CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761235Orig1s000

OTHER REVIEW(S)

FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion

****Pre-decisional Agency Information****

Memorandum

Date: January 4, 2022

To: Wendy Streight, PhD, Regulatory Project Manager
Division of Ophthalmology (DO)

From: Carrie Newcomer, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Jim Dvorsky, Team Leader, OPDP

Subject: OPDP Labeling Comments for VABYSMO (faricimab-svoa) injection, for intravitreal use

BLA: 761235

In response to the Division of Ophthalmology (DO) consult request dated June 10, 2021, OPDP has reviewed the proposed product labeling (PI) and carton and container labeling for the original BLA submission for VABYSMO (faricimab-svoa) injection, for intravitreal use.

Labeling: OPDP's comments on the proposed labeling are based on the draft labeling located in SharePoint on January 2, 2022 and are provided below.

Carton and Container Labeling: OPDP has reviewed the attached proposed carton and container labeling received by electronic email from DO on January 4, 2022 and we do not have any comments.

Thank you for your consult. If you have any questions, please contact Carrie Newcomer at (301) 796-1233 or Carrie.Newcomer@fda.hhs.gov.

16 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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CARRIE A NEWCOMER
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Clinical Inspection Summary

Date	December 6, 2021
From	Roy Blay, Ph.D. Karen Bleich, M.D. Kassa Ayalew, MD, MPH Good Clinical Practice Assessment Branch (GCPAB) Division of Clinical Compliance Evaluation (DCCE) Office of Scientific Investigations (OSI)
To	Lucious Lim, M.D., Reviewing M.O. William Boyd, M.D., Supervisory M.O. Wendy Streight, Ph.D., P.M. Division of Ophthalmology
BLA	761235
Applicant	Genentech, Inc.
Drug	Vabysmo, (faricimab, RO6867461)
NME	N/A
Therapeutic Classification	Bispecific monoclonal antibody
Proposed Indication(s)	Treatment of patients with: • Neovascular (Wet) Age-Related Macular Degeneration (nAMD) • Diabetic Macular Edema (DME) • Diabetic Retinopathy (DR)
Consultation Request Date	7 Jul 21
Summary Goal Date	7 Dec 21
Action Goal Date	28 Jan 22
PDUFA Date	28 Jan 22

I. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

The clinical sites of Drs. Rich, Hu, Sheth, Wells, and Warrow were inspected in support of this NDA. Based on the results of these inspections, Protocols GR40306, GR40844, GR40349, and GR40398 appear to have been conducted adequately and the data generated by these sites appear acceptable in support of the respective indications.

II. BACKGROUND

The Applicant submitted this NDA to support the use of Vabysmo (faricimab), in the treatment of Neovascular (Wet) Age-Related Macular Degeneration (nAMD), Diabetic Macular Edema (DME), and Diabetic Retinopathy (DR).

Inspections were requested for the following four protocols in support of this application:

1. **Protocol GR40306:** A Phase III, Multicenter, Randomized, Double-Masked, Active Comparator-controlled Study To Evaluate The Efficacy And Safety Of Faricimab In Patients With Neovascular Age-Related Macular Degeneration (Tenaya)

2. **Protocol GR40844:** A Phase III, Multicenter, Randomized, Double-Masked, Active Comparator-controlled Study To Evaluate The Efficacy And Safety Of Faricimab In Patients With Neovascular Age-Related Macular Degeneration (Lucerne)

3. **Protocol GR40349:** A Phase III, Multicenter, Randomized, Double-Masked, Active Comparator-Controlled Study To Evaluate The Efficacy And Safety Of RO6867461 In Patients With Diabetic Macular Edema (Yosemite)

4. **Protocol Gr40398**: A Phase III, Multicenter, Randomized, Double-Masked, Active Comparator-controlled Study To Evaluate The Efficacy And Safety Of RO6867461 In Patients With Diabetic Macular Edema (Rhine)

Protocols GR40306 and GR40844 were identically designed studies for the investigation of the treatment of AMD with Vabysmo. They were Phase III, multicenter, randomized, active comparator-controlled, double-masked, parallel-group, 112-week studies to investigate the efficacy, safety, durability, and pharmacokinetics of the 6-mg dose of faricimab administered at up to 16-week intervals to treatment-naive patients with nAMD. Subjects were randomized 1:1 to either the investigational product (IP) or the comparator arm (aflibercept). The primary efficacy endpoint was the change from baseline in Best Corrected Visual Acuity (BCVA) as measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters based on an average at Weeks 40, 44, and 48. Protocol GR40306 was conducted at 149 domestic and international sites with 671 subjects randomized to the study. The first subject was enrolled in February of 2019 and the last subject was randomized in November of 2019. The data cutoff for the primary analysis of the study was 26 Oct 2020. Protocol GR40844 was conducted at 122 domestic and international sites with 658 subjects randomized to the study. The first subject was enrolled in March of 2019 and the last subject was randomized in November of 2019. The data cutoff for the primary analysis of the study was 5 Oct 2020.

