CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

216675Orig1s000

PRODUCT QUALITY REVIEW(S)

RECOMMENDATION

☒ Approval
☐ Approval with Post-Marketing Commitment
☐ Complete Response

NDA 216675
Assessment # 1

Drug Product Name	Perfluorohexyloctane (F6H8) Ophthalmic Solution
Dosage Form	Solution
Strength	100%
Route of Administration	Topical ophthalmic solution
Rx/OTC Dispensed	Rx
Applicant	Bausch & Lomb Incorporated
US agent, if applicable	

Submission(s) Assessed	Document Date	Discipline(s) Affected
Original	June 28, 2022	All disciplines
Quality Amendment	Aug 30, 2022	Drug substance
Quality Amendment	Nov 01, 2022	Manufacturing process
Quality Amendment	Jan 17, 2023	Quality microbiology and drug substance
Quality Amendment	Feb 24, 2023	Quality microbiology, drug product and drug substance

QUALITY ASSESSMENT TEAM

Discipline	Primary Assessor	Secondary Assessor
Drug Substance	Joseph Leginus	Sithamalli Chandramouli
Drug Product	Ravindra K Kasliwal	Chunchun Zhang
Manufacturing	Qiang Han	Kamal Tiwari
Microbiology	Ash Bekele	Laura Wasil
Biopharmaceutics	NA	NA
Regulatory Business Process Manager	Shazma Aftab	
Application Technical Lead	Chunchun Zhang	
Laboratory (OTR)	NA	

Environmental	Ravindra K Kasliwal	Chunchun Zhang

QUALITY ASSESSMENT DATA SHEET

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

DMF #	Type	Holder	Item Referenced	Status	Date Assessment Completed	Comments
(b) (4)	III		(b) (4)	NA		
	III			NA		
	III			NA		
	III			NA		

B. OTHER DOCUMENTS: *IND, RLD, RS, Approved NDA*

Document	Application Number	Description
IND	130558	This product during IND development

2. CONSULTS

Discipline	Status	Recommendation	Date	Assessor
Biostatistics		NA		
Pharmacology/Toxicology		Adequate	2/21/2023	Aling Dong/ Mukesh Summan
CDRH		NA		CDRH confirmed that no CDRH consult is necessary on 7/11/2022

Clinical		NA		
Other		NA		

EXECUTIVE SUMMARY

I. RECOMMENDATIONS AND CONCLUSION ON APPROVABILITY

Satisfactory information and responses have been submitted to support the drug substance, drug product, quality microbiology and manufacturing process aspects.

The product has been recommended for NME on 8/19/2022 in DARRTS since it has not been previously approved or marketed from internet/database searching. The product is regulated as a drug device combination product per the Genus decision. The product is packaged in a multi-dose eyedropper and is considered low risk, therefore CDRH confirmed that no CDRH consult is necessary on 7/11/2022. OPMA has issued an overall acceptable recommendation for all the facilities on 9/13/2022. Therefore, NDA 216675 is recommended approval from Product Quality perspective.

Labeling recommendations from the Product Quality perspective will be provided to the OND PM for consideration during final labeling discussion.

II. SUMMARY OF QUALITY ASSESSMENTS

A. Product Overview

The drug product Perfluorohexyloctane (F6H8) Ophthalmic Solution, 100% is a sterile clear colorless solution and packaged in a 5 mL multi-dose polypropylene eyedropper with 3 mL fill volume.

Proposed Indication(s) including Intended Patient Population	For treatment of the signs and symptoms of dry eye disease (DED) associated with meibomian gland dysfunction (MGD); one drop 4 times/eye/daily
Duration of Treatment	one drop 4 times/eye/daily
Maximum Daily Dose	117.74 mg/day. As above (see the package insert for details)
Alternative Methods of Administration	NA

B. Quality Assessment Overview

Drug Substance: Adequate

The drug substance Perfluorohexyloctane (F6H8) is a clear, colorless, practically odorless liquid. Sufficient CMC information including manufacturing process, impurities limits and stability data was provided.

Drug Product: Adequate

Perfluorohexyloctane (F6H8) ophthalmic solution, 100% is a sterile clear colorless solution. The drug product composition doesn't contain any excipients.

The revised drug product specifications are acceptable and include the following quality attributes: description, identification, assay, visible particles, minimum fill weight, pH, particulate matter, impurities/degradants and sterility. All the analytical methods are adequately validated. Evaluation of the risk assessment of the elemental impurities and nitrosamine impurities showed low risk. Extractable/leachable studies were performed; none of the extracted substances have a level of concentration above the safety level.

