CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761109Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

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

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

Date of This Review:	February 5, 2020
Application Type and Number:	BLA 761109
Product Name and Strength:	Lyumjev (insulin lispro) injection, 100 units/mL Lyumjev KwikPen (insulin lispro) injection, 100 units/mL and 200 units/mL Lyumjev Junior KwikPen (insulin lispro) injection, 100 units/mL Lyumjev Tempo Pen (insulin lispro) injection, 100 units/mL
Total Product Strength:	1,000 units per 10 mL vial 300 units per 3 mL cartridge 300 units per 3 mL prefilled pen 600 units per 3 mL prefilled pen
Product Type:	Single Ingredient Product, Combination Product (Drug-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Eli Lilly and Company (Lilly)
Panorama #:	2019-36466842 and 2019-36666813
DMEPA Safety Evaluator:	Ariane O. Conrad, PharmD, BCACP, CDE
DMEPA Team Leader:	Hina Mehta, PharmD
DMEPA Associate Director:	Mishale Mistry, PharmD, MPH

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary names, Lyumjev, Lyumjev KwikPen, Lyumjev Junior KwikPen, and Lyumjev Tempo Pen 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. Lilly submitted a self-conducted name study for the proposed proprietary names. In addition, they submitted an external name study conducted by (b) (4) which assessed the placement of a modifier within the proposed proprietary name.

1.1 REGULATORY HISTORY

Lilly submitted the proposed proprietary name (b) (4) unacceptable due to orthographic similarities, phonetic similarities (b) (4)

Under BLA 761109, Lilly submitted the proposed proprietary name (b) (4) uring a December 2, 2019 teleconference with Lilly, we communicated ongoing concerns of orthographic similarities (b) (4) and submitted the proposed proprietary names, Lyumjev, Lyumjev KwikPen, Lyumjev Junior KwikPen, and Lyumjev Tempo Pen for review on December 13, 2019.[d]

1.2 PRODUCT INFORMATION

The following product information is provided in the prescribing information (PI) submitted on August 28, 2019 and the proprietary name submission dated December 13, 2019.

(b) (4)

- Intended Pronunciation: [redacted]
- Nonproprietary Name: insulin lispro
- Indication of Use: To improve glycemic control in adults with diabetes mellitus
- Route of Administration: subcutaneous or intravenous
  - most patients will administer subcutaneously; however, it can also be administered intravenously in a hospital setting under medical supervision.
- Dosage Form: injection
- Strength: 100 units/mL and 200 units/mL
- Dose and Frequency: Individualize dosage based on route of administration, the individual's metabolic needs, blood glucose monitoring results and glycemic control goal
  - Subcutaneous injection: [redacted] within 20 minutes after starting a meal
- How Supplied:
  - 100 units/mL (U-100) is available as:
    - 10 mL multiple-dose vial
    - 3 mL single-patient-use KwikPen®
    - 3 mL single-patient-use Junior KwikPen®
    - 3 mL single-patient-use Tempo Pen™
    - 3 mL single-patient-use cartridges
  - 200 units/mL (U-200) is available as:
    - 3 mL single-patient-use KwikPen®
- Storage:

  [redacted] unopened [redacted] vials, pens, and cartridges [redacted] between 36°F to 46°F (2°C to 8°C) [redacted]

  Do not freeze or use [redacted] if it has been frozen. [redacted]

  [redacted]

  When stored at room temperature, [redacted] can only be used for a total of 28 days including both not in-use (unopened) and in-use (opened) storage time.

---

[e] Although the sponsor states that intended pronunciation is [redacted] we considered possible alternative pronunciations (e.g., Ly-OOM-jev) based on the proposed spelling of the name in our evaluation of risk for sound-alike confusion.

In-use (opened) vials, whether or not refrigerated, must be used within 28 days. (b) (4) [redacted]

- Reference Listed Drug/Reference Product: n/a

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Lyumjev, Lyumjev KwikPen, Lyumjev Junior KwikPen, and Lyumjev Tempo Pen would not misbrand the proposed product per their January 10, 2020 email. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Metabolism and Endocrinology Products (DMEP) concurred with the findings of OPDP's assessment for Lyumjev, Lyumjev KwikPen, Lyumjev Junior KwikPen, and Lyumjev Tempo Pen.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proposed proprietary name, Lyumjev[f].