Protocols GR40349 and GR40398 were identically designed studies for investigation of the treatment of DME and DR with Vabysmo. Protocols GR40349 and GR40398 were Phase III, multicenter, randomized, active comparator-controlled, double-masked, parallel-group studies evaluating the efficacy, safety, and pharmacokinetics and optimal treatment frequency of RO6867461 administered by IVT injection at 8-week intervals or personal treatment intervals (PTI) of approximately 100 weeks duration (not including the screening period) to patients with DME. Subjects were randomized in a 1:1:1 ratio to the IP administered every four weeks, 8 weeks or PTI. The primary efficacy endpoint is the change from baseline in BCVA (as measured on the ETDRS chart at a starting distance of 4 meters) at one year. Specifically, the primary efficacy endpoint is the change from baseline in BCVA averaged over Weeks 48, 52, and 56.

Protocol GR40349 was conducted at 179 domestic and international sites with 940 subjects randomized to the study. The first subject was enrolled in September of 2019 and the last subject was randomized in September of 2019. The data cutoff for the primary analysis of the study was October 20, 2020. Protocol GR40398 was conducted at 174 domestic and international sites with 951 subjects randomized to the study. The first subject was enrolled in September of 2019 and the last subject was randomized in September of 2019. The data cutoff for the primary analysis of the study was October 19, 2020.

Dr. Rich conducted Protocol GR40306; Dr. Hu conducted Protocol GR40349; Dr. Sheth conducted Protocol GR40398; and Drs. Wells and Warrow conducted Protocol GR40844. Selection of the sites was left to the discretion of OSI by the reviewing division, the Division of Ophthalmology. These sites were selected for inspection because of their relatively high enrollment of study subjects and/or a lack of a history of recent inspections. In addition, Drs. Hu and Warrow were also selected for inspection in response to a complaint (#9446) alleging improper blood collection techniques, failure to collect necessary specimens for analysis, falsified freezer temperature recordings, misplacement of subject files, and disorganization and carelessness in implementation of the study plan. The goals of these inspections were the evaluation of study conduct and the verification of the primary efficacy endpoint, in addition to determining the validity of the allegations against Drs. Hu and Warrow.

III. Results (by site):

1. **Ryan Rich, MD**
   Retina Consultants of Southern Colorado
   2770 North Union Blvd., Suite 140
   Colorado Springs, CO 80909

   Site: 319471
   Protocol: GR40306
   Inspection Dates: 9/23-29/21

At this site, 20 subjects were screened, 15 were enrolled (5 screen fails), three subjects withdrew, and four subjects remained in the extension phase of study. The study records of the 15 enrolled subjects were reviewed for the primary efficacy endpoint (BCVA), adverse events, visit progress notes, medical records, and protocol deviations. Other study records reviewed included informed consent, financial disclosure, site training records, delegation of duties, investigational product (IP) control, and sponsor monitor, and IRB correspondence.

The inspection compared the source records as noted above with the data listings and no significant discrepancies were observed. Adherence to the regulations and the investigational plan was adequate.

2. Allen Hu, M.D.
Cumberland Valley Retina PC
1150 Opal Court
Hagerstown, MD 21740

Site: 311827
Protocol: GR40349
Inspection Dates: 9/22-27/21

At this site, 48 subjects were screened, 35 were enrolled, and 32 completed the study. Three subjects discontinued from the study: Subject (b) (6) was discontinued for noncompliance with the visit schedule (COVID concerns) after the data cutoff date, Subject (b) (6) was discontinued from this site and rejoined the study at another site under the same protocol, and Subject (b) (6) discontinued prior to Week 48 due to a diagnosis of terminal cancer.

The study records of the 35 enrolled subjects were reviewed for the primary efficacy endpoint (BCVA), adverse events, and protocol deviations. Other study records reviewed included IRB documentation, financial disclosure, site training records, informed consent forms, subjects' source records, IP control, and study and monitoring correspondence.

