CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208088Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME MEMORANDUM

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

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

Date of This Review:	April 24, 2020
Application Type and Number:	NDA 208088
Product Name and Strength:	Tlando (testosterone undecanoate) Capsule 112.5 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Lipocine Inc. (Lipocine)
Panorama #:	2020-39085895
DMEPA Safety Evaluator:	Denise V. Baugh, PharmD, BCPS
DMEPA Team Leader:	Briana Rider, PharmD, CPPS

1 INTRODUCTION

This memorandum is to reassess the proposed proprietary name, Tlando, which was found conditionally acceptable under NDA 208088 on April 11, 2016,[a] November 17, 2017,[b] and August 1, 2019.[c] However, NDA 208088 received a Complete Response on June 28, 2016, May 8, 2018, and November 8, 2019, respectively. Thus, Lipocine re-submitted the name Tlando for review with their Class 2 Resubmission of NDA 208088 on February 28, 2020. We note that all product characteristics remain the same.

2 METHODS AND DISCUSSION

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Tlando would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Urology, Obstetrics, and Gynecology (DUOG) concurred with the findings of OPDP's assessment for Tlando.

2.2 SAFETY ASSESSMENT

For re-assessment of the proposed proprietary name, we evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the proposed proprietary name. Additionally, we searched the United States Adopted Name (USAN) stem list to determine if the proposed proprietary name contains any USAN stems as of the last USAN updates. The April 22, 2020 search of USAN stems did not find any USAN stems in the proposed proprietary name, Tlando.

2.3 COMMUNICATION OF DMEPA'S ANALYSIS AT MIDPOINT OF REVIEW

We communicated our findings to the Division of Urology, Obstetrics, and Gynecology (DUOG) via e-mail on April 24, 2020. At that time, we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Urology, Obstetrics, and Gynecology (DUOG) on April 24, 2020, they stated no additional concerns with the proposed proprietary name, Tlando.

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[a] White, L. Proprietary Name Review for Tlando (testosterone undecanoate) NDA 208088, Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2016 APR 11. RCM No.: 2016-2933656.

[b] Whaley, E. Proprietary Name Review for Tlando (testosterone undecanoate) NDA 208088, Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 NOV 17. RCM No.: 2017- 17380941.

[c] Stewart, J. Proprietary Name Review for Tlando (NDA 208088). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 AUG 01. Panorama No.: 2019-31589103.

3 CONCLUSION

Our re-assessment did not identify any names that represent a potential source of drug name confusion. Therefore, we maintain that the proposed proprietary name, Tlando, is acceptable.

If you have any questions or need clarifications, please contact Oyinlola Fashina, OSE project manager, at 301-796-4446.

3.1 COMMENTS TO LIPOCINE

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

If any of the proposed product characteristics as stated in your submission, received on February 28, 2020, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCE

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

   USAN Stems List contains all the recognized USAN stems.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

DENISE V BAUGH
04/24/2020 12:33:49 PM

BRIANA B RIDER
04/24/2020 12:42:58 PM

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:	August 1, 2019
Application Type and Number:	NDA 208088
Product Name and Strength:	Tlando (testosterone undecanoate) Capsule, 112.5 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Lipocine Inc. (Lipocine)
Panorama #:	2019-31589103
DMEPA Safety Evaluator:	Janine Stewart, PharmD
DMEPA Team Leader (Acting):	Briana Rider, PharmD

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Tlando, 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. Lipocine did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

The Applicant previously submitted the proposed proprietary name, (b) (4) on October 31, 2014 under IND 106476. However, the Office of Prescription Drug Promotion (OPDP) determined that the proposed name would misbrand the proposed product because (b) (4) (b) (4) (b) (4) (b) (4) The Division of Bone, Reproductive, and Urologic Products (DBRUP) and DMEPA concurred with their findings and found the name unacceptable. The Applicant then submitted the proposed proprietary name, (b) (4) on May 13, 2015 under IND 106476 and NDA 208088. However, DMEPA found the proposed name unacceptable due to (b) (4) in OSE Review 2015-453678 dated September 29, 2015. The Applicant then submitted (b) (4) on December 16, 2015 under NDA 208088 but withdrew that name on March 1, 2016 after DMEPA expressed concerns with (b) (4) (b) (4) during a teleconference on February 29, 2016.

The Applicant then submitted the name, Tlando, for review on March 1, 2016. The proposed proprietary name, Tlando, was found conditionally acceptable under the first review cycle for NDA 208088.[a] At the time, the proposed strengths of Tlando were (b) (4) (b) (4) 112.5 mg. NDA 208088 received a Complete Response on June 28, 2016.

The Applicant submitted a Class 2 Resubmission on August 8, 2017. Thus, the Applicant submitted the name, Tlando, for review on September 1, 2017. We noted that since our previous review, the product strength changed (b) (4) to 112.5 mg (b) (4) Additionally, the previous review noted a dosage regimen of 225 mg twice daily (2 X 112.5 mg twice a day) (b) (4) (b) (4). The August 8, 2017 Tlando PNR request listed a dosage regimen of 225 mg twice daily (2 X 112.5 mg twice a day) (b) (4) Based on our review, the proposed proprietary name, Tlando, was found conditionally acceptable under NDA 208088 in OSE Review 2017-17380941 dated November 17, 2017[b]. However, the Application received a subsequent Complete Response on May 8, 2018.

