CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761106Orig1s000

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:	December 3, 2018
Application Type and Number:	BLA 761106
Product Name and Strength:	Herceptin Hylecta (trastuzumab and hyaluronidase human-xxxx)[a] Injection, 120 mg and 2,000 units/mL
Total Product Strength:	600 mg and 10,000 units/5 mL
Product Type:	Multiple Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Genentech, Inc. (Genentech)
Panorama #:	2018-25980339
DMEPA Safety Evaluator:	Tingting Gao, PharmD
DMEPA Team Leader (Acting):	Sevan Kolejian, PharmD, MBA
DMEPA Deputy Director:	Danielle Harris, PharmD, BCPS

[a] The proposed nonproprietary name has not yet been conditionally accepted. We therefore refer to the proposed product as "trastuzumab and hyaluronidase human-xxxx" throughout this review in place of the nonproprietary name for this product.

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Herceptin Hylecta, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed proprietary name are outlined in the reference section and Appendix A respectively. Genentech submitted an external name study, conducted by (b) (4), for this proposed proprietary name.

1.1 REGULATORY HISTORY

Genentech previously submitted the proposed proprietary name, (b) (4) on May 1, 2018 under BLA 761106. However, we found the name, (b) (4) unacceptable because the proposed name, (b) (4) (b) (4) (b) (4) Therefore, the proposed proprietary name, (b) (4), is misleading pursuant to 21 CFR 201.6(b).[b]

Thus, Genentech submitted the name, Herceptin Hylecta, for review on September 17, 2018.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on September 17, 2018.

- Intended Pronunciation: her sep' tin hye lek' tah
- Active Ingredient: trastuzumab and hyaluronidase human-xxxx
- Indication of Use:
    - Adjuvant Breast Cancer: indicated for adjuvant treatment of HER2 overexpressing node positive or node negative (ER/PR negative or with one high risk feature breast cancer
        - as part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel
        - as part of a treatment regimen with docetaxel and carboplatin
        - as a single agent following multi modality anthracycline based therapy.
    - Metastatic Breast Cancer: indicated
        - In combination with paclitaxel for first line treatment of HER2 overexpressing metastatic breast cancer
        - As a single agent for treatment of HER2 overexpressing breast cancer in patients who have received one or more chemotherapy regimens for metastatic disease.
- Route of Administration: Subcutaneous

[b] Gao, T. Proprietary Name Review for (b) (4) (BLA 761106). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 JUL 26. Panorama No. 2018-22736159.

- Dosage Form: Injection
- Strength: 120 mg and 2,000 units/mL (600 mg and 10,000 units/5 mL)
- Dose and Frequency: 600 mg/10,000 units every 3 weeks
- How Supplied: Each carton contains 1 single-dose vial.
- Storage: Store vials at 2-8°C. Do not freeze. Store in the original package in order to protect from light.

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Herceptin Hylecta would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Oncology Products 1 (DOP1) concurred with the findings of OPDP's assessment for Herceptin Hylecta.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proposed proprietary name[c].

2.2.2 Components of the Proposed Proprietary Name

Genentech indicated in their submission that the proposed proprietary name, Herceptin Hylecta, is derived from "Herceptin", which is an FDA approved name; and the modifier "Hylecta" is intended to link to hyaluronidase. This proprietary name is comprised of multiple words that contain the root name "Herceptin" and modifier "Hylecta". The use of the rootname "Herceptin" and modifier "Hylecta" is evaluated in Section 2.2.6.

2.2.3 Comments from Other Review Disciplines at Initial Review

In response to the OSE, October 3, 2018 e-mail, the Division of Oncology Products 1 (DOP1) did not forward any comments or concerns relating to Herceptin Hylecta at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Forty-six practitioners participated in DMEPA's prescription studies for Herceptin Hylecta. One participant in the outpatient prescription study and one participant in the verbal prescription study omitted the modifier "Hylecta" in their responses "Herceptin". We discuss the omission of

[c] USAN stem search conducted on October 10, 2018.

the modifier in Section 2.2.6. The remaining 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 Medication Error Data Selection of Cases

We searched the FDA Adverse Event Reporting System (FAERS) database using the strategy listed in Table 2 (see Appendix A1 for a description of FAERS database) for name confusion errors involving Herceptin that would be relevant for this review.

