CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

214511Orig1s000

PRODUCT QUALITY REVIEW(S)

NDA 214511, LUMISIGHT
OPQ Integrated Quality Assessment (IQA)

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Office of Pharmaceutical Quality

New Drug Application (NDA) 214511

Executive Summary

RECOMMENDATION

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

NDA 214511
Assessment 1

Drug Product Name	LUMISIGHT
Dosage Form	Injection
Strength	39 mg
Route of Administration	Intravenous
Rx/OTC Dispensed	Rx
Applicant	Lumicell, Inc.
US agent, if applicable	N/A

Submission(s) Assessed	Document Date	Discipline(s) Affected
Quality Amendment	11/07/2023	DP
Quality Amendment	10/25/2023	DP, Process
Quality Amendment	10/23/2023	DP, Process
Quality Amendment	10/19/2023	DP
Quality Amendment	9/18/2023	DP, Process
Quality Amendment	9/7/2023	Process
Quality Amendment	9/5/2023	DP, Process
Quality Amendment	8/30/2023	DP
Quality Amendment	8/25/2023	Process
Quality Amendment	8/24/2023	Process
Quality Amendment	8/13/2023	Process
Quality Amendment	8/3/2023	DP, Process
Quality Amendment	7/13/2023	Process
Quality Amendment	7/5/2023	DS, DP, Process
Quality Amendment	6/23/2023	Micro
Quality Amendment	5/23/2023	Micro
Quality Amendment	5/12/2023	DS, Process
NDA 214511 Original	3/17/2023	DS, DP, Process and Micro
Quality Amendment	3/8/2023	DS, DP, Process and Micro
Quality Amendment	11/12/2021	DS, DP, Process and Micro

QUALITY ASSESSMENT TEAM

Discipline	Primary Assessor	Secondary Assessor
Drug Substance	Joseph Leginus	Sithamalli Chandramouli
Drug Product	Dhana Kasi	Danae Christodoulou
Manufacturing	Rose Xu	Vidya Pai
Microbiology	David Bateman	Laura Wasil
Biopharmaceutics	N/A	
Regulatory Business Process Manager	Anika Lalmansingh	
Application Technical Lead	Dhana Kasi	
Laboratory (OTR)	N/A	
Environmental	N/A	

QUALITY ASSESSMENT DATA SHEET

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

DMF #	Type	Holder	Item Referenced	Status	Date Assessment Completed	Comments
DMF (b) (4)	II	(b) (4)		Adequate	4/25/2023	

2. CONSULTS

Discipline	Status	Recommendation	Date	Assessor
Biostatistics	N/A			
Pharmacology/Toxicology	N/A			
CDRH	N/A			
Clinical	N/A			
Other	N/A			

EXECUTIVE SUMMARY

I. RECOMMENDATIONS AND CONCLUSION ON APPROVABILITY

OPQ team recommendation Approval.

Several issues were identified during the NDA review of drug substance, drug product, manufacturing and facilities, microbiology, and labeling sections. Applicant provided necessary quality information to resolve all the quality issues. Initial assessment of the facility team related to the drug substance and drug product facilities have been approved based on the firm's history of inspections and manufacturing experience. Recently, the drug product manufacturing facility, (b) (4) was inspected for another drug product and the issues related to quality systems were addressed through704(a)(4) assessment. The drug product facility is recommended for approval.

