

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**217370Orig1s000**

**PRODUCT QUALITY REVIEW(S)**

**NDA 217370**

**From: Chunchun Zhang, ATL, OPQ/OPQII/DPQAIX**

**Date: Mar 20, 2025**

**Re: NDA 217370, Acotremone ophthalmic solution, 0.003%**

**Product quality final recommendation: Approval**

---

NDA 217370, Acotremone ophthalmic solution, 0.003% was originally recommended for Approval from product quality perspective, refer to IQA #1 on Jan 28, 2025. In order to comply with USP <771>, the agency asked the applicant to include the particulate matter test to comply with USP <790> for topical ophthalmic products. The revised drug product specifications were provided on Mar 18, 2025 and were found acceptable by the drug product reviewer Dr. Milton Sloan, refer to the Drug Product addendum dated Mar 20, 2025. All the other OPQ disciplines uphold the approval recommendations without any change. Therefore, NDA 217370 is recommended for approval from product quality perspective.

Chunchun Zhang, Ph.D.

ATL for 217370

**ADDENDUM**

DIVISION OF OPHTHALMOLOGY OFFICE OF SPECIALTY MEDICINE  
OFFICE OF NEW DRUGS CENTER FOR DRUG EVALUATION AND  
RESEARCH FOOD AND DRUG ADMINISTRATION

**DATE:** March 19, 2025

**TO:** **NDA #217370, Drug Product Review #1**

**THROUGH :** Chunchun Zhang, Ph.D., Sr. Pharm Quality Assessor,  
CDER/OPQ/OPQAII/DPQAIX

**FROM:** Milton J. Sloan, Ph. D., Sr. Chemist, CDER/OPQ/OPQAII/DPQAIX

**SUBJECT:** Drug Product review and assessment of Quality Amendment to NDA  
217370

**Agency Information Request (Mar 12, 2025)**

**Drug Product**

**1. We recommend as part of the drug product specification for particulate and foreign matter conformance with USP <790> for the topical ophthalmic solution. Refer to the current USP <771> Ophthalmic Products-Quality Tests for consistency with compendial methods and acceptance criteria. Revise the appropriate NDA section.**

**Applicant Response**

(b) (4)



(b) (4)

**Table 1 Release and Stability Specifications for Acoltremon Ophthalmic Solution 0.003%**

Test Description	Release Acceptance Criteria	Shelf-Life Acceptance Criteria
Description	Colorless liquid, essentially free of visible particles	
Clarity (NTU)	(b) (4)	
Identification of AR-15512 by HPLC Retention Time <sup>1</sup>	The retention time of the main peak in the sample's chromatogram corresponds to that of the AR-15512 reference standard's chromatogram.	Not Applicable
Identification of AR-15512 by DAD/UV Spectrum <sup>1</sup>	The UV spectrum of the main peak in the sample's chromatogram corresponds to that of the AR-15512 reference standard's chromatogram.	Not Applicable
pH	(b) (4)	
Osmolality (mOsm/kg)	280 – 330	
AR-15512 Content (% Label Claim)	(b) (4)	(b) (4)
AR-15512 Degradation Products (% w/w) (b) (4)	Not more than (b) (4)	
Unspecified Degradation Products <sup>2</sup>	Not more than (b) (4)	
Total Degradation Products	Not more than (b) (4)	
Minimum Fill Volume <sup>1</sup>	Meets the requirements of USP <755>  Stage 1 (n=10 units) Mean is not less than the labeled amount and no unit has < 90% labeled amount	





Milton  
Sloan

Digitally signed by Milton Sloan  
Date: 3/20/2025 10:37:08AM  
GUID: 508da72000029fa0e17abc24c6841f0a



Chunchun  
Zhang

Digitally signed by Chunchun Zhang  
Date: 3/20/2025 10:41:59AM  
GUID: 51269608000064178e75377202fe6c5d