Table 2. FAERS Search Strategy	
Search Date	October 1, 2018
Drug Name	Herceptin [product name]
Event (MedDRA Terms)	**DMEPA Official PNR Name Confusion Search Terms Event List:** Preferred Terms: CIRCUMSTANCE OR INFORMATION CAPABLE OF LEADING TO MEDICATION ERROR DRUG ADMINISTRATION ERROR DRUG DISPENSING ERROR DRUG PRESCRIBING ERROR INTERCEPTED DRUG DISPENSING ERROR INTERCEPTED DRUG PRESCRIBING ERROR INTERCEPTED MEDICATION ERROR MEDICATION ERROR PRODUCT NAME CONFUSION TRANSCRIPTION MEDICATION ERROR Lower Level Terms: INTERCEPTED PRODUCT SELECTION ERROR INTERCEPTED WRONG DRUG PRODUCT SELECTED INTERCEPTED WRONG DRUG SELECTED PRODUCT SELECTION ERROR WRONG DEVICE DISPENSED WRONG DRUG ADMINISTERED WRONG DRUG DISPENSED WRONG DRUG PRESCRIBED WRONG DRUG PRODUCT SELECTED WRONG DRUG SELECTED WRONG PRODUCT SELECTED
Date Limits	May 1, 2018[d] to October 1, 2018

[d] Date of last search in Gao, T. Proprietary Name Review for (b) (4) (BLA 761106). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 JUL 26. Panorama No. 2018-22736159.

Each report was reviewed for relevancy and duplication. Duplicates were merged into a single case. The NCC MERP Taxonomy of Medication Errors was used to code the case outcome and error root causes when provided by the reporter.

After individual review, 7 reports were not included in the final analysis because they did not describe name confusion.

Following exclusions, the search yielded no relevant cases.

2.2.6 Safety assessment of the root name and modifier

The proposed proprietary name is comprised of two words: the root name "Herceptin" and the modifier "Hylecta". The root name, "Herceptin", is available for intravenous administration in strengths of 150 mg/vial and 440 mg/vial. Genentech has developed a co-formulation of trastuzumab and hyaluronidase human for subcutaneous injection and proposes to use the modifier "Hylecta" to differentiate this subcutaneous formulation from the currently marketed intravenous formulation of Herceptin. Differences between the proposed subcutaneous formulation and the currently marketed intravenous formulation are listed in Table 2 below.

Table 2. Product Characteristics of Herceptin and Herceptin Hylecta

	Herceptin[e] BLA 103792	**Herceptin Hylecta (proposed) BLA 761106**
Intended Pronunciation:	her sep' tin	her sep' tin hye lek' tah
Active Ingredient	trastuzumab	trastuzumab and hyaluronidase human
Indication of Use	The treatment of HER2-overexpressing breast cancer. The treatment of HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma.	treatment of HER2-overexpressing breast cancer (adjuvant breast cancer and metastatic breast cancer).
Route of Administration	Intravenous	Subcutaneous
Dosage Form	For Injection	Injection
Strength	150 mg/vial, 440 mg/vial	600 mg and 10,000 units/5 mL
Dose and Frequency	Adjuvant Treatment of HER2 Overexpressing Breast Cancer Administer at either: • Initial dose of 4 mg/kg over 90 minute intravenous infusion, then 2 mg/kg over 30 minute intravenous infusion weekly for the first 12 weeks (with paclitaxel or docetaxel) or 18 weeks (with docetaxel/carboplatin). One	600 mg and 10,000 units subcutaneously over approximately 2-5 minutes every three weeks. Patients with metastatic breast cancer should be treated until disease progression. Patients with adjuvant breast cancer should be treated for 52 weeks or until disease recurrence, whichever occurs first.

[e] Herceptin. Drugs@FDA. U.S. Food and Drug Administration; April 2017. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/103792s5337lbl.pdf.

Table 2. Product Characteristics of Herceptin and Herceptin Hylecta		
	Herceptin[e] **BLA 103792**	**Herceptin Hylecta (proposed)** **BLA 761106**
	week after the last weekly dose of Herceptin, administer 6 mg/kg as an intravenous infusion over 30−90 minutes every three weeks to complete a total of 52 weeks of therapy. • Initial dose of 8 mg/kg over 90 minutes intravenous infusion, then 6 mg/kg over 30-90 minutes intravenous infusion every three weeks for 52 weeks. • Metastatic HER2 Overexpressing Breast Cancer • Initial dose of 4 mg/kg as a 90 minute intravenous infusion followed by subsequent weekly doses of 2 mg/kg as 30 minute intravenous infusions. Metastatic HER2 Overexpressing Gastric Cancer • Initial dose of 8 mg/kg over 90 minutes intravenous infusion, followed by 6 mg/kg over 30 to 90 minutes intravenous infusion every 3 weeks.	
How Supplied	One carton containing 150 mg Single dose vial One carton containing 420 mg multi-dose vial and Bacteriostatic Water for Injection	Single dose vial
Storage	2°C to 8°C (36°F to 46°F)	2°C to 8°C (36°F to 46°F)

Given the Genentech's proposal to use Herceptin as the root name with the addition of a modifier, we considered the following (addressed respectively below): (1) evaluation of the use of the same root name, (2) whether use of a modifier is sufficient to adequately distinguish the products, and (3) evaluation of the proposed modifier "Hylecta".

