

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

212097Orig1s000

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:	November 7, 2018
Application Type and Number:	NDA 212097
Product Name and Strength:	Gvoke HypoPen and Gvoke PFS (glucagon injection) 0.5 mg/0.1 mL and 1 mg/0.2 mL
Total Product Strength:	0.5 mg/0.1 mL and 1 mg/0.2 mL
Product Type:	Combination Product (Drug-Device)
Rx or OTC:	Rx
Applicant/Sponsor Name:	Xeris Pharmaceuticals, Inc.
Panorama #:	2018-25165264 and 2018-26035460
DMEPA Safety Evaluator:	Stephanie DeGraw, PharmD
DMEPA Team Leader:	Hina Mehta, PharmD
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1 INTRODUCTION

This review evaluates the proposed proprietary names, Gvoke HypoPen and Gvoke PFS, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed names are outlined in the reference section and Appendix A respectively. Xeris Pharmaceuticals, Inc. did not submit an external name study for these proposed proprietary names.

1.1 REGULATORY HISTORY

The Applicant previously submitted the proposed proprietary name, (b) (4)***, on February 17, 2016. However, we found the name, (b) (4)***, unacceptable because it would overstate the (b) (4) of the drug under IND 115091 on April 11, 2016.^a

Subsequently, the Applicant submitted the proposed proprietary name, (b) (4)***, on September 26, 2016. We found the name, (b) (4)***, unacceptable due to orthographic and phonetic similarity, as well as overlapping product characteristics, with (b) (4), under IND 115091 on March 14, 2017.^b

The Applicant then submitted the proposed proprietary name, (b) (4) HypoPen***, for review on October 16, 2017. However, we found the name, (b) (4) HypoPen***, unacceptable due to orthographic similarity, as well as overlapping product characteristics, with (b) (4) under IND 115091 on April 12, 2018.^c

Thus, the Applicant submitted the names, Gvoke HypoPen and Gvoke PFS, for review on August 10, 2018 and September 10, 2018 respectively.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on August 10, 2018.

- Intended Pronunciation: G-VOKE Hypo-Pen (no intended pronunciation provided for Gvoke PFS)
- Active Ingredient: glucagon
- Indication of Use: treatment of severe hypoglycemia
- Route of Administration: subcutaneous injection into abdomen, outer thigh, or outer upper arm
- Dosage Form: injection
- Strength: 0.5 mg/0.1 mL and 1 mg/0.2 mL

^a Conrad, A. Proprietary Name Review for (b) (4)*** (IND 115091). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2016 APR 11. Panorama No. 2016-2820090.

^b Vee, S. Proprietary Name Review for (b) (4)*** (IND 115091). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 MAR 14. Panorama No. 2016-10386146.

^c Rimmel, S. Proprietary Name Review for (b) (4) HypoPen (IND 115091). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 APR 12. Panorama No. 2017-18306869.

- Dose and Frequency: administered as needed for severe hypoglycemia
 - o Pediatric patients <12 years that weigh <45 kg = 0.5 mg
 - o Adults and pediatric patients ≥12 years or <12 years that weigh ≥45 kg = 1 mg
- How Supplied: available as a ready-to-use, pre-filled, pre-measured, single-dose, disposable auto-injector or pre-filled syringe with a plunger rod and backstop containing either 0.5 mg or 1 mg of glucagon. Each is packaged in a foil pouch and supplied in the following pack configurations:
 - o Carton of 2 auto-injectors, each containing 1 mg/0.2 mL
 - o Carton of 2 pre-filled syringes, each containing 1 mg/0.2 mL
 - o Carton of 2 auto-injectors, each containing 0.5 mg/0.1 mL
 - o Carton of 2 pre-filled syringes, each containing 0.5 mg/0.1 mL
- Storage: controlled room temperature 20° to 25°C (68° to 77°F)

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that the proposed names would not misbrand the proposed product. 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 of the proposed names.