-----  
**This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.**  
-----

/s/  
-----

CHUNCHUN N ZHANG  
03/20/2025 11:02:35 AM

## NDA Executive Summary

### 1. Application/Product Information

<b>NDA Number</b>	217370		
<b>Applicant Name</b>	Alcon Laboratories, Inc.		
<b>Drug Product Name</b>	Acoltremon ophthalmic solution		
<b>Dosage Form</b>	Solution		
<b>Proposed Strength(s)</b>	0.003%		
<b>NDA Classification</b>	Type 1 - NME		
<b>Route of Administration</b>	Ophthalmic		
<b>Maximum Daily Dose</b>	(b) (4)		
<b>Rx/OTC Dispensed</b>	Rx		
<b>Proposed Indication</b>	Treatment of the signs and symptoms of dry eye disease		
<b>Drug Product Description</b>	Acoltremon ophthalmic solution, 0.003% is a clear to slightly opalescent, colorless, sterile, preservative-free isotonic aqueous solution and packaged in a low-density polyethylene (LDPE) (b) (4) single-dose vial. Five single-dose vials (b) (4) are packaged together in an aluminum pouch.		
<b>Co-packaged product information</b>	NA		
<b>Device information</b>	Single dose (b) (4) vial. CDRH consult was determined to be not necessary on 6/6/2024.		
<b>Storage Temperature/ Conditions</b>	2°C to 8°C		
<b>Review Team</b>	<b>Discipline</b>	<b>Primary</b>	<b>Secondary</b>
	<i>Drug Substance</i>	Fardokht Abulwerdi	Zhengfu Wang

	<i>Drug Product/ Labeling</i>	Milton Sloan	Chunchun Zhang
	<i>Manufacturing</i>	Wenchun Feng	Sudipan Karmakar
	<i>Biopharmaceutics</i>	NA	NA
	<i>Microbiology</i>	David Quan	Yeissa ChabrierRosello
	<i>Other (specify)</i>	NA	
	<i>RBPM</i>	Shazma Aftab	
	<i>ATL</i>	Chunchun Zhang	
<b>Consults</b>	NA		

**2. Final Overall Recommendation - Approval**

**3. Action Letter Information**

**a. Expiration Dating:** The shelf life of 18 months for acoltremon ophthalmic solution is granted when stored at 2°C to 8°C.

**b. Additional Comments for Action:** NA

**4. Basis for Recommendation:**

**a. Summary of Rationale for Recommendation:**

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

*The product is regulated as a drug and device combination product per the Genus decision. CDRH confirmed that no CDRH consult was necessary on Jun 6, 2024.*

*OPMA issued an overall recommendation of “approval” on Jul 2, 2024. Therefore, NDA 217370 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.*

**b. Is the overall recommendation in agreement with the individual discipline recommendations? Yes**

**Recommendation by Subdiscipline:**

<b>Drug Substance</b>	-	<b>Adequate</b>
<b>Drug Product</b>	-	<b>Adequate</b>
<b>Quality Labeling</b>	-	<b>Adequate</b>
<b>Manufacturing</b>	-	<b>Adequate</b>
<b>Biopharmaceutics</b>	-	<b>N/A</b>
<b>Microbiology</b>	-	<b>Adequate</b>

**Environmental Assessment:** Categorical Exclusion - Adequate  
**QPA for EA(s):** No

**5. Life-Cycle Considerations**

**Established Conditions per ICH Q12:** No

**Comments:** NA

**Comparability Protocols (PACMP):** No

**Comments:** NA

**Additional Lifecycle Comments:** NA

***Application Technical Lead Name and Date:*** Chunchun Zhang, Ph. D., Jan 28, 2025

83 Page(s) have been Withheld in Full as b4 (CCI/TS)  
immediately following this page

# CHAPTER IV: LABELING

## [IQA NDA Assessment Guide Reference](#)

### 1.0 PRESCRIBING INFORMATION

#### Assessment of Product Quality Related Aspects of the Prescribing Information:

#### 1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

Item	Information Provided in the NDA	Assessor's Comments
<b>Product Title in Highlights</b>		
Proprietary name	Yes	Refer to DMEPA review
Established name(s)	Yes	
Route(s) of administration	Yes	
<b>Dosage Forms and Strengths Heading in Highlights</b>		
Summary of the dosage form(s) and strength(s) in metric system.	Yes	
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.	N/A	

(b) (4)



2

Item	Information Provided in the NDA	Assessor's Comments
<b>DOSAGE AND ADMINISTRATION section</b>		
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	

**Section 3 (DOSAGE FORMS AND STRENGTHS)**



Item	Information Provided in the NDA	Assessor's Comments
<b>DOSAGE FORMS AND STRENGTHS section</b>		
Available dosage form(s)	Yes	
Strength(s) in metric system	Yes	
If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance	N/A	
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, and imprinting	N/A	
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 labeling term (e.g., single-dose, multiple-dose, single-patient-use). Other package type terms include pharmacy bulk package and imaging bulk package.	N/A	Single-dose term is recommended.