Thus, as part of the NDA 208088 resubmission, Lipocine submitted the name, Tlando, for review on May 9, 2019.

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[a] White, L. Proprietary Name Review for Tlando (testosterone undecanoate) NDA 208088, Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2016 APR 11. RCM No.: 2016- 2933656.

[b] Whaley, E. Proprietary Name Review for Tlando (testosterone undecanoate) NDA 208088, Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 NOV 17. RCM No.: 2017- 17380941.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on May 9, 2019.

- Intended Pronunciation: TEE-lan-DOH
- Active Ingredient: testosterone undecanoate
- Indication of Use: indicated for testosterone replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone.
    - Primary hypogonadism (congenital or acquired): testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (follicle stimulating hormone (FSH), luteinizing hormone (LH)) above the normal range.
    - Hypogonadotropic hypogonadism (congenital or acquired): gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range.
- Route of Administration: oral
- Dosage Form: capsule
- Strength: 112.5 mg
- Dose and Frequency: 225 mg testosterone undecanoate ((b) (4) (b) (4)) taken as two 112.5 mg capsules. Tlando should be taken twice daily, with food, (b) (4)
- How Supplied: Supplied in HDPE bottles with a foil liner and a child resistant cap
- Storage: Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F). [See USP controlled room temperature.]

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Tlando 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 Tlando.

2.2 SAFETY ASSESSMENT

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

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

Lipocine did not provide a derivation or intended meaning for the proposed proprietary name, Tlando, 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, May 23, 2019 e-mail, the Division of Bone, Reproductive and Urologic Products (DBRUP) did not forward any comments or concerns relating to Tlando at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Sixty-two practitioners participated in DMEPA's prescription studies for Tlando. The responses did not directly overlap with any currently marketed products or any products in the pipeline.

One respondent in the inpatient study interpreted the proposed proprietary name as "Teando" which is a close variation to the currently marketed product, Treanda. Treanda is an injectable product indicated for treatment of chronic lymphocytic leukemia and indolent B cell non-Hodgkin's Lymphoma. We previously evaluated the name pair, Tlando and Treanda, and found that there are sufficient orthographic, phonetic, and product characteristic differences between the name pair[b]. We maintain our previous position regarding this name pair.

Orthographically, the second letter of Tlando is an upstroke letter "l" whereas the second letter in Treanda is a curved letter "r". Phonetically, the first syllable ('Tee-' vs. 'Tree-') and second syllable ('-lan-' vs. '-an-') of the name pair sound different. Additionally, there are no overlaps in route of administration (oral vs. intravenous infusion), strength (112.5 mg vs. 25 mg, 100 mg, 45 mg/0.5 mL and 180 mg/2 mL), dosage form (capsule vs. injection solution and powder for injection) or indication (testosterone replacement therapy in males vs. treatment of chronic lymphocytic leukemia and indolent B-cell non-Hodgkin lymphoma). While there is minimal opportunity for dose overlap between Tlando 225 mg and Treanda 225 mg, Treanda dosing is (b) (4), (b) (4) In totality, we find that given the differences in the other product characteristics there is minimal risk of name confusion for this name pair (see Appendix E).

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

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[c] USAN stem search conducted on June 13, 2019.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search[d] identified seventy-four names with the combined score of ≥55% or individual orthographic or phonetic score of ≥70%. We had identified and evaluated most of the names in our previous proprietary name review. 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 5 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 ≥70%	2
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	4
Low similarity name pair: combined match percentage score ≤54%	0

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

Our analysis of the 6 names contained in Table 1 determined none of the names will pose a risk for confusion with Tlando 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 26, 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 August 1, 2019, they stated no additional concerns with the proposed proprietary name, Tlando.

[d] POCA search conducted on May 30, 2019 in version 4.3.

3 CONCLUSION

The proposed proprietary name, Tlando, is acceptable.

If you have any questions or need clarifications, please contact Oyinlola Fashina, OSE project manager, at 301-796-4446.

3.1 COMMENTS TO LIPOCINE INC.

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

If any of the proposed product characteristics as stated in your submission, received on May 9, 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 ≥70%.
- Moderately similar pair: combined match percentage score ≥55% to ≤ 69%.

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

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

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 3).
- Moderately similar names are further evaluated to identify the presence of attributes that are known to cause name confusion.
    - Name attributes: We note that the beginning of the drug name plays a significant role in contributing to confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are major contributing factor in the confusion of drug names[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

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

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

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

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 ≥ 70%).

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

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

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

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

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

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

Appendix B: Prescription Simulation Samples and Results

Figure 1. Tlando Study (Conducted on June 26, 2019)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order: Tlando 225mg po twice daily Outpatient Prescription: Patient _____ Date _____ Address _____ ℞ Tlando 2 capsules PO BID with food #120 MEDWATCH 1-800-FDA-1088 Refill(s):_____ Dr. _____ DEA No._____ Address _____ Telephone _____	Tlando Take 2 capsules by mouth twice daily with food. Disp# 120

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

218 People Received Study

62 People Responded

Study Name: Tlando

Total	**32**	**11**	**19**	
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
DLANDO	2	0	0	2
FLANDO	3	0	0	3
ILANDA	0	0	1	1
ILANDO	2	0	1	3
JLANDO	1	0	0	1
TEANDO	0	0	1	1
TEELANDO	0	2	0	2
TELANDO	0	9	0	9
TLANDA	0	0	1	1
TLANDO	24	0	15	58