Perfluorohexyloctane (F6H8) ophthalmic solution, 100% is packaged in a 5 mL (b) (4) bottle with 3 mL fill volume. The container closure system was demonstrated to be suitable for the proposed drug product and cause no safety concerns.

The applicant has submitted three drug product primary stability batches at 1/5 of the proposed commercial scale with 18 months stability data when stored at long term storage condition (25°C/60%RH) and 6 months at accelerated condition (40°C/75%RH). All the quality attributes met the specifications. Photostability study indicated the drug product is not sensitive to light. Freeze-thaw study with three cycles were conducted to support the proposed shipping plan. Therefore, the expiration date of 24 months for commercial products is granted when stored at 15 °C to 25 °C (59 °F to 77 °F) and no additional precautionary statement is recommended.

The storage statement is "Store at 15 °C to 25 °C (59 °F to 77 °F)." and will be finalized at the OND's labeling meeting.

Labeling: Adequate

Labeling recommendations from the Product Quality perspective will be communicated to the OND PM.

Manufacturing: Adequate

The manufacturing process includes (b) (4) . All the process related concerns have been resolved. All

the manufacturing sites are acceptable based on the previous inspection history and manufacturing capability.

Biopharmaceutics: N/A

Microbiology (if applicable): Adequate

The applicant has provided adequate sterility assurance. (b) (4) Sterility is tested for release of finished drug product.

C. Risk Assessment

From Initial Risk Identification			Assessment		
Attribute/ CQA	**Factors that can impact the CQA**	**Initial Risk Ranking**	**Risk Mitigation Approach**	**Final Risk Evaluation**	**Lifecycle Considerations/ Comments**
Assay (API), stability	• Formulation • Container closure • Raw materials	L	(b) (4)	L	
Impurities	• Formulation • Container closure • Process parameters • Scale/equipment	H		L	
Particulate matter	• Formulation • Container closure	L		L	
Sterility	• Formulation • Container closure • Process parameters • Scale/equipment	H		M	

D. List of Deficiencies for Complete Response

1. Overall Quality Deficiencies *(Deficiencies that affect multiple sub-disciplines)*

NA

2. Drug Substance Deficiencies

NA

3. Drug Product Deficiencies

NA

4. Labeling Deficiencies

Communicate to the OND PM

5. Manufacturing Deficiencies

NA

6. Biopharmaceutics Deficiencies

NA

7. Microbiology Deficiencies

NA

8. Other Deficiencies *(Specify discipline, such as Environmental)*

NA

Application Technical Lead Name and Date:

Chunchun Zhang, Ph. D., March 2, 2023

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Sithamalli Chandramouli

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CHAPTER II: DRUG PRODUCT

Product Information	
NDA Number	**216675**
Assessment Cycle Number	1
Drug Product (DP) Name / Strength	Meibo (perfluorohexyloctane) ophthalmic solution, 100%
Route of Administration	Topical
Drug Product Manufacturer	Bausch & Lomb Americas Inc., Bridgewater, NJ 08807
RLD Information (Brand Name of Product, Applicant)	None
RLD/RS Number	None
Proposed Indication	Treatment of the signs and symptoms of dry eye disease (DED) associated with meibomian gland dysfunction (MGD).

Assessment Recommendation: *Adequate*

Assessment Summary:

The proposed drug product, Perfluorohexyloctane Ophthalmic Solution, 100%, is a one component product consisting of only perfluorohexyloctane and there are no excipients. The company has only one packaging configuration for commercial use, a 3 mL fill size in a 5 mL bottle.

Perfluorohexyloctane is practically insoluble in water, and the two liquids do not mix. Because perfluorohexyloctane does not mix or contain water, it exhibits no pH, osmolality, or water activity, and is not able to support microbial growth. Therefore, Perfluorohexyloctane Ophthalmic Solution, 100%, may be used as a preservative-free product itself.

The primary packaging consists of a 5-mL multi-dose polypropylene bottle, (b) (4) dropper tip and (b) (4) cap. Perfluorohexyloctane is not photosensitive (does not degrade in light). Therefore, primary container does not need to provide protection from light to the drug product. The commercial product, however, includes opaque secondary packaging components. The container closure system (CCS) is capable of delivering a reproducible and consistent average drop size of 11 µL (delivered dose of 14.7 mg perfluorohexyloctane with a density of 1.338 g/mL at 20°C).). The product is regulated as a drug device combination product per the Genus decision. However, the eyedropper is a multi-dose container and is considered a low risk, CDRH confirmed that a CDRH consult is not necessary on 7/11/2022.

