

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

761083Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME MEMORANDUM

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

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

Date of This Review:	November 1, 2017
Application Type and Number:	BLA 761083
Product Name and Strength:	Hemlibra (emicizumab) Injection 30 mg/mL, 105 mg/0.7 mL, 60 mg/0.4 mL, and 150 mg/mL
Total Product Strength:	30 mg/mL and 150 mg/mL
Product Type:	Single Ingredient Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Genentech, Inc.
Panorama #:	2017-18296191
DMEPA Safety Evaluator:	Casmir Ogbonna, PharmD, MBA, BCPS, BCGP
DMEPA Team Leader:	Hina Mehta, PharmD

1 INTRODUCTION

This memorandum is to reassess the proposed proprietary name, Hemlibra, which was found conditionally acceptable under IND 122954 on August 17, 2016.^a Subsequently, under BLA 761083, the proposed proprietary name, Hemlibra, was found to be vulnerable to medication errors due to confusion with another product, (b) (4)*** (IND (b) (4) under review at the time, and was found unacceptable on August 17, 2017.^b Therefore, the ultimate acceptability of the proposed proprietary name, Hemlibra, was dependent upon which underlying application was approved first.

We note that the goal date for BLA 761083 is February 8, 2018 with a tentative early action date of November 15, 2017, whereas the underlying application for (b) (4)*** remains in IND status. Therefore, if the proposed proprietary name, Hemlibra, is granted approval under BLA 761083 on or before February 8, 2018, this application approval will precede approval of the application with the conflicting proposed name, (b) (4)***. Thus, the applicant resubmitted the proposed proprietary name, Hemlibra, on October 13, 2017 for review.

2 METHODS AND DISCUSSION

2.1 SAFETY ASSESSMENT

For re-assessment of the proposed proprietary name, DMEPA 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, DMEPA searched the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. The October 19, 2017, search of USAN stems did not find any USAN stems in the proposed proprietary name.

Finally, DMEPA evaluated the status of the underlying application of the conflicting name, (b) (4)***. We determined the underlying application for (b) (4)*** remains in IND status. Therefore, if the proposed proprietary name, Hemlibra, is granted approval under BLA 761083 on or before the November 15, 2017 early action goal date or before the February 8, 2018 goal date for the application, this application approval will precede approval of the application with the conflicting proposed name, (b) (4)***.

Based upon our safety assessment of the proposed proprietary name, Hemlibra, the application goal date for BLA 761083, and the status of the underlying application for (b) (4)***, we find Hemlibra conditionally acceptable.

^a Rahimi, L. Proprietary Name Review for Hemlibra IND 122954. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2016 August 17. RCM No.: 2016-8402343.

^b Ogbonna, C. Proprietary Name Review for Hemlibra BLA 761083. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 August 16. RCM No.: 2017-16037244.

2.2 COMMUNICATION OF DMEPA'S ANALYSIS AT MIDPOINT OF REVIEW

DMEPA communicated our findings to the Division of Hematology Products (DHP) via e-mail on October 24, 2017. At that time, we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DHP on October 30, 2017, they stated no additional concerns with the proposed proprietary name, Hemlibra.

3 CONCLUSIONS

We conclude that the proposed proprietary name, Hemlibra, is acceptable.

If you have any questions or need clarifications, please contact Wana Manitsitkul, OSE project manager, at 240-402-4156.

3.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your October 13, 2017, submission are altered prior to approval of the marketing application, the name must be resubmitted for review.

If your application receives a complete response, please submit a new request for review of your proposed proprietary name when you respond to the application deficiencies.

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.

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/s/

CASMIR I OGBONNA
11/01/2017

HINA S MEHTA
11/01/2017

MEMORANDUM
NONPROPRIETARY NAME SUFFIX

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)

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Date of This Review:	September 19, 2017
Requesting Office or Division:	Division of Hematology Products (DHP)
Application Type and Number:	BLA 761083
Product Name and Strength:	Hemlibra (emicizumab-kxwh) Injection 30 mg/mL, 105 mg/0.7 mL, 60 mg/0.4 mL, and 150 mg/mL
Total Product Strength:	150 mg/mL, and 30 mg/mL
Product Type:	Single ingredient product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Genentech, Inc.
Panorama #:	2017-1521
DMEPA Primary Reviewer:	Casmir Ogbonna, PharmD, MBA, BCPS, BCGP
OMEPRM Deputy Director (Acting):	Lubna Merchant, MS, PharmD

1 PURPOSE OF MEMO

This memorandum summarizes our evaluation of the four-letter suffix for inclusion in the nonproprietary name and communicates our recommendation for the nonproprietary name for BLA 761083.