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

No.	**Proposed name:** Tlando **Established name:** testosterone undecanoate **Dosage form:** Capsule **Strength(s):** 112.5 mg **Usual Dose:** 225 mg (2 capsules) taken twice daily, with food, (b) (4)	**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.	Tlando	100	The subject of this review.
2.	(b) (4)	71	(b) (4)

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

No.	Name	POCA Score (%)
3.	Slynd	64
4.	Tulana	66

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

No.	**Proposed name:** Tlando **Established name:** testosterone undecanoate **Dosage form:** Capsule **Strength(s):** 112.5 mg **Usual Dose:** 225 mg (2 capsules) taken twice daily, with food, (b) (4)	**POCA Score (%)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
5.	Treanda	65	This name pair has sufficient orthographic ('Tl-' vs. 'Tr-') and phonetic differences ('Tee-' vs. 'Tree-' and '-lan-' vs. '-an-') There are no overlaps in route of administration (oral vs. intravenous infusion), strength (112.5 mg vs. 25

No.	**Proposed name:** Tlando **Established name:** testosterone undecanoate **Dosage form:** Capsule **Strength(s):** 112.5 mg **Usual Dose:** 225 mg (2 capsules) taken twice daily, with food, (b) (4)	**POCA Score (%)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
			mg, 100 mg, 45 mg/0.5 mL and 180 mg/2 mL), dosage form (capsule vs. injection solution and powder for injection) or indication (testosterone replacement therapy in males vs. treatment of chronic lymphocytic leukemia and indolent B-cell non-Hodgkin lymphoma). While there is minimal opportunity for dose overlap between Tlando 225 mg and Treanda 225 mg, Treanda dosing is (b) (4) , (b) (4) In totality, we find that given the differences in the other product characteristics there is minimal risk of name confusion for this name pair

Appendix F: Low Similarity Names (e.g., combined POCA score is ≤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
6.	Selank	56	Name identified in RxNorm database. This product is a bulk ingredient for animal drug compounding.

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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/s/

JANINE A STEWART
08/01/2019 02:46:31 PM

BRIANA B RIDER
08/01/2019 07:42:23 PM

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:	November 17, 2017
Application Type and Number:	NDA 208088
Product Name and Strength:	Tlando (testosterone undecanoate) capsule, 112.5 mg
Product Type:	Single-ingredient
Rx or OTC:	Rx
Applicant/Sponsor Name:	Lipocine Inc.
Panorama #:	2017-17380941
DMEPA Safety Evaluator:	Ebony Whaley, PharmD, BCPPS
DMEPA Team Leader:	Lolita White, PharmD

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Tlando, 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 did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

The Applicant previously submitted the proposed proprietary name, (b) (4) on October 31, 2014 under IND 106476. However, the Office of Prescription Drug Promotion (OPDP) determined that the proposed name would misbrand the proposed product because (b) (4) (b) (4) (b) (4) (b) (4) The Division of Bone, Reproductive, and Urologic Products (DBRUP) and DMEPA concurred with their findings and found the name unacceptable. The Applicant then submitted the proposed proprietary name, (b) (4) on May 13, 2015 under IND 106476 and NDA 208088. However, DMEPA found the proposed name unacceptable due to (b) (4) in OSE Review 2015-453678 dated September 29, 2015. The Applicant then submitted (b) (4) on December 16, 2015 under NDA 208088 but withdrew that name on March 1, 2016 after DMEPA expressed about concerns with (b) (4) (b) (4) during a teleconference on February 29, 2016.

The Applicant then submitted the name, Tlando, for review on March 1, 2016. The proposed proprietary name, Tlando, was found conditionally acceptable under the first review cycle for NDA 208088.[a] At the time, the proposed strengths of Tlando were (b) (4) (b) (4) (b) (4) 112.5 mg. NDA 208088 received a Complete Response on June 28, 2016.

The Applicant submitted a Class 2 Resubmission on August 8, 2017. Thus, the Applicant submitted the name, Tlando, for review on September 1, 2017. We note that since our previous review, the product strength has changed (b) (4) to 112.5 mg only. Additionally, the previous review noted a dosage regimen of 225 mg twice daily (2 X 112.5 mg twice a day) (b) (4) (b) (4). The current Tlando PNR request lists a dosage regimen of 225 mg twice daily (2 X 112.5 mg twice a day) only. The updated information is included in Section 1.2 Product Information.

1.2 PRODUCT INFORMATION

The following product information is provided in the September 1, 2017 proprietary name submission.

- Intended Pronunciation: TEE-lan-DOH
- Active Ingredient: testosterone undecanoate
- Indication of Use: indicated for testosterone replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone.

[a] White, L. Proprietary Name Review for Tlando (testosterone undecanoate) NDA 208088, Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2016 APR 11. RCM No.: 2016- 2933656.

- Primary hypogonadism (congenital or acquired): testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (follicle stimulating hormone (FSH), luteinizing hormone (LH)) above the normal range.
- Hypogonadotropic hypogonadism (congenital or acquired): gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range.

- Route of Administration: oral
- Dosage Form: capsule
- Strength: 112.5 mg
- Dose and Frequency: 225 mg testosterone undecanoate ((b) (4) (b) (4)) taken as two 112.5 mg capsules. Tlando should be taken twice daily, with food, (b) (4)
- How Supplied: Supplied in HDPE bottles with a foil liner and a child resistant cap
- Storage: Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F). [See USP controlled room temperature.]