The proposed proprietary name modifier, Junior, contains the United States Adopted Name (USAN) stem "-io-". The "-io-" USAN stem in the infix position is used by the USAN council to indicate iodine containing products. Although FDA recommends against the incorporation of USAN stems in the position that USAN designates for the stem, we note that the word "Junior" is an English word that can only be spelled using the stem in the position designated by USAN. We have no expectation that the word "Junior" should be spelled differently to avoid inclusion of the USAN stem "-io-". Therefore, we will not object to the proposed proprietary name based on the presence of a USAN stem in this instance.

2.2.2 Components of the Proposed Proprietary Name

Lilly indicated in their submission that the proposed proprietary name, Lyumjev, has no specific derivation. The proprietary names Lyumjev KwikPen, Lyumjev Junior KwikPen, and Lyumjev Tempo Pen are comprised of the root name Lyumjev and the device modifiers KwikPen, Junior KwikPen, and Tempo Pen, respectively.

We determined that the root name, Lyumjev, does not contain any components (i.e. route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

[f] USAN stem search conducted on January 13, 2020.

Per the submission, the KwikPen modifier denotes the specific type of pen injector used for the product that will be packed as a prefilled pen (Lyumjev U-100 KwikPen and Lyumjev U-200 KwikPen). The *Junior* KwikPen modifier distinguishes the pen injector which dials in 0.5-unit increments from the other KwikPen devices. This is consistent with the Lilly brand of approved KwikPen disposable pens (i.e., Humalog KwikPen (U-100), Humalog KwikPen (U-200), and Humalog Junior KwikPen). We note that the naming convention of adding a modifier to represent a specific device has been used before to differentiate various presentations within a product line (in this case, to differentiate between the different pen injector presentations and the vial/cartridge presentations).

Additionally, per the submission, the proposed proprietary name Lyumjev Tempo Pen is intended to distinguish their modified pen device from the proprietary name used for Lilly's currently marketed KwikPen device. The Tempo Pen has been modified to enable it to be used in a connected care environment and use of the "Tempo Pen" modifier for this device is consistent with the approach used to differentiate the Humalog KwikPen and Basaglar KwikPen from the currently approved Humalog Tempo Pen and Basaglar Tempo Pen (approved November 15, 2019).

We note that omission and oversight of a modifier is cited in literature as a common cause of medication error. As with any product that is available in multiple presentations, the prescriber would need to indicate in the prescription, the intended product on the prescription. If the modifiers "KwikPen", "Junior KwikPen", or "Tempo Pen" are omitted, the intended presentation and insulin concentration (U-100 or U-200) may be clarified by the pharmacist prior to dispensing, or the patient may receive the vial or cartridge presentation. We note that the proposed presentations share the same active ingredient, indication, route of administration, dosage form, dose and frequency. Furthermore, the KwikPen, Junior KwikPen and the Tempo Pen use the same device platform; therefore, there is no concern that the wrong product would be dispensed if the modifier is dropped. In the event the KwikPen was dispensed instead of the Tempo Pen, the patient would be able to administer their prescribed dose; however, the patient would not have connectivity to the mobile application. We note that the "KwikPen", "Junior KwikPen", and "Tempo Pen" devices are not available on their own and we do not anticipate that the modifiers will be written without the root name. Thus, while modifiers may be omitted, they can assist in differentiating products and may help to prevent potential selection errors when used. An alternative to using modifier to distinguish these presentations is to use a different root name for each presentation. However, marketing the presentations under unique proprietary names also carries a risk of medication errors, such as therapeutic duplication and overdoses. Thus, we do not object to the use of modifiers to distinguish the products.

In summary, we acknowledge that the use of the proposed modifiers, "KwikPen", "Junior KwikPen", and "Tempo Pen" are consistent with the naming strategy used for other products and provide a means to differentiate between the pen injectors and the vial/cartridge presentation.

