CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

210821Orig1s000

PRODUCT QUALITY REVIEW(S)

QUALITY ASSESSMENT

Recommendation: Approval

NDA 210821
Review # 2
Mar 1, 2019

Drug Name/Dosage Form	***Tetracaine hydrochloride Ophthalmic Solution USP***
Strength	*0.5%*
Route of Administration	*Topical ophthalmic*
Rx/OTC Dispensed	*Rx*
Applicant	*Valeant Pharmaceuticals*
US agent, if applicable	*NA*

SUBMISSION(S) REVIEWED	DOCUMENT DATE
Resubmission	*2/25/2019*

Quality Review Team

DISCIPLINE	PRIMARY REVIEWER	SECONDARY REVIEWER
Application Technical Lead	Chunchun Zhang	NA
Drug Substance	Rajan Pragani	Su (Suong) Tran
Drug Product	Shrikant Pagay	Balajee Shanmugam
Microbiology	Renee Marcsisin	Jess Wells
Biopharmaceutics	Qi Zhang	Jing Li
Process	Lixia Cai	Dan Obrzut
Facility	Lixia Cai	Dan Obrzut
Regulatory Business Process Manager	Kristine Leahy	NA
ORA Lead	Caryn McNabb	NA
Laboratory (OTR)	NA	NA
Environmental Assessment (EA)	Shrikant Pagay	Balajee Shanmugam

Quality Review Data Sheet

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

DMF #	Type	Holder	Item Referenced	Status[1]	Date Review Completed	Comments
(b) (4)	Type II	(b) (4)	Tetracaine hydrochloride drug substance	Adequate	1/2/2019	LoA: 6/15/2017 Reviewed by Erin Skoda
	Type III		(b) (4)	NA		LoA: 8/30/2017
	Type III			NA		LoA: 8/17/2017
	Type III			NA		LoA: 8/17/2017
	Type III			NA		LoA: 8/17/2017
	Type III			NA		LoA: 9/8/2017
	Type III			NA		LoA: 8/17/2017
	Type III			NA		LoA: 8/17/2017

[1]NA (There is enough data in the application, therefore the DMF did not need to be reviewed).

B. Other Documents: *IND, RLD, or sister applications*

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NA		

2. CONSULTS

NA

Executive Summary

I. Recommendations and Conclusion on Approvability

Drug substance, drug product, biopharmaceutics, manufacturing process and quality micro reviewers have recommended approval of NDA 210821 as documented in IQA #1 dated 11/2/2018.

The drug product manufacturing facility, Bausch & Lomb at Tampa, FL (FEI: 1000113778) is classified as NAI based on the recent inspection ending Jan 30, 2019. The Office of Process and Facilities has issued an overall acceptable recommendation for all the facilities on Feb 28, 2019. Therefore, NDA 210821 is recommended for APPROVAL from the Product Quality perspective.

Labeling recommendations from the Product Quality perspective were provided to the OND PM for consideration during the original NDA review cycle.

II. Summary of Quality Assessments

A. Product Overview

Proposed Indication(s) including Intended Patient Population	For the treatment of procedures requiring a rapid and short-acting topical ophthalmic anesthetic, in pediatric and adult patients.
Duration of Treatment	One drop topically in the eye(s) as needed. See package insert for the recommended dosage in patients.
Maximum Daily Dose	As above (see the package insert for details).
Alternative Methods of Administration	NA

B. Quality Assessment Overview

i. Drug Substance Quality Summary

The drug substance, tetracaine hydrochloride, is a white to almost white crystalline powder. It is manufactured by (b) (4). The drug substance referenced in DMF (b) (4) was found adequate by Erin Skoda on 1/2/2019.

ii. Drug Product Quality Summary

Refer to IQA #1 dated 11/2/2018 for the detailed discussion. The expiration date of 24 months is granted when stored at (b) (4) 25 °C. The storage statement is "Store at (b) (4) 25 °C (b) (4) 77 °F). Protect from light." and was finalized at original NDA review cycle.

The drug product manufacturing site Bausch & Lomb at Tampa, FL (FEI: 1000113778) is classified as NAI from the outcome of the recent inspection ending 1/30/2019. All the other facilities are acceptable based on the profile. Therefore, the overall recommendation of "Approval" was entered for the NDA into Panorama by OPF on 2/28/2019.