1. Evaluation of the Use of the same root name

Herceptin has been marketed as the proprietary name for trastuzumab for injection since 1998. The proposed multi-ingredient product contains both trastuzumab and hyaluronidase human. Because the proposed product shares the active ingredient

trastuzumab and indication (breast cancer), the use of the same root name Herceptin appears appropriate. In addition, we performed a FAERS search on October 1, 2018 to identify cases of name confusion with the root name Herceptin. Our search did not identify any medication errors that could be attributed to name confusion involving Herceptin. Thus, we do not object to use of the same root name for this product.

2. Whether use of a modifier is sufficient to adequately distinguish the products

According to Genentech, the addition of the hyaluronidase human to the active ingredient trastuzumab improves subcutaneous delivery by facilitating local dispersion and enhancing systemic absorption.[f] Therefore, if the intravenous formulation was inadvertently administered subcutaneously, the trastuzumab would be very slowly absorbed, which may lead to the potential for underdose as the peak concentration would not be achieved. On the other hand, if the subcutaneous formulation was inadvertently administered intravenously, it may lead to the potential for overdose.

Genentech proposes to differentiate the products by using a modifier in the proprietary name nomenclature. We considered the risk of name confusion if the modifier is dropped. 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. Postmarket experience shows that the introduction of product line extensions may result in medication errors if the modifier is omitted and the product characteristics are similar or overlap. An alternative to using a modifier to distinguish this product from the currently marketed products is to use a different root name. However, marketing the new product under a unique proprietary name also carries a risk of medication errors, such as therapeutic duplication and overdoses. Thus, we agree that a modifier may assist in differentiating between the intravenous and subcutaneous formulations.

3. Evaluation of the proposed modifier "Hylecta"

Genentech indicated that the modifier "Hylecta" is intended to link to hyaluronidase. Genentech believes this modifier will enable healthcare providers, pharmacists, and users to distinguish between the proposed product and the currently approved Herceptin. Our review of the external study conducted by (b) (4) found that none of the healthcare practitioners (HCPs) understood the meaning of the proposed modifier "Hylecta" (see Table 3 below).

Table 3. Number and Percentage of responses for modifier meaning from 150 healthcare practitioners, data from external study conducted by (b) (4)

	Responses for modifier meaning	**#**	**%**

[f] Genentech, Inc. 2.4 Nonclinical Overview (rHuPH20). South San Francisco (CA): Genentech, Inc. 2018 MAY 1. Available at \\cdsesub1\evsprod\bla761106\0001\m2\24-nonclin-over\nonclinical-overview-rhuph20.pdf.

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

(b) (4)

Modifier alone, unaided: “Hylecta”	Breast cancer	1	0.7%
	Fictional character	1	0.7%
	Immunosuppressant	1	0.7%
	Incontinence	1	0.7%
	Oncology	1	0.7%
	Scientific	1	0.7%
	Water	1	0.7%
Base brand plus modifier, unaided: “Herceptin Hylecta”	Breast cancer	4	2.7%
	Antineoplastic	3	2%
	Monoclonal Antibody	2	1.3%
	Cancer	1	0.7%
	Chemotherapy	1	0.7%
	Depression	1	0.7%
	HER2 breast cancer	1	0.7%
	Liver	1	0.7%
	Oncology	1	0.7%

(b) (4) asserts that the results shown above are to be expected with first exposure to the existing base brand and modifier name combination until such time that HCPs become familiar with the new product. We agree that the modifier “Hylecta” is novel and has no well understood standard meaning in drug nomenclature. However, it is reasonable to expect that, like any novel modifier, awareness among healthcare practitioners will increase with market uptake of the product. Additionally, we determined that the modifier does not contain any components such as USAN stem, route of administration, or dosage form that is misleading or can contribute to medication error. Thus, it appears to provide adequate differentiation between the currently marketed Herceptin (single-ingredient product, weight-based dosing, and intravenous administration) and the proposed drug product (multiple-ingredient product, fixed dosing of 600 mg/10,000 units, and subcutaneous administration). Thus, we do not object to the modifier “Hylecta”.