2 RESULTS

The following sections provide 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. 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 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[b].

[b] USAN stem search conducted on September 12, 2017.

2.2.2 Components of the Proposed Proprietary Name

The Applicant did not provide a derivation or intended meaning for the proposed name, Tlando, 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, September 19, 2017 e-mail, the Division of Bone, Reproductive, and Urologic Products (DBRUP) 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 practitioners participated in DMEPA's prescription studies. The responses did not directly overlap with any currently marketed products or any products in the pipeline. However, two responses to the outpatient portion of the study responses ("Trando") look similar to the currently marketed product, Treanda. Treanda is an injectable product indicated for treatment of chronic lymphocytic leukemia and indolent B cell non-Hodgkins Lymphoma. We evaluated the name pair, Tlando and Treanda, further and find that there are sufficient orthographic, phonetic and product characteristic differences between the name pair. Orthographically, the second letter of Tlando is an upstroked letter "l" whereas the second letter in Treanda is a curved letter "r". Phonetically, the first syllable ('Tee-' vs. 'Tree-') and second syllable ('-lan-' vs. '-an-') of the name pair sound different. Additionally, there are no overlaps in route of administration (oral vs. intravenous infusion), strength (112.5 mg vs. 25 mg, 100 mg, 45 mg/0.5 mL and 180 mg/2 mL), dosage form (capsule vs. injection solution and powder for injection) or indication (testosterone replacement therapy in males vs. treatment of chronic lymphocytic leukemia and indolent B-cell non-Hodgkin lymphoma). While there is dose overlap between Tlando 225 mg and Treanda 225 mg, we find that given the differences in the other product characteristics there is minimal risk of name confusion for this name pair (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[c] identified 83 names with a combined phonetic and orthographic score of ≥55% or an individual phonetic or orthographic score ≥70%**.** These names are included in Table 1 below.

2.2.6 Names with Strength Overlap and Potential Orthographic, Spelling, and Phonetic Similarities

The proposed product, Tlando, will be available in a 112.5 mg strength. Since this is not a typical strength that is commonly marketed, we searched the Electronic Drug Registration and Listing System (eDRLS) database to identify names with strength overlap. The eDRLS search did not identify names with strength overlap and potential orthographic, spelling, and phonetic similarities with Tlando that were not identified in POCA.

[c] POCA search conducted on September 7, 2017 in version 4.1.

2.2.7 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. Similarity Category	**Number of Names**
Highly similar name pair: combined match percentage score ≥70%	2
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	66
Low similarity name pair: combined match percentage score ≤54%	15

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

Our analysis of the 83 names contained in Table 1 determined none of the names will pose a risk for confusion as described in Appendices C through H.

2.2.9 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 November 16, 2017. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DBRUP on November 17, 2017, they stated no additional concerns with the proposed proprietary name, Tlando.

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, Tlando, and have concluded that this name is acceptable.

If any of the proposed product characteristics as stated in your September 1, 2017 submission are altered prior to approval of the marketing application, the name must be resubmitted for review.

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 supports 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. [d]

[d] 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 ≥70%.
   - Moderately similar pair: combined match percentage score ≥55% to ≤ 69%.
   - Low similarity: combined match percentage score ≤54%.

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

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 3).
- Moderately similar names are further evaluated to identify the presence of attributes that are known to cause name confusion.
    - Name attributes: We note that the beginning of the drug name plays a significant role in contributing to confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are major contributing factor in the confusion of drug names[e]. 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.,

[e] 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 ≥ 70%).

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

Y/N	Is there different number or placement of cross-stroke or dotted letters present in the names?	Y/N	Across a range of dialects, are the names consistently pronounced differently?
Y/N	Do the infixes of the name appear dissimilar when scripted?		
Y/N	Do the suffixes of the names appear dissimilar when scripted?		

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

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

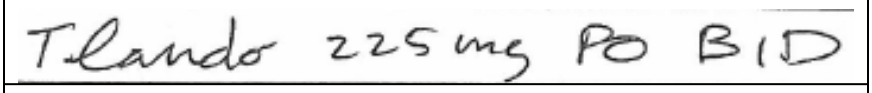
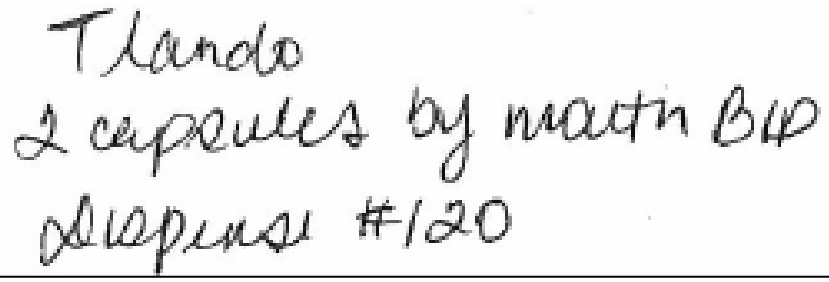
<table>
<tr><td>Step 2</td><td colspan="2">Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names <u>with</u> overlapping or similar strengths or doses.</td></tr>
<tr><td></td><td>Orthographic Checklist (Y/N to each question)
Do the names begin with different first letters?
Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.
Are the lengths of the names dissimilar* when scripted?
*FDA considers the length of names different if the names differ by two or more letters.
Considering variations in scripting of some letters (such as z and f), is there a different number or placement of upstroke/downstroke letters present in the names?
Is there different number or placement of cross-stroke or dotted letters present in the names?
Do the infixes of the name appear dissimilar when scripted?
Do the suffixes of the names appear dissimilar when scripted?</td><td>Phonetic Checklist (Y/N to each question)
Do the names have different number of syllables?
Do the names have different syllabic stresses?
Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?
Across a range of dialects, are the names consistently pronounced differently?</td></tr>
</table>

