

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
**206538Orig1s000**

**PROPRIETARY NAME REVIEW(S)**

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**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\*\*\***

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<b>Date of This Review:</b>	July 2, 2014
<b>Application Type and Number:</b>	NDA 206538
<b>Product Name and Strength:</b>	Toujeo SoloStar (insulin glargine [rDNA origin]) injection, 300 units/mL
<b>Product Type:</b>	Combination (Drug + Device)
<b>Rx or OTC:</b>	Rx
<b>Applicant/Sponsor Name:</b>	Sanofi
<b>Submission Date:</b>	April 30, 2014
<b>Panorama #:</b>	2014-17289
<b>DMEPA Primary Reviewer:</b>	Sarah K. Vee, PharmD
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## 1 INTRODUCTION

This review evaluates the proposed proprietary name, Toujeo SoloStar, from a safety and promotional perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively. The Applicant submitted an external name study, conducted by [REDACTED] <sup>(b) (4)</sup> for this product.

### 1.1 PRODUCT INFORMATION

The following product information is provided in the April 30, 2014 proprietary name submission.

- Intended Pronunciation: TWO-jee-oh SOH-loh-STAR
- Active Ingredient: insulin glargine
- Indication of Use: long- acting human insulin analog indicated to improve glycemic control in adults with diabetes mellitus
- Route of Administration: subcutaneous injection
- Dosage Form: solution
- Strength: 300 units/mL
- Dose and Frequency: individualized once daily at any time of the day
- How Supplied: 1.5 mL SoloStar disposable prefilled pen
- Storage:

	<b>Not in-use (unopened) Refrigerated</b>	<b>In-use (opened) (See Temperature Below)</b>
1.5 mL SoloStar <sup>®</sup> disposable prefilled pen	Until expiration date	<sup>(b) (4)</sup> days om temperature only (Do not refrigerate)

- Container and Closure Systems: The insulin glargine solution for injection is packaged in a multidose container (cartridge) closed with a flanged cap with [REDACTED] <sup>(b) (4)</sup> sealing disk and a plunger stopper and housed in a disposable pen.

## 2 RESULTS

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

### 2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Metabolic and Endocrinology Products (DMEP) concurred with the findings of OPDP's promotional assessment of the proposed name.

## 2.2 SAFETY ASSESSMENT

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

### 2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proprietary name<sup>1</sup>.

### 2.2.2 Components of the Proposed Proprietary Name

The Applicant did not provide a derivation or intended meaning for the proposed name, Toujeo 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.

The Applicant submitted “SoloStar” as a modifier to reflect the drug product as part of the pen injector. This is to remain consistent with the Sanofi brand of approved SoloStar disposable pens, e.g., Lantus SoloStar and Apidra SoloStar.

### 2.2.3 FDA Name Simulation Studies

108 practitioners participated in DMEPA’s prescription studies. The interpretations did not overlap with any currently marketed products nor did the misinterpretations sound or look similar to any currently marketed products or any products in the pipeline. There was a wide range of interpretations of the voice prescription where “Tugio” or “Tugeo” being the most common misinterpretation. Among the written prescriptions, “Turyeo” or “Turyio” was the most common misinterpretation. SoloStar component of the proposed proprietary name was generally interpreted correctly. 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, May 6, 2014 e-mail, DMEP did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

### 2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Table 1 lists the number of names with the combined orthographic and phonetic score of  $\geq 50\%$  retrieved from our POCA search organized as highly similar, moderately similar or low similarity for further evaluation. Table 1 also includes names identified (b) (4)

Table 1. POCA Search Results	Number of Names
Highly similar name pair: combined match percentage score $\geq 70\%$	1

<sup>1</sup>USAN stem search conducted on May 8, 2014.

Moderately similar name pair: combined match percentage score $\geq 50\%$ to $\leq 69\%$	28
Low similarity name pair: combined match percentage score $\leq 49\%$	19

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

Our analysis of the 48 names contained in Table 1 determined 48 names will not pose a risk for confusion as described in Appendices C through G.

### 2.2.7 Communication of DMEPA’s Analysis at Midpoint of Review

DMEPA communicated our findings to DMEP via e-mail on June 6, 2014. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from DMEP on June 10, 2014, they stated no additional concerns with the proposed proprietary name, Toujeo SoloStar.