2 ASSESSMENT OF THE NONPROPRIETARY NAME

Genentech, Inc. was notified of the Agency's intention to designate a proper name that includes a four-letter distinguishing suffix that is devoid of meaning for its product in an advice letter^a.

1. emicizumab-kxwh

FDA generated a four letter suffix, -kxwh. This suffix was evaluated against the criteria described in the guidance^b.

We determined that the FDA-generated suffix "-kxwh", is not too similar to any other product's suffix designation, does not look similar to the names of other currently marketed products, that the suffix is devoid of meaning, and does not make any misrepresentations with respect to safety or efficacy of this product.

These findings were shared with the TBBS, ORP, OCC and OPDP. In email correspondence dated September 14, 2017 the workgroup concurred with DMEPA's assessment and conclusion.

3 CONCLUSION

We find the suffix "-kxwh" acceptable and recommend the nonproprietary name be revised throughout the draft labels and labeling to emicizumab-kxwh.

3.1 RECOMMENDATIONS FOR GENENTECH, INC.

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

^a Merchant, L. Advice letter for BLA 761083. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 AUG 1.

^b 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>

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/s/

CASMIR I OGBONNA
09/19/2017

LUBNA A MERCHANT
09/19/2017

PROPRIETARY NAME REVIEW

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

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Date of This Review:	August 17, 2017
Application Type and Number:	BLA 761083
Product Name and Strength:	Hemlibra (emicizumab) Injection 30 mg/mL, 105 mg/0.7 mL, 60 mg/0.4 mL, and 150 mg/mL
Total Product Strength:	30 mg/mL and 150 mg/mL
Product Type:	Single Ingredient Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Genentech, Inc.
Panorama #:	2017-16037244
DMEPA Primary Reviewer:	Casmir Ogbonna, PharmD, MBA, BCPS, BCGP
DMEPA Team Leader:	Hina Mehta, PharmD
DMEPA Associate Director (Acting):	Mishale Mistry, PharmD, MPH
DMEPA Director:	Todd Bridges, Rph

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Hemlibra (emicizumab), from a safety and misbranding perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively. The Applicant submitted an external name study by Drug Safety Institute, Inc. (DSI) that was already reviewed under IND 122954, OSE RCM # 2016-8402343^a.

1.1 REGULATORY HISTORY

The Applicant previously submitted the proposed proprietary name, Hemlibra on June 6, 2016, under IND 122954. The Division of Medication Error Prevention and Analysis (DMEPA) found the name Hemlibra conditionally acceptable in OSE Review #2016-8402343, dated August 17, 2016.^a Thus, the Applicant re-submitted the name, Hemlibra, for review on June 28, 2017 under BLA 761083.

1.2 PRODUCT INFORMATION

The following product information is provided in the June 28, 2017, proprietary name submission.

- Intended Pronunciation: hem-lē-brā
- Active Ingredient: emicizumab
- Indication of Use: For routine prophylaxis to prevent bleeding or reduce the frequency of bleeding episodes in patients with hemophilia A (congenital factor VIII deficiency) with factor VIII inhibitors.
- Route of Administration: subcutaneous
- Dosage Form: injection
- Strength: 30 mg/mL, 105 mg/0.7 mL, 60 mg/0.4 mL, and 150 mg/mL
- Dose and Frequency: 3 mg/kg by subcutaneous injection once weekly for the first 4 weeks, followed by 1.5 mg/kg once weekly.
- How Supplied: as a sterile, colorless to pale yellow liquid for SC injection in single-dose 3-mL glass vials. The nominal fill volumes for each product strength include: 1.0 mL (150 mg or 30 mg), 0.7 mL (105 mg), and 0.4 mL (60 mg). Each strength will be secondary packed as 1 vial/pack.
- Storage: Store vials in a refrigerator between 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. Do not freeze. Do not shake. Prior to administration, unopened vials (b) (4)

^a Rahimi, L. Proprietary Name Review for Hemlibra IND 122954. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2016 August 17. RCM No.: 2016-8402343.