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

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

Appendix B: Prescription Simulation Samples and Results

Figure 1. Tlando Study (Conducted on September 15, 2017)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order:  Outpatient Prescription:  	Tlando 2 capsules by mouth twice daily Dispense #120

FDA Prescription Simulation Responses

304 People Received Study
74 People Responded

Study Name: Tlando

Total	24	23	27	
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
KELONDO	0	1	0	1
LANDO	1	0	0	1
TALANDO	0	1	0	1
TEELANDO	0	2	0	2
TELANDO	0	8	0	8
TELONDO	0	3	0	3
THANDO	1	0	0	1
TILANDO	0	7	0	7
TINLONDO	0	1	0	1
TLANDO	20	0	26	46

T-LANDO	0	0	1	1
TRANDO	2	0	0	2

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

No.	**Proposed name:** Tlando **Established name:** testosterone undecanoate **Dosage form:** capsule **Strength(s):** 112.5 mg **Usual Dose:** 225 mg (2 capsules) taken twice daily, with food, (b) (4)	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.	Tlando	100	Subject of review
2.	(b) (4)	76	Previous proposed PN for this NDA 208088. (b) (4) is considered withdrawn as of March 1, 2016.

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

No.	Name	POCA Score (%)
3.	Trancot	62
4.	Pronto	59
5.	Lazanda	58
6.	Pandel	58
7.	Flanders	56
8.	Silanol	56
9.	Soolantra	56
10.	Teladar	56
11.	Prandin	55

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

No.	**Proposed name:** Tlando **Established name:** testosterone undecanoate **Dosage form:** capsule **Strength(s):** 112.5 mg **Usual Dose:** 225 mg (2 capsules) taken twice daily, with food, (b) (4)	POCA Score (%)	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
12.	Plan B	66	This name pair has sufficient orthographic and phonetic differences.

No.	**Proposed name:** Tlando **Established name:** testosterone undecanoate **Dosage form:** capsule **Strength(s):** 112.5 mg **Usual Dose:** 225 mg (2 capsules) taken twice daily, with food, (b) (4) (b) (4)	POCA Score (%)	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
13.		65	This name pair has sufficient orthographic and phonetic differences.
14.	Treanda	65	This name pair has sufficient orthographic ('Tl-' vs. 'Tr-') and phonetic differences ('Tee-' vs. 'Tree-' and '-lan-' vs. '-an-') Tlando is a single strength oral capsule intended for self-administration and Treanda is a multiple strength injectable product available as a solution or powder for injection for infusion by a healthcare professional.
15.	P-Tann D	64	This name pair has sufficient orthographic and phonetic differences. Additionally, if the modifier 'D' is included this further differentiates the name pair.
16.	Tandem	64	This name pair has sufficient orthographic and phonetic differences.
17.	Xtandi	64	This name pair has sufficient orthographic and phonetic differences.
18.	J-Tan D	63	This name pair has sufficient orthographic and phonetic differences. Additionally, if the modifier 'D' is included this further differentiates the name pair.
19.	Dytan-D	62	This name pair has sufficient orthographic and phonetic differences. Additionally, if the modifier 'D' is included this further differentiates the name pair.
20.	Panadol	62	This name pair has sufficient orthographic and phonetic differences.
21.	Tramadol	61	This name pair has sufficient orthographic and phonetic differences.
22.	Nilandron	60	This name pair has sufficient orthographic and phonetic differences.
23.	Lantus	59	This name pair has sufficient orthographic and phonetic differences.

No.	**Proposed name:** Tlando **Established name:** testosterone undecanoate **Dosage form:** capsule **Strength(s):** 112.5 mg **Usual Dose:** 225 mg (2 capsules) taken twice daily, with food, (b) (4)	**POCA Score (%)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
24.	Mylanta	58	This name pair has sufficient orthographic and phonetic differences.
25.	Plenvu***	58	This name pair has sufficient orthographic and phonetic differences.
26.	Toradol	58	This name pair has sufficient orthographic and phonetic differences.
27.	T-Panol	58	This name pair has sufficient orthographic and phonetic differences.
28.	Trandate	58	This name pair has sufficient orthographic and phonetic differences.
29.	Tylenol	58	This name pair has sufficient orthographic and phonetic differences.
30.	Dilantin	56	This name pair has sufficient orthographic and phonetic differences.
31.	Dilantin-125	56	This name pair has sufficient orthographic and phonetic differences. Additionally, if the modifier '125' is included this further differentiates the name pair.
32.	Stadol	56	This name pair has sufficient orthographic and phonetic differences.
33.	Tandem Ob	56	This name pair has sufficient orthographic and phonetic differences. Additionally, if the modifier 'Ob' is included this further differentiates the name pair.
34.	Taladine	55	This name pair has sufficient orthographic and phonetic differences.
35.	Tandem F	55	This name pair has sufficient orthographic and phonetic differences. Additionally, if the modifier 'F' is included this further differentiates the name pair.
36.	Trulance	55	This name pair has sufficient orthographic and phonetic differences.
37.	Patanol	54	This name pair has sufficient orthographic and phonetic differences.