## 3 DISCUSSION OF DUAL PPROPRIETARY NAME

Insulin glargine, 100 units/mL, was approved on April 20, 2000 under the proprietary name, Lantus, for NDA 21081. The product is available in a vial as well as a cartridge integrated into a disposable pen injector (SoloStar).

Sanofi is now seeking a dual proprietary name, Toujeo SoloStar, for a new concentration (300 units/mL) of insulin glargine, (referred to as HOE901-U300), which will be available as a cartridge integrated into a disposable pen injector. Sanofi indicates that: *The proposed name contains “SoloStar” as a modifier to reflect that insulin glargine U-300 will be available as a solution for injection in 1.5 mL cartridges that are irreversibly integrated into a disposable prefilled pen injector (SoloStar®). This is to remain consistent with the Sanofi brand of approved SoloStar disposable pens, e.g., Lantus SoloStar and Apidra SoloStar.* Thus, this review focuses on Toujeo component of the dual proprietary name.

Sanofi provided a survey of Healthcare professionals (HCPs) supporting the use of a dual proprietary name that was conducted by (b) (4) in their request for proposed proprietary name review, dated April 20, 2014.

Sanofi has assessed two potential naming strategies for insulin glargine U-300:

- Use of a new brand name rather than the Lantus brand name
- Use of the Lantus brand name with a modifier (e.g. Lantus 100 and Lantus 300)

(b) (4) surveyed 101 Healthcare professionals (HCPs) to assess whether a new brand name for insulin glargine U-300 would help to reduce the risk of confusion with Lantus. Majority (80.2%) of the HCPs surveyed felt that it would be safer if the new concentration used a new proprietary name in terms of medication error prevention (see Appendix H for details of the study). Additionally, PK/PD studies submitted to NDA

206538 stated that insulin glargine U-100 and U-300 concentrations have different PK/PD profiles (see Appendix I for details).

In light of the information that we gathered from internal and external sources, we considered different naming approaches such as whether the product could be safely managed using the existing name Lantus, Lantus plus a modifier, or a dual proprietary name, and considered different medication error risks with each approach.

With the use of dual proprietary name, we are typically concerned with duplicate therapy. However, this is less of a concern with this particular product for several reasons. We anticipate that duplicate therapy is unlikely since the drug regimen for diabetes patients would be expected to be managed by a single clinician or a team of clinicians who are familiar with a given patient's drug regimen. Furthermore, patients are expected to be educated about the different types of insulins that they are using. In addition the risk of duplicate therapy with the dual proprietary name for insulin glargine U-300 would be similar to introducing a new basal insulin to the market. The clinician would need to discontinue the existing therapy with Lantus in order to switch the patient's basal insulin to the new insulin glargine U-300 same as he would to switch to another basal insulin (e.g. Levemir). Furthermore, due to differences in PK/PD profiles, the products should not be substituted for each other (e.g. unit to unit). Thus, using different proprietary names appears to be the most efficient way to convey to HCPs that the products are not the same to help prevent medication errors with dosing.

We also considered other naming options: use of the existing name, Lantus and use of the existing name, Lantus with a modifier. Using the root name, Lantus, for the two different concentrations that are different in their PK/PD profile may be misleading because it may signal to HCPs that manipulating the doses of one or the other concentration may provide the same glycemic control, which may not be the case.

Using the existing name, Lantus plus a modifier is another option we considered. However, it will be difficult to communicate the difference in the two products' strengths and PK/PD profiles through a modifier. Moreover, adding another modifier to Lantus SoloStar may be more confusing and complicated. Additionally, postmarketing experience indicates that modifiers can be dropped in the medication order process. This type of error could lead to the outcome where the prescription would be interpreted to mean insulin glargine U-100.

In conclusion, among the three naming approaches, it appears that using a dual proprietary name poses the least risk of medication errors and this approach would not be introducing additional risk of medication errors. As a result we find the proprietary name, Toujeo SoloStar, acceptable for insulin glargin U-300.

#### **4 CONCLUSIONS**

The proposed proprietary name is acceptable from both a promotional and safety perspective.

If you have further questions or need clarifications, please contact Lyle Canida, OSE project manager, at 301-796-1637.

#### **4.1 COMMENTS TO THE APPLICANT**

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

If any of the proposed product characteristics as stated in your April 30, 2014 submission are altered, the name must be resubmitted for review.

