CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761091Orig1s000

PROPRIETARY NAME REVIEW(S)

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)

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

Date of This Review:	September 20, 2018
Responsible OND Division:	Division of Oncology Products 1 (DOP1)
Application Type and Number:	BLA 761091
Product Name and Strength:	Herzuma (trastuzumab-pkrb) for Injection, 420 mg/vial
Product Type:	Single Ingredient Product
Applicant/Sponsor Name:	Celltrion, Inc.
FDA Received Date:	June 18, 2018
OSE RCM #:	2018-1311
DMEPA Primary Reviewer:	Tingting Gao, PharmD
DMEPA Deputy Director:	Danielle Harris, PharmD, BCPS

1 PURPOSE OF MEMO

This memorandum is to reassess the proposed suffix, (b) (4) for BLA 761091, which was found conditionally acceptable on July 19, 2017[a], for inclusion in the nonproprietary name and communicates our recommendation for the nonproprietary name for BLA 761091.

1.1 Regulatory History

Celltrion previously submitted a list of 10 suffixes, in their order for preference for BLA 761091. FDA found the proposed suffix, (b) (4) for BLA 761091, conditionally acceptable on July 19, 2017[a]. However, BLA 761091 received a Complete Response (CR) letter on March 30, 2018[b]. Thus, Celltrion submitted a Class 2 Resubmission on June 15, 2018.

On June 18, 2018, Celltrion submitted a list of 10 suffixes, in their order of preference, to be used in the nonproprietary name of their product[c]. Table 1 presents a list of suffixes submitted by Celltrion in their Class 2 Resubmission:

Table 1. Suffixes submitted by Celltrion***	
1.	(b) (4)
2.	
3.	
4.	pkrb
5.	(b) (4)
6.	
7.	
8.	
9.	
10.	

We reviewed Celltrion's proposed suffixes in order of preference listed by Celltrion, along with the supporting data[c] they submitted, using the principles described in the applicable guidance.[d] We note the first proposed suffix was previously evaluated and found conditionally acceptable during the previous review cycle.[a]

[a] Gao, T. Nonproprietary Name Suffix Memorandum for trastuzumab (b) (4) (BLA 761091). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 JUL 19. RCM No.: 2017-1057.

[b] Beaver, J. Complete Response (BLA 761091). Silver Spring (MD): FDA, CDER, OND, DOP1 (US); 2018 MAR 30.

[c] Nonproprietary Name Review Request and Supporting Analysis: Proposed Suffixes for Herzuma (BLA 761091). Yeonsu-gu, Incheon (Republic of Korea): Celltrion, Inc.; document dated 2017 May 12. Available from: \\cdsesub1\evsprod\bla761091\0042\m1\us\non-proprietary-names.pdf (received on 2018 Jun 18).

[d] 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 ASSESSMENT OF THE NONPROPRIETARY NAME

(b) (4)

2.4 trastuzumab-pkrb

Celltrion's fourth proposed suffix, -pkrb, is comprised of four distinct letters ("p", "k", "r" and "b").

We determined that the proposed suffix -pkrb, 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, TBBS, and ORP. In email correspondence dated September 7, 2018, the workgroup concurred with DMEPA's assessment and conclusion. DMEPA also communicated our findings to the Division of Oncology Products 1 (DOP1) via e-mail on September 20, 2018.

