CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

212905Orig1s000

PRODUCT QUALITY REVIEW(S)

NDA Executive Summary

1. Application/Product Information

NDA Number.	212905 Resubmission 3
Applicant Name	Verrica Pharmaceuticals, Inc.
Drug Product Name	YCANTH® (cantharidin)
Dosage Form.	Solution
Proposed Strength(s)	0.7%
Route of Administration	Topical
Maximum Daily Dose	AS prescribe and applied by a healthcare professional
Rx/OTC Dispensed	Rx
Proposed Indication	Treatment of molluscum contagiosum
Drug Product Description	The applicant, Verrica Pharmaceuticals, Inc. has resubmitted this 505(b)(1) new drug application for YCANTH® (cantharidin) Solution, 0.7% (b) (4) for topical administration for the treatment of molluscum contagiosum. The active ingredient, cantharidin is not a synthetic drug. I (b) (4) s produced by and isolated from several species of blister beetles. Cantharidin is a potent blister agent and is highly toxic if ingested. Cantharidin drug substance for this application (b) (4) . YCANTH is a slightly viscous, light violet to dark purple, topical solutio (b) (4) and will be applied to affected skin area only by healthcare professionals. Upon topical admini (b) (4) . Each mL of YCANTH contains 7mg of cantharidin as the active ingredient and acetone, camphor, castor oil, ethanol, gentian violet, hydroxypropyl cellulose, and nitrocellulose as inactive ingredients. The formulation also contains an

	oral deterrent (denatonium benzoate) to help mitigate the risk of accidental ingestion. YCANTH solution is supplied in a sealed glass ampule contained within a single-use applicator and enclosed in a protective paperboard sleeve. Each ampule of YCANTH contains approximately 0.45 mL of 0.7% cantharidin solution. A YCANTH Break Tool is co-packaged as (b) (4) per each carton of applicators. YCANTH should be stored at 20°C – 25°C (68°F – 77°F): excursion permitted from 15°C – 30°C (59°F to 87°F) [USP Controlled Room Temperature], protected from light. Based on the stability data provided in this application, an expiration dating period of 24 months is granted to this drug product.		
Co-packaged product information	A YCANTH Break Tool is co-packaged as (b) (4) per each carton of applicators		
Device information:	Description, performance attributes or N/A		
Storage Temperature/ Conditions	20°C – 25°C (68°F – 77°F): excursion permitted from 15°C – 30°C (59°F to 87°F) [USP Controlled Room Temperature], protected from light. °C		
Review Team	**Discipline**	**Primary**	**Secondary**
	Drug Substance	No updates were submitted N/A	N/A
	Drug Product/ Labeling	Zhengfang Ge, Ph.D.	Hamid Shafiei, Ph.D.
	Manufacturing	Mesfin Abdi, Ph.D.	Jean Tang, Ph.D.
	Biopharmaceutics	N/A	N/A
	Microbiology	Dustin Thomas, Ph.D.	Jesse Wells, Ph.D.
	Other (specify): Environmental Assessment	Zhengfang Ge, Ph.D.	Hamid Shafiei, Ph.D.
	RBPM	Melinda Bauerlien, M.S.	

	ATL	Hamid Shafiei, Ph.D.
Consults	N/A	

2. Final Overall Recommendation - Approval

This application is recommended for approval from the OPQ perspective with an expiration dating period of 24 months.

4. Basis for Recommendation:

a. Summary of Rationale for Recommendation:

This is the third class 2 resubmission for this application. The original application as well as the next two resubmissions received complete response due to inadequate facilities.

- The applicant of this 505(b)(1) new drug application has provided sufficient CMC information to assure the identity, purity, strength, and quality of the drug substance, cantharidin and the drug product, Trade Name (cantharidin) Solution, 0.7% (b) (4)) for topical use.
- The Office of Pharmaceutical Manufacturing Assessment has made the overall recommendation of adequate regarding the facilities involved in this application.
- The CMC issues on labels/labeling have been satisfactorily resolved in this review cycle.
- The applicant's request for categorical exclusion from the environmental assessment has been granted.

Therefore, this resubmission of this application is recommended for approval from the OPQ perspective with an expiration dating of 24 months.

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

Recommendation by Subdiscipline:

Drug Substance - Adequate
Drug Product - Adequate
Quality Labeling - Adequate
Manufacturing - Adequate
Biopharmaceutics - Adequate
Microbiology - Adequate

Environmental Assessment: Choose an item.
QPA for EA(s): Choose Yes or No.