## 5 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](http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther_biological)).

### *RxNorm*

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

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

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

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

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

## APPENDICES

### Appendix A

FDA's Proprietary Name Risk Assessment considers the promotional and safety aspects of a proposed proprietary name.

1. **Promotional Assessment:** For prescription drug products, the promotional review of the proposed name is conducted by OPDP. For over-the-counter (OTC) drug products, the promotional review of the proposed name is conducted by DNCE. OPDP or DNCE evaluates proposed proprietary names to determine if they are overly fanciful, so as to misleadingly imply unique effectiveness or composition, as well as to assess whether they contribute to overstatement of product efficacy, minimization of risk, broadening of product indications, or making of unsubstantiated superiority claims. OPDP or DNCE provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment:** The safety assessment is conducted by DMEPA, and includes the following:
  - a. **Preliminary Assessment:** We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2\*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.<sup>2</sup>

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

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

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

- b. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@fda, CernerRxNorm, and names in the review pipeline using a 50% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:
- Highly similar pair: combined match percentage score  $\geq 70\%$ .
  - Moderately similar pair: combined match percentage score  $\geq 50\%$  to  $\leq 69\%$ .
  - Low similarity: combined match percentage score  $\leq 49\%$ .

Using the criteria outlined in the check list (Table 3-5) that corresponds to each of the three categories (highly similar pair, moderately similar pair, and low similarity), DMEPA evaluates the name pairs to determine the acceptability or non-acceptability of a proposed proprietary name. Based on our root cause analysis of post marketing experience errors, we find the expression of strength and dose, which is often located in close proximity to the drug name itself on prescriptions and medication orders, is an important factor in mitigating or potentiating confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion is limited (e.g., route, frequency, dosage form, etc.).

- For highly similar names, there is little that can mitigate a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of  $\geq 70$  percent are likely to be rejected by FDA. (See Table 3)
- Moderately similar names with overlapping or similar strengths or doses represent an area for concern for FDA. The dosage and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics (e.g., route, frequency, dosage form, etc.) to mitigate confusion may be limited when the strength or dose overlaps. FDA will review these names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4)
- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist (See Table 5).

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

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

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

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

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

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

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

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

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

Answer the questions in the checklist below. Affirmative answers to these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion, provided that the pair do not share a common strength or dose (see Step 1 of the Moderately Similar Checklist).			
<u>Orthographic Checklist</u>		<u>Phonetic Checklist</u>	
<b>Y/N</b>	Do the names begin with different first letters? <i>Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.</i>	<b>Y/N</b>	Do the names have different number of syllables?
<b>Y/N</b>	Are the lengths of the names dissimilar* when scripted?  <i>*FDA considers the length of names different if the names differ by two or more letters.</i>	<b>Y/N</b>	Do the names have different syllabic stresses?
<b>Y/N</b>	Considering variations in scripting of some letters (such as <i>z</i> and <i>f</i> ), is there a different number or placement of upstroke/downstroke letters present in the names?	<b>Y/N</b>	Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?
<b>Y/N</b>	Is there different number or placement of cross-stroke or dotted letters present in the names?	<b>Y/N</b>	Across a range of dialects, are the names consistently pronounced differently?
<b>Y/N</b>	Do the infixes of the name appear dissimilar when scripted?		
<b>Y/N</b>	Do the suffixes of the names appear dissimilar when scripted?		

**Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is  $\geq 50\%$  to  $\leq 69\%$ ).**

<p>Step 1</p>	<p>Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths have a higher potential for confusion and should be evaluated further (see Step 2).</p> <p>For single strength products, also consider circumstances where the strength may not be expressed.</p> <p>For any combination drug products, consider whether the strength or dose may be expressed using only one of the components.</p> <p>To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion:</p> <ul style="list-style-type: none"> <li>○ 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.</li> <li>○ Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity.</li> <li>○ Similar sounding doses: 15 mg is similar in sound to 50 mg</li> </ul>
<p>Step 2</p>	<p>Answer the questions in the checklist below. Affirmative answers to these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion between moderately similar names <b>with</b> overlapping or similar strengths or doses.</p>