4 CONCLUSION

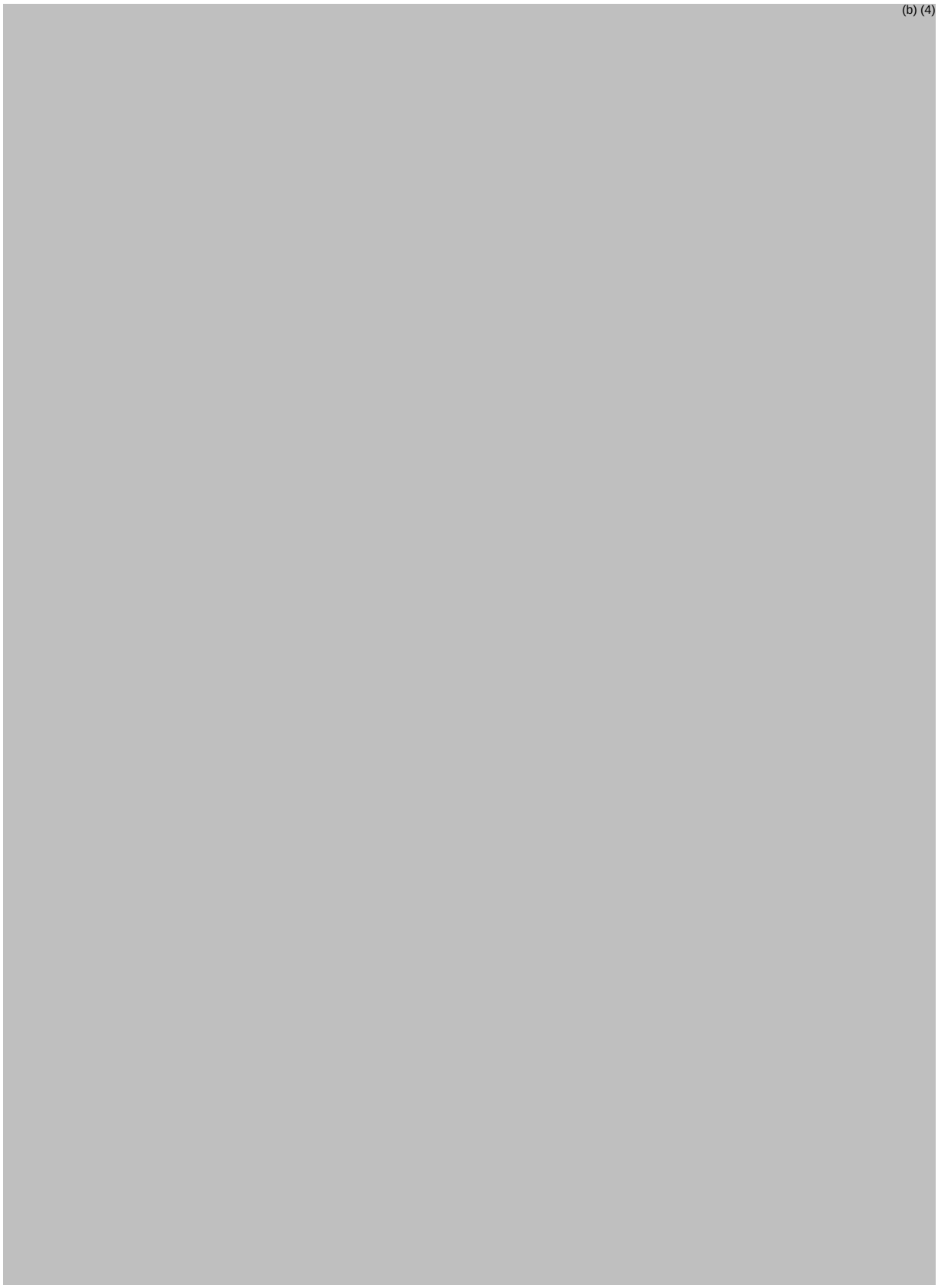
We find Celltrion's proposed suffix -pkrb acceptable and recommend the nonproprietary name be revised throughout the draft labels and labeling to trastuzumab-pkrb.

4.1 Recommendations for Celltrion

We find the nonproprietary name, trastuzumab-pkrb, conditionally acceptable for your proposed product. Should your 351(k) BLA be approved during this review cycle, trastuzumab-pkrb 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 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.