5. Life-Cycle Considerations

Established Conditions per ICH Q12: No
Comments:

Comparability Protocols (PACMP): No
Comments:

Additional Lifecycle Comments: None

Hamid Shafiei

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Memorandum

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

Date: **May 31, 2023**

From: **Zhengfang Ge, Ph.D.**
Reviewer, ONDP/Division II/Branch IV

Through: **Hamid Shafiei, Ph.D.**
SPQAL, ONDP/Division II/Branch IV

To: **Labeling Review of NDA 212905: Ycanth (cantharidin) topical solution**

Subject: **Final Recommendation for Labeling/Labels**

The labeling review #1 has noted the following issues:

The following deficiencies in the carton/container labels were conveyed to the applicant

1. change (b) (4) mg to 0.7 mg in the "each 1 mL of solution contains (b) (4) mg cantharidin" on carton. The quantitative composition provided in section 3.2.P.1.2 is (b) (4) 0.7% (b) (4) This information should also be displayed on the applicator label.
2. Add lot number and expiration date on carton and container labels
3. Provide the amount of alcohol on applicator label

The following changes were implemented in the PI in sharePoint

1. The drug product name should be changed from "VP-102" to "Ycanth" throughout the labeling

Section 3 Dosage form:

2. The strength should be 0.7% (b) (4) a description of "each mL of solution contains 7 mg (0.7%) of cantharidin" should be added to describe the strength

Section 11 Description

3. Revise to “Topical solution, 0.7% each mL of solution contains 7 mg (0.7%) of cantharidin in a light violet to dark purple, slightly viscous liquid, free of visual particulates”
4. Enter (b) (4) for alcohol content, it should be displayed in terms of percent volume of absolute alcohol

5. Delete (b) (4)
6. Remove paragraphs for (b) (4)

Section 16 How Supplied

1. Change dosage form from “solution” to “topical solution”
2. delete (b) (4) from the strength.0.7%, add a descriptor “each mL of solution contains 7 mg (0.7%) of cantharidin”
3. Add drug product appearance “light violet to dark purple, slightly viscous liquid, free of visual particulates”
4. Change the storage condition to “Store at 20°C to 25°C (68° to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature, protect from light”

Evaluation of Revised Labeling/Labels

The revised container/carton labels are satisfactory and provided in the **Attachment**. The labeling review decision is pending due to ongoing negotiations with the applicant. There are only minor labeling deficiencies from the CMC perspective, and we expect the applicant will accept our recommendations. Refer to the CMC sections of the final approved labeling

Recommendation:

This NDA is **now** recommended for **Approval** from the labeling perspective.

Attachment:

Carton Label (6 count applicators and 2 break tools):

(b) (4)

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Zhengfang Ge

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Hamid Shafiei

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U.S. FOOD & DRUG ADMINISTRATION

RECOMMENDATION

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

NDA 212905
Assessment 3 (Resub 2)

Drug Product Name	YCANTH (cantharidin)
Dosage Form	Solution
Strength	0.7%
Route of Administration	Topical
Rx/OTC Dispensed	Rx
Applicant	Verrica Pharmaceuticals, Inc.
US agent, if applicable	N/A

Submission(s) Assessed	Document Date	Discipline(s) Affected
Class 2 Resubmissions 2	11/24/2021	All
General Correspondence	11/29/2021	All
Clinical Study Report	12/14/2021	Clinical
Human Factor Study Validation Report	01/07/2022	Clinical and DMEPA
Human Factor Study Related Report	01/28/2022	Clinical and DMEPA
Administrative Change	02/04/2022	All
Clinical Study Report/Human Factor	03/08/2022	Clinical and DMEPA

QUALITY ASSESSMENT TEAM

Discipline	Primary Assessor	Secondary Assessor
Drug Substance	Martin Haber, Ph.D. / Fredrich Burnett, Ph.D.	Donna Christner, Ph.D.
Drug Product	Zhengfang Ge, Ph.D.	Moo-Jhong Rhee, Ph.D. / Wendy Wilson-Lee, Ph.D.
Manufacturing	Youmin Wang, Ph.D.	Jean Tang, Ph.D. Yubing Tang, Ph.D.
Microbiology	Eric Adeeku, Ph.D.	Jesse Wells, Ph.D.

Biopharmaceutics	N/A	N/A
Regulatory Business Process Manager	Melinda Bauerlien, MS	
Application Technical Lead	Hamid Shafiei, Ph.D.	
Laboratory (OTR)	N/A	N/A
Environmental	Zhengfang Ge, Ph.D.	Moo-Jhong Rhee, Ph.D.