**Section 11 (DESCRIPTION)**

(b) (4)



Item	Information Provided in the NDA	Assessor's Comments
<b>DESCRIPTION section</b>		
Proprietary and established name(s)	Yes	
Dosage form(s) and route(s) of administration	Yes	
If the active ingredient is a salt, apply the USP Salt Policy and include the equivalency statement per FDA Guidance.	N/A	
List names of all inactive ingredients. Use USP/NF names. Avoid Brand names.	Yes	
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	Single-dose term is recommended.
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	N/A	
Statement of being sterile (if applicable)	Yes	
Pharmacological/therapeutic class	Yes	
Chemical name, structural formula, molecular weight	Yes	
If radioactive, statement of important nuclear characteristics.	N/A	
Other important chemical or physical properties (such as pKa or pH)	Yes	

**Section 11 (DESCRIPTION) Continued**

Item	Information Provided in the NDA	Assessor's Comments
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")	N/A	

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



Item	Information Provided in the NDA	Assessor's Comments
<b>HOW SUPPLIED/STORAGE AND HANDLING section</b>		
Available dosage form(s)	Yes	
Strength(s) in metric system	Yes	
Available units (e.g., bottles of 100 tablets)	Yes	
Identification of dosage forms, e.g., shape, color, coating, scoring, imprinting, NDC number	N/A	
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.	N/A	

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

Item	Information Provided in the NDA	Assessor's Comments
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.)	None	
If the product contains a desiccant, ensure the size and shape differ from the dosage form and desiccant has a warning such as "Do not eat."	None	

Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature.	Yes. Based on the in-use and accelerated stability data, the patient may store the drug product at temperatures from 2°C - 25°C (36°F-77°F) for up to 30 days, and up to 7 of those 30 days may be outside of the secondary foil pouch container, i.e., only in the primary plastic container.	
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	

### 2.2.1 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 parenterals, sulfites, FD&C Yellow Number 5 (tartrazine), and benzyl alcohol]. Please notify the prescription drug 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.

### 2.2.2 Manufacturing Information After Section 17 (for drug products)

Item	Information Provided in the NDA	Assessor's Comments
<b>Manufacturing Information After Section 17</b>		
Name and location of business (street address, city, state and zip code) of the manufacturer, distributor, and/or packer	Yes	

## 2.0 PATIENT LABELING

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

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

## 3.0 CARTON AND CONTAINER LABELING



Item	Information Provided in the NDA	Assessor's Comments about Carton Labeling
Proprietary name, established name, and dosage form (font size and prominence)	Yes	
Dosage strength	Yes	
Route of administration	Yes	
If the active ingredient is a salt, include the equivalency statement per FDA Guidance	N/A	
Net contents (e.g. tablet count)	N/A	
"Rx only" displayed on the principal display	Yes	
NDC number	Yes	Space is reserved
Lot number and expiration date	Yes	Space is reserved
Storage conditions. If applicable, include a space on the carton labeling for the user to write the new BUD.	(b) (4)	
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use)	N/A	Single-dose term is recommended
Other package terms include pharmacy bulk package and imaging bulk package which require "Not for direct infusion" statement.	N/A	
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	N/A	
Bar code	Yes	

Item	Information Provided in the NDA	Assessor's Comments about Carton Labeling
Name of manufacturer/distributor	Yes	
Medication Guide (if applicable)	Yes	
No text on Ferrule and Cap over seal	Yes	
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.	N/A	
And others, if space is available	N/A	

**Assessment of Carton and Container Labeling:** *Adequate*

***Any deficiencies should be listed at the end in the “ITEMS FOR ADDITIONAL ASSESSMENT.”***

## **ITEMS FOR ADDITIONAL ASSESSMENT**

**None**

### ***Overall Assessment and Recommendation:***

The NDA is adequate for Approval from the Drug Product perspective.

