CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

210850Orig1s000

PRODUCT QUALITY REVIEW(S)

RECOMMENDATION

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

NDA 210850 Resubmission
Assessment 1

Drug Product Name	Sincalide for Injection, 5 mcg/vial
Dosage Form	Powder for reconstitution
Strength	5 mcg/vial
Route of Administration	Intravenous
Rx/OTC Dispensed	Rx
Applicant	MAIA Pharmaceuticals, Inc.
US agent, if applicable	NA

Submission(s) Assessed	Document Date	Discipline(s) Affected
Resubmission, eCTD SDN 0016	09/26/2022	DS, DP, OPMA, labeling, and micro
Amendment, SDN 0017	10/07/2022	DP, OPMA, micro
Amendment, SDN 0018	10/25/2022	DP, OPMA, micro
Amendment, SDN 0020	11/14/2022	Labeling

NDA Executive Summary

1. Application/Product Information

NDA Number.	NDA 210850 Resubmission #1 (SDN 0016)		
Applicant Name	MAIA Pharmaceuticals, Inc.		
Drug Product Name	Sincalide for Injection, 5 mcg/vial		
Dosage Form.	Powder for reconstitution		
Proposed Strength(s)	5 mcg		
Route of Administration	Intravenous		
Maximum Daily Dose	0.12 mcg per kg		
Rx/OTC Dispensed	Rx		
Proposed Indication	(1) to stimulate gallbladder contraction, (2) to stimulate pancreatic secretion, and (3) to accelerate the transit of a barium meal through the small bowel		
Drug Product Description	Each single-dose vial of sincalide provides a sterile nonpyrogenic lyophilized white to off-white cake or powder consisting of 5 mcg sincalide with 30 mg arginine hydrochloride, 15 mg lysine hydrochloride,170 mg mannitol, 4 mg methionine, 2 mg pentetic acid, and 0.04 mg sodium metabisulfite		
Co-packaged product information	N/A		
Device information:	N/A		
Storage Temperature/ Conditions	Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [See USP Controlled Room Temperature]		
Review Team	**Discipline**	**Primary**	**Secondary**
	Drug Substance	Sam Bain	Lawrence Perez
	Drug Product/ Labeling	Zhengfang Ge	Nina Ni

	Manufacturing	Yan Xu	Tianhong Tim Zhou
	Biopharmaceutics	N/A	N/A
	Microbiology	Dustin Thomas	Jesse Wells
	Other (specify):	N/A	N/A
	RBPM	Melinda Bauerlien	
	ATL	Nina Ni	
Consults	N/A		

2. Final Overall Recommendation - Approval

3. Action Letter Information

a. Expiration Dating: 24 months

b. Additional Comments for Action: N/A

4. Basis for Recommendation:

a. Summary of Rationale for Recommendation:

The NDA was tentatively approved in the previous review cycle, dated 02/23/2018. In the current resubmission, the applicant requested a final approval with updated 24 months stability data for 3 registration batches. There are no other CMC changes included in the resubmission.

OPQ recommends APPROVAL of NDA 210850 for commercialization of Sincalide for Injection, 5 mcg/vial. Based on our evaluation of the available information, the applicant provided sufficient information to support an approval recommendation from the product quality perspective. The applicant provided adequate chemistry, manufacturing, and controls (CMC) information to ensure the identity, strength, purity, and quality of the

proposed drug product. The overall manufacturing inspection recommendation is approval for all the facilities associated with this application. The proposed labeling and labels include adequate information to meet the regulatory requirements.