U.S. FOOD & DRUG ADMINISTRATION

EXECUTIVE SUMMARY

For more details about the items in this template, please see the Executive Summary chapter of the NDA IQA Guide

I. RECOMMENDATIONS AND CONCLUSION ON APPROVABILITY

- The applicant of this 505(b)(1) new drug application has provided sufficient CMC information to assure the identity, purity, strength, and quality of the drug substance, cantharidin and the drug product, Trade Name (cantharidin) Solution, 0.7% (b) (4) for topical use.
- The Office of Pharmaceutical Manufacturing Assessment has made the overall recommendation of "**withhold**" regarding the facilities involved in this application.
- The CMC issues on labels/labeling **have not** been satisfactorily resolved in this review cycle.
- The applicant's request for categorical exclusion from the environmental assessment has been granted.

Therefore, from the OPQ perspective, this NDA **is not** recommended for **approval** in its present form per 21 CFR 314.125(b)(6),(13).

II. SUMMARY OF QUALITY ASSESSMENTS

A. Product Overview

The applicant, Verrica Pharmaceuticals, Inc. has resubmitted this 505(b)(1) new drug application for YCANTH® (cantharidin) Solution, 0.7% (b) (4) for topical administration for the treatment of molluscum contagiosum on November 24, 2021. This is the second class 2 resubmission of this application. This application was originally submitted on September 13, 2019 and resubmitted as a class 2 resubmission on December 23, 2020 and received the complete response (CR) on July 13, 2020 and on September 16, 2021, respectively. The resubmission dated December 23, 2020 received the CR due to inadequate manufacturing facilities.

YCANTH is a slightly viscous, light violet to dark purple, topical solution with (b) (4) and will be applied to affected skin area only by healthcare professionals. (b) (4)

The active ingredient cantharidin is not a synthetic drug. It is a (b) (4) that is produced by and isolated from several species of blister beetles.

Cantharidin is a potent blister agent and is highly toxic if ingested. Cantharidin drug substance for this application is (b) (4) [redacted]

This abbreviated executive summary is to capture the OPQ review of the information provided in the second class 2 resubmission dated November 24, 2021. For the full review of this application refer to IQA for the review # 1 dated June 11, 2020 and the review of class 2 resubmission dated September 11, 2021.

Proposed Indication(s) including Intended Patient Population	Molluscum contagiosum lesions of the skin
Duration of Treatment	Every 3 weeks (b) (4) [redacted]
Maximum Daily Dose	Not more than two applicators per each treatment
Alternative Methods of Administration	N/A

B. Quality Assessment Overview

Drug Substance: Adequate

No additional drug substance information was submitted in this resubmission.

Drug Product: Adequate

No additional drug product information was submitted in this resubmission.

Labeling: Inadequate

The CMC section of the PI labeling as well as container and carton labels have been reviewed by the Drug Product Reviewer, Dr. Zhengfang Ge. Dr. Ge has identified multiple labeling/label deficiencies from the CMC deficiencies. Since the overall recommendation from the Office Pharmaceutical Manufacturing Assessment regarding the facilities involved in this application is "withhold", the labeling negotiations with the applicant will not be pursued in this review cycle.

Manufacturing: Inadequate

No additional manufacturing process information was submitted in this application.

However, during a recent inspection of the (b) (4) [redacted], manufacturing

facility and (b) (4)

Satisfactory resolution of these deficiencies is required before this application may be approved. Therefore, the Office of Pharmaceutical Manufacturing Assessment Reviewer, Dr. Youmin Wang has concluded that this application cannot be recommended for approval in its present form per 21 CFR 314.125(b)(13).

Dr. Wang's review is provided in the Manufacturing Chapter of the abbreviated IQA 2.

Biopharmaceutics: Adequate

Not applicable.

Microbiology (if applicable): Adequate

No additional microbiology information was provided in this class 2 resubmission.

C. Risk Assessment: Not Applicable

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**

D. List of Deficiencies for Complete Response

1. Labeling Deficiencies

PI Labeling as well as container and carton labels are not reviewed in this review cycle since this resubmission will receive a complete response due to inadequate manufacturing facilities status.

2. Manufacturing Deficiencies

Inadequacy of the (b) (4) , manufacturing facility and (b) (4) with the recommendation of "withhold".