Since the primary container is a polypropylene bottle and the drug product is 100% perfluorohexyloctane without any excipients, there may be some weight lost during storage. However, the weight loss does not have an effect on the intended composition or potency of the product.

The unspecified impurities (each) are controlled at NMT (b) (4)% (equal to (b) (4) mg for a total daily dose of 120 mg), in accordance with ICH Q3B(R2) for new drug products. Total impurities are not to exceed a limit of (b) (4)%.

The company has proposed adequate control strategy, including the drug product specifications to assure identity, strength, purity, and quality of the drug product. The available stability data support the conclusion that the drug product, when packaged in natural polypropylene bottles with (b) (4) dropper tips and white (b) (4) closures and stored at **25ºC/60%RH will be stable for the proposed 24-month expiry for the drug product**. The proposed drug product is considered as a non-aqueous, it is acceptable to conduct the stability studies under relative high humidity although it is packaged in a semipermeable container.

The thermal cycling studies have demonstrated that potential **temperature excursions during shipment and storage would not expect to have a negative impact on product quality or stability**.

In use study confirm that the drug product is safe for the intended duration of **use of 4 weeks**.

CQAs	Initial Risk Ranking	Comments	Updated Risk Ranking after Assessment Cycle #	Comments
Appearance	Low	Tested	Low	Tested
Assay, stability	Low	Tested	Low	Tested for assay and Impurities
Particulate matter	Medium	Comply with USP <788>	Low	Stability data show low particle count in each size throughout stability studies.
Leachable / extractable	Low	-	Low	Studies show that leachable are well below 20 ppm.

List Submissions Being Assessed (table):

Document(s) Assessed	Date Received
Original (0001)	**28-Jun-2022**
Amendment (0009)	**24-Feb-2023**

Highlight Key Issues from Last Cycle and Their Resolution: None

Concise Description of Outstanding Issue: None

P.1 DESCRIPTION AND COMPOSITION

Component/Composition Table

The proposed drug product consists of the semi fluorinated alkane (1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluorotetradecane) drug substance. The drug product only contains drug substance and contains no additional excipients.

Component	Reference to Quality Standard	Function	Concentration (g/mL)	Quantity per Unit (g/3 mL)
Perfluorohexyloctane	In-house	Active	1.338	4.014

Assessment: *{Adequate}*

Perfluorohexyloctane Ophthalmic Solution, 100% is a one component product consisting of only perfluorohexyloctane, a semifluorinated alkane, and there are no excipients. The company has only one packaging configuration for commercial use, a 3 mL fill size in a 5 mL bottle.

Perfluorohexyloctane is a colorless liquid with a refractive index very close to water. It is physically, chemically, and physiologically inert, undergoes neither catabolism nor metabolism in the human body and has favorable physical properties for use in the eye. This includes low surface and interface tension, physical properties that by reducing shearing forces between surfaces provide excellent spreading and wetting abilities. The product is intended to substitute the lipid layer of the eye to reduce evaporation of the tear film and thereby protecting the ocular surface from evaporation.

P.2 PHARMACEUTICAL DEVELOPMENT

(b) (4)

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CHAPTER III: ENVIRONMENTAL

R REGIONAL INFORMATION

Environmental

The applicant has requested categorical exclusion from preparation of an environmental assessment under 21 CFR 25.31(b) and has stated that to the applicant's knowledge, no extraordinary circumstances exist (21 CFR 25.15(d)).

(b) (4)

[redacted]

Assessment: *Adequate*

Since the potential introduction concentration is less than 1 ppb, this product qualifies for a categorical exclusion from preparation of an environmental assessment.