We also note that your first three proposed suffix candidates are unacceptable for the following reasons:

(b) (4)




(b) (4)

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/s/

TINGTING N GAO
09/20/2018

DANIELLE M HARRIS
09/21/2018

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:	August 24, 2018
Application Type and Number:	BLA 761091
Product Name and Strength:	Herzuma (trastuzumab-xxxx) for Injection, 420 mg/vial
Product Type:	Single Ingredient Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Celltrion, Inc.
Panorama #:	2018-23847264
DMEPA Safety Evaluator:	Tingting Gao, PharmD
DMEPA Team Leader:	Chi-Ming (Alice) Tu, PharmD

1 INTRODUCTION

This memorandum is to reassess the proposed proprietary name, Herzuma, which was found conditionally acceptable under BLA 761091 on August 14, 2017.[a]

We note that there is a (b) (4) 420 mg/vial for BLA 761091. All other product characteristics remain the same.

2 METHODS AND DISCUSSION

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 Oncology Products 1 (DOP1) concurred with the findings of OPDP's assessment of the proposed name.

2.2 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. We also evaluated previously identified names taking into account the (b) (4) 420 mg/vial.[b] Our evaluation has not 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 July 19, 2018 search of USAN stems did not find any USAN stems in the proposed proprietary name.

2.3 COMMUNICATION OF DMEPA'S ANALYSIS AT MIDPOINT OF REVIEW

DMEPA communicated our findings to the Division of Oncology Products 1 (DOP1) via e-mail on August 16, 2018. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DOP1 on August 24, 2018, they stated no additional concerns with the proposed proprietary name, Herzuma.

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[a] Gao, T. Proprietary Name Review for Herzuma (BLA 761091). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 AUG 14. Panorama No. 2017-15373147.

[b] (b) (4) BLA 761091 for the 420 mg/vial presentation. See Minie, L. FDA Communication: RE: BLA 761091: (b) (4) Silver Spring (MD): FDA, CDER, OND, OHOP, DOP1 (US); 2018 May 10. BLA 761091.

3 CONCLUSION

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

If you have any questions or need clarifications, please contact Frances Fahnbulleh, OSE project manager, at 301-796-0942.

3.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your submission, received on June 18, 2018, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

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

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/s/

TINGTING N GAO
08/24/2018

CHI-MING TU
08/24/2018

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:	February 14, 2018
Application Type and Number:	BLA 761091
Product Name and Strength:	Herzuma (trastuzumab-(b) (4)) for Injection, 420 mg/vial
Product Type:	Single ingredient product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Celltrion
Panorama #:	2017-15373147-1
DMEPA Safety Evaluator:	Tingting Gao, PharmD
DMEPA Team Leader:	Chi-Ming (Alice) Tu, PharmD

1 INTRODUCTION

This memorandum is to reassess the proposed proprietary name, Herzuma, based on (b) (4) the 420 mg/vial.[a] The proposed proprietary name, Herzuma, was found acceptable under BLA 761091 on August 14, 2017.[b]

2 METHODS AND DISCUSSION

2.1 SAFETY ASSESSMENT

For re-assessment of the proposed proprietary name, Herzuma, DMEPA evaluated the previously identified names (b) (4). Our evaluation has not 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 January 29, 2018 search of USAN stems did not find any USAN stems in the proposed proprietary name.

3 CONCLUSION

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

If you have any questions or need clarifications, please contact Frances Fahnbulleh, OSE project manager, at 301-796-0942.

[a] Minie, L. General Advice Letter (BLA 761091); 2018 Jan 25. This General Advice Letter checked into DARRTS are email communications between FDA and McNamara, L. of Celltrion for BLA 761091. (b) (4)

[b] Gao, T. Proprietary Name Review for Herzuma (BLA 761091). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 AUG 14. Panorama No. 2017-15373147.