Application Technical Lead:

Hamid Shafiei, Ph.D.
Branch IV/DNDP2/ONDP/OPQ

Hamid Shafiei

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CHAPTER VII: MICROBIOLOGY

IQA NDA Assessment Guide Reference

Product Information	
NDA Number	212905
Assessment Cycle Number	03
Drug Product Name/ Strength	Cantharidin / 0.7 % (b) (4)
Route of Administration	Topical
Applicant Name	Verrica Pharmaceuticals Inc.
Therapeutic Classification/ OND Division	N/A
Manufacturing Site	(b) (4)
Method of Sterilization	Non-sterile

Assessment Recommendation: **Adequate**

Assessment Summary:

List Submissions being assessed (table):

Document(s) Assessed	Date Received
Seq 0069	01/23/2023

Highlight Key Issues from Last Cycle and Their Resolution: This is a resubmission after a Complete Response Letter issued to the firm on 05/25/2022. The original marketing submission (dated Sep 24, 2019) was sent to a Complete Response due to a Facilities issue, but the Microbiology review of the original (N212905MR01.docs, dated 04/28/2020) submission and of the CRL response (N212905MR02.docx, 03/07/2022) were found Adequate. The current submission proposes a new (b) (4) manufacturing facility, however, no changes to the proposed drug product (DP), DP manufacturer, specifications, or information pertaining to Microbiology are proposed.

Remarks: None

Concise Description of Outstanding Issues: None

Supporting Documents:

- Microbiology review, N212905MR01.docs, dated 04/28/2020, for the review of proposed DP (Adequate).
- Microbiology review, N212905MR02.docx, dated 03/07/2022, for the CRL response (Adequate).

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Dustin Thomas

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Comments: Micro review of the resubmission is complete. We find it adequate.

Jesse Wells

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CHAPTER IV: LABELING

IQA NDA Assessment Guide Reference

1.0 PRESCRIBING INFORMATION

Assessment of Product Quality Related Aspects of the Prescribing Information:

The Prescribing Information is deemed not ADEQUATE as proposed until it is revised satisfactorily to meet the regulatory requirements (See the **List of Deficiencies** at the end of this review).

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

(b) (4)

[redacted]

Item	Information Provided in the NDA	Assessor's Comments
Product Title in Highlights		
Proprietary name	**YCANTH**	**Not Adequate** The proposed proprietary name "Ycanth" was considered acceptable by DMEPA. "VP-102"

		should be changed to Ycanth throughout the labeling
Established name(s)	(cantharidin) topical solution	**Adequate**
Route(s) of administration	topical	**Adequate**
Dosage Forms and Strengths Heading in Highlights		
Summary of the dosage form(s) and strength(s) in metric system.	Topical solution, 0.7% (b) (4)	**Not Adequate** Per discussion with Jibril from PQL, the strength should be 0.7% (b) (4) a description of "each mL of solution contains 7 mg/mL (0.7%) of cantharidin" should be added in section 3 to describe the content
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	

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)

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Item	Information Provided in the NDA	Assessor's Comments
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)	- single-use drug device combination product	**Adequate** - It's a single use highly toxic applicator by healthcare provider. - Warnings and use instruction are provided.

1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)

(b) (4)

Item	Information Provided in the NDA	Assessor's Comments
DOSAGE FORMS AND STRENGTHS section		
Available dosage form(s)	Not Provided	**Not Adequate** Revise this section to the following: Topical solution, 0.7% each mL of solution contains 7 mg/mL (0.7%) of cantharidin in a light violet to dark purple, slightly viscous liquid, free of visual particulates
Strength(s) in metric system	0.7% (b) (4)	**Not Adequate** - delete (b) (4) - Add "each mL of solution contains 7 mg/mL (0.7%) of cantharidin"
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	light violet to dark purple, slightly viscous liquid, , free of visual particulates	**Adequate**
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	

1.2.3 Section 11 (DESCRIPTION)

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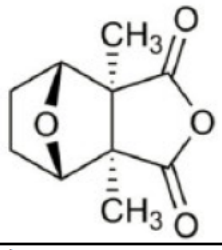
Item	Information Provided in the NDA	Assessor's Comments
DESCRIPTION section		
Proprietary and established name(s)	VP-102	**Not Adequate** Change to: Ycanth (cantharidin) topical solution
Dosage form(s) and route(s) of administration	solution	**Not Adequate** - Change to topical solution - Replace (b) (4) with "(7 mg/mL)"
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.	inactive ingredients: acetone, camphor, castor oil, ethanol, gentian violet, hydroxypropyl cellulose, and nitrocellulose. The formulation also contains an oral deterrent (denatonium benzoate) to help mitigate the risk of accidental ingestion.	**Adequate**
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	Not Provided	**Not Adequate** - Enter (b) (4) for alcohol concentration, the alcohol concentration should be displayed in terms of percent volume of absolute alcohol
Statement of being sterile (if applicable)	N/A	
Pharmacological/ therapeutic class	Lipophilic compound	**Defer to clinical pharmacology**