Primary Environmental Assessor Name and Date: 24-Feb-2023

Ravindra K Kasliwal, Ph.D.
Review Chemist, Branch-6, DNDP-3, ONDP, OPQ

Secondary Assessor Name and Date: 24-Feb-2023

Chunchun Zhang, Ph.D.
SPQA, Branch-6, DNDP-3, ONDP, OPQ

Ravindra Kasliwal

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Chunchun Zhang

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CHAPTER VII: MICROBIOLOGY

For more details about the items in this template, please see Chapter VII (Microbiology) of the NDA IQA Guide

Product Information	Indicated for the treatment of the signs and symptoms of dry eye disease (DED) associated with meibomian gland dysfunction (MGD)
NDA Number	216675
Assessment Cycle Number	1
Drug Product Name/ Strength	MEIBO, (Perfluorohexyloctane Ophthalmic Solution, 100%, (b) (4) g/mL).
Route of Administration	Ophthalmic/drop
Applicant Name	Bausch & Lomb Incorporated
Therapeutic Classification/ OND Division	CDER/OND/OSM/DO
Manufacturing Site	(b) (4)
Method of Sterilization	(b) (4)

Assessment Recommendation: **Adequate**

Assessment Summary: Recommended for Approval

List Submissions Being Assessed (table):

Document(s) Assessed	Date Received
Seq 0001 (1), Original submission	06/28/2022
Seq 0004 (4), CMC IR response	08/30/2022
Seq 0006 (6), CMC IR response	11/01/2022
Seq 0007 (7), CMC IR response	01/17/2023

Seq 0009 (9), CMC IR response	02/24/2023

Highlight Key Issues from Last Cycle and Their Resolution: Not applicable.

Remarks: The drug product is a sterile ophthalmic solution, consists of only the drug substance (perfluorohexyloctane, 100%) as the single ingredient in the formulation.

Concise Description of Outstanding Issues *(list bullet points with key information and update as needed)*: None

Supporting Documents: None

S DRUG SUBSTANCE

The drug substance is tested for bioburden (Limits: (b) (4) for both total aerobic microorganisms and total yeast and mold). The drug substance is not reviewed for sterility assurance since it is sterilized in the manufacturing process of the drug product.

Assessment: (*Adequate*)

P.1 DESCRIPTION OF THE COMPOSITION OF THE DRUG PRODUCT

(Section 3.2.P.1, Description and Composition of the Drug Product)

Description of drug product – The proposed drug product is a sterile ophthalmic solution (100%), consists of the semi-fluorinated alkane perfluorohexyloctane (drug substance) as the single ingredient in the formulation. The product is packaged as multiple doses in 5 mL (3 mL fill) polypropylene bottles with dropper tips and screw caps.

Table 2.3.P.1–1 Qualitative and quantitative composition drug product

Component	Reference to Quality Standard	Function	Concentration (g/mL)	Quantity per Unit (g/3 mL)
Perfluorohexyloctane	In-house	Active	1.338	4.014

Description of container closure system –A description of the primary container closure system along with the manufacturer's information is provided in

the following applicant table modified from " Table 3.2.P.7.1–1 Summary of primary packaging components" and drawings in Section 3.2.P.7

Description of the primary container closure

Component	Description	Manufacturer	DMF
Bottle	5 mL, natural, polypropylene (PP) bottle, (b) (4)	(b) (4)	(b) (4)
Dropper			
Cap			

Assessment: (*Adequate*)
The applicant provided acceptable description of the drug product and the container closure system. (b) (4)

P.2 PHARMACEUTICAL DEVELOPMENT
P.2.5 MICROBIOLOGICAL ATTRIBUTES

(b) (4)

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CHAPTER IV: LABELING

1.0 PRESCRIBING INFORMATION

Assessment of Product Quality Related Aspects of the Prescribing Information:

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Product Title in Highlights		
Established name(s)[1]	Inadequate	Currently the indicated name is <TRADENAME> (b) (4) Recommend changing to: "**<TRADENAME>(perfluorohexyloctane ophthalmic solution)** (b) (4)
Route(s) of administration	Inadequate	The route of administration is not indicated along with Trademark and established name, "**for topical ophthalmic use**" should be added after the name.
Dosage Forms and Strengths Heading in Highlights		
Summary of the dosage form(s) and strength(s) in metric system	Inadequate	Currently the dosage form and strength are described as (b) (4) It is incorrect and should be changed to: "**Ophthalmic solution, containing perfluorohexyloctane, 100% (3 mL).**"
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored".	N/A	

[1] Established name = [Drug] [Route of Administration] [Dosage Form]

For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package.	Adequate	Not an injectable product.
If the drug product contains an active ingredient that is a salt, clearly state whether the strength is based on the active moiety (e.g., Tablets: 10 mg of drug-x) or active ingredient (e.g., Tablets: 10 mg of drug-x hydrochloride).	N/A	