C. Special Product Quality Labeling Recommendations (NDA only)

NA

D. Final Risk Assessment (see Attachment)

I. From Initial Risk Identification			Review Assessment		
Attribute/CQA	Factors that can impact the CQA	Initial Risk Ranking	Risk Mitigation Approach	Final Risk Eval.	Lifecycle Considerations Comments
Sterility	Formulation Container closure[1] Process parameters Scale/equipment Site	H	Sterilization has been validated.	L	Post-approval stability protocol will test sterility.
Endotoxin Pyrogen	Formulation Container closure[1] Process parameters Scale/equipment	L	This is a topical product and therefore does not require testing for endotoxin.	L	No endotoxin testing required.
Assay (API), stability	Formulation Container closure[1] Raw materials	L	Robust analytical method validated for assay; no trend on stability; levels remain within the proposed specification. Label claim will be delivered.	L	
Assay (preservative)	Formulation Container closure[1] Process parameters Scale/equipment	L	Preservative chlorobutanol is added in the formulation.	L	

Uniformity of Dose (Fill Vol/ Deliverable volume)	Formulation Container closure[1] Process parameters Scale/equipment	**M**	A colorless to slightly yellow ophthalmic solution. A fill volume of 15mL in a 15mL LDPE bottle.	**L**	
pH	Formulation Container closure[1] Process parameters Scale/equipment	**L**	(b) (4) formulation; No trend on stability observed. Impact on other quality attributes is very minimal.	**L**	
Particulate matter	Formulation Container closure[1] Process parameters Scale/equipment	M	Particulate matter test was included in the drug product specification, comply with USP <789>.	L	

[1]Stability studies demonstrate container closure compatibility with the drug product for all quality attributes.

This NDA is recommended for Approval from the Product Quality perspective.

On behalf of the OPQ team
Chunchun Zhang, Ph.D. ATL for NDA 210821

FACILITIES

Product Background: Ophthalmic solution for topical ophthalmic anesthetic application
NDA/ANDA: N210821
Drug Product Name/Strength: Tetrcaine Hydrochloride Ophthalmic Solution USP, 0.5%
Route of Administration: Ophthalmic

Review Summary:
The manufacturing and testing sites considered in this review, and the acceptability of the sites from a facilities assessment standpoint, are summarized below.

(b) (4)

Bausch & Lomb, Incorporated

Location: 8500 Hidden River Parkway, Tampa, FL 33637 FEI 1000113778.
Function: DP manufacture, testing, and packaging, incoming DS and excipients quality release for use in formulation (profile SLQ)
Review Conclusion:
A pOAI alert was issued for this DP site during a (10Aug2018) inspection of the manufacturing facility, our field investigator observed objectionable conditions at the facility and conveyed that information to the representative of the facility at the close of the inspection.
A Follow up inspection was finished on 30Jan2019 with an final recommendation of NAI with a few verble observations. Based on the resolution of the observations from the inspection on 10Aug2018 is satisfactory, the the recommendation has been updated from "Withhold Approval" to "Approve".
Review Conclusion: Acceptable from a facilities assessment standpoint.

(b) (4)

(b) (4)

CONCLUSION: Subject NDA210821 (RESUB) is recommended for Approval from a facilities assessment standpoint.

List Submissions being reviewed
NDA 210821 (Sequence 0001, received 02/20/2018)
NDA 210821-ORIG-1-RESUB-11 (received 02/25/2019)
Highlight Key Outstanding Issues from Last Cycle: Facility "Withhold Approval" due to OAI classification issued to facility, Bausch & Lomb, Incorporated, FEI 1000113778 (was reclassified to NAI after reinspection).
Concise Description Outstanding Issues Remaining: None

3.2.S.2 Manufacture

(b) (4)

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Bausch & Lomb, Inc. is currently approved for U.S. distribution of multiple ophthalmic solution products, (b) (4) The subject NDA proposes the product has been commercially manufactured as an unapproved drug and distributed by Bausch & Lomb, Inc. on the market for more than 20 years.