No.	**Proposed name:** Tlando **Established name:** testosterone undecanoate **Dosage form:** capsule **Strength(s):** 112.5 mg **Usual Dose:** 225 mg (2 capsules) taken twice daily, with food, (b) (4)	**POCA Score (%)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
38.	Tapentadol	52	This name pair has sufficient orthographic and phonetic differences.
39.	Anadrol-50	49	This name pair has sufficient orthographic and phonetic differences. Additionally, if the modifier '50' is included this further differentiates the name pair.
40.	Andro LA 200	49	This name pair has sufficient orthographic and phonetic differences. Additionally, if the modifiers 'LA 200' are included this further differentiates the name pair.

Appendix F: Low Similarity Names (e.g., combined POCA score is ≤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
41.	Slo-Indo	68	International product marketed in United Kingdom.
42.	(b) (4)	66	Previous proposed PN for this NDA 208088; found unacceptable in OSE Review #2015-453678 due to having (b) (4)
43.	C Tan D	64	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
44.	Mandol	64	Brand discontinued with no generic equivalent available. NDA 50504 and ANDA 62560 withdrawn FR effective 3/13/2009 and 4/6/2006, respectively.
45.	Tylan	63	Veterinary product.

No.	Name	POCA Score (%)	Failure preventions
46.	Balanta	62	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
47.	Tindal	62	Brand discontinued with no generic equivalent available. NDA 12254 withdrawn pending FR notice.
48.	Poly Tan D	60	Brand discontinued with no generic equivalent available.
49.	Prondol	60	This is an international drug marketed in UK and Ireland.
50.	Ganda	58	International product marketed in Europe and Africa.
51.	Trandide	58	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
52.	Dilantin-30	56	Brand discontinued with no generic equivalent available.
53.	Chendol	56	International product formerly marketed in Europe and Australia.
54.	Telazol	56	Veterinary product.
55.	Tilade	56	Brand discontinued with no generic equivalents available. NDA 19660 withdrawn FR effective 07/21/2017. NDA 20750 withdrawn FR effective 03/20/2000
56.	Tusana D	56	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
57.	Talinolol	55	International product formerly marketed in Germany, Russia, and the Czech Republic.
58.	Tiadenol	55	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
59.	Allantoin	54	Product is not a drug but a compound used as an active ingredient in over the counter cosmetic products.
60.	Restandol	54	International product marketed in United Kingdom.
61.	Tanoral	52	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
62.	Gantanol	50	Brand discontinued with no generic equivalent available. NDA 12715 and NDA 13664 withdrawn FR effective 9/17/2001 and 1/9/1997, respectively.
63.	Tiadilon	50	International product formerly marketed in France.

No.	Name	POCA Score (%)	Failure preventions
64.	1,2-octanediol	50	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases
65.	1-Octanol	50	Product is not a drug. Product is an organic compound.
66.	2-Octanol	50	Product is not a drug. Product is an organic compound.
67.	Octanediol	50	Product is not a drug. Product is an organic compound.
68.	Andro LA	49	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
69.	Otoalgan	48	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.

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

No.	Name	POCA Score (%)
70.	Ztlido***	65
71.	Clodan	62
72.	Dolono	62
73.	C-Tanna 12D	60
74.	D-Tann Cd	60
75.	D-Tann Dm	60
76.	Plendil	60
77.	Linde	59
78.	Platinol	59
79.	Clinsol	56
80.	Drontal	56
81.	Latuda	56
82.	Clinpro 5000	55
83.	(b) (4)	55

[f] 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

Appendix I: Names identified in the eDRLS database not likely to be confused due to notable spelling, orthographic and phonetic differences.

No.	Name
	N/A

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

/s/

EBONY A WHALEY
11/17/2017

LOLITA G WHITE
11/17/2017

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:	April 11, 2016
Application Type and Number:	NDA 208088
Product Name and Strength:	Tlando (testosterone undecanoate) Capsules (b) (4) (b) (4) 112.5 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Lipocine, Incorporated
Panorama #:	2016- 2933656
DMEPA Primary Reviewer:	Lolita White, PharmD
DMEPA Team Leader:	Danielle Harris, PharmD, BCPS

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Tlando***, 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 did not submit an external name study for this proposed proprietary name for this product.

1.1 REGULATORY HISTORY

The Applicant previously submitted the proposed proprietary name, [redacted] on October 31, 2014. However, the Office of Prescription Drug Promotion (OPDP) determined that the proposed name would misbrand the proposed product because it [redacted] Both the Division of Bone, Reproductive, and Urologic Products (DBRUP) and DMEPA concurred with their findings and found the name unacceptable. The Applicant then submitted the proposed proprietary name, [redacted] on May 13, 2015. However, DMEPA found the proposed name unacceptable due to [redacted] in OSE Review 2015-453678 dated September 29, 2015. The Applicant then submitted [redacted] on December 16, 2015 but withdrew that name on March 1, 2016 after DMEPA expressed about concerns with [redacted] during a teleconference with Lipocine, Inc on February 29, 2016

Thus, the Applicant submitted the name, Tlando***, for review on March 1, 2016.

1.2 PRODUCT INFORMATION

The following product information is provided in the March 1, 2016, proprietary name submission.