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

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

**Appendix B: Prescription Simulation Samples and Results**

**Figure 1. Toujeo SoloStar Study (Conducted on May x, 2014)**

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Medication Order:</u></p> <p><i>Toujeo Solostar Inject (b)(4) units subcutaneously once daily</i></p> <p><u>Outpatient Prescription:</u></p> <p><i>Toujeo Solostar (b)(4) units subcutaneously once daily #5</i></p>	<p>Toujeo SoloStar Inject (b)(4) units subcutaneously once daily #5</p>

**FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)**

269 people received study  
108 people responded  
study name: toujeo SoloStar

total	36	31	41	
interpretation	outpatient	voice	inpatient	total
2 g o solostar	0	1	0	1
2go celestar	0	1	0	1
2go selestar	0	1	0	1
illegible (solostar)??	0	0	1	1

interpretation	outpatient	voice	inpatient	total
jugeo solostar	0	1	0	1
jujio selistar	0	1	0	1
jujio solastar	0	1	0	1
jujio solostar	0	2	0	2
smoking cessation	1	0	0	1
tgo-selestar	0	1	0	1
togio filistar	0	1	0	1
toiyco solostar	0	0	3	3
toiyeo solostar	0	0	1	1
toiyio solastar	1	0	0	1
tojuo solostar	0	1	0	1
tonryio solastar	1	0	0	1
toriyic solostar	1	0	0	1
torjeo solastas	1	0	0	1
torjio solastar	1	0	0	1
toryces solostar inject	0	0	1	1
toryco solostar	0	0	9	9
toryco solostar inject 45 units	0	0	1	1
toryeo solostar	1	0	16	17
toryeo solostar inject	0	0	1	1
toryeo solstar	0	0	1	1
toryes solostar	0	0	1	1
toryia solastar	1	0	0	1
toryia solostar	1	0	0	1
toryie solostar	1	0	0	1
toryio solastar	4	0	0	4
toryio solastoar	1	0	0	1
toryio solostar	20	0	0	20
toufeo solostar	0	0	1	1
toujeo solostar	1	0	0	1
touyco solestar inject	0	0	1	1
touyeo solostar	0	0	1	1
toyco	0	0	1	1
toyeo	0	0	1	1
toyyeo solostar	0	0	1	1
trugio celestar	0	1	0	1
tugeo selastar	0	1	0	1
tugeo solastar	0	1	0	1
tugeo solostar	0	2	0	2
tugeo zolistar	0	1	0	1
tugio celestar	0	1	0	1

interpretation	outpatient	voice	inpatient	total
tugio folostar	0	1	0	1
tugio philistar	0	1	0	1
tugio solarstar	0	1	0	1
tugio solastar	0	1	0	1
tugio solistar	0	2	0	2
tugio velostar	0	1	0	1
tu-g-o felistar	0	1	0	1
tujio solostar	0	1	0	1
tuogeo solostar	0	1	0	1
two geo filistar	0	1	0	1
twogeo solistar	0	1	0	1
twogeo solostar	0	1	0	1

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

N/A

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

No.	Proposed name: Toujeo Solostar Strength: 300 units/mL Usual Dose: individualized once daily	POCA Score (%)
1.	Taurgo ***	61
2.	Tazia	50

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

No.	Proposed name: Toujeo Solostar Strength: 300 units/mL Usual Dose: individualized once daily	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.	Forteo	55	The infix of this name pair have sufficient orthographic differences The first and second syllables of this name pair sound different.
2.	(b) (4) ***	54	The first and second syllables of this name pair sound different.
3.	Taurine	52	The suffix of this name pair have sufficient orthographic differences The second syllables of this name pair sound different.
4.	(b) (4) ***	50	The prefix and suffix of this name pair have sufficient orthographic differences The first and second syllables of this name pair sound different. Toujeo contains one extra syllable.
5.	Kurvelo	50	The prefix and suffix of this name pair have sufficient orthographic differences The first, second, and third syllables of this name pair sound different.

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**Appendix F:** Low Similarity Names (i.e., combined POCA score is  $\leq 49\%$ )

No.	Name	POCA Score (%)
1.	Cardio	47
2.	Kal D	47
3.	Pau D'arco	46
4.	Tarceva	46
5.	Targin	46
6.	Osteo	45
7.	Da Zao	44
8.	Souci	44
9.	Toux/Cough	44
10.	Bai Shao	42
11.	Paeonia	42
12.	Tco	42
13.	Cardio3-Q10	40
14.	Cardia	36
15.	Januvia	< 50
16.	Lantus	< 50
17.	Toviaz	< 50
18.	Tradjenta	< 50
19.	Tussend	< 50

**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.	Toujeo <sup>***</sup>	100	Subject of this review
2.	Touro	68	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.