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DOSAGE AND ADMINISTRATION section		
Special instructions for product preparation (e.g., reconstitution and resulting concentration, dilution, compatible diluents, storage conditions needed to maintain the stability of the reconstituted or diluted product)	N/A	

Important administration instructions supported by product quality information (e.g., do not crush or chew extended-release tablets, instructions for mixing with food)	Adequate	Contact lenses should be removed prior to the administration of <TRADENAME>. Other pictorial directions are adequate.
For parenteral products: include statement: *"Parenteral drug products must be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit"*	N/A	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled. Note the labeling requirement may be applicable to another section of the PI (e.g., Section 11).	N/A	
For radioactive products, include radiation dosimetry for the patient and healthcare practitioner(s) who administer the drug	N/A	
For hazardous products, include the statement *"DRUG X is a hazardous drug. Follow applicable special handling and disposal procedures.[x]"* with	N/A	

x numerical citation to "OSHA Hazardous Drugs".		

1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)

APPEARS THIS WAY ON ORIGINAL

QUALITY ASSESSMENT

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DOSAGE FORMS AND STRENGTHS section		
Available dosage form(s)	Inadequate	Currently the dosage form is described as "(b) (4) ophthalmic solution". **It should be changed to "Ophthalmic solution".**
Strength(s) in metric system	Inadequate	The currently described statement (b) (4) should be revised to, "**Ophthalmic solution, containing clear, colorless, and sterile perfluorohexyloctane, 100% (3mL).".**
If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance. Clearly state whether the strength is based on the active moiety (e.g., Tablets: 10 mg of drug-x) or active ingredient (Tablets: 10 mg of drug-x hydrochloride).	N/A	
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable	Adequate	Sterile is added. The color of the solution should be indicated as "colorless".
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	N/A	

For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package type terms include pharmacy bulk package and imaging bulk package.	Adequate	Not an injectable product.

Section 11 (DESCRIPTION)

Current Description:

11 DESCRIPTION

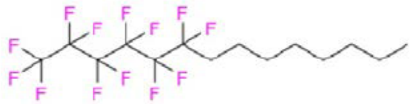
(b) (4)

[redacted]

The description should be revised to:

<TRADENAME> >(perfluorohexyloctane ophthalmic solution), (b) (4) is a sterile liquid containing 100% perfluorohexyloctane, for topical ophthalmic use.

The active ingredient is 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluorotetradecane is a semifluorinated alkane. It has a molecular formula of $C_{14}H_{17}F_{13}$and a molecular weight of 432.26 g/mol. The chemical structure is:



Perfluorohexyloctane is practically immiscible with water. It is miscible with ethanol and most organic solvents.

Each multiple-dose, bottle contains 3 mL of perfluorohexyloctane, (b) (4) as a clear and colorless liquid. It does not contain any other ingredient or a preservatives.

QUALITY ASSESSMENT

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DESCRIPTION section		
Proprietary and established name(s)	Inadequate	Established name was not provided. See proposed revision above.
Dosage form(s) and route(s) of administration	Inadequate	Dosage form and route of administration is not provided. See proposed revision above.
If the active ingredient is a salt, apply the USP Salt Policy and include the equivalency statement per Salt Guidance and MAPP. For example: "TRADENAME contains 100 mg of drug-x (equivalent to 123.7 mg of drug-x hydrochloride)"	N/A	
List names of all inactive ingredients. Use USP/NF names in alphabetical order. Avoid brand names.	N/A	There are no inactive ingredients in the product.
For parenteral injectable dosage forms, include the name and quantities of all inactive ingredients. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect.	N/A	
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	N/A	
Sterility statement (if applicable)	Adequate	Word sterile is indicated. See revised recommendation above.

Pharmacological/Therapeutic class	Adequate	Was not included. Recommend including for topical ophthalmic use. See revised description.
Chemical name, structural formula, molecular weight	Adequate	It is specified.
If radioactive, statement of important nuclear characteristics.	N/A	
Other important chemical or physical properties (such as pKa or pH)	N/A	It is a single component product. There are no inactive ingredients.