II. SUMMARY OF QUALITY ASSESSMENTS

A. Product Overview

Pegulicianine for injection from Lumicell Inc. is a new molecular entity and it was granted breakthrough device (scanner) designation on 03/28/2018 and received fast track designation in 10/29/2020. This application is a 505 b (1) application. The drug product, Pegulicianine for injection (b) (4) It is indicated for use in patients undergoing breast conserving surgery (lumpectomy) to remove breast cancer. Pegulicianine produces a fluorescent signal after its peptide backbone is cleaved by the proteases in tumor tissue. After cleavage the fluorescence quencher, QSY21 separates from the rest of the molecule leaving the Cy5 containing fragment which give the fluorescence signal. Cy5 fragments are found in higher concentrations in tumor tissue in humans and creates the signal contrast between tumor and normal tissue. Pegulicianine for injection is a (b) (4) single dose lyophilized powder containing 40 mg/vial of pegulicianine, mannitol and phosphate (b) (4) The drug product is supplied in a (b) (4) 10-mL glass vial with grey (b) (4) rubber stopper with crimp and blue flip-off seal. Each vial contains 40 mg of dark blue lyophilized powder for reconstitution in 4 mL of 0.45% sodium chloride for injection. The extractable volume of the reconstituted drug product is determined by gravimetric analysis and it is 3.9 mL. The strength of the drug product is 39 mg. Applicant listed six impurities as specified impurities by RRT ranges based on our recommendation and acceptance criteria was established based on non-clinical data. The acceptance criterion for unspecified impurity was

(b) (4) % based on FDA's recommendation. The recommended dose of Pegulicianine is 1 mg/kg. (b) (4) The shelf life of 36 months is granted at (b) (4) °C.

The drug substance, pegulicianine acetate is a fluorescent imaging agent contains a fluorophore (CY5 monoacid), a dark quencher (QSY21 carboxylic acid), an amino acid backbone, and a polyethylene glycol (PEG) moiety (methoxy-PEG, ~20k Dalton). A retest date of (b) (4) months is granted for pegulicianine drug substance when stored at (b) (4)

The drug product manufacturing process includes (b) (4) The drug product is manufactured by (b) (4) (b) (4), and drug substance at (b) (4) (b) (4) The drug substance manufacturing facility is acceptable based on file review. The drug product manufacturing facility, (b) (4) was covered as part of (b) (4) inspection for lyophilized (b) (4) products with no major issues. Later, a pre-approval inspection was conducted *for another NDA (b) (4) there were concerns regarding facility cleaning and control procedures. A 704(a)(4) assessment was conducted in (b) (4) and the facility issues were resolved through information requests. The drug product facility is recommended for approval to support this NDA.*

The drug product is (b) (4)

Proposed Indication(s) including Intended Patient Population	(b) (4)
Duration of Treatment	N/A
Maximum Daily Dose	(b) (4)
Alternative Methods of Administration	N/A

Reference (b) (4) 5274733

B. Quality Assessment Overview

Drug Substance: Adequate

CMC information related to drug substance, pegulicianine acetate is provided in DMF (b) (4) from (b) (4) Letter of authorization is provided (b) (4). DMF (b) (4) was reviewed by J. Leginus on (b) (4) and found adequate to support NDA 214155.

Pegulicianine acetate is a fluorescent dye with (b) (4) and molecular weight for the drug substance is f 22,000 Da. The drug substance is a dark blue amorphous powder and it is hygroscopic. Proposed levels of impurities in the drug substance specification have been adequately justified. The proposed level of specified impurity RRT (b) (4) to (b) (4) at (b) (4)% by RP-HPLC has been concluded by Pharm/Tox to be acceptable based on nonclinical studies. Applicant included 5 additional specified impurities by RRT ranges with their respective limits, and the limit of "All other single impurities" is (b) (4)% for the pegulicianine drug substance is acceptable and is supported by nonclinical data according to the Pharm/Tox team. Further, the limit of (b) (4)% for (b) (4) high molecular weight (HMW) impurities is supported by clinical safety based on clinical batch data. A retest date of (b) (4) months is granted for pegulicianine drug substance when stored at (b) (4)

Drug Product: Adequate

Pegulicianine for injection is a (b) (4), single dose lyophilized powder containing pegulicianine, mannitol and phosphate (b) (4) The excipients used in the drug product formulation are commonly used for injectable products. Each vial contains 40 mg of dark blue lyophilized powder for reconstitution in 4 mL of 0.45% sodium chloride for injection. The drug product is supplied in a (b) (4) 10-mL glass vial with grey (b) (4) rubber stopper with crimp and blue flip-off seal. The drug product is tested for all the critical quality attributes at release and stability. The acceptance criteria for specified impurities by RRT are supported by non-clinical data. Applicant listed five additional impurities as specified impurities based on our recommendation and acceptance criteria was established based on non-clinical data. The acceptance criterion for unspecified impurity was (b) (4) % based on FDA's recommendation. The batch analysis data showed that the test results are within the specified limits. The shelf life of 36 months is granted at (b) (4) °C. The reconstituted drug product solution is stable for 4 h at room temperature and 24 h at 2-8 °C.