The following adverse events listed in the source documentation and the EDC system were not reported in the data listings per the following table:

Table 1: Unreported AEs

Subject, Treatment Arm	Treatment Start Date	Adverse Event	Adverse Event Date
(b) (6) Arm C	2/14/2019	Worsening DME (OS), mild	(b) (6)
		CKD stage 2, moderate	
(b) (6) Arm C	4/8/2020	Physical deconditioning, severe	
		Pseudo-obstruction of bowel, severe	
		Onychomycosis of fingernail, mild	
		Chronic kidney disease, Stage 3, severe	
		Acute metabolic encephalopathy	
		Bilateral pleural effusions	

Reviewer comments: The unreported AEs listed for Subject (b) (6) *in the table started concurrently with the reported SAE for newly diagnosed adenocarcinoma for which the subject withdrew from the study. The AEs are provided here for the consideration of the review team.*

In January of 2020, the agency received a complaint (C#9446) regarding study conduct at Dr. Hu's site. The complaint referenced several clinical trials, including Protocol GR40306. Specific allegations included failure to collect lab specimens and improper specimen collection procedures. Review of the source records at the site substantiated the complaint, including several instances in which protocol required labs were not collected in 2019. For example, 10 subjects did not have labs collected at week 4 for plasma PK, PD, and ADA samples as required by protocol; 3 subjects did not have urine collected at week 56 for urinalysis; 4 subjects had blood drawn in error when not required by protocol (3 at day 7, 1 at week 68) and 1 subject had a Day 1 DNA collection in error (the subject had not consented to DNA collection). The sample collection errors occurred in 2019 and early 2020.

A note to file at the site dated 4/4/2019 acknowledged multiple lab collection errors and described staff retraining. The lab collection errors persisted, and additional corrective actions were taken in 2020, including hiring additional personnel and the creation of a system to ensure that labs were obtained when required.

An additional protocol violation included the enrollment of a study subject who was ineligible for the study given a hemoglobin A1c greater than 10 at the screening visit. This is adequately described in the data listings. Dr. Hu's preventive action plan includes the institution of a secondary review of eligibility for all study subjects prior to randomization.

Reviewer comments: The preventive actions appear to be reasonable. There is no evidence of harm to the study subjects related to the protocol violations.

Additional allegations in complaint #9446 included inadequate temperature monitoring of refrigerator for IP storage and misplaced patient files. Records at the site demonstrate adequate documentation and procedures related to temperature monitoring.

The regulatory violations at the site do not appear to impact the reliability of the study data generated at the site.

3. **Veeral Sheth, M.D.**
   University Retina and Macula Associates, PC
   6320 W. 159th St., Suite A
   Oak Forest, IL 60452

   Site: 313958
   Protocol: GR40398
   Inspection Dates: 10/4-8/21

At this site, 64 subjects were screened, 39 were enrolled in the study, and 32 subjects completed the study. The study records of the 39 enrolled subjects were reviewed for the primary efficacy endpoint (BCVA), adverse event reporting, protocol adherence, laboratory reports, concomitant medications, and IP control. Other study records reviewed included monitoring reports, case report forms, site signature logs, and site training documentation.

Electronic case report forms (eCRFs) were used in the study. Access was controlled via password/usernames. Source data was transcribed to the eCRFs via authorized users who could make changes via a query system. Audit trails were available for review. Electronic records appeared adequate.

The following unreported adverse events in source documentation and the EDC system were not reflected in the data listings:

Table 2: Unreported AEs

Subject Treatment arm	Treatment Start Date	Adverse Event	Adverse Event Date
(b) (6), Arm B	(b) (6)	Shortness of breath	(b) (6)
(b) (6), Arm B	(b) (6)	Chronic fatigue-mild	

Some concomitant medications captured in the source records and EDC system were not reflected in the data listings. For example, Subjec (b) (6) was prescribed ampicillin for treatment of a urinary tract infection that began (b) (6) and resolved (b) (6). The AE was reported in the data listings but not the use of ampicillin for its treatment. Other medications that were begun on (b) (6) but were not reported in the data listings include glargine, Rocephin, dextrose 10%, NaCl, 0.9%, aspirin, Labetalol, ferrous sulfate, and Lantus insulin.