Section 11 (DESCRIPTION) Continued

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
For oral prescription drug products, include gluten statement (if applicable)	N/A	
Remove statements that may be misleading or promotional (e.g., "synthesized and developed by Drug Company X," "structurally unique molecular entity")	Adequate	Promotional statements are not included in the revised proposed description.
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled. Note the labeling requirement may be applicable to another section of the PI (e.g., Section 2).	N/A	

1.2.4 Section 16 (HOW SUPPLIED/STORAGE AND HANDLING)

Current Description:

(b) (4)

Recommend Revising to:

HOW SUPPLIED/STORAGE AND HANDLING

<TRADENAME> (perfluorohexyloctane ophthalmic solution), (b) (4) is supplied as a sterile, clear, colorless liquid in a multiple-dose 5 mL polypropylene bottles with dropper tips and screw caps, packaged in a carton. – NDC 24208-377-05

Storage

Store <TRADENAME> at 20ºC to 25ºC (68ºF to 77ºF); (b) (4)

After opening, <TRADENAME> can be used until the expiration on the bottle.

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
HOW SUPPLIED/STORAGE AND HANDLING section		
Available dosage form(s)	Inadequate	Recommend revising – see above.
Strength(s) in metric system	Inadequate	Recommend revising – see above.
Available units (e.g., bottles of 100 tablets)	Adequate	
Identification of dosage forms (e.g., shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable); Include NDC(s)	Inadequate	Color and clarity are not described. Recommend revising – see above.
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	N/A	
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package.	Inadequate	Multiple dose container is not included which should be included. Recommend adding "for single-patient use" Recommend revising – see above.

Special handling about the supplied product (e.g., protect from light, refrigerate). If there is a statement to "Dispense in original container," provide reason why (e.g., to protect from light or moisture, to maintain stability, etc.). For hazardous drugs, state "DRUG X is a hazardous drug. Follow applicable special handling and disposal procedures.[x]" with x numerical citation to "OSHA Hazardous Drugs."	Adequate	No special precautions are required.

Section 16 (HOW SUPPLIED/STORAGE AND HANDLING) (Continued)

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature.	Adequate	
Latex: If product does not contain latex and manufacturing of product and container did not include use of natural rubber latex or synthetic derivatives of natural rubber latex, state: *"Not made with natural rubber latex. Avoid statements such as "latex-free."*	N/A	
Include information about child-resistant packaging	N/A	

1.2.5 Other Sections of Labeling

There may be other sections of labeling that contain product-quality related information. For example, there are specific required/recommended warnings for certain inactive ingredients [e.g., aspartame, aluminum in large and small volume parenteral, sulfites, FD&C Yellow Number 5 (tartrazine), and benzyl alcohol]. Please notify the prescription drug review division if the product contains any of these inactive ingredients.

Please include your comments about other sections of labeling if they contain product quality information.

1.2.6 Manufacturing Information After Section 17 (for drug products)

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Manufacturing Information After Section 17		
Name and location of business (street address, city, state, and zip code) of the manufacturer, distributor, and/or packer	Adequate	Distributed by: Bausch & Lomb Americas Inc., Bridgewater, NJ 08807

2.0 PATIENT LABELING – There is no patient labeling provided.

Assessment of Product Quality Related Aspects of Patient Labeling (e.g., Medication Guides, Instructions for Use, Patient Information):

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Carton Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Established name[2]	N/A	
Special preparation instructions (If applicable)	N/A	
Storage and handling information (If applicable)	N/A	
If the product contains a desiccant, ensure the desiccant has a warning (e.g., "Do not eat.") and the size and shape of the desiccant differs from the dosage form.	N/A	
Active ingredient(s) (if applicable)	N/A	
Alphabetical listing of inactive ingredients (if applicable)	N/A	
Name and location of business (street address, city, state, and zip code) of manufacturer, distributor, and/or packer	N/A	

Any deficiencies should be listed at the end in the "ITEMS FOR ADDITIONAL ASSESSMENT."

3.0 CONTAINER AND CARTON LABELING

3.1 Container Labels

(Copy/paste or refer to a representative example of a proposed container)