2.2.3 Comments from Other Review Disciplines at Initial Review

In response to the OSE January 14, 2020 e-mail, the Division of Metabolism and Endocrinology Products (DMEP) did not forward any comments or concerns relating to Lyumjev at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Eighty practitioners (80) participated in DMEPA's prescription study for Lyumjev and Lyumjev KwikPen. In addition, 77 practitioners participated in the Lyumjev Junior KwikPen and Lyumjev Tempo Pen, respectively. One hundred seventy-nine (179) participants interpreted the names correctly: "Lyumjev" (48 out of 80 participants), "Lyumjev KwikPen (42 out of 80 participants), "Lyumjev Junior KwikPen" (44 out of 77 participants), and "Lyumjev Tempo Pen" (45 out of 77 participants). 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 prescription simulation studies.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search[g] identified six 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 Retrieved for Review Organized by Name Pair Similarity

Table 1 lists the 11 names retrieved from our POCA search and Lilly's internal name 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%	2
Low similarity name pair: combined match percentage score ≤54%	7

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

Our analysis of the 11 names contained in Table 1 determined none of the names will pose a risk for confusion with Lyumjev 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 Metabolism and Endocrinology Products (DMEP) via email on February 5, 2020. At that time, we also requested additional information

[g] POCA search conducted on January 13, 2020 in version 4.3.

or concerns that could inform our review. Per email correspondence from the Division of Metabolism and Endocrinology Products (DMEP) on February 5, 2020, they stated no additional concerns with the proposed proprietary name, Lyumjev.

3 CONCLUSION

The proposed proprietary name, Lyumjev, is acceptable.

If you have any questions or need clarifications, please contact Terrolyn Thomas, OSE project manager, at 240-402-3981.

3.1 COMMENTS TO ELI LILLY AND COMPANY

We have completed our review of the proposed proprietary names, Lyumjev, Lyumjev KwikPen, Lyumjev Junior KwikPen, and Lyumjev Tempo Pen and have concluded that these names are acceptable.

If any of the proposed product characteristics as stated in your submission, received on December 13, 2019, are altered prior to approval of the marketing application, the names must be resubmitted for review.

4 REFERENCES

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

USAN Stems List contains all the recognized USAN stems.

2. Phonetic and Orthographic Computer Analysis (POCA)

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

Drugs@FDA

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

RxNorm

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

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

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

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

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

APPENDICES

Appendix A

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

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

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

[h] National Coordinating Council for Medication Error Reporting and Prevention. 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[i]. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.
    - Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).

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

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

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

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

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

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

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

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

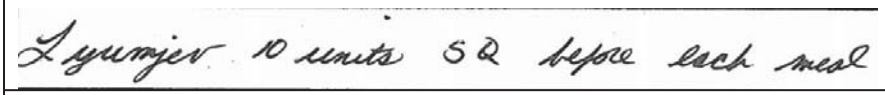
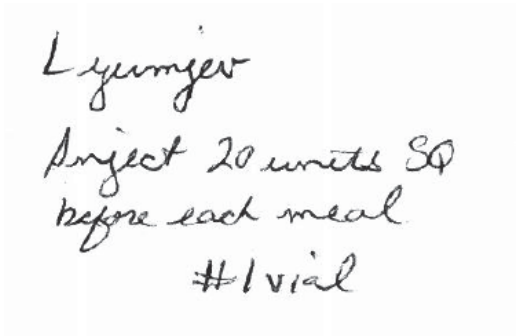
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length 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. Lyumjev Study (Conducted on January 17, 2020)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order:  	Lyumjev Inject 20 units SQ before each meal Dispense # 1 vial
Outpatient Prescription:  	
CPOE Study Sample (Font: sans-serif, 12 point, bold)	
Lyumjev	

FDA Prescription Simulation Responses (Aggregate Report)