Chemical name, structural formula, molecular weight	chemical name: 1,2-dimethyl-3,6-epoxyperhydrophthalic molecular weight: 196.20 g/mol molecular formula: C10H12O4 Structure: 	**Adequate**
If radioactive, statement of important nuclear characteristics.	N/A	
Other important chemical or physical properties (such as pKa or pH)	Cantharidin is a white to off-white solid at room temperature and is only very slightly soluble in water. (b) (4) [redacted]	**Not Adequate** - Delete (b) (4) [redacted] - Remove paragraphs for (b) (4) [redacted]

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"		- Delete (b) (4) [redacted]

1.2.4 Section 16 (HOW SUPPLIED/STORAGE AND HANDLING)

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Item	Information Provided in the NDA	Assessor's Comments
HOW SUPPLIED/STORAGE AND HANDLING section		
Available dosage form(s)	solution	**Not Adequate:** Change to: 1. topical solution
Strength(s) in metric system	0.7% (b) (4)	**Not Adequate** - delete (b) (4) - add "(7 mg/mL), each mL of topical solution contains 7 mg cantharidin"
Available units (e.g., bottles of 100 tablets)	6 or 12 per carton	**Adequate**
Identification of dosage forms, e.g., shape, color, coating, scoring, imprinting, NDC number	VP-102 Solution is supplied in a sealed glass ampule contained within a single-use applicator and enclosed in a protective paperboard sleeve. Each ampule of VP-102 contains approximately 0.45 mL of 0.7% (b) (4) cantharidin solution. A VP-102 Break Tool is co-packaged as (b) (4) per each carton of applicators. NDC numbers are provided	**Adequate** 2. Add "light violet to dark purple, slightly viscous liquid, free of visual particulates"
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	
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.)	(b) (4)	**Adequate**
If the product contains a desiccant, ensure the size and shape differ from the dosage form	N/A	

and desiccant has a warning such as "Do not eat."		
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature.	(b) (4) [redacted]	**Not Adequate** Change to "Store at 20°C to 25°C (68° to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature, protect from light"
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

N/A

1.2.6 Manufacturing Information After Section 17 (for drug products)

Item	Information Provided in the NDA	Assessor's Comments
Manufacturing Information After Section 17		
Name and location of business (street address, city, state and zip code) of the manufacturer, distributor, and/or packer	Manufactured by: Pharmaceutical Packaging Solutions 341 JD Yarnell Industrial Pkwy, Clinton, TN 37716 For: Verrica Pharmaceuticals Inc. 10 North High Street, Suite 200 West Chester, PA 19380.	**Adequate**

2.0 PATIENT LABELING

The following CMC information provided in the Patient Labeling is adequate

What is VP-102

3. VP-102 contains a violet-colored dye, which may be temporarily visible on the skin.
4. VP-102 contains a bittering agent to discourage young children from putting it in their mouths.

3.0 CARTON AND CONTAINER LABELING

Label for Single tube applicator

(b) (4)

Label for paperboard sleeve

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Item	Information Provided in the NDA	Assessor's Comments about Carton Labeling
Proprietary name, established name, and dosage form (font size and prominence	(b) (4)	**Adequate**
Dosage strength	0.7% approximately 0.45 mL of 0.7% cantharidin solution. Each 1 mL of solution contains (b) (4) cantharidin. Recommended Dosage: See prescribing information. For Topical Use Only.	**Not Adequate** 5. change (b) (4) mg to 0.7 mg. The quantitative composition provided in sect P.1 is (b) (4) 0.7% (b) (4)
Route of administration	Topical solution For topical use only	**Adequate**
If the active ingredient is a salt, include the equivalency statement per FDA Guidance	N/A	
Net contents (e.g. tablet count)	6. "Single use applicator contains 0.45mL of 0.7% cantharidin solution" on carton and container labels 7. "6 (or 12) applicators and 2 break tools" on carton labels	**Adequate**
"Rx only" displayed on the principal display	Provided	**Adequate**
NDC number	Provided	**Adequate**
Lot number and expiration date	Not Provided	**Not Adequate** 8. Add lot number and expiration date on carton and container labels
Storage conditions. If applicable, include a space on the carton labeling for the user to write the new BUD.	Store at 20°C to 25°C (68° to 77°F). Excursions permitted between 15°C to 30°C (59°F to 86°F). Protect from light. YCANTH Solution contains (b) (4) alcohol	**Adequate**
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use)	N/A	