2.2.7 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 November 30, 2018. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Oncology Products 1 (DOP1) on December 3, 2018, they stated no additional concerns with the proposed proprietary name, Herceptin Hylecta.

3 CONCLUSION

The proposed proprietary name, Herceptin Hylecta, 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 GENENTECH, INC.

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

If any of the proposed product characteristics as stated in your submission, received on September 17, 2018, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

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

USAN Stems List contains all the recognized USAN stems.

2. Phonetic and Orthographic Computer Analysis (POCA)

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

Drugs@FDA

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

RxNorm

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

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

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

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

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

APPENDICES

Appendix A

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

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

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

[i] 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[j]. 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.

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[j] 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 ≥ 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%).

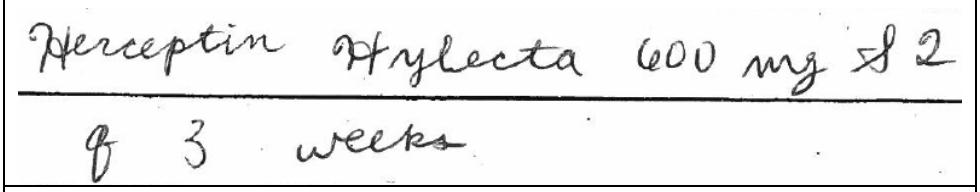
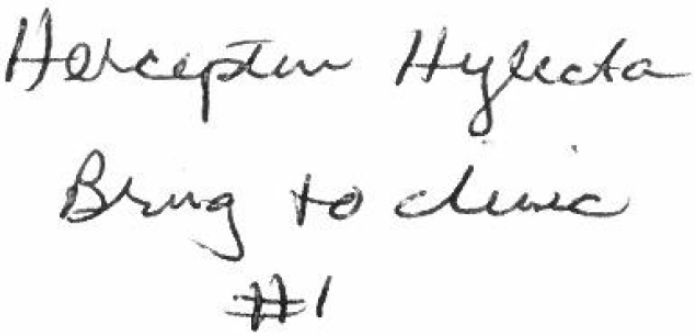
Names with low similarity are generally acceptable unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity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

Appendix A1: Description of FAERS

The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support the FDA's postmarket safety surveillance program for drug and therapeutic biologic products. The informatic structure of the FAERS database adheres to the international safety reporting guidance issued by the International Conference on Harmonisation. FDA's Office of Surveillance and Epidemiology codes adverse events and medication errors to terms in the Medical Dictionary for Regulatory Activities (MedDRA) terminology. Product names are coded using the FAERS Product Dictionary. More information about FAERS can be found at: http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm.

Appendix B: Prescription Simulation Samples and Results

Figure 1. Herceptin Hylecta Study (Conducted on September 28, 2018)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order:  Outpatient Prescription:  	Herceptin Hylecta Bring to clinic Dispense number one

FDA Prescription Simulation Responses (Aggregate Report)
Study Name: Herceptin Hylecta

306 People Received Study
46 People Responded

Study Name: Herceptin Hylecta

Total	19	12	15	
INTERPRETATION	OUTPATIENT	VOICE	INPATIENT	TOTAL
HERCEPTI HYLECTA	1	0	0	1
HERCEPTIN	1	1	0	2
HERCEPTIN HELECTA	0	1	0	1
HERCEPTIN HIGHLECTA	0	1	0	1
HERCEPTIN HILECTA	0	2	0	2
HERCEPTIN HILEPTA	0	1	0	1
HERCEPTIN HYLECTA	17	2	14	33
HERCEPTIN HYLECTA IV	0	0	1	1
HERPECTIN HYLEPTA	0	1	0	1
HERSEPTIN HILECKA	0	1	0	1
PERCEPTIN HYLECTA	0	1	0	1
PERCEPTIN ILAPTA	0	1	0	1

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/s/

TINGTING N GAO
12/03/2018

SEVAN H KOLEJIAN
12/03/2018

DANIELLE M HARRIS
12/03/2018

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:	July 26, 2018
Application Type and Number:	BLA 761106
Product Name and Strength:	(b) (4) (trastuzumab and hyaluronidase human) Injection, 120 mg and 2,000 Units/mL
Total Product Strength:	600 mg and 10,000 Units/5 mL
Product Type:	Multi-Ingredient Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Genentech, Inc.
Panorama #:	2018-22736159
DMEPA Safety Evaluator:	Tingting Gao, PharmD
DMEPA Team Leader:	Chi-Ming (Alice) Tu, PharmD
DMEPA Deputy Director:	Danielle Harris, PharmD, BCPS

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TINGTING N GAO
07/26/2018

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07/26/2018

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07/26/2018