Conclusion

Based on the most updated compliance record and District Office recommendation, the firm has been produced the product since 1991 and obtained previous approvals for U.S. distribution of numerous ophthalmic solution products, the firm has demonstrated that it has the facilities, equipment, personnel and expertise required for DP production as described in the subject NDA. Bausch & Lomb, Inc. is recommended for **Approval** for Tetracaine Hydrochloride Ophthalmic Solution 0.5% DP manufacture from the standpoint of facilities assessment.

Comparability Protocols

Reviewer's Assessment: N/A

Post-Approval Commitments (For NDA only)

Reviewer's Assessment: N/A

Lifecycle Management Considerations

None

List of Deficiencies:

02/27/2019: None

Primary Facilities Reviewer Name and Date:
Lixia Cai, Chemist OPQ/OPF/DPA III/PABVII, 09/25/2018, 02/27/2019
Secondary Reviewer Name and Date:
Daniel L. Obrzut, Chemist OPQ/OPF/DPA III/PABVII, 9/26/2018, 2/28/2019

Lixia Cai

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Daniel Obrzut

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Chunchun Zhang

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QUALITY ASSESSMENT

Recommendation: Complete Response

NDA 210821
Review # 1
Nov 2, 2018

Drug Name/Dosage Form	***Tetracaine hydrochloride Ophthalmic Solution USP***
Strength	*0.5%*
Route of Administration	*Topical ophthalmic*
Rx/OTC Dispensed	*Rx*
Applicant	*Valeant Pharmaceuticals*
US agent, if applicable	*NA*

SUBMISSION(S) REVIEWED	DOCUMENT DATE
Original	*2/22/2018*
Amendment	*4/6/2018*
Amendment	*7/26/2018*
Amendment	*8/1/2018*
Amendment	*8/23/2018*
Amendment	*9/4/2018*
Amendment	*10/25/2018*

Quality Review Team

DISCIPLINE	PRIMARY REVIEWER	SECONDARY REVIEWER
Application Technical Lead	Chunchun Zhang	NA
Drug Substance	Rajan Pragani	Su (Suong) Tran
Drug Product	Shrikant Pagay	Balajee Shanmugam
Microbiology	Renee Marcsisin	Jess Wells
Biopharmaceutics	Qi Zhang	Jing Li
Process	Lixia Cai	Dan Obrzut
Facility	Lixia Cai	Dan Obrzut
Regulatory Business Process Manager	Kristine Leahy	NA
ORA Lead	Caryn McNabb	NA
Laboratory (OTR)	NA	NA
Environmental Assessment (EA)	Shrikant Pagay	Balajee Shanmugam

Quality Review Data Sheet

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

DMF #	Type	Holder	Item Referenced	Status[1]	Date Review Completed	Comments
(b) (4)	Type II	(b) (4)	Tetracaine hydrochloride drug substance (b) (4)	Adequate	9/21/2018	LoA: 6/15/2017 Rajan Pragani
	Type III			NA		LoA: 8/30/2017
	Type III			NA		LoA: 8/17/2017
	Type III			NA		LoA: 8/17/2017
	Type III			NA		LoA: 8/17/2017
	Type III			NA		LoA: 9/8/2017
	Type III			NA		LoA: 8/17/2017
	Type III			NA		LoA: 8/17/2017

[1]NA (There is enough data in the application, therefore the DMF did not need to be reviewed).

B. Other Documents: *IND, RLD, or sister applications*

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NA		

2. CONSULTS

DISCIPLINE	STATUS	RECOMMENDATION	DATE	REVIEWER
Biostatistics	NA			
Pharmacology/Toxicology	NA			
CDRH	NA			
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 micro, manufacturing process, and biopharmaceutics aspects.

At the current time, GMP inspection of the manufacturing facilities supporting the NDA application indicates lack of compliance and OPF has issued an overall recommendation of "Withhold". In particular, the compliance status of the drug product manufacturing facility, Bausch & Lomb (FEI 1000113778), was found unacceptable and the Office of Compliance further confirmed the OAI classification through email communication on 11/1/2018. In agreement with the above recommendation, NDA 210821 is recommended for Complete Response from Product Quality perspective.

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

The following CR statement about the unacceptable manufacturing facility (Bausch & Lomb) should be included in the CR letter:

During a recent inspection of the Bausch & Lomb (FEI 1000113778) manufacturing facility for this NDA, our field investigator observed objectionable conditions at the facility and conveyed that information to the representative of the facility at the close of the inspection. Satisfactory resolution of the observations is required before this NDA may be approved.