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	"YCANTH Solution contains (b) (4) alcohol" is provided on the carton label, but not on the applicator label	**Not Adequate** 9. Provide the amount of alcohol on container label
Bar code	Provided	**Adequate**

Item	Information Provided in the NDA	Assessor's Comments about Carton Labeling
Name of manufacturer/distributor	Manufactured by: Pharma Packaging Solutions, Inc. Clinton, TN 37716 Manufactured for: Verrica Pharmaceuticals Inc. West Chester, PA 19380 www.verrica.com Patented: www.verrica.com/patents	**Adequate**
Medication Guide (if applicable)	10. For administration by a healthcare professional only 11. Recommended Dosage: See prescribing information. 12. Carefully follow step-by-step directions in the package insert to prepare for application.	**Adequate**
No text on Ferrule and Cap overseal	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.	N/A	
And others, if space is available	**WARNING:** Flammable Liquid **WARNING:** Highly Toxic! • Wear gloves and eye protection during YCANTH preparation and administration. • Remove paperboard sleeve and inspect the applicator before using the break tool.	**Adequate**

Assessment of Carton and Container Labeling: *Inadequate*

1. change (b) (4) mg to 0.7 mg in the "each 1 mL of solution contains (b) (4) mg cantharidin" on carton. The quantitative composition provided in sect P.1 is (b) (4) 0.7% (b) (4) This information should also be displayed on the applicator label.

2. Add lot number and expiration date on carton and container labels
3. Provide the amount of alcohol on applicator label

ITEMS FOR ADDITIONAL ASSESSMENT

List of Deficiencies

The following deficiencies in the carton/container labels need to be conveyed to the applicant

1. change [redacted] mg to 0.7 mg in the "each 1 mL of solution contains [redacted] mg cantharidin" on carton. The quantitative composition provided in section 3.2.P.1.2 is [redacted] 0.7% [redacted]. This information should also be displayed on the applicator label.
2. Add lot number and expiration date on carton and container labels
3. Provide the amount of alcohol on applicator label

The following changes have been implemented in the PI in sharePoint

1. The drug product name should be changed from "VP-102" to "Ycanth" throughout the labeling

Section 3 Dosage form:

2. The strength should be 0.7% [redacted] a description of "each mL of solution contains 7 mg (0.7%) of cantharidin" should be added to describe the strength

Section 11 Description

3. Revise to "Topical solution, 0.7% each mL of solution contains 7 mg (0.7%) of cantharidin in a light violet to dark purple, slightly viscous liquid, free of visual particulates"
4. Enter [redacted] for alcohol content, it should be displayed in terms of percent volume of absolute alcohol
5. Delete [redacted]

6. Remove paragraphs for [redacted] (b) (4)

Section 16 How Supplied

1. Change dosage form from "solution" to "topical solution"
2. delete [redacted] (b) (4) from the strength.0.7%, add a descriptor "each mL of solution contains 7 mg (0.7%) of cantharidin"
3. Add drug product appearance "light violet to dark purple, slightly viscous liquid, free of visual particulates"
4. Change the storage condition to "Store at 20°C to 25°C (68° to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature, protect from light"

Overall Assessment and Recommendation:

The NDA is not ready for approval in its present form per CFR 314.125(b)(6) until the outstanding labeling issues listed in the **List of Deficiencies** are satisfactorily resolved.

Primary Labeling Assessor Name and Date:

Zhengfang Ge, Ph. D.
Reviewer, BRANCH IV/DIVISION II
OFFICE OF NEW DRUG PRODUCT

Secondary Assessor Name and Date (and Secondary Summary, as needed):

Hamid Shafiei, Ph. D.
SPQAL, BRANCH IV/DIVISION II
OFFICE OF NEW DRUG PRODUCT

Zhengfang Ge

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Hamid Shafiei

Digitally signed by Hamid Shafiei
Date: 3/24/2023 03:38:43PM
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FDA U.S. FOOD & DRUG ADMINISTRATION