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 names^d.

2.2.2 *Components of the Proposed Proprietary Name*

The proprietary name consists of a root name, Gvoke, and a modifier HypoPen or PFS. Xeris Pharmaceuticals, Inc. indicated in their submission that the proposed name, Gvoke, is derived from “*Glucagon Hypoglycemia Auto-injector Pen.*” The Applicant indicated in their submission that the proposed modifier, HypoPen, “*describes a single-use, pre-filled injection device ready-to-use for severe hypoglycemia.*” The Applicant indicated in their submission that the proposed modifier, PFS, refers to the proposed prefilled syringe presentation. Therefore, we evaluated whether the proposed name requires the modifiers and the appropriateness of the proposed modifiers ‘HypoPen’ and ‘PFS’. Our evaluation is discussed in Section 2.2.8.

^d USAN stem search conducted on August 30, 2018 and September 21, 2018.

2.2.3 Comments from Other Review Disciplines at Initial Review

In response to the OSE, August 30, 2018 e-mail, the Division of Metabolism and Endocrinology Products (DMEP) did not forward any comments or concerns relating to the proposed proprietary name, Gvoke HypoPen at the initial phase of the review.

In response to the OSE, October 2, 2018 e-mail, the Division of Metabolism and Endocrinology Products (DMEP) did not forward any comments or concerns relating to the proposed proprietary name, Gvoke PFS at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Forty-eight practitioners participated in DMEPA's prescription studies for Gvoke HypoPen. Fifty-one practitioners participated in DMEPA's prescription studies for Gvoke PFS. One participant omitted the modifier 'PFS'. We discuss the omission of the modifier in Section 2.2.8. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline.

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

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search^e identified 15 names with a combined phonetic and orthographic score of $\geq 55\%$ or an individual phonetic or orthographic score $\geq 70\%$. These names are included in Table 1 below.

2.2.6 Names Retrieved for Review Organized by Name Pair Similarity

Table 1 lists the number of names retrieved from our POCA search. 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 $\geq 70\%$	3
Moderately similar name pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$	11
Low similarity name pair: combined match percentage score $\leq 54\%$	1

^e POCA search conducted on September 21, 2018 in version 4.3.

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

Our analysis of the 15 names contained in Table 1 determined none of the names will pose a risk for confusion as described in Appendices C through H.

2.2.8 Analysis of the Proposed Modifiers “PFS” and “HypoPen”

Proposed modifier ‘HypoPen’:

Xeris proposes to use the root name ‘Gvoke’ and the device-related modifier ‘HypoPen’ for the auto-injector presentation for the glucagon injection. We evaluated the use of the modifier ‘HypoPen’ in our previous review and do not find the modifier to be misleading or vulnerable to confusion, and therefore, acceptable for this product.^f We maintain our evaluation of the modifier ‘HypoPen’ for this product.

Proposed Modifier ‘PFS’:

Xeris proposes to use the root name ‘Gvoke’ and the device-related modifier ‘PFS’ for the prefilled syringe presentation for the glucagon injection. We considered the following (addressed respectively below): 1) use of a modifier to adequately distinguish the products and 2) whether the use of the modifier ‘PFS’ is appropriate.

- 1. Whether use of a modifier is sufficient to adequately distinguish the products:** 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, the modifier ‘PFS’ proposes to distinguish the prefilled syringe presentation from the autoinjector presentation). We considered the risk of name confusion if the modifier is omitted. We note that omission and oversight of modifiers is cited in literature as a common cause of medication error.^g Although modifiers may be omitted, they can assist in differentiating products and may help to prevent potential selection errors when used. As with any product that is available in multiple packaging presentations, the prescriber would need to indicate the intended product on the prescription. If the modifier ‘PFS’ is omitted (as seen in the FDA Name Simulation Study), the pharmacist should call the prescriber to seek clarification to determine which presentation the prescriber intended. However, since the 0.5 mg/0.1 mL and 1 mg/0.2 mL strengths are available in both the prefilled syringe and autoinjector presentations, the patient would receive the correct active ingredient and dose even if the modifier is omitted and the unintended presentation is dispensed. Thus, we do not object to the use of a modifier to distinguish the product presentations, in this case.
- 2. Safety Assessment of the Modifier PFS:** As stated in the Xeris submission, the proposed modifier, PFS, refers to the prefilled syringe presentation. We note that the modifier ‘PFS’ has been used previously for marketed products (e.g., Idamycin PFS and Vincasar PFS), but has not been used to indicate the prefilled syringe device presentation that a drug product is