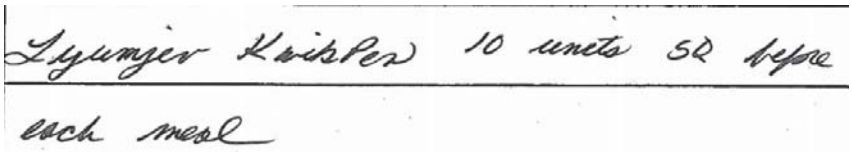
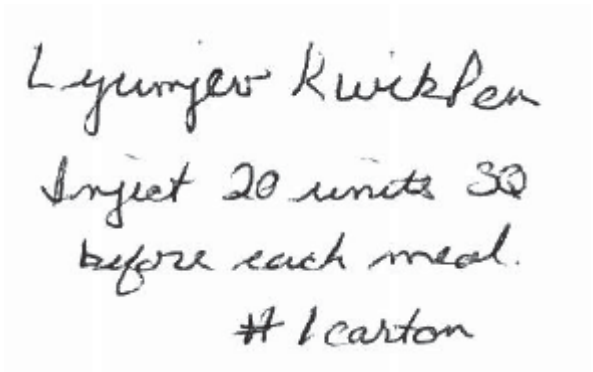
Study Name: Lyumjev
As of Date 1/29/2020

211 People Received Study
80 People Responded

Study Name: Lyumjev

Total	19	18	26	17	
INTERPRETATION	**OUTPATIENT**	**CPOE**	**VOICE**	**INPATIENT**	**TOTAL**
BLOOMJEV	0	0	2	0	2
BLUMGEV	0	0	1	0	1
BLUMJEZ	0	0	1	0	1
GLUMJEV	0	0	1	0	1
LOOMJEV	0	0	2	0	2
LOOVJEV	0	0	1	0	1
LUMEJEV	0	0	1	0	1
LUMGEV	0	0	2	0	2
LUMJAV	0	0	2	0	2
LUMJEV	0	0	12	0	12
LUNJEV	0	0	1	0	1
LYEVMIEV	1	0	0	0	1
LYUMJER	0	0	0	1	1
LYUMJEV	17	18	0	12	47
LYUMJEV INJECTION	0	0	0	1	1
LYUMJIV	1	0	0	0	1
ZYUMJEV	0	0	0	3	3

Figure 1. Lyumjev KwikPen Study (Conducted on January 17, 2020)

Handwritten Medication Order/Prescription	**Verbal Prescription**
Medication Order:  	Lyumjev KwikPen Inject 20 units SQ before each meal Dispense # 1 carton
Outpatient Prescription:  	
CPOE Study Sample (Font: sans-serif, 12 point, bold)	
Lyumjev KwikPen	

FDA Prescription Simulation Responses (Aggregate Report)

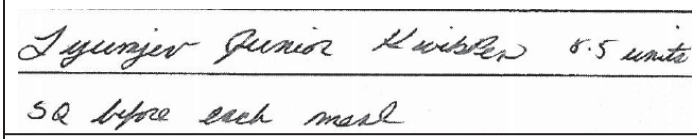
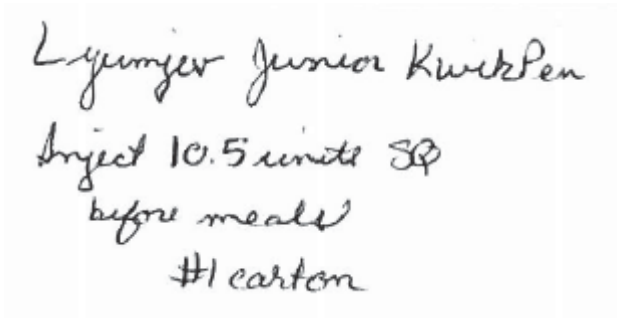
Study Name: Lyumjev KwikPen
As of Date 1/29/2020