According to the protocol, previous anti-VEGF treatment was a randomization stratification factor. Subject (b) (6) who was in Arm B 6 mg RO6867461 (PTI) and randomized on (b) (6) was incorrectly identified as not having received prior anti-VEGF treatment. The subject's medical records confirmed previous anti-VEGF treatment and the EDC was updated during the inspection. Subject (b) (6) was stratified correctly with respect to anti-VEGF treatment. An additional subject at the site (Subjec (b) (6)) was incorrectly stratified with regards to prior anti-VEGF treatment; in the case of Subject (b) (6) the problem was identified and corrected and is appropriately reported in the data listings.

Additional regulatory violations include the late reporting of SAEs for Subjects (b) (6) (all adequately reported in the data listings), the enrollment of a subject who did not meet the inclusion criteria regarding the use of medication for diabetes (adequately reported in the data listings), the loss of two kits of the IP, and the randomization of a subject to the study prior to receipt of documentation of coagulation laboratory results (required to assess eligibility).

4. John A. Wells, MD
Palmetto Retina Center
124 Sunset Court
West Columbia, SC 29169

Site: 319534
Protocol: GR40844
Inspection Dates:

At this site, 37 subjects were screened. Of the 24 subjects initially enrolled in the study, 15 subjects completed the study, an additional five subjects had not completed the study having had visits at Weeks 104 or 108 (the final visit being Week 112), and of the four remaining enrolled subjects, Subject (b) (6) transferred to another site; Subjects (b) (6) withdrew consent during the study; and Subject (b) (6) died of Covid/pneumonia on (b) (6), after the data cut-off date of 10/05/2020. Study record review included informed consent forms, medical and ocular histories, subject eligibility, study treatments, IP control, concomitant medications, the primary efficacy endpoint data, adverse events, protocol deviations, quality of life questionnaires, and electronic data. The case histories for all 23 enrolled subjects (less one transferred subject) were compared with the data listings. Other study records reviewed included training logs, delegation of duties logs, sponsor, monitor, and IRB correspondence, and financial disclosure forms.

There was one unreported AE of posterior vitreous detachment, for Subject (b) (6) (randomized to the faricimab treatment arm on (b) (6)) which occurred on (b) (6).

Reviewer comment: The review division may wish to determine the significance, if any, of the observed isolated finding of post vitreous detachment on safety assessment.

Determination of Central Subfield Thickness (CST) is a measure of active disease and determines the treatment interval for subjects. The initial CST finding at Week 20 for Subject (b) (6) did not meet active disease criteria by comparison with previous CST findings at Weeks 12 and 16 and indicated a treatment interval of every 12 weeks. At Week 24, the investigator revised the Week 20 CST finding such that active disease criteria were met and a treatment interval of every eight weeks was indicated. The revision resulted in the initial treatment interval for this subject not being in compliance with the protocol. This major protocol violation was reported to the IRB and is reported in the protocol deviation line listings. The investigator stated that he would be reviewing CST values prior to treatment administration for ongoing/future studies.

The inspection compared the source records as noted above with the data listings and no significant discrepancies were observed. Adherence to the regulations and the investigational plan appeared adequate.

5. David Warrow, M.D.
Cumberland Valley Retina PC
1150 Opal Court
Hagerstown, MD 21740

Site: 319532
Protocol: GR40844
Inspection Dates: 9/28/21-10/1/21

At this site, 28 subjects were screened, 20 were enrolled and randomized to the study, and nine subjects completed the study. Subject (b) (6) discontinued due to diagnosis of terminal cancer and died off-study on (b) (6), after the data cut-off date of 10/05/20. Study record review of the 20 enrolled subjects included informed consent, inclusion/exclusion criteria, laboratory tests, progress notes, protocol deviations, demographics, physical examinations, medical histories including ocular medical histories and ophthalmic examination findings, the primary efficacy endpoint (BCVA), concomitant medications, adverse event reporting, and concurrent ocular procedures. Other study records reviewed included training logs, delegation of duties logs, IP control, sponsor, monitor, and IRB correspondence, and financial disclosure forms.

The inspection compared the source records as noted above with the data listings and no significant discrepancies were observed. There was insufficient evidence to substantiate the allegations in the complaint (#9446) described above (see **Background**) alleging improper study conduct. Adherence to the regulations and the investigational plan appeared adequate.