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	**-**	**N/A**
Microbiology	**-**	**Adequate**

Environmental Assessment: Categorical Exclusion - Adequate
QPA for EA(s): Yes

5. Life-Cycle Considerations

Established Conditions per ICH Q12: No
Comments: N/A

Comparability Protocols (PACMP): No
Comments: N/A

Additional Lifecycle Comments:

In the resubmission SDN 0016, dated 09/26/2022, the applicant originally also proposed addition of the alternate USP (b) (4) glass vial with (b) (4) for the packaging of the drug product; however, release and stability data for drug product batch manufactured using the alternate vials were not included in the submission. Thus, per Agency's recommendation, in the amendment SDN 0017, dated 10/07/2022, the applicant submitted a comparability protocol for the proposed alternate vials as a post-approval change. However, the process assessment team, Drs. Yan Xu and Tim Zhou found inadequate manufacturing process information of using the alternate vials was provided in the comparability protocol. Thus, in the amendment SDN 0018, dated 10/25/2022, the applicant removed the comparability protocol per Agency's recommendation (b) (4) (b) (4)

Nina Ni

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NDA_210850_SD_16_NAI

In the amendment dated 26-SEP-2022 (SD_16), the NDA applicant has requested full approval of the NDA, which was tentatively approved on 23-FEB-2018.

The NDA applicant has referenced DMF (b) (4) for the drug substance CMC. The tentative approval of the NDA was based upon the adequate status of the DMF, Review #2, dated 16-OCT-2017. Since then, the only significant change to the DMF has been the extension of retest period for the drug substance to (b) (4) months, based upon updated stability data. This is reflected by the DMF review dated 24-OCT-2022, Adequate (NAI), S. Bain.

Based upon the current adequacy of the DMF, the NDA remains approvable from the drug substance perspective, with a retest period of (b) (4) months for the drug substance, for a shelf-life storage condition of (b) (4)

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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: **Nov. 14, 2022**

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

Through: **Nina Ni, Ph.D.**
SPQA, ONDP/Division II/Branch IV

To: **Labeling Review of NDA 210850**

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

The Labeling of the original submission was found acceptable during the original review cycle. In the amendment of the resubmission dated 14 -Nov-2022, the applicant further accepted the Agency's recommendation to revise the storage condition to "Store at 20°C to 25°C (68°F to 77°F), excursions permitted between 15°C to 30°C (59° to 86°F) [See USP Controlled Room Temperature]" throughout the labeling.

Recommendation:
This NDA is **now** recommended for approval from the labeling perspective.

Attachment: Final container/carton labels

Zhengfang Ge

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Nina Ni

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CHAPTER VII: MICROBIOLOGY

IQA NDA Assessment Guide Reference

Product Information	
NDA Number	202872
Assessment Cycle Number	MR02
Drug Product Name/ Strength	Sincalide for Injection, 5 mcg/vial
Route of Administration	Intravenous
Applicant Name	MAIA Pharmaceuticals, Inc
Therapeutic Classification/ OND Division	
Manufacturing Site	Gland Pharma Limited Survey No. 143-148, 150 & 151 Near Gandimasamma Cross Roads D.P. Pally, Dundigal – Gandiamaisamma Mandal, Medchal – Malkajgiri District Hyderabad, Telengana, India 500043
Method of Sterilization	(b) (4)

Assessment Recommendation: **Adequate**

Assessment Summary:

List Submissions being assessed (table):

Document(s) Assessed	Date Received
0014 (16)	**09/26/2022**
0015 (17)	**10/07/2022**

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

Remarks: The submission is in the eCTD format. The submission dated 09/26/2022 is the Request for Approval submission which contains the CCIT validation data. The submission dated 10/07/2022 is a response to an IR in which the applicant changes the submission to a comparability protocol.

Concise Description of Outstanding Issues
(List bullet points with key information and update as needed): N/A

Supporting Documents: N/A

The applicant submitted a Class-2 request for approval to add an alternative vial with (b) (4) on 09/26/2022. It was determined a comparability protocol is required for the

change and was submitted on 10/07/2022. The drug product is a lyophilized intravenous product. The approved vial depyrogenation validation and media fill studies cover the proposed vial since the vial falls within the validation brackets. The applicant provided an updated CCIT validation study of the proposed vial.

P.1 Description of the Composition of the Drug Product

Description of drug product – Clear colorless solution.