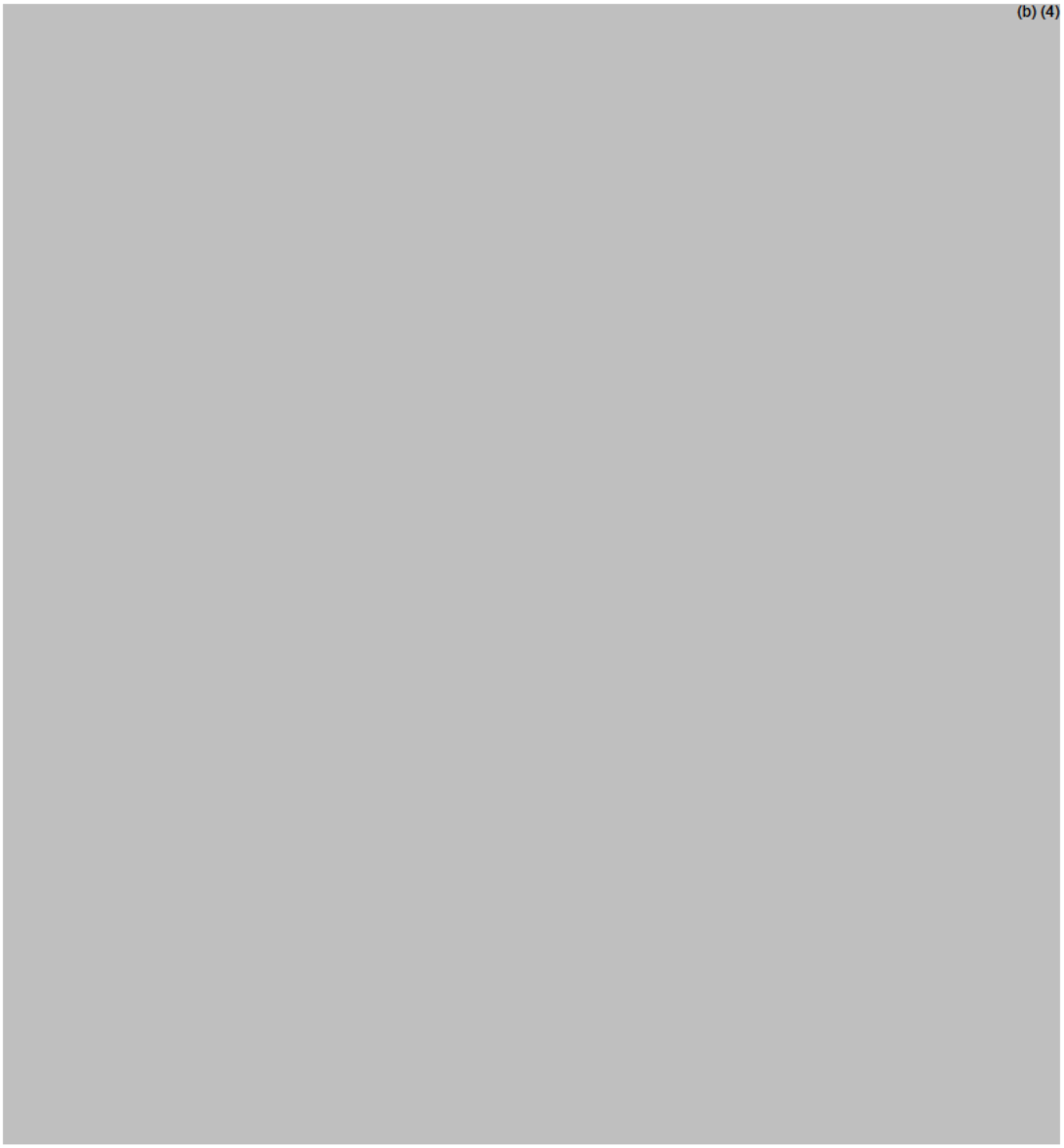
[2] Established name = [Drug] [Route of Administration] [Dosage Form]

(b) (4)

3.2 Carton Labeling

(Copy/paste or refer to a representative example of a proposed carton labeling)

(b) (4)



Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Carton Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Established name[3], (font size and prominence)	Inadequate	Change to: (perfluorohexyloctane) ophthalmic solution, (b) (4)
Strength(s) in metric system	Adequate	(perfluorohexyloctane) (b) (4)
Route(s) of administration	Adequate	For Topical Ophthalmic Solution.
If the active ingredient is a salt, include the equivalency statement per Salt Guidance and MAPP.	N/A	
Net contents (e.g., tablet count, volume of liquid)	Adequate	3 mL is indicated.
"Rx only" displayed on the principal display	Adequate	"Rx Only" is displayed.
NDC	Adequate	It is displayed.
Lot number and expiration date	Adequate	Space is designated.
Storage conditions. If applicable, include a space on the carton labeling for the user to write the new beyond-use-date (BUD).	Adequate	
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package, and these products require a "Not for direct infusion" statement.	Inadequate	"Multiple Dose Container" is not included. It should be included on PDP.