*Primary Drug Product Assessor Name and Date:*

*Milton. J. Sloan, PhD,  
Sr. Chemistry Reviewer  
OPQ/ONDP/Div3/Branch 6*

*Secondary Assessor Name and Date (and Secondary Summary, as needed)*  
*Chunchun Zhang, Ph.D.,*  
*Quality Assessment Lead,*  
*OPQ/ONDP/Div3/Branch 6*



Milton  
Sloan

Digitally signed by Milton Sloan  
Date: 1/23/2025 10:24:25PM  
GUID: 508da72000029fa0e17abc24c6841f0a



Chunchun  
Zhang

Digitally signed by Chunchun Zhang  
Date: 1/24/2025 10:09:39AM  
GUID: 51269608000064178e75377202fe6c5d

66 Page(s) have been Withheld in Full as b4 (CCI/TS)  
immediately following this page

## CHAPTER VII: MICROBIOLOGY

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

<b>Product Information</b>	
<b>NDA Number</b>	217370
<b>Assessment Cycle Number</b>	01
<b>Drug Product Name/ Strength</b>	Acoltremon Ophthalmic Solution 0.003%
<b>Route of Administration</b>	Topical Ophthalmic
<b>Applicant Name</b>	Alcon Laboratories
<b>Therapeutic Classification/ OND Division</b>	CDER/OND/OSM/DO
<b>Manufacturing Site</b>	(b) (4)  France FEI: (b) (4)
<b>Method of Sterilization</b>	(b) (4)

**Assessment Recommendation: Adequate**

**Assessment Summary:**

**List Submissions Being Assessed (table):**

Document(s) Assessed	Date Received
Sequence 0001	05/30/2024
Sequence 0008	10/01/2024

**Highlight Key Issues from Last Cycle and Their Resolution: N/A**

**Remarks:** Topical Ophthalmic solution for the treatment of signs and symptoms of dry eye disease. Standard review. Non-complex drug product. This review includes microbiological quality information requests sent on 09/16/2024 and sponsor responses received on 10/01/2024.

**Concise Description of Outstanding Issues: None**

**Supporting Documents: None.**

### S DRUG SUBSTANCE

(b) (4) a product quality microbiology review of the drug substance is not reviewed.

**P.1 DESCRIPTION OF THE COMPOSITION OF THE DRUG PRODUCT**

Acoltremon Ophthalmic Solution 0.003% is a clear to slightly opalescent, colorless, sterile, preservative-free isotonic aqueous solution at a pH of approximately 7, packaged in a low-density polyethylene (LDPE) (b) (4) single-use (b) (4) vial. Each vial contains 0.4 mL of solution.

**Drug product composition**

Component	Function	Concentration	
		Quantity (mg/mL)	Quantity (% w/v)
Acoltremon (AR-15512)	Active Ingredient	(b) (4)	0.003
Hypromellose (b) (4)	(b) (4)	(b) (4)	
Polyoxyl 35 Castor Oil (b) (4)			
Sodium Dihydrogen Phosphate Dihydrate			
Sodium Chloride			
Sodium Hydroxide <sup>4</sup>	pH Adjuster	q.s. to pH 7	q.s. to pH 7
Purified Water	(b) (4)	(b) (4)	