- Intended Pronunciation: "TEE-lan-DOH"
- Active Ingredient: testosterone undecanoate
- Indication of Use: Testosterone replacement in adult males for conditions associated with a deficiency or absence of endogenous testosterone – primary hypogonadism (congenital or acquired) or secondary hypogonadism (congenital or acquired)
- Route of Administration: Oral
- Dosage Form: Capsule
- Strength [redacted] 112.5 mg
- Dose and Frequency: [redacted] dose of 225 mg twice daily (2 X 112.5 mg twice a day). [redacted]
- How Supplied/ Container and Closure Systems : Supplied in HDPE bottles with a foil liner and a child resistant lid. Each bottle contains 120 capsules.
- Storage: Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).

2 RESULTS

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 (DBRUP) 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[1].

2.2.2 Components of the Proposed Proprietary Name

The Applicant did not provide a derivation or intended meaning for the proposed name, Tlando*** in their submission. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 FDA Name Simulation Studies

Sixty-nine 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.

2.2.4 Comments from Other Review Disciplines at Initial Review

In response to the OSE, March 9, 2016 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.

[1]USAN stem search conducted on 3/2/16.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Table 1 lists the number of names with the combined orthographic and phonetic score of ≥50% retrieved from our POCA search[2] organized as highly similar, moderately similar or low similarity for further evaluation.

Table 1. POCA Search Results	**Number of Names**
Highly similar name pair: combined match percentage score ≥70%	3
Moderately similar name pair: combined match percentage score ≥50% to ≤ 69%	72
Low similarity name pair: combined match percentage score ≤49%	0

2.2.6 Names with Potential Orthographic, Spelling, and Phonetic Similarities that overlap in strength

The proposed product, Tlando*** will be available in strength of 112.5 mg. Since this is not a typical strength that is commonly marketed, we searched the Electronic Drug Registration and Listing System (eDRLS) database to identify any names with potential orthographic, spelling, and phonetic similarities with Tlando*** that were not identified in POCA, and found to have an overlap in strength with Tlando***.

Table 1A. eDRLS Search Results[3]	**POCA score**
n/a	

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

Our analysis of the 75 names contained in Table 1 determined none of the 75 names will 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 April 7, 2016. At that time we also requested additional information or concerns that could inform our review. Per e-mail

[2] POCA search conducted on 3/2/16.

[3] eDRLS search conducted on 3/2/16

correspondence from the DBRUP on April 11, 2016, they stated no additional concerns with the proposed proprietary name, Tlando.

3 CONCLUSIONS

The proposed proprietary name is acceptable.

If you have any questions or need clarifications, please contact Shawnetta M. Jackson, M.S., OSE project manager, at 301-796-4952.

3.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your March 1, 2016 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 supports 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. [4]

[4] 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 medical and/or coined abbreviations in the proprietary name?**
	Proprietary names should not incorporate medical abbreviations (e.g., QD, BID, or others commonly used for prescription communication) or coined abbreviations that have no established meaning.
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 50% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:

- Highly similar pair: combined match percentage score ≥70%.
- Moderately similar pair: combined match percentage score ≥50% to ≤ 69%.
- Low similarity: combined match percentage score ≤49%.

Using the criteria outlined in the check list (Table 3-5) that corresponds to each of the three categories (highly similar pair, moderately similar pair, and low similarity), DMEPA evaluates the name pairs to determine the acceptability or non-acceptability of a proposed proprietary name. 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 with overlapping or similar strengths or doses represent an area for concern for FDA. The dosage and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and it 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, etc.) may be limited when the strength or dose overlaps. We review 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 ≥ 70%).

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

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is ≥50% to ≤69%).

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

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

Table 5: Low Similarity Name Pair Checklist (i.e., combined score is ≤49%).

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

Appendix B: Prescription Simulation Samples and Results

Figure 1. Tlando Study (Conducted on March 4, 2016)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order: Tlando 112.5mg two capsules po twice daily	Tlando (b) (4) mg Take two capsules by mouth twice daily. dispense (b) (4)
Outpatient Prescription: Tlando (b) (4) mg 2 capsules po bid #120	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

261 People Received Study
69 People Responded

Study Name: Tlando

Total	21	26	22	
INTERPRETATION	OUTPATIENT	VOICE	INPATIENT	TOTAL
ELANDO	1	0	0	1
FLANDO	2	0	0	2
TALANDO	0	2	0	2
TALONDO	0	3	0	3
TEANDO	0	0	3	3
TELANDO	0	2	0	2
TELLONDO	0	1	0	1
TELONDO	0	7	0	7

TELONDRO	0	1	0	1
TILANDO	1	0	0	1
TLANDE	0	0	1	1
TLANDO	16	0	17	33
TLANDO 112.5 MG	0	0	1	1
TLANDS	1	0	0	1
TOLANDO	0	6	0	6
TOLONDO	0	3	0	3
TULONDO	0	1	0	1

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

No.	**Proposed name:** Tlando **Established name:** Testosterone Undecanoate **Dosage form:** capsule **Strength(s)** (b) (4) 112.5 mg **Usual Dose:** (b) (4) 225 day	**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.	tlando***	100	Proposed proprietary name under review.
2.	(b) (4)	76	Name withdrawn by sponsor on 3/1/16.
3.	Slo-Indo	70	International Product used in the United Kingdom.