{See appended electronic signature page}

Roy Blay, Ph.D.
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
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OSI/Office Director/David Burrow
OSI/DCCE/Division Director/Kassa Ayalew
OSI/DCCE/ Acting Branch Chief/Kassa Ayalew
OSI/DCCE/Team Leader/Karen Bleich
OSI/DCCE/GCPAB Reviewer/Roy Blay
OSI/GCPAB/Program Analyst/Yolanda Patague

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LABEL AND LABELING REVIEW
Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
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 10, 2021
Requesting Office or Division:	Division of Ophthalmology (DO)
Application Type and Number:	BLA 761235
Product Name and Strength:	Vabysmo (faricimab-svoa) injection, 6 mg/0.05 mL
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Genentech, Inc.
FDA Received Date:	May 28, 2021
OSE RCM #:	2021-1108
DMEPA 1 Safety Evaluator:	Nasim Roosta, PharmD
DMEPA 1 Team Leader:	Valerie S. Vaughan, PharmD

1 REASON FOR REVIEW

As part of the approval process for Vabysmo (faricimab-svoa) injection, the Division of Ophthalmology (DO) requested that we review the proposed Vabysmo prescribing information (PI), container label and carton labeling for areas of vulnerability that may lead to medication errors.

2 MATERIALS REVIEWED

Table 1. Materials Considered for this Label and Labeling Review

Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B- N/A
ISMP Newsletters*	C- N/A
FDA Adverse Event Reporting System (FAERS)*	D- N/A
Other	E- N/A
Labels and Labeling	F

N/A=not applicable for this review
*We do not typically search FAERS or ISMP Newsletters for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

3 CONCLUSION AND RECOMMENDATIONS

The proposed prescribing information (PI), container label and carton labeling may be improved to promote the safe use of this product from a medication error perspective. We provide the identified medication error issues, our rationale for concern, and our proposed recommendations to minimize the risk for medication error in Section 4 for the Division and in Section 5 for Genentech, Inc.

4 RECOMMEDATIONS FOR DIVISION OF OPHTHALMOLOGY (DO)

Table 2. Identified Issues and Recommendations for Division of Ophthalmology (DO)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Prescribing Information, Container Label and Carton Labeling			
1.	The non-proprietary name suffix is denoted by the placeholder "-xxxx".	The non-proprietary name suffix "-svoa" was found conditionally acceptable on November 09, 2021.[a]	Replace "-xxxx" with the conditionally acceptable non-proprietary name suffix, "-svoa".
Prescribing Information- Section 16: How Supplied/Storage and Handling			
1.	In section 16.1, *How Supplied*, there is no mention of the overfill supplied in the vial.	Each vial contains (b) (4) of solution to deliver a 0.05 mL dose volume. Wrong dose errors could occur if the healthcare provider inadvertently injects more volume than needed to achieve the dose. Additionally, wrong technique in product use could occur if a healthcare provider (HCP) attempts to use the single dose vial to administer a 0.05 mL dose from one vial to both eyes. A statement of overfill might be useful to alert the HCP that more volume than required for a single dose is contained within the vial.	Add a statement to Section 16.1, notifying the HCP of the overfill contained within the vial. We recommend, a similar statement regarding the overfill amount be included on the container label and carton labeling to minimize risk of medication error during preparation and administration. For example: "Each glass vial contains (b) (4) mg VABYSMO in (b) (4) mL solution. This provides an overfill amount to allow for administration of a single 0.05 mL dose of solution containing 6 mg of VABYSMO".

5 RECOMMENDATIONS FOR GENENTECH, INC.

[a] Chan, I. Nonproprietary Name Suffix- Advice for BLA 761235. Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2021 NOV 09. RCM No.: 2021-1, 2021-41.

Table 3. Identified Issues and Recommendations for Genentech, Inc. (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Container Label and Carton Labeling			
1.	We note that the placeholder, "TRADENAME" is included on the container label and the carton label. Additionally, the placeholder, "-xxxx" is presented for the non-proprietary name suffix.	The proposed proprietary name, Vabysmo, was found to be conditionally acceptable on August 24, 2021[b] and the non-proprietary name suffix, -svoa, was found conditionally acceptable on November 09, 2021[a]. The proprietary name and non-proprietary name suffix found conditionally acceptable, "Vabysmo" and "-svoa", respectively, should be used throughout the container label and carton labeling.	Replace the placeholder, "TRADENAME", with the conditionally acceptable proprietary name, "Vabysmo". Replace the placeholder, "-xxxx", with the conditionally acceptable non-proprietary name suffix, "-svoa".
2.	The format for expiration date is not defined.	Clearly defining the expiration date will minimize confusion and risk for deteriorated drug medication errors.	Identify the expiration date format you intend to use. FDA recommends that the human-readable expiration date on the drug package label include a year, month, and non-zero day. FDA recommends that the expiration date appear in YYYY-MM-DD format if only numerical characters are used or in YYYY-MMM-DD if alphabetical characters are used to represent the month. If there are space limitations on the drug package, the human-readable text may

[b] Chan, I. Proprietary Name Review – Advice for Vabysmo IND 119225. Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2021 AUG 24. RCM: 2021-1044724002.