The strength of the drug product was determined by testing the extractable volume of the reconstituted drug product by gravimetric analysis. The drug product vial (40 mg) was reconstituted with 4 mL of

0.45 % saline. The extractable volume study was performed by 3 analysts testing 6 drug product vials. The test result indicates that the extractable volume is in the range of (b) (4) mL to (b) (4) mL with the average of 3.9 mL and assay range of the reconstituted drug product is 96 – 99 %. The strength of the drug product is 39 mg and the drug product label will be updated.

Labeling: Adequate

Numerous issues were identified in the labeling and revisions made included those to dosage forms and strengths, description and how supplied section. The extractable volume of the reconstituted drug product was determined by gravimetric analysis, and it was 3.9 mL. The drug product label will be updated with the strength of 39 mg.

Manufacturing: Adequate

The manufacturing process includes (b) (4) The drug product is manufactured by (b) (4) and drug substance at (b) (4) The drug substance manufacturing facility is acceptable based on file review. The drug product manufacturing facility, (b) (4) was covered as part of (b) (4) inspection for lyophilized (b) (4) products with no major issues. However, at the end of the review cycle, a pre-approval inspection for a different lyophilized product (b) (4) A 704(a)(4) was conducted for this application in (b) (4) No significant issues were found during the review of submitted records. The firm is recommended for approval to support this NDA.

Microbiology: Adequate

The drug product is (b) (4)

Application Technical Lead Name and Date:

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CHAPTER IV: LABELING

1.0 PRESCRIBING INFORMATION

Assessment of Product Quality Related Aspects of the Prescribing Information: Adequate with revisions provided below.

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

Item	Information Provided in the NDA	Assessor's Comments
Product Title in Highlights		
Proprietary name Established name(s) Route(s) of administration	LUMISIGHT™ (pegulicianine) for Injection, for intravenous use	Adequate
Dosage Forms and Strengths Heading in Highlights		
Summary of the dosage form(s) and strength(s) in metric system.	For Injection: (b) (4) in a single dose vial (b) (4)	Revision: For injection: (b) (4) lyophilized powder in a single dose vial (b) (4)
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	NA	
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.		

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)

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)	Multiple vials may be used for dosing	

1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)

Item	Information Provided in the NDA	Assessor's Comments
DOSAGE FORMS AND STRENGTHS section		
Available dosage form(s)	For Injection: (b) (4)	Revision: For injection: (b) (4) dark blue lyophilized powder in a single-dose vial (b) (4)
Strength(s) in metric system	in a single dose vial (b) (4)	
If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance		
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, and imprinting		
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"		
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.		

Item		Assessor's Comments
DESCRIPTION:		
Proprietary and established name(s)	LUMISIGHT (b) (4) (b) (4)	Revision: Chemical name, molecular weight structural formula updated to include the acetate ion.
Dosage form(s) and route(s) of administration		
If the active ingredient is a salt, apply the USP Salt Policy and include the equivalency statement per FDA Guidance.		
List names of all inactive ingredients. Use USP/NF names. Avoid Brand names.	LUMISIGHT (pegulicianine) for Injection is supplied as a sterile, (b) (4) Each vial contains 40 mg of pegulicianine, (b) (4)	
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.		
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol		
Statement of being sterile (if applicable)		
Pharmacological/ therapeutic class		
Chemical name, structural formula, molecular weight		
If radioactive, statement of important nuclear characteristics.		
Other important chemical or physical properties (such as pKa or pH)		

Section 11 (DESCRIPTION) Continued

Item	Information Provided in the NDA	Assessor's Comments
For oral prescription drug products, include gluten statement if applicable	None.	
Remove statements that may be misleading or promotional (e.g., "synthesized and developed by Drug Company X," "structurally unique molecular entity"	None.	