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/

TINGTING N GAO
02/14/2018

CHI-MING TU
02/14/2018

PROPRIETARY NAME REVIEW

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

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

Date of This Review:	August 14, 2017
Application Type and Number:	BLA 761091
Product Name and Strength:	Herzuma (trastuzumab-xxxx) for Injection, (b) (4) 420 mg/vial
Product Type:	Single ingredient product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Celltrion
Panorama #:	2017-15373147
DMEPA Primary Reviewer:	Tingting Gao, PharmD
DMEPA Team Leader:	Chi-Ming (Alice) Tu, PharmD

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Herzuma, 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, conducted by (b) (4), for this product.

1.1 PRODUCT INFORMATION

The following product information is provided in the May 31, 2017 proprietary name submission.

- Intended Pronunciation: her zoo' mah
- Active Ingredient: Trastuzumab
- Indication of Use: Treatment of HER2 overexpressing breast cancer and the treatment of HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma
- Route of Administration: Intravenous
- Dosage Form: Lyophilized, sterile powder for injection
- Strength: (b) (4) 420 mg/vial
- Dose and Frequency:
    - Adjuvant Treatment of HER2-Overexpressing Breast Cancer:
        - (b) (4)
        -
    - Metastatic HER2-Overexpressing Breast Cancer:
        - (b) (4)
    - Metastatic HER2-Overexpressing Gastric Cancer:
        - (b) (4)
- How Supplied

  (b) (4)
    - 420 mg/vial: Each carton contains one multiple-dose vial of Herzuma and one vial (20 mL) of Bacteriostatic Water for Injection (BWFI), USP
- Storage: Refrigerated at 2−8°C

- Container and Closure Systems:

  [redacted] (b) (4)

  - 420 mg/vial: a clear, 50 mL [redacted] (b) (4) glass vial closed with a stopper which has a [redacted] (b) (4) 20 mm aluminum seal with a flip-off button.

- Reference Product: Herceptin (trastuzumab), BLA 103792

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 Oncology Products 1 (DOP1) 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[a].

2.2.2 Components of the Proposed Proprietary Name

The Applicant stated the derivation for the proposed name, Herzuma, is [redacted] (b) (4) 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, June 30, 2017 e-mail, the Division of Oncology Products 1 (DOP1) 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

Eighty 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.

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[a] USAN stem search conducted on July 13, 2017.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search[b] identified 18 names with a combined phonetic and orthographic score of ≥55% or an individual phonetic or orthographic score ≥70**.** These names are included in Table 1 below.

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

The proposed product, Herzuma will be available in (b) (4) 420 mg/vial strength (b) (4) Since this is not a typical strength that is commonly marketed, we searched the Electronic Drug Registration and Listing System (eDRLS) database to identify names with strength overlap. None of the names identified in the eDRLS database are likely to be confused due to notable spelling, orthographic and phonetic differences. The names identified in the eDRLS database not likely to be confused due to notable spelling, orthographic, and phonetic differences are listed in Appendix I.

2.2.7 Names Retrieved for Review Organized by Name Pair Similarity

Table 1 lists the number of names retrieved from our POCA search and the Drug Safety Institute external study. These name pairs are organized as highly similar, moderately similar or low similarity for further evaluation.

Table 1. Similarity Category	**Number of Names**
Highly similar name pair: combined match percentage score ≥70%	1
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	14
Low similarity name pair: combined match percentage score ≤54%	15

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

Our analysis of the 30 names contained in Table 1 determined 30 names will not pose a risk for confusion as described in Appendices C through H.

2.2.9 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Oncology Products 1 (DOP1) via e-mail on July 24, 2017. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DOP1 on August 14, 2017, they stated no additional concerns with the proposed proprietary name, Herzuma.

[b] POCA search conducted on July 13, 2017 in version 4.1.

3 CONCLUSIONS

The proposed proprietary name is acceptable.

If you have any questions or need clarifications, please contact Frances Fahnbulleh, OSE project manager, at 301-796-0942.

3.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your May 31, 2017 submission are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

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

   USAN Stems List contains all the recognized USAN stems.