Table 3. Identified Issues and Recommendations for Genentech, Inc. (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			include only a year and month, to be expressed as: YYYY-MM if only numerical characters are used or YYYY-MMM if alphabetical characters are used to represent the month. FDA recommends that a hyphen or a space be used to separate the portions of the expiration date.
3.	The net quantity statement is missing from the container label and carton labeling.	The net quantity statement is required per 21 CFR 201.51(a).	Add the net quantity to the container label and carton labeling in accordance with 21 CFR 201.51(a). Additionally, we recommend that the net quantity statement appear on the principal display panel but separated from and less prominent than the statement of strength (e.g., not highlighted, boxed, or bolded). See *Draft guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors*[c].
Carton Labeling			
1.	The trade carton labeling does not include the machine readable 2D data matrix barcode product identifier.	The DSCSA requires certain prescription drugs to have a human-readable and machine-readable (2D data matrix barcode) product identifier on the smallest	We recommend that you review the draft guidance to determine if the product identifier requirements apply to your product's labeling. See Guidance for Industry: Product

[c] When final, this guidance will represent FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

Table 3. Identified Issues and Recommendations for Genentech, Inc. (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
		saleable unit (usually the carton) for tracking and tracing purposes. NDC: [insert product's NDC] SERIAL: [insert product's serial number] LOT: [insert product's lot number] EXP: [insert product's expiration date]	Identifiers under the Drug Supply Chain Security Act - Questions and Answers (June 2021).[d] Note that the guidance recommends that the human-readable portion be located near the 2D data matrix barcode.

[d] Guidance for Industry: Product Identifiers Under the Drug Supply Chain Security Act - Questions and Answers. 2021. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/product-identifiers-under-drug-supply-chain-security-act-questions-and-answers.

APPENDICES: METHODS & RESULTS FOR EACH MATERIAL REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 4 presents relevant product information for Vabysmo that Genentech, Inc. submitted on May 28, 2021.

Table 4. Relevant Product Information for Vabysmo	
Initial Approval Date	N/A
Active Ingredient	Faricimab
Indication	Treatment of patients with: Neovascular (wet) Age-Related Macular Degeneration (nAMD), Diabetic Macular Edema (DME), Diabetic Retinopathy (DR)
Route of Administration	Intravitreal injection
Dosage Form	Ophthalmic solution
Strength	6 mg/0.05 mL
Dose and Frequency	6 mg (0.05 mL) administered by intravitreal injection every 4 weeks (approximately every 28 ± 7 days, monthly) for the first 4 doses, followed by 6 mg (0.05 mL) via intravitreal injection at a dosing interval of up to every 16 weeks (4 months).
How Supplied	Supplied as a clear to opalescent, colorless to brownish-yellow 6 mg/0.05 mL solution in a single-dose glass vial. Each glass vial contains (b) (4) a single dose of 0.05 mL solution containing 6 mg of VABYSMO. Each VABYSMO carton (NDC 50242-096-01) contains one glass vial and one sterile 5 µm blunt transfer filter needle (18-gauge x 1½ inch, 1.2 mm x 40 mm).
Storage	Refrigerate 2°C to 8°C (36°F to 46°F), Do not freeze, do not shake. (b) (4) Keep the vial in the original carton to protect form light. Prior to use, the unopened glass vial of VABYSMO may be kept at room temperature, 20°C to 25°C (68°F to 77°F), for up to 24 hours.
Container Closure	Vial with aluminum seal and plastic flip-off cap

APPENDIX F. LABELS AND LABELING

F.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[e] along with postmarket medication error data, we reviewed the following Vabysmo labels and labeling submitted by Genentech, Inc.

- Container label received on May 28, 2021
- Carton labeling received on May 28, 2021
- Prescribing Information (Image not shown) received on July 15, 2021, available from \\CDSESUB1\evsprod\bla761235\0005\m1\us\annotated-draft-labeling-text.pdf

F.2 Label and Labeling Images

Container label

(b) (4)

[e] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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