RECOMMENDATION

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

NDA 212905
Assessment # 1

Drug Product Name	Trade Name (cantharidin)
Dosage Form	Solution
Strength	0.7% (b) (4)
Route of Administration	Topical
Rx/OTC Dispensed	Rx
Applicant	Verrica Pharmaceuticals, Inc.
US agent, if applicable	N/A

Submission(s) Assessed	Document Date	Discipline(s) Affected
Resubmission of the NDA	12/23/2020	All
Quality Information	12/28/2020	All
Response to Human Factor Information Request	02/19/2021	All
Response to Information Request - Quality	03/04/202021	ONDP and OPMA
Response to Information Request - Quality	03/08/2021	OPMA
Response to Information Request - Quality	03/24/2021	OPMA and ONDP
Response to Information Request - Quality	03/24/2021	OPMA and ONDP
Administrative Change	04/05/2021	All
Response to Information Request - Quality	04/20/2021	OPMA
Meeting Request in Response to the Discipline Letter	05/13/2021	All
Response the Discipline Letter	05/14/2021	All
Response to Information Request – Human Factor Study	05/18/2021	Clinical and DMEPA

Human Factor Study Report	06/21/2021	Clinical and DMEPA
Administrative Change	08/13/2021	All
Response to Human Factor Study Advice	08/25/2021	Clinical and DMEPA

QUALITY ASSESSMENT TEAM

Discipline	Primary Assessment	Secondary Assessment
Drug Substance	Martin Haber, Ph.D. / Fredrich Burnett, Ph.D.	Donna Christner, Ph.D.
Drug Product	Zhengfang Ge, Ph.D.	Moo-Jhong Rhee, Ph.D. / Wendy Wilson-Lee, Ph.D.
Manufacturing	Youmin Wang, Ph.D.	Jean Tang, Ph.D. Yubing Tang, Ph.D.
Microbiology	Eric Adeeku, Ph.D.	Jesse Wells, Ph.D.
Biopharmaceutics	N/A	N/A
Regulatory Business Process Manager	Melinda Bauerlien, MS	
Application Technical Lead	Hamid Shafiei, Ph.D.	
Laboratory (OTR)	N/A	N/A
Environmental	Zhengfang Ge, Ph.D.	Moo-Jhong Rhee, Ph.D.

FDA U.S. FOOD & DRUG ADMINISTRATION

EXECUTIVE SUMMARY

For more details about the items in this template, please see the Executive Summary chapter of the NDA IQA Guide

I. RECOMMENDATIONS AND CONCLUSION ON APPROVABILITY

- The applicant of this 505(b)(1) new drug application has provided sufficient CMC information to assure the identity, purity, strength, and quality of the drug substance, cantharidin and the drug product, Trade Name (cantharidin) Solution, 0.7% (b) (4) for topical use.
- The Office of Pharmaceutical Manufacturing Assessment has made the overall recommendation of "**withhold**" regarding the facilities involved in this application.
- The CMC issues on labels/labeling **have not** been satisfactorily resolved in this review cycle.
- The applicant's request for categorical exclusion from the environmental assessment has been granted.

Therefore, from the OPQ perspective, this NDA **is not** recommended for **approval** in its present form per 21 CFR 314.125(b)(6),(13).

II. SUMMARY OF QUALITY ASSESSMENTS

A. Product Overview

The applicant, Verrica Pharmaceuticals, Inc. has resubmitted this 505(b)(1) new drug application for YCANTH® (cantharidin) Solution, 0.7% (b) (4) for topical administration for the treatment of molluscum contagiosum on December 23, 2020. This application was originally submitted on September 13, 2019 and received a complete response on July 13, 2020. The review clock for this resubmission was extended due to the submission of a major amendment and the new PDUFA goal date for this class 2 resubmission has been reset to September 23, 2021.

YCANTH is a slightly viscous, light violet to dark purple, topical solution with (b) (4) and will be applied to affected skin area only by healthcare professionals. Upon topical administration, (b) (4) (b) (4) It is indicated for the treatment of molluscum contagiosum.

The active ingredient cantharidin is not a synthetic drug. It is a (b) (4) that is produced by and isolated from several species of blister beetles. Cantharidin is a potent blister agent and is highly toxic if ingested.

Cantharidin drug substance for this application is [redacted] (b) (4) [redacted] (b) (4) This abbreviated executive summary is to capture the OPQ review of the information provided in the class 2 resubmission dated December 23, 2020. For the full review of this application refer to IQA for the review # 1 dated June 11, 2020.