**Container Closure System**

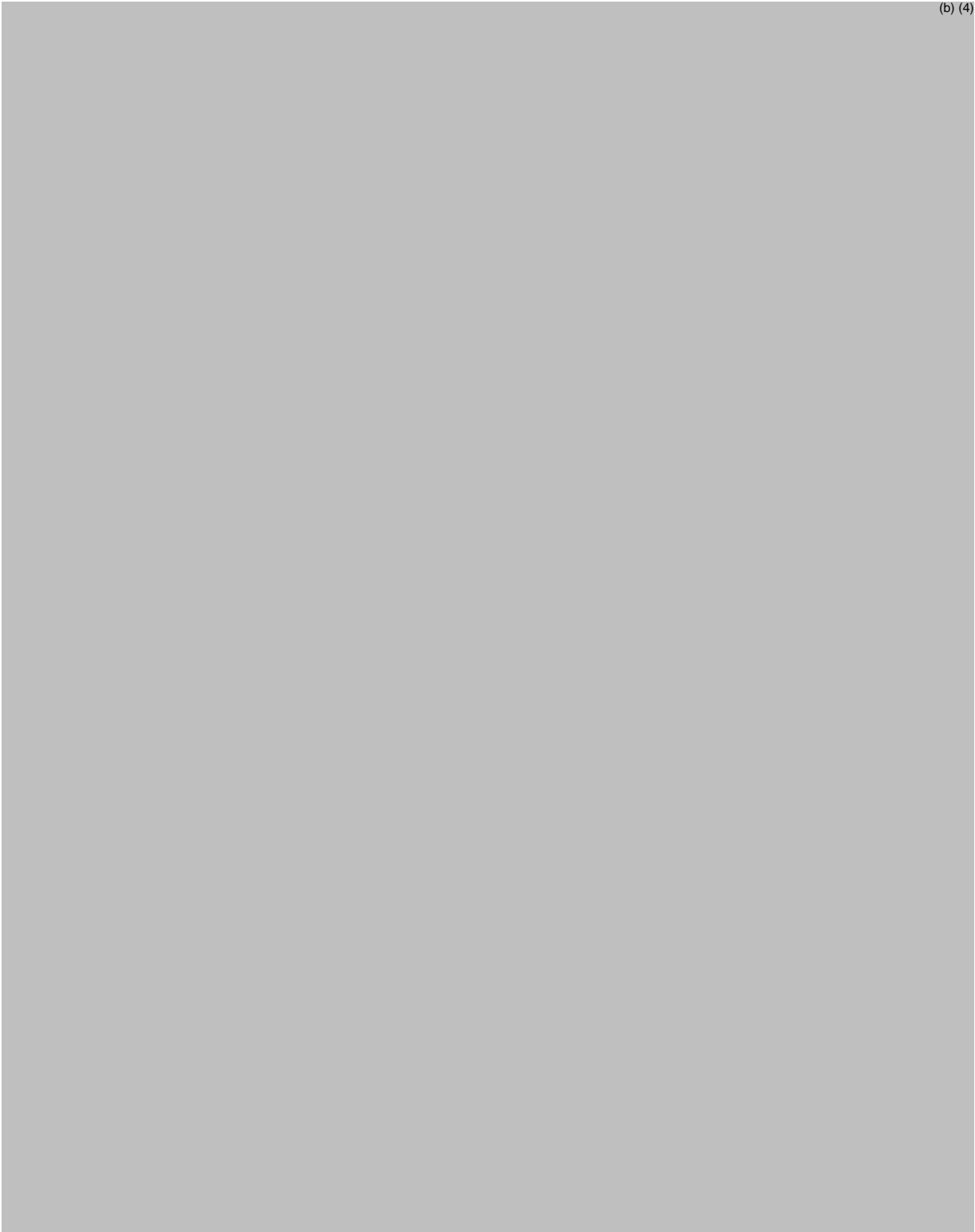
(source: seq0001, container-closure-system-(b) (4).pdf in eCTD 3.2.P.7)

Component	Description	Manufacturer
(b) (4)		

**Assessment: Adequate**

The information provided for the description of the drug product and the container closure system meet regulatory expectations.

## **P.2 PHARMACEUTICAL DEVELOPMENT**



(b) (4)



David  
Quan

Digitally signed by David Quan  
Date: 1/16/2025 01:34:05PM  
GUID: 653ff941000bf1cb71c860d4c33b4ffe



Yeissa  
Chabrier Rosello

Digitally signed by Yeissa Chabrier Rosello  
Date: 1/16/2025 01:36:52PM  
GUID: 5317ea990000ce969cecabfa83284493

-----  
**This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.**  
-----

/s/  
-----

CHUNCHUN N ZHANG  
01/28/2025 10:04:14 AM