

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

206333Orig1s000

MICROBIOLOGY / VIROLOGY REVIEW(S)

Product Quality Microbiology Review

01 December 2014

NDA: 206333

Drug Product Name

Proprietary: (b) (4) (not approved at the time of review submission)

Non-proprietary: Deoxycholic Acid

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
13 MAY 2014	13 MAY 2014	23 MAY 2014	28 MAY 2014
25 JUL 2014	25 JUL 2014	N/A	N/A
29 OCT 2014	29 OCT 2014	N/A	N/A

Applicant/Sponsor

Name: Kythera Biopharmaceuticals, Inc.

Address: 27200 West Agoura Road, Calabasas, CA 91301

Representative: Diane Stroehmann

Telephone: 818-587-4521

Name of Reviewer: Erika Pfeiler, Ph.D.

Conclusion: Recommended for Approval

Product Quality Microbiology Data Sheet

- A.**
- 1. TYPE OF SUBMISSION:** 505(b)(1)
 - 2. SUBMISSION PROVIDES FOR:** Initial marketing of a sterile drug product
 - 3. MANUFACTURING SITE:**
[REDACTED] (b) (4)
 - 4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
 - Sterile Solution
 - Subcutaneous injection
 - 10 mg/mL
 - 5. METHOD(S) OF STERILIZATION:** Terminal [REDACTED] (b) (4) sterilization
 - 6. PHARMACOLOGICAL CATEGORY:** Improvement of appearance associated with submental fat in adults.
- B. SUPPORTING/RELATED DOCUMENTS:**
Microbiology Review 24 of DMF [REDACTED] (b) (4), DARRTS Date 26 April 2013
Microbiology Review 1 of DMF [REDACTED] (b) (4), DARRTS Date 29 October 2009
- C. REMARKS:** N/A

filename: N206333R1.doc

Executive Summary

I. Recommendations

- A. **Recommendation on Approvability** - Recommended for Approval
- B. **Recommendations on Phase 4 Commitments and/or Agreements, if Approvable** – N/A

II. Summary of Microbiology Assessments

- A. **Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology** – Product is terminally sterilized
(b) (4)
- B. **Brief Description of Microbiology Deficiencies** – N/A
- C. **Contains Potential Precedent Decision(s)**- ☐ Yes ☒ No

III. Product Quality Microbiology Risk Assessment

A. Initial Product Quality Microbiology Risk Assessment

CQA	Risk Factor	Prob. of Occ. (O)	Modifier for O ^(3, 4, 5)	Severity of Effect (S)	Detect. (D)	Risk Priority Number ⁶ (RPN)	Additional Review Emphasis based on Risk (in addition to normal review process)
Ster.	(b) (4)	6	-1	5	5	125	(b) (4)
Endo		4		4	4	64	(b) (4)

3 = Anti-Microbial Formulation (e.g., meets USP <51>),

RPN <50 = **Low Risk**; RPN 50-120 = **Moderate Risk**; RPN >120 = **High Risk**

B. Final Risk Assessment – The applicant has presented adequate information to mitigate risks outlined in the initial product quality microbiology risk assessment.

IV. Administrative

A. Reviewer's Signature _____

Erika Pfeiler, Ph.D.
Microbiologist

B. Endorsement Block _____

Stephen Langille, Ph.D.
Senior Review Microbiologist

C. CC Block
N/A

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

Erika A. Pfeiler -S

Digitally signed by Erika A. Pfeiler -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People,
0.9.2342.19200300.100.1.1=2000396533, cn=Erika A. Pfeiler -S
Date: 2014.12.01 07:34:07 -05'00'

Stephen E.
Langille -A

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ou=People, 0.9.2342.19200300.100.1.1=1300151320,
cn=Stephen E. Langille -A
Date: 2014.12.01 07:36:08 -05'00'

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 206333

Applicant: Kythera
Biopharmaceuticals, Inc.

Letter Date: 13 May 2014

Drug Name: KYBELLA™
(proposed)

NDA Type: 505(b)(1)

Stamp Date: 13 May 2014

The following are necessary to initiate a review of the NDA application:

	Content Parameter	Yes	No	Comments
1	Is the product quality microbiology information described in the NDA and organized in a manner to allow substantive review to begin? Is it legible, indexed, and/or paginated adequately?	X		
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	X		
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	X		
4	Are any study reports or published articles in a foreign language? If yes, has the translated version been included in the submission for review?			The submission is in English.
5	Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies?	X		
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	X		
7	Has the applicant submitted the results of analytical method verification studies?		X	See Additional Comments.
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?			N/A
9	If sterile, are extended post-constitution and/or post-dilution hold times in the draft labeling supported by microbiological data?	X		
10	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: This product is a sterile solution for subcutaneous injection, 2 mL in a 2 mL vial, intended for single use. The drug product is terminally sterilized (b) (4). The application did not contain method verification studies for sterility and endotoxin testing. An information request for these and other minor deficiencies will be conveyed to the applicant in the 74-day letter.

Erika Pfeiler, Ph.D.

Date

Stephen Langille, Ph.D.

Date

Please convey the following information requests to the applicant in the 74-day letter.

1. Your application describes dye ingress studies to ensure container closure integrity. How did the preparation of the units used in dye ingress testing compare to production parameters? (In production, (b) (4).) If parameters used to prepare units for dye ingress testing were different than those used in production, provide a rationale for the handling method that you describe.
2. Confirm that production sterilization parameters for the drug product include a (b) (4).
3. Your application states that you use methods described in USP <85> for endotoxin testing, but you do not provide the results of method verification studies with the drug product. Provide a summary of any method verification studies.
4. Your application states that you use methods described in USP <71> for sterility testing, but you do not provide the results of method verification studies with the drug product. Provide a summary of any method verification studies.
5. Your application briefly describes the use of a (b) (4) test used to test container closure integrity in commercial production. Provide a more thorough description of the validation studies performed for this testing. Provide a description of test parameters, including positive and negative controls used in routine testing.
6. Describe culturing and handling methods for biological indicators (b) (4) requalification studies.
7. Your application states that endotoxin and container closure integrity will be tested as part of the stability program. State the specifications for these attributes, including test method and acceptance criteria.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ERIKA A PFEILER
06/25/2014

STEPHEN E LANGILLE
06/25/2014