<sup>\*\*\*</sup> This document contains proprietary information that should not be released to the public

No.	Name	POCA Score (%)	Failure preventions
3.	Koussou	60	Identified (b) (4) Not a drug. Homeopathic substance.
4.	Touro A&H	58	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
5.	Touro LA	58	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
6.	Touro CC	56	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
7.	(b) (4) ***	56	Found unacceptable in OSE (b) (4) for IND (u) (4)
8.	(b) (4) ***	56	Found unacceptable in OSE # (b) (4) 2010 for IND (u) (4)
9.	Taurate	54	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
10.	Gou Ji	54	Identified (b) (4) Unable to find product characteristics in commonly used drug databases.
11.	Poudre	52	Identified (b) (4) Unable to find product characteristics in commonly used drug databases.
12.	Sauge	52	Identified (b) (4) Unable to find product characteristics in commonly used drug databases.
13.	Tongo	52	Identified (b) (4) Not a drug. Homeopathic substance.

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No.	Name	POCA Score (%)	Failure preventions
14.	Touro DM	52	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
15.	Touro HC	52	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
16.	(b) (4)***	51	Name Entered by Safety Evaluator. Unable to find product characteristics in commonly used drug databases.
17.	Targel	51	Identified by (b) (4) Unable to find product characteristics in commonly used drug databases.
18.	Touro EX	51	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
19.	Tegison	50	Name identified in Drugs At FDA database. Withdrawn FR effective 09/10/2003 (NDA 19369; no generics)
20.	Toco.E.	50	Identified (b) (4) Unable to find product characteristics in commonly used drug databases.
21.	Tone	50	Identified (b) (4) Unable to find product characteristics in commonly used drug databases.
22.	Tri-Sudo	50	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.

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**Appendix H:** (b) (4) **FMEA**

In the first section of the naming strategy assessment research, respondents were reminded that Product X is *insulin glargine 300 U/mL* rather than the current 100 U/mL Lantus. Next, respondents were asked if they felt that it would reduce the risk of confusion between Lantus and the new *insulin glargine 300 U/mL* if the new *insulin glargine* utilized a new brand name rather than the Lantus brand name. Finally, respondents were asked why they felt that way.

In the second section of the naming strategy assessment research, respondents were again reminded that Product X is *insulin glargine 300 U/mL* rather than the current 100 U/mL Lantus. Respondents were then asked if they felt that Product X could safely coexist with Lantus if Product X also utilized the Lantus brand name with a modifier (e.g. Lantus 100 and Lantus 300) instead of a completely new name. Finally, respondents were asked why they felt that way.

One hundred and one (101) healthcare professionals were asked to assess whether a new brand name for *insulin glargine 300 U/mL* would help to reduce the risk of confusion with Lantus. The table below shows the results:

<b>Use of New Name (n=101)</b>	
Yes, it would reduce confusion	80.2%
No, it would not reduce confusion	19.8%

Of the 101 respondents, 81 felt that a new brand name would reduce the risk of confusion between Lantus and the new *insulin glargine 300 U/mL* rather than the new *insulin glargine* utilizing the Lantus brand name. These 81 respondents identified the following reasons why they believe that a new brand name would reduce the risk of confusion:

<b>Reasons New Name would Reduce Confusion</b>	
Differentiate the concentration/strength	27
Reduce confusion/risk of medication error	18
Differentiate the products	10
Different name	7
Including units only is not enough	6
Easier	3
Enough confusion already exists	1
Reduce risk to patients	1
Unrelated responses	8

Of the 101 respondents, only 20 felt that a new brand name would not reduce the risk of confusion between Lantus and the new *insulin glargine 300 U/mL* rather than the new *insulin glargine* utilizing the Lantus brand name. These 20 respondents identified the following reasons why they believe that a new brand name would not reduce the risk of confusion:

<b>Reasons New Name would not Reduce Confusion</b>	
Strength is sufficient	5
More confusing with different names	2
Brand would be different	4
No need to change	3
Different packaging would be better	2
There won't be a problem/risk of confusion	2
It's the same product	1
Unrelated responses	2