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

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

Drugs@FDA

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

RxNorm

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

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

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

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

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

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

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

APPENDICES

Appendix A

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

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

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

[c] 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[d]. 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.,

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

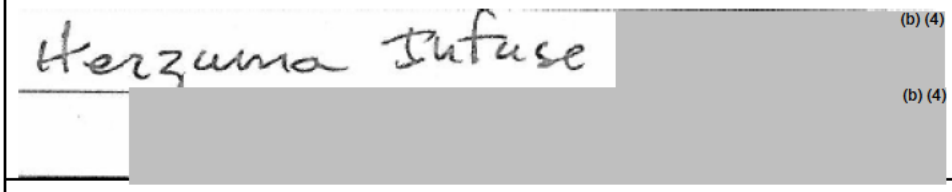
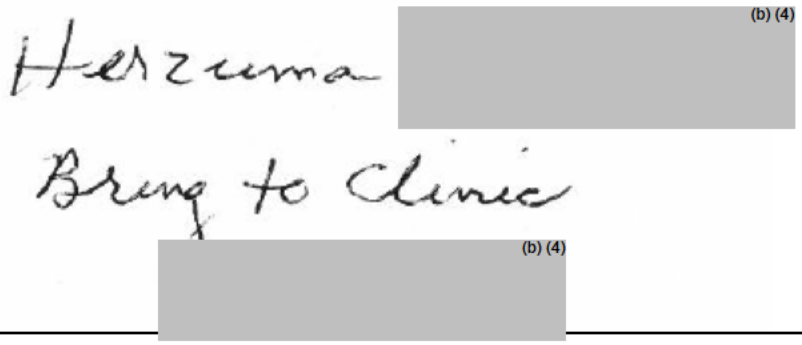
Step 2	Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names **with** overlapping or similar strengths or doses.	
	Orthographic 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. Herzuma Study (Conducted on June 23, 2017)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order:  	Herzuma (b) (4) (b) (4) Bring to clinic (b) (4)
Outpatient Prescription:  	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

Study Name: Herzuma

291 People Received Study

80 People Responded

Total	**31**	**25**	**24**	
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
HERZCEMA	1	0	0	1
HERZUINA	0	0	2	2
HERZUMA	30	16	20	66
HERZUMA VIAL	0	1	0	1
HERZURNA	0	0	2	2
PERSUMA	0	1	0	1
PERZUMA	0	7	0	7

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

No.	**Proposed name:** Herzuma **Established name:** trastuzumab-xxxx **Dosage form:** For injection **Strength(s):** (b) (4) 420 mg/vial **Usual Dose:** 2mg/kg to 8 mg/kg intravenous infusion (frequency varies depending on the indication)	**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.	Herzuma	100	Name 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 (%)
2.	Verluma	68

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

No.	**Proposed name:** Herzuma **Established name:** trastuzumab-xxxx **Dosage form:** For injection **Strength(s):** (b) (4) 420 mg/vial **Usual Dose:** 2 mg/kg to 8 mg/kg intravenous infusion (frequency varies depending on the indication)	**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**
3.	(b) (4) ***	55	This name pair has sufficient orthographic and phonetic differences.
4.	Harvoni	61	This name pair has sufficient orthographic and phonetic differences.
5.	Herbon	67	This name pair has sufficient orthographic and phonetic differences.
6.	Pertuzumab	58	This name pair has sufficient orthographic and phonetic differences.

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

No.	Name	POCA Score (%)
7.	Alrheumat	54
8.	Arzerra	50
9.	Cyramza	50
10.	Hepsera	48
11.	Herceptin	46
12.	Herplex	42
13.	Hizentra	54
14.	Humira	48
15.	Humulin	38
16.	Kanuma	48
17.	Rheumate	52
18.	Rheumatrex	40
19.	Thermazene	51
20.	Valturna	37
21.	Zovirax	20

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
22.	Helium	57	Not a drug, a gas.
23.	Herpid	56	International product marketed in United Kingdom.
24.	Hetrazan	64	NDA 006459 Withdrawn FR Effective 12/07/2007 and there are no generics available.