Proposed Indication(s) including Intended Patient Population	Molluscum contagiosum lesions of the skin
Duration of Treatment	Every 3 weeks [redacted] (b) (4)
Maximum Daily Dose	Not more than two applicators per each treatment
Alternative Methods of Administration	N/A

B. Quality Assessment Overview

Drug Substance: Adequate

No additional drug substance information was provided in this class 2 resubmission. The drug substance review team had recommended approval of this application from the drug substance perspective based on the review the information that had been provided in the original submission of this application. Refer to IQA # 1 dated June 11, 2020.

Drug Product: Adequate

During the first cycle review of this application, the Drug Product Reviewer, Dr. Zhengfang Ge had found multiple CMC deficiencies and recommended that the application could not be approved in the form it was presented until the deficiencies delineated in the drug product review are adequately addressed. The drug product related deficiencies identified by Dr. Ge are captured in the IQA # 1 and will not be repeated here. The drug product related deficiencies were communicated to applicant in the Complete Response Letter (CRL) dated July 13, 2020.

The applicant resubmitted this application on December 23, 2020 with additional drug product information in order to address the drug product deficiencies noted in the CRL. Dr. Ge has reviewed the drug product information provided in this resubmission and has found that the additional information provided in the resubmission has adequately addressed all deficiencies noted in her original drug product review. Dr. Ge has recommended the approval of this application from the drug

product perspective. Dr. Ge's review is provided in the DRUG product Chapter of this abbreviated IQA.

Labeling: Inadequate

The CMC section of the PI labeling as well as container and carton labels have been reviewed by the Drug Product Reviewer, Dr. Zhengfang Ge. Dr. Ge has identified multiple labeling/label deficiencies from the CMC deficiencies. Since the overall recommendation from the Office Pharmaceutical Manufacturing Assessment regarding the facilities involved in this application is "withhold", the labeling negotiations with the applicant will not be pursued in this review cycle.

Manufacturing: Inadequate

During the first cycle review of this application, the Office of Pharmaceutical Manufacturing Assessment (OPMA) Reviewer, Dr. Zhao Wang had found multiple manufacturing process related deficiencies and recommended that the application could not be approved in the form it was presented until the deficiencies delineated in the manufacturing process review are adequately addressed. The manufacturing process related deficiencies identified by Dr. Wang are captured in the IQA # 1 and will not be repeated here. The deficiencies related to manufacturing process were communicated to applicant in the Complete Response Letter (CRL) dated July 13, 2020.

In addition to manufacturing process, due to COVID-19 pandemic the required inspections of the of (b) (4) (b) (4) (b) (4) were still pending at the conclusion of the first review cycle.

The additional manufacturing process information provided in the resubmission of this application in response to the deficiencies conveyed in the CRL has been reviewed by the OPMA Reviewer, Dr. Youmin Wang. Dr. Wang has concluded that the manufacturing process information provided in the resubmission has adequately addressed all process deficiencies that were conveyed to the applicant. Therefore, Dr. Wang has recommended the approval of this application from the manufacturing process perspective. However, Dr. Wang has made the recommendation of "withhold" regarding two manufacturing facilities involved in this (b) (4)

Based on overall facilities recommendation of inadequate by Dr. Wang, this application cannot be recommended for approval in its present form per 21 CFR 314.125(b)(13).

Dr. Wang's review is provided in the Manufacturing Chapter of the abbreviated IQA.

Biopharmaceutics: Adequate

Not applicable. During the review of the original submission, it was determined that this application does not need biopharmaceutics review.

Microbiology (if applicable): Adequate

No additional microbiology information was provided in this class 2 resubmission. The microbiology review team had recommended approval of this application from the microbiology perspective based on the review of the information that had been provided in the original submission of this application. Refer to IQA # 1 dated June 11, 2020.

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**
Applicator's performance and drug delivery	Much higher crushing force needed to break the glass ampule inside the applicator compared to currently marketed	M	The applicant has submitted a new human factor study based on the recommendation by DMEPA. DMEPA has found the human factor study adequate.	L Acceptable	None

D. List of Deficiencies for Complete Response

1. Labeling Deficiencies

PI Labeling as well as container and carton labels are not reviewed in this review cycle since this resubmission will receive a complete response due to inadequate manufacturing facilities status.

2. Manufacturing Deficiencies

Inadequacy of the (b) (4)

(b) (4)

[redacted] (b) (4) facilities with the recommendation of "withhold".

Application Technical Lead:

Hamid Shafiei, Ph.D.
Branch IV/DNDP2/ONDP/OPQ

Hamid Shafiei

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/s/

HAMID R SHAFIEI
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