Drug product composition – Unchanged

Description of container closure system –

Glass vial	Rubber stopper	Seal
5 mL USP (b) (4) clear glass (b) (4) vial with 20 mm neck (b) (4) Material Code No. (b) (4)	20 mm (b) (4) rubber stoppers (b) (4) Material Code No. (b) (4)	20 mm Aluminum flip off seals with (b) (4) (Blue color) button (matte top) Material Code No. (b) (4)

P.2 Pharmaceutical Development

P.2.5 Microbiological Attributes

Container/Closure and Package Integrity

(b) (4)

Comparability Protocols – This submission is classified as a comparability protocol and the relevant data is reviewed above.

Reviewer's Assessment: N/A

List of Deficiencies: N/A

Primary Microbiology Assessor: Dustin Thomas, Ph.D. 10/20/2022

Secondary Microbiology Assessor: Jesse Wells, Ph.D. 10/20/2022

Jesse Wells

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Dustin Thomas

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CHAPTER VII: MICROBIOLOGY

IQA NDA Assessment Guide Reference

Product Information	
NDA Number	210850
Assessment Cycle Number	MR03
Drug Product Name/ Strength	Sincalide for Injection, 5 mcg/vial
Route of Administration	Intravenous
Applicant Name	MAIA Pharmaceuticals, Inc
Therapeutic Classification/ OND Division	
Manufacturing Site	Gland Pharma Limited Survey No. 143-148, 150 & 151 Near Gandimasamma Cross Roads D.P. Pally, Dundigal – Gandiamaisamma Mandal, Medchal – Malkajgiri District Hyderabad, Telengana, India 500043
Method of Sterilization	(b) (4)

Assessment Recommendation: **Adequate**

Assessment Summary:

List Submissions being assessed (table):

Document(s) Assessed	Date Received
0014 (16)	**09/26/2022**
0015 (17)	**10/07/2022**
0016 (18)	**10/25/2022**

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

Remarks: The submission is in the eCTD format. The submission dated 09/26/2022 is the Request for Approval submission which contains the CCIT validation data. The submission dated 10/07/2022 is a response to an IR in which the applicant changes the submission to a comparability protocol. The submission dated 10/25/2022 is for the withdrawal of the CP and alternative vial.

Concise Description of Outstanding Issues
(List bullet points with key information and update as needed): N/A

Supporting Documents: N210850MR02.docx, adequate 10/25/2022. Review of Comparability Protocol proposing an [redacted] (b) (4) This submission has been withdrawn following approval of the review.

The applicant withdrew the proposed Comparability Protocol submitted on 10/07/2022. The proposed [redacted] (b) (4)

Post-dilution/reconstitution hold time

The applicant proposes an 8 hour post-dilution hold time at room temperature in the package insert, which was covered in the original review (N210850MR01.docx, 01/09/2018, adequate).

Assessment: *Adequate*

Comparability Protocols – N/A

Reviewer's Assessment: N/A

List of Deficiencies: N/A

Primary Microbiology Assessor: Dustin Thomas, Ph.D. 11/17/2022

Secondary Microbiology Assessor: Jesse Wells, Ph.D. 11/17/2022

Jesse Wells

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Dustin Thomas

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Nina Ni

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/s/

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QUALITY ASSESSMENT

Recommendation: As of this review, this 505 (b)(2) NDA is *not* ready for Approval in its present form per 21 CFR 314.125(b)(6).

NDA 210850
OPQ Review #1

Drug Name/Dosage Form	Sincalide for Injection
Strength	Each single-dose vial contains 5 mcg of sincalide for reconstitution
Route of Administration	Intravenous Injection
Rx/OTC Dispensed	Rx
Applicant	MAIA Pharmaceuticals, Inc.; Princeton, NJ
US agent, if applicable	NA

SUBMISSION(S) REVIEWED	DOCUMENT DATE	DISCIPLINE(S) AFFECTED
Original	8/25/2017	OPQ
Amendment	11/17/2017	OPQ
Amendment	12/08/2017	ONDP
Amendment	12/18/2017	ONDP/DNDAPI/ONDP/OPF
Amendment	1/24/2018	ONDP/DNDAPI/ONDP/OPF