II. Summary of Quality Assessments

A. Product Overview

Proposed Indication(s) including Intended Patient Population	For the treatment of procedures requiring a rapid and short-acting topical ophthalmic anesthetic, in pediatric and adult patients.
Duration of Treatment	One drop topically in the eye(s) as needed. See package insert for the recommended dosage in patients.
Maximum Daily Dose	As above (see the package insert for details).
Alternative Methods of Administration	NA

B. Quality Assessment Overview

i. Drug Substance Quality Summary

The drug substance, tetracaine hydrochloride, is a white to almost white crystalline powder. It is manufactured by (b) (4). The drug substance referenced in DMF (b) (4) was found adequate by Rajan Pragani on 9/21/2018.

ii. Drug Product Quality Summary

Tetracaine Hydrochloride Ophthalmic Solution USP, 0.5%, an ester local anesthetic, is indicated for procedures requiring a rapid and short-acting topical ophthalmic anesthetic, in pediatric and adult patients. The drug product is packaged as 15 mL fill in multi-dose 15 cc low density polyethylene bottles using linear low-density polyethylene tips and 15 mm polypropylene closure. Each vial is packaged in an individual carton with a package insert.

The drug product has been marketed since 1992. All excipients used in the formulation are adequately qualified. No novel excipients are used in the formulation. There are (b) (4) of preservatives chlorobutanol used in the formulation which have been used since 1992. The drug product specification includes tests for appearance, identity, assay, impurities (specified, unspecified and total), chlorobutanol assay, pH, osmolality, water loss, sterility, particulate matter, antimicrobial effectiveness, and minimum fill volume. Evaluation of the risk assessment of the elemental impurities was performed and indicates the results are lower than the permitted daily exposure (PDE) as noted in ICH Q3D guidance. Extractable and one-time leachable studies were performed, per the agency's recommendation, the applicant has committed to provide leachable data for 3 batches placed under the long-term storage condition through the proposed expiry period in the amendment dated 10/25/2018. The updated specification was submitted on 10/25/2018 with the revised limits on the chlorobutabol assay. All analytical methods are described in reasonable detail and have been adequately validated, particularly the method ((b) (4)) for assay and related substances was found acceptable by OTR on 10/24/2018.

Batch analyses are provided for 5 primary stability batches for the commercial fill configuration manufactured at the commercial site Bausch & Lomb at Tampa, FL. All batches complied with the proposed specification.

The applicant has submitted 5 primary stability batches with 24 months stability data when stored at long term storage condition, three batches were tested under 25°C/40%RH while the other two batches were tested under 25°C/60%RH. All the batch sizes are commercial scale ((b) (4)). No accelerated study was performed. All the quality attributes remain within the proposed specifications. Therefore, the expiration date of 24 months is granted when stored at (b) (4) 25 °C.

The storage statement is "Store at (b) (4) 25 °C (b) (4) 77 °F). Protect from light." and will be finalized at the OND's labeling meeting.

The proposed drug product manufacturing process consists of: (b) (4)

This 505(b)(2) NDA relies for approval on the literature-based clinical data to support the safety and effectiveness of the proposed product. Biopharmaceutics reviewer Dr. Zhang has found the bridge between the proposed drug product and those used in the literature studies has been established.

OPF has issued a withhold recommendation for the drug product manufacturing site Bausch & Lomb at Tampa, FL (FEI: 1000113778) from the outcome of the recent inspection; the Office of Compliance further confirmed the OAI classification through email communication on 11/1/2018. All the other facilities are acceptable based on the profile. Therefore, the overall recommendation of "withhold" was entered for the NDA into Panorama by OPF on 9/17/2018.

C. Special Product Quality Labeling Recommendations (NDA only)

NA

D. Final Risk Assessment (see Attachment)

I. From Initial Risk Identification			Review Assessment		
Attribute/CQA	Factors that can impact the CQA	Initial Risk Ranking	Risk Mitigation Approach	Final Risk Eval.	Lifecycle Considerations Comments
Sterility	Formulation Container closure[1] Process parameters Scale/equipment Site	H	Sterilization has been validated.	L	Post-approval stability protocol will test sterility.