211 People Received Study
80 People Responded

Study Name: Lyumjev KwikPen

Total	19	18	26	17	
INTERPRETATION	**OUTPATIENT**	**CPOE**	**VOICE**	**INPATIENT**	**TOTAL**
BLOOMJEV QUICK PEN	0	0	1	0	1
GLUMJEV QUICK PEN	0	0	1	0	1
LOOMJEV QUICK PEN	0	0	1	0	1
LOOMJEV QUIK PEN	0	0	2	0	2
LUMEJEV QUIKPEN	0	0	1	0	1
LUMGEV KWIKPEN	0	0	1	0	1
LUMGEV QUICK PEN	0	0	1	0	1
LUMGEV QUICKPEN	0	0	1	0	1
LUMJAV QUICKPEN	0	0	1	0	1
LUMJAV QUIK PEN	0	0	1	0	1
LUMJEV	0	0	1	0	1
LUMJEV KWIKPEN	0	0	2	0	2
LUMJEV QUICK PEN	0	0	4	0	4
LUMJEV QUICKPEN	0	0	3	0	3
LUMJEV QUIK PEN	0	0	1	0	1
LUMJEV QUIKPEN	0	0	1	0	1
LUMJEV QWICKPEN	0	0	1	0	1
LUMJEV QWIKPEN	0	0	1	0	1
LUMJEZ QUICK PEN	0	0	1	0	1
LYSOZYME	0	1	0	0	1
LYUMIEV KWIKPEN	1	0	0	0	1
LYUMJER	0	0	0	1	1
LYUMJER KWIKPEN	0	0	0	1	1
LYUMJEV KWICKPEN	2	0	0	0	2
LYUMJEV KWIK PEN	1	0	0	4	5
LYUMJEV KWIKPEN	13	17	0	7	37
LYUMJEV QUICK PEN	1	0	0	0	1
LYUMJIV KWIKPEN	1	0	0	0	1
ZYUMJER KWIKPEN	0	0	0	1	1
ZYUMJEV	0	0	0	1	1
ZYUMJEV KWIK PEN	0	0	0	2	2

Figure 1. Lyumjev Junior KwikPen Study (Conducted on January 21, 2020)

Handwritten Medication Order/Prescription	**Verbal Prescription**
Medication Order:  	Lyumjev Junior KwikPen Inject 10.5 units SQ before meals Dispense # 1 carton
Outpatient Prescription:  	
CPOE Study Sample (Font: sans-serif, 12 point, bold)	
Lyumjev Junior KwikPen	

FDA Prescription Simulation Responses (Aggregate Report)

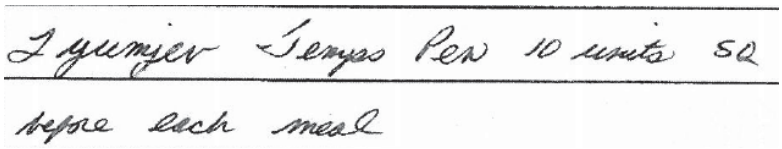
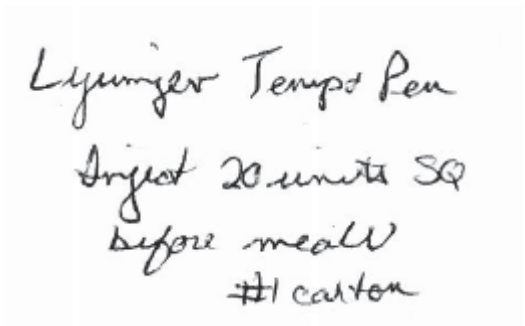
Study Name: Lyumjev Junior KwikPen
As of Date 1/29/2020