Section 16 (HOW SUPPLIED/STORAGE AND HANDLING)

Item	Information Provided in the NDA	Assessor's Comments
HOW SUPPLIED/STORAGE AND HANDLING section		
Available dosage form(s) Strength(s) in metric system Available units (e.g., bottles of 100 tablets) Identification of dosage forms, e.g., shape, color, coating, scoring, imprinting, NDC number Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored" 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.	How supplied LUMISIGHT (pegulicianine for Injection) is (b) (4) 10 vials (NDC 82292-040-10). (b) (4)	Revision: How supplied LUMISIGHT (pegulicianine) for injection is supplied (b) (4) as a dark blue lyophilized powder in cartons of 10 vials (NDC 82292-040-10). Storage and Handling Store vials of LUMISIGHT frozen at -25°C to -15°C (-13°F to 5°F) in the original carton to protect from light.

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.)	N/A	
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."	N/A	
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature.		
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."	See above. N/A	
Include information about child-resistant packaging	No Information included.	

1.2.3 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	(b) (4)	Manufactured for: Lumicell, Inc. 275 Washington Street, Suite 200 Newton, MA 02458

2.0 PATIENT LABELING

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

No Information included.

3.0 CARTON AND CONTAINER LABELING

Revised Container and Carton Labels:

3.1 Container Label

3.2 Carton Labeling

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

Lumicell accepted FDA's recommendations and it is adequate.

Overall Assessment and Recommendation:

Lumicell accepted FDA's recommendations, and it is adequate.

Dhanalakshmi Kasi

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Danae Christodoulou

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CHAPTER VII: MICROBIOLOGY

IQA NDA Assessment Guide Reference

Product Information	
NDA Number	214511
Assessment Cycle Number	MR01
Drug Product Name/ Strength	Pegulicianine 40 mg/4mL single-dose vial
Route of Administration	Intravenous injection
Applicant Name	Lumicell, Inc.
Therapeutic Classification/ OND Division	Division of Medical Imaging and Radiation Medicine
Manufacturing Site	(b) (4)
Method of Sterilization	

Assessment Recommendation: **Adequate**

Assessment Summary:

The drug product is (b) (4)

List Submissions being assessed (table):

Document(s) Assessed	Date Received
eCTD Seq #0000	July 15, 2021
eCTD Seq #0001	November 15, 2023
eCTD Seq #0002	March 8, 2023
eCTD Seq #0009	May 23, 2023
eCTD Seq #0012	June 23, 2023

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

Remarks: The drug product is supplied as a lyophilized powder in 10 mL vials.

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

Supporting Documents:

DMF (b) (4) (adequate)

DMF (b) (4)
manufacturing facility:

Microbiology review [redacted] (adequate).

Microbiology review [redacted]

Microbiology review [redacted]

(adequate).

P.1 Description of the Composition of the Drug Product

- **Description of drug product:** A sterile dark blue lyophilized powder for reconstitution in 4 mL of 0.45% sodium chloride for injection (USP).

- **Drug product composition:**

Ingredient	Content per mL
LUM015 acetate	10 mg
Mannitol, USP	9.8 [redacted] mg
Sodium phosphate, monobasic monohydrate, USP	0.9 [redacted] mg
Sodium Phosphate dibasic, heptahydrate, USP	0.80 mg
Sterile water for injection, USP	Removed during lyophilization

- **Description of container closure system:**

Component	Description	Manufacturer
Vial	10 mL [redacted] clear glass tubing vial	[redacted]
Stopper	[redacted] 20 mm [redacted] rubber [redacted] stopper	
Cap	20 mm blue aluminum flip-off seal	

Adequate

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

P.2 Pharmaceutical Development

P.2.5 Microbiological Attributes

Container/Closure and Package Integrity

(3.2.P.2 Pharmaceutical development, page)

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DHANALAKSHMI KASI
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