^f Rimmel, S. Proprietary Name Review for (b) (4) HypoPen (IND 115091). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 APR 12. Panorama No. 2017-18306869.

^g Lesar TS. Prescribing Errors Involving Medication Dosage Forms. J Gen Intern Med. 2002; 17(8): 579-587.

contained in. The examples given of 'PFS' as a modifier indicate that the product is a preservative-free solution. Therefore, we considered whether the modifier for this product may be misinterpreted as 'preservative-free'. However, based on email confirmation from Office of Pharmaceutical Quality, we note that the proposed solution is a preservative-free, sterile solution, and therefore, we did not identify plausible risk associated with the misinterpretation of the proposed modifier 'PFS.'

In summary, we determined that the use of the proposed modifier, 'PFS', may assist in differentiating the prefilled syringe presentation from the autoinjector presentation. Therefore, based on the totality of the information considered above, we find the use of the proposed modifier 'PFS' acceptable for this product.

2.2.9 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Metabolism and Endocrinology Products (DMEP) via e-mail on November 2, 2018. At that time, we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DMEP on November 6, 2018, they stated no additional concerns with the proposed proprietary names, Gvoke Hypopen and Gvoke PFS.

3 CONCLUSION

The proposed proprietary names, Gvoke HypoPen and Gvoke PFS are acceptable.

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

3.1 COMMENTS TO THE APPLICANT/SPONSOR

We have completed our review of the proposed proprietary names, Gvoke HypoPen and Gvoke PFS, and have concluded that these names are acceptable.

If any of the proposed product characteristics as stated in your submission, received on August 10, 2018 and September 10, 2018, are altered prior to approval of the marketing application, the names must be resubmitted for review.

4 REFERENCES

1. **USAN Stems** (<http://www.ama-assn.org/ama/pub/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/approved-stems.page>)

USAN Stems List contains all the recognized USAN stems.

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

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

Drugs@FDA

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

RxNorm

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

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

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

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

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

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment 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 $\geq 70\%$.
 - Moderately similar pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$.
 - Low similarity: combined match percentage score $\leq 54\%$.

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

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 3).
- Moderately similar names are further evaluated to identify the presence of attributes that are known to cause name confusion.
 - Name attributes: We note that the beginning of the drug name plays a significant role in contributing to confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are major contributing factor in the confusion of drug namesⁱ. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.
 - Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).
- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

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

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

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

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

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

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

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

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

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

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

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

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

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 <u>with</u> 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?
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Table 5: Low Similarity Name Pair Checklist (i.e., combined score is $\leq 54\%$).

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

Appendix B: Prescription Simulation Samples and Results

Figure 1. Gvoke HypoPen Study (Conducted on 09/21/2018)

Handwritten Medication Order/Prescription	Verbal Prescription
<u>Medication Order:</u> <i>Gvoke Hypopen 0.5mg SubQ prn for severe hypoglycemia</i>	Gvoke Hypopen 1 mg Inject subcutaneously as needed for very low blood sugar Dispense 2 pack
<u>Outpatient Prescription:</u> <i>Gvoke Hypopen 1mg Inject subcutaneously prn for very low blood sugar 2 pack</i>	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