211 People Received Study
77 People Responded

Study Name: Lyumjev Junior KwikPen

Total	32	14	14	17	
INTERPRETATION	**OUTPATIENT**	**CPOE**	**VOICE**	**INPATIENT**	**TOTAL**
LOOMJAV JUNIOR QUICKPEN	0	0	1	0	1
LUMGEV JR QUIKPEN	0	0	1	0	1
LUMJEV JR QWIKPEN	0	0	1	0	1
LUMJEV JR. QUICK PEN	0	0	1	0	1
LUMJEV JR. QUICK PENN	0	0	1	0	1
LUMJEV JUNIOR KWIKPEN	0	0	1	0	1
LUMJEV JUNIOR QUICK PEN	0	0	3	0	3
LUMJEV JUNIOR QUICKPEN	0	0	2	0	2
LUMJEVE JUNIOR QUICK PEN	0	0	1	0	1
LUMZAS JR KWIKPEN	0	0	1	0	1
LYEMJEV JUNIER KWIKPEN	1	0	0	0	1
LYMJEV JUNIOR KWIKPEN	1	0	0	0	1
LYMMMJIUS JUNIOR KWIKPEN	1	0	0	0	1
LYUEMJEV JUNIOR KWIKPEN	1	0	0	0	1
LYUMIEV	0	0	0	1	1
LYUMJEM JR KWIKPEN	0	0	1	0	1
LYUMJEV	2	0	0	0	2
LYUMJEV JUNIOR KWIKPEN	1	0	0	0	1
LYUMJEV JUNION KWIKPEN	2	0	0	0	2
LYUMJEV JUNIOR KRIKPEN	1	0	0	0	1
LYUMJEV JUNIOR KWICKPEN	4	0	0	0	4
LYUMJEV JUNIOR KWIKPEN	17	14	0	10	41
LYUMJIV JUNIOR KWIKPEN	0	0	0	1	1
LYUMZEVJUNIOR KWIKPEN	1	0	0	0	1
LYUNJEV JINIOR KWIKPEN	0	0	0	1	1
LYUNJEV JUNIOR KWIKPEN	0	0	0	2	2
LYUNJIEV JUNIOR KWIKPEN	0	0	0	1	1
TYUMJEV JUNIOR KWIKPEN	0	0	0	1	1

Figure 1. Lyumjev Tempo Pen Study (Conducted on January 21, 2020)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order:  	Lyumjev Tempo Pen Inject 20 units SQ before meals Dispense # 1 carton
Outpatient Prescription:  	
CPOE Study Sample (Font: sans-serif, 12 point, bold)	
Lyumjev Tempo Pen	

FDA Prescription Simulation Responses (Aggregate Report)

Study Name: Lyumjev Tempo Pen
As of Date 1/29/2020

211 People Received Study
77 People Responded

Study Name: Lyumjev Tempo Pen

Total	32	14	14	17	
INTERPRETATION	**OUTPATIENT**	**CPOE**	**VOICE**	**INPATIENT**	**TOTAL**
LOOMJAV TEMPLE PEN	0	0	1	0	1
LUMGEV TEMPO PEN	0	0	1	0	1
LUMJEV TEMPO PEN	0	0	8	0	8
LUMJEV TEMPOPEN	0	0	1	0	1
LUMJEVE TAMPO PEN	0	0	1	0	1
LUMZAS TEMPO PEN	0	0	1	0	1
LYMJEV TEMPO PEN	1	0	0	0	1
LYMMJEV	1	0	0	0	1
LYUEMJEV TEMPO PEN	1	0	0	0	1
LYUMGEV TEMPO PEN	1	0	0	0	1
LYUMIEV TENYSS PENN	0	0	0	1	1
LYUMJEV	1	0	0	0	1
LYUMJEV TEMPS PEN	1	0	0	0	1
LYUMJEV TEMP PEN	2	0	0	0	2
LYUMJEV TEMPA PEN	1	0	0	0	1

LYUMJEV TEMPO PEN	19	14	1	10	44
LYUMJEV TEMPOPEN	1	0	0	0	1
LYUMJEV TEMPT PEN	1	0	0	0	1
LYUMJEV TEMYSS PEN	0	0	0	1	1
LYUMJEV TENYSS PEN	0	0	0	1	1
LYUMJEVTEMPOPEN	1	0	0	0	1
LYUMJIV TEMPO PEN	0	0	0	1	1
LYUMZEV TEMP PEN	1	0	0	0	1
LYUNJEV TENYSS PEN	0	0	0	1	1
LYUNJIEV TEMPO PEN	0	0	0	1	1
TYUMJEV TEMPO PEN	0	0	0	1	1

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

No.	**Proposed name:** Lyumjev[KwikPen], [Junior KwikPen], [Tempo Pen] **Established name:** insulin lispro **Dosage form:** injection **Strength(s):** 100 units/mL and 200 units/mL **Usual Dose:** dose administered (b) (4) within 20 minutes of starting a meal	**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.	Lyumjev*** Lyumjev Kwikpen*** Lyumjev Tempo Pen***	100 52 49	These names are subjects of the review.
2.	(b) (4) ***	89	This name was proposed for this (b) (4) and found unacceptable by DMEPA (b) (4) Sponsor submitted an alternative name, which is the subject of this review.