Quality Review Team

DISCIPLINE	REVIEWER	BRANCH/DIVISION
Drug Substance	Joseph Leginus	CDER/OPQ/ONDP/ DNDAPI/NDBII
Drug Product and Labeling	Zhengfang Ge	CDER/OPQ/ONDP/ DNDPII/NDPBV
Process	Yaodong Hong	CDER/OPQ/OPF/ DPAIII/PABVIII
Biopharmaceutics	Bryan Ericksen	CDER/OPQ/ONDP/DB/BBII
Microbiology	Paul Dexter	CDER/OPQ/OPF/DMA/MABI
Facility	Vidya Pai	CDER/OPQ/OPF/DIA/IABIII
Regulatory Business Process Manager	Oumou Barry	CDER/OPQ/OPRO/DR BPMI/RBPMBI
Application Technical Lead	Hitesh Shroff	CDER/OPQ/ONDP/ DNDPII/NDPBV
Laboratory (OTR)	N/A	N/A
Environmental Analysis (EA)	Zhengfang Ge	CDER/OPQ/ONDP/ DNDPII/NDPBV

Quality Review Data Sheet

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

DMF #	Type	Holder	Item Referenced	Status	Date Review Completed	Comments
(b) (4)	Type II	(b) (4)		Active	Adequate (Reviewed by Joseph Leginus, Ph.D. on 10/16/2017)	LOA: 07/10/2017
	Type III			Active	NA	LOA: 02/15/2017
	Type III			Active	Adequate (Reviewed by V. Amspacher on 11/29/2016)	LOA: 02/14/2017
	Type V			Active	NA	LOA: 09/13/2016

NA: Sufficient information provided in this application so this DMF was not reviewed.

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

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NA	NA	NA

2. CONSULTS: None

DISCIPLINE	STATUS	RECOMMENDATION	DATE	REVIEWER
Biostatistics	N/A			
Pharmacology/Toxicology	N/A			
CDRH	N/A			
Clinical	N/A			

Executive Summary

I. Recommendations and Conclusion on Approvability

The applicant has provided sufficient CMC information to assure the identity, strength, purity, and quality of the drug product.

*This drug product is recommended for approval for only **intravenous administration** from biopharmaceutics perspective.*

The claim for the Categorical Exclusion for the Environmental Assessment is granted.

The Office of Process and Facilities (OPF) has made a final overall "Approval" recommendation for the facilities involved in this application as of this review.

The label/labeling issues have ***not*** been satisfactorily resolved.

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

II. Summary of Quality Assessments

A. Product Overview

Sincalide for Injection contains sincalide as an active ingredient. Sincalide is a cholecystokinin (CCK) analog to stimulate gallbladder contraction, pancreatic secretion or to accelerate the transit of barium meal through the small bowel.

The drug product is supplied as sterile, lyophilized powder for reconstitution in a 5 mL single-dose clear glass vial. Each vial contains 5 mcg sincalide. The inactive ingredients include: mannitol (b) (4) L-arginine hydrochloride, L-lysine hydrochloride and L-methionine (b) (4) pentetic acid (b) (4) and sodium hydroxide or hydrochloric acid to adjust pH to 6.5 to 7.5.

Sincalide for Injection must be reconstituted with 5 mL of sterile water for IV injection. The reconstituted solution is diluted with 0.9% Sodium Chloride Injection, USP for IV infusion. This drug product is recommended for approval for only intravenous administration from biopharmaceutics perspective.