306 People Received Study
48 People Responded

Study Name: Gvoke Hypopen

Total	19	11	18	
INTERPRETATION	OUTPATIENT	VOICE	INPATIENT	TOTAL
GEBOLK HYPOPEN	0	1	0	1
GEEVOK PIPOPEN 1MG	0	1	0	1
GEEVOKE HYPOPEN	0	1	0	1
GEOAK HYPO PEN	0	1	0	1
GEOKE HYPOPEN	0	1	0	1
GEVOCK HYPO PEN	0	1	0	1
GEVOK HYPOPEN	0	2	0	2
GIVOK HYPOPEN	0	1	0	1
GIVOQ HYPOPEN	0	1	0	1
GROKE HYPOPEN	2	0	0	2
GVOKE HYPOPEN	16	1	17	51
GVOKE HYPOPEN SUBQ	0	0	1	1
YVOKE HYPOPEN	1	0	0	1

Figure 1. Gvoke PFS Study (Conducted on 10/15/2018)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order: <i>Gvoke PFS 1mg sub 2 prn</i>	Gvoke PFS 0.5 mg Inject subcutaneously as needed for severe hypoglycemia Dispense 1 carton
Outpatient Prescription: <i>Gvoke PFS 0.5mg</i> <i>Inject subcutaneously</i> <i>as needed for severe hypoglycemia</i> <i>#1 carton</i>	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

306 People Received Study
51 People Responded

Study Name: Gvoke PFS

Total	22	12	17	51
INTERPRETATION	OUTPATIENT	VOICE	INPATIENT	TOTAL
GEEVOC PSS	0	1	0	1
GEVOK PFS	0	1	0	1
GEVOK PPS	0	1	0	1
GEVOK PSS	0	1	0	1
GEVOK TSS	0	1	0	1
GEVOKE PFF	0	1	0	1
GEVOKE PSS	0	2	0	2
GEVOKE TSS	0	1	0	1
GIVOK GSS 0.5 MG	0	1	0	1
GIVOKE PFS	0	1	0	1
GRABE PFS	1	0	0	1
GRAKE PFS	1	0	0	1
GROKE PFS	1	0	0	1
GUAKE PFS	2	0	0	2
GVABE PFS	1	0	0	1

GVAKE PFS	9	0	0	9
GVOBE PFS	1	0	0	1
GVOKE PFS	4	0	16	39
GVOKE PFS SUBLINGUAL	0	0	1	1
IVAKE PFS	1	0	0	1
JEEVOKE TSS	0	1	0	1
YVOKE	1	0	0	1

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

No.	Proposed name: Gvoke Hypopen, Gvoke PFS Established name: glucagon Dosage form: solution Strength(s): 0.5 mg/0.1 mL and 1 mg/0.2 mL Usual Dose: 0.5 mg or 1 mg as needed	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.	Gvoke***	100	Root name subject of this review
2.	Gvoke Hypopen***	100	Subject of this review
3.	Gvoke PFS***	100	Subject of this review

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

No.	Name	POCA Score (%)
4.	D-Vert	56
5.	Gleevec	56
6.	Go-Evac	60
7.	Gonak	58
8.	Folex pfs	57

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

No.	Proposed name: Gvoke Hypopen, Gvoke PFS Established name: glucagon Dosage form: solution Strength(s): 0.5 mg/0.1 mL and 1 mg/0.2 mL Usual Dose: 0.5 mg or 1 mg as needed	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
9.	Hypopen***	60	Subject of this review as modifier for the device component.

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

No.	Name	POCA Score (%)
10.	Evekeo	46

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
11.	(b) (4) Hypopen***	64	Name denied for same proposed product under review (IND 115091) on April 12, 2018.
12.	G-Vent	62	Name identified in RxNorm database. Discontinued phenylpropanolamine (PPA) product for public health safety. No generic equivalents available.

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

No.	Name	POCA Score (%)
13.	Cosopt Pf	55
14.	Excof-Sf	56
15.	Ketoseb Ps	58

^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

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