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.	Lumizyme	59
4.	Symjepi	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 --- N/A

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

No.	Name	POCA Score (%)
5.	Lumigan	51
6.	Lupon Depot-Ped	29
7.	Levemir FlexPen	28
8.	Orovite Compliment	18

No.	Name	POCA Score (%)
9.	Primoteston Depot	14

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

Appendix H: Names not likely to be confused due to absence of attributes that are known to cause name confusion[j]. --- N/A

[j] 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

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/

ARIANE O CONRAD
02/05/2020 02:13:19 PM

HINA S MEHTA
02/06/2020 08:58:28 PM

MISHALE P MISTRY
02/07/2020 08:30:36 AM

MEMORANDUM
SUFFIX REVIEW FOR NONPROPRIETARY NAME

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:	February 3, 2020
Responsible OND Division:	Division of Metabolism and Endocrinology Products (DMEP)
Application Type and Number:	BLA 761109
Product Name and Strength:	Lyumjev[a] (insulin lispro-aabc) injection, U-100 and U-200
Product Type:	Combination Product (Biologic-Device)
Applicant/Sponsor Name:	Eli Lilly and Company (Lilly)
FDA Received Date:	August 15, 2019
OSE RCM #:	2019-2447
DMEPA Primary Reviewer:	Carlos M Mena-Grillasca, BS Pharm
DMEPA Deputy Director:	Danielle Harris, PharmD, BCPS

[a] Proposed proprietary name currently under review.

1 PURPOSE OF MEMO

This memorandum summarizes our evaluation of the four-letter suffixes proposed by Lilly for inclusion in the nonproprietary name and communicates our recommendation for the nonproprietary name for BLA 761109.

2 ASSESSMENT OF THE NONPROPRIETARY NAME

On August 15, 2019, Lilly submitted a list of 10 suffixes, in their order of preference, to be used in the nonproprietary name of their product[a]. Lilly also provided findings from an external study conducted by the (b) (4), evaluating the proposed four-letter suffixes in conjunction with the nonproprietary name, for our consideration. Table 1 presents a list of suffixes submitted by Lilly:

Table 1. Suffixes submitted by Lilly***

1.	aabc
(b) (4)	

We reviewed Lilly's proposed suffixes in order of preference listed by Lilly, along with the supporting data they submitted, using the principles described in the applicable guidance.[c]

[a] Note to Reviewer (BLA 761109). Indianapolis (IN): Eli Lilly and Company; 2019 Aug 15. Available from: \\cdsesub1\evsprod\bla761109\0001\m1\us\note.pdf

[b] Non-Proprietary Name Suffix Recommendation (BLA 761109). (b) (4) 2019 Jul 30. Available from: \\cdsesub1\evsprod\bla761109\0001\m1\us\non-proprietary-name-suffix-recommendation.pdf

[c] See Section VI which describes that any suffixes should be devoid of meaning in Guidance for Industry: Nonproprietary Naming of Biological Products. 2017. Available from: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM459987.pdf

2.1 insulin lispro-aabc

Lilly's first proposed suffix, -aabc, is comprised of 3 distinct letters.

We determined that the proposed suffix -aabc, is not too similar to any other products' suffix designation, does not look similar to the names of other currently marketed products, that the suffix is devoid of meaning, does not include any abbreviations that could be misinterpreted, and does not make any misrepresentations with respect to safety or efficacy of this product.

3 COMMUNICATION OF DMEPA'S ANALYSIS

These findings were shared with OPDP. Per an email correspondence dated January 14, 2020, OPDP did not identify any concerns that would render this proposed suffix unacceptable. DMEPA also communicated our findings to the Division of Metabolism and Endocrinology Products (DMEP) via e-mail on February 3, 2020.

4 CONCLUSION

We find Lilly's proposed suffix -aabc acceptable and recommend the nonproprietary name be revised throughout the draft labels and labeling to insulin lispro-aabc. DMEPA will communicate our findings to the Applicant via letter.