One hundred and one (101) healthcare professionals were asked to assess whether the new *insulin glargine 300 U/mL* could safely coexist with the current Lantus 100 U/mL if the new product also utilized the Lantus brand name with a modifier (e.g. Lantus 100 and Lantus 300) instead of a completely new name. The table below shows the results:

<b>Use of Lantus with a Modifier (n=101)</b>	
Yes, they could safely coexist	34.7%
No, they could not safely coexist	65.3%

Of the 101 respondents, 66 felt that the new *insulin glargine 300 U/mL* could not safely coexist with the current Lantus 100 U/mL if the new product also utilized the Lantus brand name with a modifier (e.g. Lantus 100 and Lantus 300) instead of a completely new name. These 66 respondents identified the following reasons why they believe that they could not safely coexist:

<b>Reasons could not Coexist with Modifier Alone</b>	
Confusion/risk of medication error	29
Name should be changed	10
Strength alone is not enough	8
Easy to make mistake	4
Physicians will forget to include strength	4
Names too similar	2
Unrelated responses	10

Of the 101 respondents, 35 felt that the new *insulin glargine 300 U/mL* could safely coexist with the current Lantus 100 U/mL if the new product also utilized the Lantus brand name with a modifier (e.g. Lantus 100 and Lantus 300) instead of a completely new name. These 35 respondents identified the following reasons why they believe that they could safely coexist:

<b>Reasons could Coexist with Modifier Alone</b>	
Modifier will be enough/indicate strength	10
They are different/could coexist	7
Easy/easy to remember	3
No issues	3
Similar to naming strategy for other products	3
Different packaging will make it clear	2
Less confusing	2
Unrelated responses	5

It is evident from these results that the approval of a new brand name for the new *insulin glargine 300 U/mL* product rather than the use of Lantus 300 or Lantus with an alternative modifier would minimize the risk of confusion with the current Lantus and ensure patient safety.

The failure modes for each scenario (co-existence of Lantus and Toujeo and co-existence of Lantus SoloStar and Toujeo SoloStar) were rated by 101 United States-based healthcare professionals, including 16 General Practitioners, 35 Diabetologists/Endocrinologists, 25 Retail Pharmacists, 6 Primary Care Nurses, and 19 Diabetology/Endocrinology Nurses using a predetermined scale of 1 to 10 based on three criteria: likelihood, severity, and detectability of each failure mode. The scale utilized by the respondents is below:

<b>Value</b>	<b>Likelihood of Occurrence</b>	<b>Severity of Effect</b>	<b>Detectability</b>
1	Remote	None	Immediately detectable
2	Very low	Very minor effect	Found early
3	Low	Minor	Usually found
4	Low to moderate	Low to moderate	Probably found
5	Moderate	Moderate	May be found
6	Moderate to high	Moderate to high	Less than 50% chance of detection
7	High	High	Unlikely to be detected
8	Very high	Very high	Very unlikely to be detected
9	Extremely high	Hazardous	Extremely unlikely to be detected
10	Almost certain	Disastrous	Almost impossible to detect

One hundred and one (101) healthcare professionals were asked to assess the failure modes between the co-existence of Lantus and Toujeo as well as Lantus SoloStar and Toujeo SoloStar. The table below shows the mean rating for each of the two scenarios:

<b>Failure Modes Assessment</b>	
<b>Lantus and Toujeo</b>	<b>3.2</b>
<b>Lantus SoloStar and Toujeo SoloStar</b>	<b>3.3</b>

**Appendix I: PK/PD Study Summary**

*After subcutaneous injection of HOE901-U300 in healthy subjects and in patients with Type 1 diabetes mellitus, the insulin serum concentration profiles indicated a slower and more prolonged absorption from the SC injection site. This resulted in a flatter, less fluctuating time-concentration profile than Lantus, with a plateau extending for up to 36 hours at higher doses for HOE901-U300. Steady state levels are reached after 3 to 4 days of daily HOE901-U300 administration compared with 1 to 2 days for Lantus. HOE901-U300 shows a flatter and prolonged profile of glucose-lowering activity which provides extended basal insulin coverage with lower diurnal fluctuation than Lantus. In steady state conditions, diurnal serum insulin glargine concentration and glucodynamic activity profiles of HOE901-U300 display lower maximum levels and smaller individual diurnal fluctuations than an equal dose of insulin glargine given as Lantus.*

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/s/  
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