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that the proposed name would not misbrand the proposed product. DMEPA and the Division of Hematologic Products (DHP) concurred with the findings of OPDP's assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

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

2.2.2 Components of the Proposed Proprietary Name

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

2.2.3 Comments from Other Review Disciplines at Initial Review

In response to the OSE, July 12, 2017 e-mail, the Division of Hematology Products (DHP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Sixty-nine (n=69) practitioners participated in DMEPA's prescription studies. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline. Appendix B contains the results from the verbal and written prescription studies.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA^b search identified 36 names with the combined score of $\geq 55\%$ or individual orthographic or phonetic score of $\geq 70\%$. We had identified and evaluated 57 names in our

^b POCA search conducted on July 26, 2017 in version 4.0

previous proprietary name review.^c We re-evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the name. We note that none of the product characteristics have changed and we agree with the findings from our previous review for the names evaluated previously.^d Table 1 also lists one name from our previous proprietary name review with a combined score of $\geq 70\%$ as a result of the update in POCA. Therefore, we identified 10 names not previously analyzed. These names are included in Table 1 below.

2.2.6 Names Retrieved for Review Organized by Name Pair Similarity

Table 1 lists the number of names retrieved from our POCA search. 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 $\geq 70\%$	1
Moderately similar name pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$	9
Low similarity name pair: combined match percentage score $\leq 54\%$	0

^c Rahimi, L. Proprietary Name Review for Hemlibra IND 122954. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2016 August 17. RCM No.: 2016-8402343.

^d Rahimi, L. Proprietary Name Review for Hemlibra IND 122954. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2016 August 17. RCM No.: 2016-8402343.

2.2.8 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Hematology Products (DHP) via e-mail on August 14, 2017. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DHP on August 14, 2017, they stated no additional concerns with the proposed proprietary name, Hemlibra.

3 CONCLUSIONS

The proposed proprietary name is not acceptable from a safety perspective. The proposed name is vulnerable to name confusion with (b) (4)***. Therefore, the decision to deny the name will be communicated to the Applicant/Sponsor via letter (See Section 3.1).

If you have further questions or need clarifications, please contact Wana Manitpisitkul, OSE project manager, at 240-402-4156

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Hemlibra, and have concluded that this name is unacceptable for the following reasons:

The proposed proprietary name, Hemlibra, could result in medication errors due to confusion with another product that is also under review. Therefore, the ultimate acceptability of your proposed proprietary name, Hemlibra, is dependent upon which underlying application is approved first. If another product is approved prior to your product with a name that would be confused with your proposed name of Hemlibra, you will be requested to submit another name.

REFERENCES

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

USAN Stems List contains all the recognized USAN stems.

2. Phonetic and Orthographic Computer Analysis (POCA)

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

Drugs@FDA

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

RxNorm

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

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

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

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

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

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

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

APPENDICES

Appendix A

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

1. **Misbranding Assessment:** For prescription drug products, OPDP assesses the name for misbranding concerns. . For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNDP. OPDP or DNDP evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment:** The safety assessment is conducted by DMEPA, and includes the following:
 - a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.^f

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

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

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
Y/N	Is the proposed name obviously similar in spelling and pronunciation to other names?
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	Are there inert or inactive ingredients referenced in the proprietary name?
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
Y/N	Does the proprietary name include combinations of active ingredients?
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
Y/N	Is there a United States Adopted Name (USAN) stem in the proprietary name?
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
Y/N	Is this proprietary name used for another product that does not share at least one common active ingredient?
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	Is this a proprietary name of a discontinued product?
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

- b. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@fda, CernerRxNorm, and names in the review pipeline using a 55% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:
- Highly similar pair: combined match percentage score $\geq 70\%$.
 - Moderately similar pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$.
 - Low similarity: combined match percentage score $\leq 54\%$.

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

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

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

route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).

- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.
- c. FDA Prescription Simulation Studies: DMEPA staff also conducts a prescription simulation studies using FDA health care professionals.

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

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

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

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

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

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

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

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

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

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

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

Step 1	<p>Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation.</p> <p>For single strength products, also consider circumstances where the strength may not be expressed.</p> <p>For any i.e. drug products comprised of more than one active ingredient, consider whether the strength or dose may be expressed using only one of the components.</p> <p>To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion:</p> <ul style="list-style-type: none"> • Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa. • Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. • Similar sounding doses: 15 mg is similar in sound to 50 mg
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Step 2	Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names with overlapping or similar strengths or doses.	
	<p>Orthographic Checklist (Y/N to each question)</p> <ul style="list-style-type: none"> • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length of names different if the names differ by two or more letters. • Considering variations in scripting of some letters (such as <i>z</i> and <i>f</i>), is there a different number or placement of upstroke/downstroke letters present in the names? • Is there different number or placement of cross-stroke or dotted letters present in the names? • Do the infixes of the name appear dissimilar when scripted? • Do the suffixes of the names appear dissimilar when scripted? 	<p>Phonetic Checklist (Y/N to each question)</p> <ul style="list-style-type: none"> • Do the names have different number of syllables? • Do the names have different syllabic stresses? • Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?