4.1 Recommendations for Eli Lilly and Company

We find the nonproprietary name, insulin lispro-aabc, conditionally acceptable for your proposed product. Should your 351(a) BLA be approved during this review cycle, insulin lispro-aabc will be the proper name designated in the license. You should revise your proposed labels and labeling accordingly and submit the revised labels and labeling to your BLA for our review. However, please be advised that if your application receives a complete response, the acceptability of your proposed suffix will be re-evaluated when you respond to the deficiencies. If we find your suffix unacceptable upon our re-evaluation, we would inform you of our finding.

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/

CARLOS M MENA-GRILLASCA
02/03/2020 08:53:01 AM

DANIELLE M HARRIS
02/06/2020 07:59:03 AM

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:	November 5, 2019
Application Type and Number:	BLA 761109 NON-RESPONSIVE
Product Name and Strength:	(b) (4) (insulin lispro) injection, 100 units/mL
	(b) (4) KwikPen (insulin lispro) injection, 100 units/mL and 200 units/mL
	(b) (4) Junior KwikPen (insulin lispro) injection, 100 units/mL
Total Product Strength:	1,000 units per 10 mL vial
	300 units per 3 mL cartridge
	300 units per 3 mL prefilled pen
	600 units per 3 mL prefilled pen
Product Type:	Single Ingredient Product, Combination Product (Drug-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Eli Lilly and Company (Lilly)
Panorama #:	2019-34701292
	2019-34927779 and 2019-34840196
	2019-34927889
DMEPA Safety Evaluator:	Ariane O. Conrad, PharmD, BCACP, CDE
DMEPA Team Leader:	Hina Mehta, PharmD
DMEPA Associate Director:	Mishale Mistry, PharmD, MPH

1 INTRODUCTION

This memorandum is to reassess the proposed proprietary names, [redacted] KwikPen, and [redacted] Junior KwikPen, which were found conditionally acceptable under IND 127210 on July 8, 2019.[a] 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 [redacted] KwikPen, and [redacted] Junior KwikPen would not misbrand the proposed product per their October 19, 2019 email. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Metabolism and Endocrinology Products (DMEP) concurred with the findings of OPDP's assessment for [redacted] KwikPen, and [redacted] Junior KwikPen.

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 October 2, 2019 search of USAN stems did not find any USAN stems in the proposed proprietary name, [redacted].

However, as noted in our prior review[a], the proposed proprietary name modifier, Junior, contains the United States Adopted Name (USAN) stem "-io-". In this instance, we maintain our nonobjection to the proposed proprietary name based on the presence of a USAN stem.

2.3 COMMUNICATION OF DMEPA'S ANALYSIS AT MIDPOINT OF REVIEW

We communicated our findings to the Division of Metabolism and Endocrinology Products (DMEP) via email on October 24, 2019. At that time, we also requested additional information or concerns that could inform our review. Per email correspondence from the Division of Metabolism and Endocrinology Products (DMEP) on October 24, 2019, they stated no additional concerns with the proposed proprietary names, [redacted] KwikPen, and [redacted] Junior KwikPen.

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 names, [redacted] KwikPen, and [redacted] Junior KwikPen, are acceptable.

---

[a] Conrad A. Proprietary Name Review for [redacted] KwikPen, and [redacted] Junior KwikPen (IND 127210). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 Jul 8. Panorama No.: 2019-28783141, 2019-28792853, 2019-28793655.

If you have any questions or need clarification, please contact Terrolyn Thomas, OSE project manager, at 240-402-3981.

3.1 COMMENTS TO ELI LILLY AND COMPANY (LILLY)

We have completed our review of the proposed proprietary names, (b) (4) KwikPen, and (b) (4) Junior KwikPen, and have concluded that these names are acceptable.

If any of the proposed product characteristics as stated in your submissions, received on September 25, 2019 and October 1, 2019, are altered prior to approval of the marketing application, the names must be resubmitted for review.

4 REFERENCE

1. **USAN Stems (https://www.ama-assn.org/about/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/

ARIANE O CONRAD
11/07/2019 10:17:40 AM

HINA S MEHTA
11/07/2019 10:29:54 AM

MISHALE P MISTRY
11/07/2019 11:55:57 AM