</p>	<p>STRENGTH:</p> <p>2.6 mg Levonorgestrel/ 2.3 mg Ethinyl Estradiol</p>	<p>USUAL DOSE:</p> <p>Apply one patch weekly for three weeks then off for one week</p> <p>OR</p> <p>Use as directed</p>	
<p>FAILURE MODE:</p> <p>Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>	
<p>17</p>	<p>Twinrix (Hepatitis A/Hepatitis B vaccine) Suspension for Injection 720 EI.U. inactivated hepatitis A virus/20 mcg recombinant HBsAg protein/mL</p> <p><u>Usual Dosage</u> 1 mL injected intramuscularly, given on a 0-, 1-, and 6-month schedule.</p> <p><i>Alternate dosage:</i> Inject 1 ml IM on days 0, 7, and 21 to 30, followed by a booster dose at month 12.</p>	<p><u>Orthographic</u> Both names consist of similar number of letters (7 vs. 6) and begin with the letter string ‘Twi-’.</p> <p><u>Phonetic</u> Both names consist of 2 syllables and begin with the ‘Tw’ sound.</p> <p><u>Product Strength</u> Both available as single strength or fixed-combination strength products</p> <p><u>Dosage Form</u> Both available in a single dosage form</p> <p><u>Directions for Use</u> Use as directed</p>	<p><u>Orthographic</u> The name Twirla contains 2 upstrokes vs. the name Twinrix which contains 1 upstroke which gives both names a different shape when scripted.</p> <p><u>Phonetic</u> The middle and ending (‘-inrix’ vs. ‘-irla’) of both names sounds distinct when spoken.</p> <p><u>Setting of Use</u> Twinrix would have to be administered by a healthcare professional (nurse, pharmacist, doctor) at the pharmacy, clinic, or doctor’s office vs. Twirla which is self-administered by the patient at home.</p>

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/s/

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07/03/2012

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