QUALITY ASSESSMENT

<table>
<tr><td>Proposed Indication(s) including Intended Patient Population</td><td>Sincalide for Injection is a cholecystokinin (CCK) analog indicated:
to stimulate gallbladder contraction, as may be assessed by various methods of diagnostic imaging, or to obtain by duodenal aspiration a sample of concentrated bile for analysis of cholesterol, bile salts, phospholipids, and crystals;
to stimulate pancreatic secretion (especially in conjunction with secretin) prior to obtaining a duodenal aspirate for analysis of enzyme activity, composition, and cytology;
to accelerate the transit of a barium meal through the small bowel, thereby decreasing the time and extent of radiation associated with fluoroscopy and x-ray examination of the intestinal tract.</td></tr>
<tr><td>Duration of Treatment</td><td>Only one IV administration</td></tr>
<tr><td>Maximum Daily Dose</td><td>Recommended Dosage of Sincalide for Injection by Treatment Indication
<table>
<tr><td>Indication</td><td>Sincalide for Injection</td></tr>
<tr><td>To stimulate contraction of the gallbladder</td><td>Intravenous Injection
0.02 mcg/kg as a single dose over 30 to 60 seconds. If satisfactory contraction does not occur in 15 minutes, administer a dose of 0.04 mcg/kg over 30 to 60 seconds.

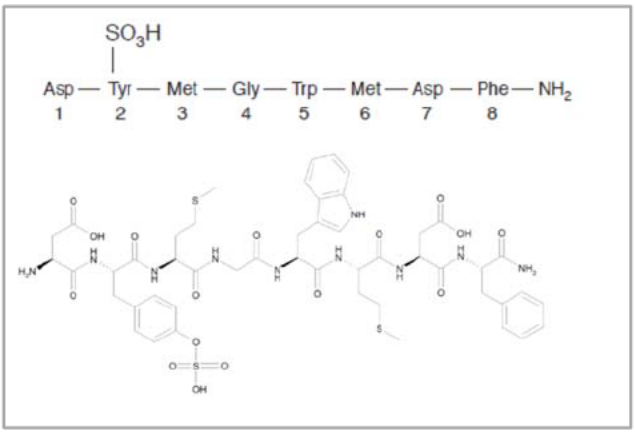
Intravenous Infusion to Reduce Gastrointestinal Adverse Reactions [see Warnings and Precautions (5.3)]
0.12 mcg/kg diluted in 100 mL of 0.9% Sodium Chloride Injection USP and infused over 50 minutes (rate of 2 mL per minute).</td></tr>
<tr><td>To stimulate pancreatic secretion 30 minutes after secretin for injection</td><td>Intravenous Infusion
0.02 mcg/kg diluted in 30 mL of 0.9% Sodium Chloride Injection USP and infused over 30 minutes at a rate of 1 mL/minute.</td></tr>
<tr><td>To accelerate the transit of a barium meal through the small intestine</td><td>Intravenous Injection
After the barium meal is beyond the proximal jejunum, administer 0.04 mcg/kg over 30 to 60 seconds.
If satisfactory transit of the barium meal has not occurred in 30 minutes, administer a dose of 0.04 mcg/kg over 30 to 60 seconds.
Intravenous Infusion to Reduce Gastrointestinal Adverse Reactions [see Warnings and Precautions (5.3)]
0.12 mcg/kg diluted in 100 mL 0.9% Sodium Chloride Injection USP and infused over 30 minutes</td></tr>
</table></td></tr>
<tr><td>Alternative Methods of Administration</td><td>N/A</td></tr>
</table>

B. Quality Assessment Overview

Drug Substances:

Sincalide is a white to off-white non-hygroscopic powder. It is a sulfated octapeptide. It is soluble in 1M ammonium hydroxide. Its specific rotation is typically $[\alpha]_D^{25} = -21°$ (1% in 1M ammonium hydroxide). It is manufactured by [redacted (b) (4)]. The CMC information including manufacturing, elucidation of structure, specification and stability of the drug substance is provided in DMF [redacted (b) (4)] from [redacted (b) (4)]. This DMF was reviewed by Dr. Joseph Leginus on October 26, 2017 and deemed adequate.