Endotoxin Pyrogen	Formulation Container closure[1] Process parameters Scale/equipment	L	This is a topical product and therefore does not require testing for endotoxin.	L	No endotoxin testing required.
Assay (API), stability	Formulation Container closure[1] Raw materials	L	Robust analytical method validated for assay; no trend on stability; levels remain within the proposed specification. Label claim will be delivered.	L	
Assay (preservative)	Formulation Container closure[1] Process parameters Scale/equipment	L	Preservative chlorobutanol is added in the formulation.	L	
Uniformity of Dose (Fill Vol/ Deliverable volume)	Formulation Container closure[1] Process parameters Scale/equipment	M	A colorless to slightly yellow ophthalmic solution. A fill volume of 15mL in a 15mL LDPE bottle.	L	
pH	Formulation Container closure[1] Process parameters Scale/equipment	L	(b) (4) formulation; No trend on stability observed. Impact on other quality attributes is very minimal.	L	
Particulate matter	Formulation Container closure[1] Process parameters Scale/equipment	M	Particulate matter test was included in the drug product specification, comply with USP <789>.	L	

[1]Stability studies demonstrate container closure compatibility with the drug product for all quality attributes.

This NDA is recommended for Complete Response from the Product Quality Perspective.

On behalf of the OPQ team
Chunchun Zhang, Ph.D. ATL for NDA 210821

Rajan Pragani

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Su (Suong) Tran

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BIOPHARMACEUTICS

NDA: 210821
Submission Type: 505(b)(2) Type 5-New Formulation
Drug Product Name/Strength: Tetracaine Hydrochloride Ophthalmic Solution USP, 0.5%.
Dosage Form: Ophthalmic Solution
Route of Administration: Ophthalmic
Applicant Name: Valeant Pharmaceuticals Ireland (Agent for Applicant: Paragon BioTeck Inc.)
Intended Use: An ester local anesthetic indicated for procedures requiring a rapid and short-acting topical ophthalmic anesthetic
Listed Drug (LD): Tetracaine Hydrochloride Ophthalmic Solution 0.5% STERI-UNIT® [NDA 208135, Alcon Research, Ltd]

REVIEW SUMMARY

This 505(b)(2) NDA relies for approval on the literature-based clinical data to support the safety and effectiveness of the proposed Tetracaine Hydrochloride Ophthalmic Solution USP, 0.5%. The Listed Drug (LD) is Tetracaine Hydrochloride Ophthalmic Solution 0.5% STERI-UNIT® [NDA 208135, Alcon Research, Ltd].

The bridge between the proposed drug product and those used in the literature studies has been established. The proposed drug product has been used in clinical since 1992, which further supported the efficacy and safety of the proposed drug product. Refer to the Clinical Review for further details. Refer to the Drug Product Reviews for additional CMC information. Refer to the FDA recommended labeling for guidelines on safe and effective use of the proposed drug product.

RECOMMENDATION: ADEQUATE

From the Biopharmaceutics perspective, NDA 210821 for Tetracaine Hydrochloride Ophthalmic Solution USP, 0.5%, is recommended for **APPROVAL**.

SIGNATURES

Primary Biopharmaceutics Reviewer Name and Date:
Qi Zhang, PhD **10/25/2018**
Division of Biopharmaceutics
Office of New Drug Products, OPQ

Secondary Biopharmaceutics Reviewer Name and Date:
Jing Li, PhD **10/25/2018**
Division of Biopharmaceutics
Office of New Drug Products, OPQ

Qi Zhang

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Jing Li

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MICROBIOLOGY

Product Background: For procedures requiring a rapid and short-acting topical ophthalmic anesthetic

NDA: 210821

Drug Product Name/Strength: Tetracaine Hydrochloride Ophthalmic Solution USP, 0.5%

Route of Administration: Topical ocular

Applicant Name: Valeant Pharmaceuticals Ireland

Manufacturing Site: Bausch & Lomb, Inc., 8500 Hidden River Parkway, Tampa, FL 33637

Method of Sterilization: (b) (4)

Review Recommendation: **Adequate**

Theme (ANDA only): **N/A**

Justification (ANDA only): **N/A**

Review Summary: **The drug product is** (b) (4)