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

No.	Name	POCA Score (%)
25.	Cerezyme	60
26.	Cerium	55
27.	Erbium	55
28.	Ergomar	60
29.	Fetzima	56
30.	Tarsum	56

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

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

No.	Name
1.	Cardizem LA
2.	Cherry Antacid
3.	Green Guard Stomach Relief
4.	Jock Itch
5.	Magnacal
6.	Medi First Antacid
7.	Medi First Plus Antacid
8.	Medi-First Antacid
9.	Medi-First Plus Antacid
10.	Medique Alcalak
11.	Medique Alcalak
12.	Mint Antacid
13.	Miralac
14.	Miralac Antiacid
15.	Moore Medical Antacid
16.	Nutralox
17.	Polaris Mint Antacid
18.	Razzmatazz Antacid
19.	Titralac
20.	Trial Antacid

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/s/

TINGTING N GAO
08/14/2017

CHI-MING TU
08/14/2017

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)

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

Date of This Review:	July 19, 2017
Requesting Office or Division:	Division of Oncology Products 1 (DOP1)
Application Type and Number:	BLA 761091
Product Name and Strength:	Herzuma (trastuzumab-(b) (4)) for Injection, (b) (4) 420 mg/vial
Product Type:	Single ingredient product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Celltrion
Panorama #:	2017-1057
DMEPA Primary Reviewer:	Tingting Gao, PharmD
OMEPRM Deputy Director (Acting):	Lubna Merchant, MS, PharmD

Reference ID: 4368375

1 PURPOSE OF MEMO

This memorandum summarizes our evaluation of the suffixes proposed by Celltrion for the nonproprietary name and communicates our recommendation for the nonproprietary name.

2 ASSESSMENT OF THE NONPROPRIETARY NAME

FDA has determined that the use of a distinguishing suffix in the nonproprietary name for Celltrion's Herzuma product is necessary to distinguish this proposed product from Herceptin (trastuzumab). As explained in FDA's Guidance for Industry, Nonproprietary Naming of Biological Products, FDA expects that a nonproprietary name for Herzuma include a distinguishing suffix that will facilitate safe use and optimal pharmacovigilance. We reviewed Celltrion's proposed suffixes against the criteria described in the guidance.

On May 30, 2017, Celltrion submitted a list of suffixes, in their order of preference, to be used in the nonproprietary name of their product. We note that the Applicant submitted ten suffixes. We conducted our review in the order of the preference listed by the Applicant.

2.1 TRASTUZUMAB-ABTR

Celltrion's first proposed suffix, (b) (4), is composed of the letters (b) (4). Celltrion stated that it is derived from (b) (4). Although we note that the suffix includes the (b) (4), we find that the composition (b) (4) in and of itself does not readily connote either the proper name or that this product is a biosimilar.

We determined that Celltrion suffix (b) (4) 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, 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 June 30, 2017, the workgroup concurred with DMEPA's assessment and conclusion.

3 CONCLUSIONS

We find that Celltrion proposed suffix (b) (4) acceptable and recommend the nonproprietary name be revised throughout the draft labels and labeling to trastuzumab-(b) (4)

3.1 RECOMMENDATIONS FOR CELLTRION

1. We find the nonproprietary name, trastuzumab-(b) (4) conditionally acceptable for your proposed product. Should your 351(k) BLA be approved during this review cycle, trastuzumab-(b) (4) 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 your proposed suffix will be re-evaluated when you respond to the deficiencies. If we find your proposal unacceptable upon our re-evaluation, we would inform you of our finding.

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/s/

TINGTING N GAO
07/19/2017

LUBNA A MERCHANT
07/19/2017

Reference ID: 4368375