Sincalide is chemically described as (3*S*)-3-amino-4-[[(2*S*)-1-[[(2*S*)-1-[[2-[[(2*S*)-1-[[(2*S*)-1-[[(2*S*)-1-amino-1-oxo-3-phenylpropan-2-yl]amino]-3-carboxy-1-oxopropan-2-yl]amino]-4-methylsulfanyl-1-oxobutan-2-yl]amino]-3-(1H-indol-3-yl)-1-oxopropan-2-yl]amino]-2-oxoethyl]amino]-4-methylsulfanyl-1-oxobutan-2-yl]amino]-1-oxo-3-(4-sulfooxyphenyl)propan-2-yl]amino]-4-oxobutanoic acid. Its molecular formula is $C_{49}H_{62}N_{10}O_{16}S_3$ and molecular mass is 1143.27.



The quality of sincalide is controlled by its specification which includes appearance, identification by infrared spectroscopy and HPLC, assay by HPLC, impurities by HPLC, residual solvents by GC, water content, [redacted (b) (4)] content and specific rotation. The drug substance specification is deemed adequate per drug substance reviewer, Dr. Joseph Leginus. (see the **Drug Substance** review). Based on the stability data provided in DMF [redacted (b) (4)] a retest period of [redacted (b) (4)] months when stored [redacted (b) (4)] was established.

The Office of Process and Facilities (OPF) reviewer, Dr. Vidya Pai has made an "Adequate" recommendation for manufacturing and testing facilities of all drug substances (See the **Facilities** review).

The drug substance manufactured by [redacted (b) (4)] described in DMF [redacted (b) (4)] is controlled to conform to the requirements (specification) to produce Sincalide for Injection.

Drug Product:
Sincalide for Injection is a sterilized lyophilized white to off-white cake or powder to be reconstituted for intravenous injection. Each vial contains 5 µg of sincalide with 170 mg mannitol, 30 mg arginine hydrochloride, 15 mg lysine hydrochloride, 4 mg methionine, 2 mg pentetic acid, 0.04 mg sodium metabisulfite. The pH (b) (4) adjusted to 6.5 to 7.5 with sodium hydroxide or hydrochloric acid prior to lyophilization. Pentetic acid is used as (b) (4) and sodium metabisulfite is used as (b) (4).

The drug product is manufactured, packaged, tested and released at Gland Pharma Ltd., Hyderabad, India. The bulk drug product solution manufacturing process consists of (b) (4) All manufacturing procedures and operations are performed in accordance with current Good Manufacturing Practices described in 21 CFR 210 and 21 CFR 211. There i (b) (4) The drug product manufacturing process was reviewed by Dr. Yaodong Huang and was deemed acceptable. (See **Process** review)

Micro:
The environmental monitoring at (b) (4) (b) (4) (b) (4) etc. were reviewed by Dr. Paul L. Dexter and recommended this NDA for approval based on sterility assurance. (See the **Microbiology** review).

Biopharm:
The proposed MAIA's drug product and the RLD (Kinavac) are identical in the dosage form and strength. However, there are differences between the formulations of the proposed MAIA's product and the RLD i.e. the absence of dibasic potassium phosphate, and the absence of polysorbate 20, and tighter pH control.

Comparison of the proposed drug product and RLD, Kinavac.

Listed Drug (KINEVAC (sincalide) for Injection, 5 mcg/vial)		MAIA Product (Sincalide for Injection, 5 mcg/vial)	
Ingredient	**Amount/vial**	**Ingredient**	**Amount**
Mannitol	170 mg	Mannitol USP	170 mg
Arginine hydrochloride	30 mg	Arginine hydrochloride USP	30 mg
Lysine hydrochloride	15 mg	Lysine hydrochloride USP	15 mg
Potassium phosphate dibasic	9 mg		
Methionine	4 mg	Methionine USP	4 mg
Pentetic acid	2 mg	Pentetic acid USP	2 mg
Sodium metabisulfite	0.04 mg	Sodium metabisulfite USP	0.04 mg
Polysorbate 20	0.005 mcg		
Sodium hydroxide/ Hydrochloric acid	Q.S to pH 6.0 to 8.0	Sodium hydroxide NF/ Hydrochloric acid NF	**Q.S to pH 6.5 to 7.5**