List Submissions Being Reviewed: 02/22/2018, 07/26/2018

Highlight Key Outstanding Issues from Last Cycle: N/A

Remarks: Tetracaine Hydrochloride Ophthalmic Solution has been marketed in the United States as an unapproved drug since the 1960's. Bausch & Lomb has been commercially producing Tetracaine Hydrochloride Ophthalmic Solution USP, 0.5% since 1992. During that time, Bausch & Lomb tested the product in accordance with the USP monograph for Tetracaine Hydrochloride Ophthalmic Solution. The API, excipients, formulation, primary container closure system, and method of manufacture of the historical product are identical to the Tetracaine Hydrochloride Ophthalmic Solution USP, 0.5% described in this NDA.

Concise Description Outstanding Issues Remaining: N/A

Supporting Documents:

- **Microbiology reviews of NDA 018086/S-077 (018086s77.doc, dated 03/23/2016, and N018086S077MR02.doc, dated 06/20/2017)**
- **Microbiology review of NDA 208254 (N208254MR01.docx, dated 08/03/2017)**

List Number of Comparability Protocols (ANDA only): N/A

P.1 Description of the Composition of the Drug Product

- **Description of drug product** – a clear, colorless, sterile, preserved, ophthalmic solution with a fill volume of 15 ml in a 15 ml low-density polyethylene plastic dropper bottle with a low-density polyethylene dropper tip and white polypropylene cap

- **Drug product composition –**

Component	Formulation Quantity	Concentration (mg/ml)	Function	Quality Standard
Tetracaine Hydrochloride[1]	0.5%[2]	(b) (4)	Active Ingredient	USP
Chlorobutanol	0.4%[3]		Antimicrobial Preservative	NF
Boric Acid	(b) (4)		(b) (4)	(b) (4)
Edetate Disodium (b) (4)				USP
Potassium Chloride				USP
Hydrochloric Acid				NF
Sodium Hydroxide				NF
			(b) (4)	USP
(b) (4)				

- **Description of container closure system –**

Components		Description
Bottle	Size	15 ml
	Description	(b) (4) Low Density Polyethylene (LDPE), (b) (4)
	Manufacturer	(b) (4)
Tip	Size	15 mm
	Description	(b) (4) LDPE, (b) (4)
	Manufacturer	(b) (4)
Closure	Size	15 mm (b)
	Description	(b) (4) Polypropylene, (b) (4)
	Manufacturer	(b) (4)

Reviewer's Assessment: ***Adequate***

The applicant provided an adequate description of the drug product composition and the container closure system designed to maintain product sterility.

All the acceptance criteria were met.

A Appendices

A.2 Adventitious Agents Safety Evaluation

A.2.1 Materials of Biological Origin

A.2.2 Testing at Appropriate Stages of Production

A.2.3. Viral Testing of Unprocessed Bulk

A. 2.4 Viral Clearance Studies

Reviewer's Assessment: N/A

R Regional Information

Executed Batch Records

Executed lot #(s): 54753, 14659, 16471, 18428, 19847, and 27328

Reviewer's Assessment: *Adequate*

The batch records confirm that validated (b) (4) manufacturing processes were used for the manufacture of the exhibit batch.

Comparability Protocols- No CP was included in the application.

Reviewer's Assessment: N/A

2. REVIEW OF COMMON TECHNICAL DOCUMENT – QUALITY (CTD-Q) MODULE 1

2.A. Package Insert

Storage temperature: 15-25 °C (59 to 77 °F). Protect from light.
Route of administration: Topical
Container: Multi-dose
15 ml fill in a 15 ml bottle

The subject drug product is not reconstituted, diluted, and is not pharmacy bulk.

Reviewer's Assessment: *Adequate*

The package insert provides adequate instructions concerning the storage and administration of the subject drug product.

Post-Approval Commitments:

Reviewer's Assessment: N/A

List of Deficiencies: **None**

Primary Microbiology Reviewer Name and Date: **Renee A. Marcsisin, Ph.D., 07/31/2018**
Secondary Reviewer Name and Date (and Secondary Summary, as needed): **Jesse Wells, Ph.D., 07/31/2018**

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Renee Marcsisin

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Jesse Wells

Digitally signed by Jesse Wells
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