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

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

Appendix B: Prescription Simulation Samples and Results

Figure 1. Hemlibra Study (Conducted on July 14, 2017)

Handwritten Medication Order/Prescription	Verbal Prescription
<p>Medication Order:</p> <p><i>Hemlibra inject 3 mg/Kg</i></p>	<p>Hemlibra 150 mg/mL</p> <p>Inject 225 mg subcutaneously once a week for 4 weeks.</p> <p>Disp. # 6 vials.</p>
<p>Outpatient Prescription:</p> <p><i>Hemlibra Bring to clinic #1 vial</i></p>	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

Study Name: Hemlibra

As of Date 8/4/2017

291 People Received Study

69 People Responded

Study Name: Hemlibra

Total	23	25	22	
INTERPRETATION	OUTPATIENT	VOICE	INPATIENT	TOTAL
EMLIBRA	0	1	0	1
EMLYBRA	0	1	0	1
HAMLIBRA	0	2	0	2
HEMLEBRA	0	1	0	1

HEMLEEBRA	0	1	0	1
HEMLIBRA	20	11	16	47
HEMLIBRA INJECT	0	0	1	1
HEMLIDYS	0	0	1	1
HEMLILYA	0	0	1	1
HEMLITYA	0	0	1	1
HEMLITYS	0	0	1	1
HEMLIYA	0	0	1	1
HEMLYBRA	0	1	0	1
HENLIBRA	0	1	0	1
HERNBIBRA	1	0	0	1
HERNLIBRA	1	0	0	1
TAMLIBRA	0	1	0	1
TEMLIBRA	0	5	0	5

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

No.	Name	POCA Score (%)
3.	Hibtiter	56
4.	(b) (4) ***	56
5.	Millipred	56
6.	(b) (4) ***	55

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

No.	Proposed name: Hemlibra Established name: emicizumab Dosage form: Subcutaneous Injection Strength(s): 30 mg/mL, 105 mg/0.7 mL, 60 mg/0.4 mL, and 150 mg/mL Usual Dose: 3 mg/kg weekly for 4 weeks as loading doses, followed by 1.5 mg/kg weekly as maintenance doses	POCA Score (%)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
7.	(b) (4) ***	64	(b) (4)

No.	Proposed name: Hemlibra Established name: emicizumab Dosage form: Subcutaneous Injection Strength(s): 30 mg/mL, 105 mg/0.7 mL, 60 mg/0.4 mL, and 150 mg/mL Usual Dose: 3 mg/kg weekly for 4 weeks as loading doses, followed by 1.5 mg/kg weekly as maintenance doses	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
8.	Minolira	56	<p>Orthographic: The prefixes ('Mi-' vs. 'Hem-'), and infixes ('-no-' vs. '-li-') of the name pair look different when scripted. Hemlibra has an additional upstroke letter 'b' in the suffix, which is absent in Minolira.</p> <p>Phonetic: This name has four syllables vs. three syllables in Hemlibra. Additionally, the name pair sounds different.</p> <p>Product Characteristics: Dosage form: Extended-release tablets vs. injection Route of administration: Oral vs. subcutaneous Strength: 105 mg and 135 mg vs. 30 mg/mL, 105 mg/0.7 mL, 60 mg/0.4 mL, and 150 mg/mL Dose/Frequency: 1 mg/kg daily up to 12 weeks vs. weight-based dosing of 3 mg/kg (xx mg) by subcutaneous injection once weekly for the first 4 weeks, followed by 1.5 mg/kg (xx mg) once weekly.</p>

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

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

No.	Name	POCA Score (%)	Failure preventions
9.	(b) (4)***	56	Proposed proprietary name found unacceptable by DMEPA (OSE # (b) (4)). An alternative proposed proprietary name has not been submitted for review.

Appendix H: Names not likely to be confused due to absence of attributes that are known to cause name confusion^h. – N/A

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

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

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/s/

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