Appendix D: Moderately Similar Names (e.g., combined POCA score is ≥50% to ≤69%) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
1.	Balanta	52
2.	Flanders	53
3.	Ganda	53
4.	lantus	52
5.	Lazanda	52
6.	Pandel	50
7.	Plan B	62
8.	Plan B One	53
9.	Tandem	60
10.	Tandem F	50
11.	Tanzeum	50
12.	Teat-Glo	50
13.	Teflaro	50
14.	Teladar	50
15.	Tencon	54

No.	Name	POCA Score (%)
16.	Trandide	58
17.	Tranmep	53
18.	Tri-Sudo	52
19.	Tusana D	52
20.	Tussend	54
21.	Tyvaso	53
22.	Xtandi	55
23.	Trancot	61
24.	Prandin	52
25.	(b) (4)	50

Appendix E: Moderately Similar Names (e.g., combined POCA score is ≥50% to ≤69%) with overlap or numerical similarity in Strength and/or Dose

No.	**Proposed name:** Tlando **Established name:** Testosterone Undecanoate **Dosage form:** capsule **Strength(s):** (b) (4) (b) (4) 112.5 mg **Usual Dose:** (b) (4) (b) (4) 225 mg po twice a (b) (4) day (b) (4)	**POCA Score (%)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
1.	Chendol	51	The prefixes and suffixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different and Tlando*** contains an extra syllable.
2.	Nilandron	50	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different .
3.	Toradol	51	The prefixes, infixes and suffixes of this name pair have sufficient orthographic differences. The first, second and third syllables of this name pair sound different.
4.	Tylenol	52	The prefixes and suffixes of this name pair have sufficient orthographic differences. The first and third syllables of this name pair sound different.
5.	Tindal	57	The suffixes of this name pair have sufficient orthographic differences. The second syllables of this name pair sound different and the name Tlando*** has an extra syllable.
6.	Tramadol	60	The prefixes, infixes and suffixes of this name pair have sufficient orthographic differences. The first, second and third syllables of this name pair sound different.

No.	**Proposed name:** Tlando **Established name:** Testosterone Undecanoate **Dosage form:** capsule **Strength(s):** (b) (4) (b) (4) 112.5 mg **Usual Dose:** (b) (4) (b) (4) (b) (4) 225 mg po twice a day (b) (4) (b) (4)	**POCA Score (%)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
7.	Trandate	57	The prefixes and suffixes of this name pair have sufficient orthographic differences. The first and second syllables sound different. The name Tlando*** has an extra syllable.
8.	Treanda	66	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
9.	Mandol	54	The prefixes and suffixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different. The name Tlando*** has an extra syllable.
10.	Trulance***	52	The prefixes and suffixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different. The name Tlando*** has an extra syllable.

Appendix F: Low Similarity Names (e.g., combined POCA score is ≤49%)

No.	Name	POCA Score (%)
1.	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
1.	(b) (4)	56	Proposed proprietary name found unacceptable by DMEPA (OSE# 2013-1771). Product approved under new proprietary name (b) (4)
2.	Prondol	52	International product marketed in the United Kingdom and Ireland.
3.	Telazol	50	Veterinary product.
4.	(b) (4)	58	Proposed propietary name withdrawn by the applicant. Approved as Ibrance in RCM# 2014-25815.
5.	(b) (4)	64	Tlando*** was submitted to replace this name and thus these two names will not coexist on the marketplace.
6.	(b) (4)	50	(b) (4)
7.	(b) (4)	50	Entire application withdrawn by sponsor on 1/28/14.
8.	(b) (4)	56	This is a secondary proposed proprietary name and the product was approved under proprietary name Trilipix.
9.	Trinza***	55	Not a proprietary drug name. It is the modifier of the proprietary Invega Trinza and will not be prescribed without the root name.
10.	Tylan	58	Veterinary product.

Appendix H: Names not likely to be confused due to notable spelling, orthographic and phonetic differences.

No.	Name	POCA Score (%)
1.	Blincyto	50
2.	C Tan D	55
3.	Claro	54
4.	Clindex	50
5.	Clinpro 5000	58
6.	Clinsol	54
7.	(b) (4)	50
8.	Dolono	53
9.	Dytan-D	51
10.	Glydo	54
11.	Io-Blend	50
12.	J-Tan D	56
13.	(b) (4)	54
14.	Kazano	52
15.	(b) (4)	57
16.	Klaron	50
17.	Linde	58
18.	(b) (4)	53
19.	Placebo	53
20.	Plendil	58
21.	Plenvu***	60
22.	Pronto	56
23.	P-Tann D	54
24.	Slentrol	50
25.	Sulindac	50
26.	Xolido	52
27.	Ztlido***	66

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/s/

LOLITA G WHITE
04/11/2016

DANIELLE M HARRIS
04/11/2016

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:	September 29, 2015
Application Type and Number:	IND 106476 NDA 208088
Product Name and Strength:	(b) (4) (testosterone undecanoate) Capsules (b) (4) (b) (4) 112.5 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Lipocine Inc.
Panorama #:	2015-453678
DMEPA Primary Reviewer:	Walter Fava, RPh., MSEd., Safety Evaluator
DMEPA Team Leader:	Danielle Harris, PharmD., BCPS
DMEPA Associate Director:	Lubna Merchant, PharmD., MS
DMEPA Director:	Todd Bridges, RPh.

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/s/

WALTER L FAVA
09/29/2015

DANIELLE M HARRIS
09/29/2015

LUBNA A MERCHANT
09/29/2015

KELLIE A TAYLOR on behalf of TODD D BRIDGES
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