[3] Established name = [Drug] [Route of Administration] [Dosage Form]

For parenteral injectable dosage forms, include the name and quantities of all active and inactive ingredients in alphabetical order. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect.	Inadequate	There are no inactive ingredients in the product. The carton indicates that " Each mL contains Active perfluorohexyloctane (b) (4) g/mL" This is incorrect. It should be revised to: Contains: 3 mL perfluorohexyloctane, (b) (4)
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	N/A	
Linear Bar code	Adequate	

QUALITY ASSESSMENT

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Carton Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Name of manufacturer/distributor /packer	Adequate	
If there is a Medication Guide, must include a statement about dispensing a Medication Guide to each patient.	N/A	
No text on Ferrule and Cap Overseal unless a cautionary statement is required.	N/A	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled.	N/A	
When a drug product differs from the relevant USP standard of strength, quality, or purity, as determined by the application of the tests, procedures, and acceptance criteria set forth in the relevant compendium, its difference shall be plainly stated on its label.	Choose an item.	
And others if space is available.	N/A	

Assessment of Carton and Container Labeling: *Inadequate*

ITEMS FOR ADDITIONAL ASSESSMENT (Deficiencies)

1. In the highlights of prescribing information
   - Revise the statement "<TRADENAME> (b) (4) to "<TRADENAME>(perfluorohexyloctane ophthalmic solution) (b) (4)".
   - Include route of administration "for topical ophthalmic use", after the trademark and established name.

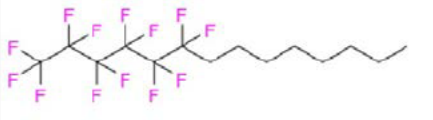
2. Revise the Dosage Forms and Strengths statement in Highlight section to: "Ophthalmic solution; containing perfluorohexyloctane, 100% (3mL)".

3. Revise section 3, DOSAGE FORMS AND STRENGTHS, to: "Ophthalmic solution; containing clear, colorless, and sterile perfluorohexyloctane, 100% (3mL)".

4. Revise section 11, "Description" as follows:

"<TRADENAME> >(perfluorohexyloctane ophthalmic solution), (b) (4) is a sterile liquid containing 100% perfluorohexyloctane, for topical ophthalmic use.

The active ingredient is 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluorotetradecane is a semifluorinated alkane. It has a molecular formula of $C_{14}H_{17}F_{13}$and a molecular weight of 432.26 g/mol. The chemical structure is:



Perfluorohexyloctane is practically immiscible with water. It is miscible with ethanol and most organic solvents.

Each multiple-dose, bottle contains 3 mL of perfluorohexyloctane, (b) (4) as a clear and colorless liquid. (b) (4)

5. Revise the "How supplied section" as follows:

<TRADENAME> (perfluorohexyloctane ophthalmic solution), (b) (4) is supplied as a sterile, clear, colorless liquid in a multiple-dose 5 mL polypropylene bottles with dropper tips and screw caps, packaged in a carton. – NDC 24208-377-05

6. Revise the established name in the container label from (b) (4) to (perfluorohexyloctane ophthalmic solution) (b) (4).

7. Revise the carton label as follows:
   - the established name from (b) (4) to (perfluorohexyloctane ophthalmic solution), (b) (4).
   - Add "Multiple-dose container" in principle display panel (PDP), below the route of administration.
   - Revise statements, "**Each mL contains**: **Active**: perfluorohexyloctane (b) (4)" to " **Contains**: 3 mL perfluorohexyloctane (b) (4)".

Overall Assessment and Recommendation:

The labeling related to product quality should be revised, as indicated above. Currently there are many missing or incorrect statements in the labeling.

Primary Labeling Assessor Name and Date:

Ravindra K Kasliwal, Ph.D. *3/1/2023*
Review Chemist, Branch-6, DNDP-3, ONDP, OPQ

Secondary Assessor

Chunchun Zhang, Ph.D. *3/1/2023*
SPQA, Branch-6, DNDP-3, ONDP, OPQ

Ravindra Kasliwal

Digitally signed by Ravindra Kasliwal
Date: 3/01/2023 07:46:31AM
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Chunchun Zhang

Digitally signed by Chunchun Zhang
Date: 3/01/2023 07:52:16AM
GUID: 51269608000064178e75377202fe6c5d

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/s/

CHUNCHUN N ZHANG
03/02/2023 12:18:16 PM