The applicant made a biowaiver request, and although, the biowaiver request for the intravenous route was found adequate and justified via a biobridge pathway under 21 CFR 320.24 (b)(6), but, the request for a waiver for the (b) (4) was found inadequate requiring further justification. This drug product is recommended for approval for only *intravenous administration* from the biopharmaceutics perspective. The biowaiver request was reviewed by Dr. Bryan Ericksen. (see **Biopharmaceutics** review)

The overall control strategy for the drug product is deemed adequate based on raw material controls, drug product specification including appearance, assay, impurities, water content, content uniformity, sterility and bacterial endotoxins limits. For assay and impurities determinations, the applicant developed and used non-compendial, validated in-house methods. The controls for appearance, water content, pH and particulate matter also deemed adequate. Based on long-term and accelerated stability data of the drug product assuring the identity, strength, purity and quality, a 24-month of expiration dating period when stored between 20ºC to 25ºC in the proposed container closure system is granted. (See the **Drug Product** review by Dr. Zhengfang Ge).

The Office of Process and Facilities (OPF) reviewer, Dr. Vidya Pai, has made an "Adequate" recommendation for the drug substances and drug product manufacturing and testing facilities involved in this NDA. (See the **Facility** review).

The claim of a categorical exclusion from the requirements of an environmental assessment (EA) in accordance with 21 CFR Part 25.31 (a) and no extraordinary circumstances exists under 21 CFR 25.15 (d) warrant preparation of an environmental assessment was deemed acceptable.

The labels and labeling issues are ***not*** yet satisfactorily resolved from the CMC perspective according to the labeling reviewer, Dr. Zhengfang Ge. Therefore, this application is ***not*** deemed ready for approval in its present form per 21CFR 314.125(b)(6) from the OPQ perspective until the deficiencies listed below are satisfactorily resolved. (See the **Labeling** review).

C. Lifecycle Management Consideration

<u>The Office of Process and Facilities:</u>

A. Regarding Facilities:
A post approval inspection at Gland Pharma Limited, Hyderabad India, FEI#3002647489, the drug product manufacturer is recommended.

The process review notes that the firm has used (b) (4) overfill, which presents scale-up risks that may present themselves at the (b) (4) L scale and may not be readily apparent at the (b) (4) L exhibit batch scale. Therefore, a post-approval inspection

is recommended to support this NDA to review the firm's validation activities and ensure that the selected manufacturing process delivers the critical quality attributes for the drug product.

B. Regarding Manufacturing Process:

(b) (4)

[redacted]

Biopharmaceutics:

This drug product is recommended for approval for IV route only from the Biopharmaceutics perspective. However, for approval of the (b) (4) the Applicant should address the following issues:

(b) (4)

1. [redacted]

2.

3. [redacted] (b) (4)

[redacted] (b) (4)

[redacted] (b) (4)

E. Special Product Quality Labeling Recommendations (NDA only)

None

F. Final Risk Assessment (see Attachment)

E. List of Deficiencies:

The following labeling comments should be resolved with the applicant.

A. Regarding PI

a) Highlight Section
The Highlight section should include [redacted] (b) (4),
including [redacted] (b) (4) in the Title

b) Full Prescribing Information

#3: Dosage Forms and Strengths
The section 3 should include a description of "lyophilized white powder".

#11: Description
The section 11 should be rearranged for the inactive ingredients in an alphabetic order.

#16: How Supplied/Storage and Handling
The section 16 should include Manufacturer/distributor name and contact information.

B. Regarding Container/Carton Labels:

- Clarify that "batch details" to be printed on the container and carton labels includes Lot No and expiration date.
- Include "excursions permitted from 15°C to 30°C (59°F-86°F) [see USP Controlled Room Temperature]" for the storage condition in the carton label
- List the inactive ingredients in alphabetic order on the carton label

Application Technical Lead Name and Date:

Hitesh Shroff, Ph.D.
Application Technical Lead, Branch V
Division of New Drug Products II
February 12, 2018

Hitesh N. Shroff -S
Digitally signed by Hitesh N. Shroff -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=2000348333, cn=Hitesh N. Shroff -S
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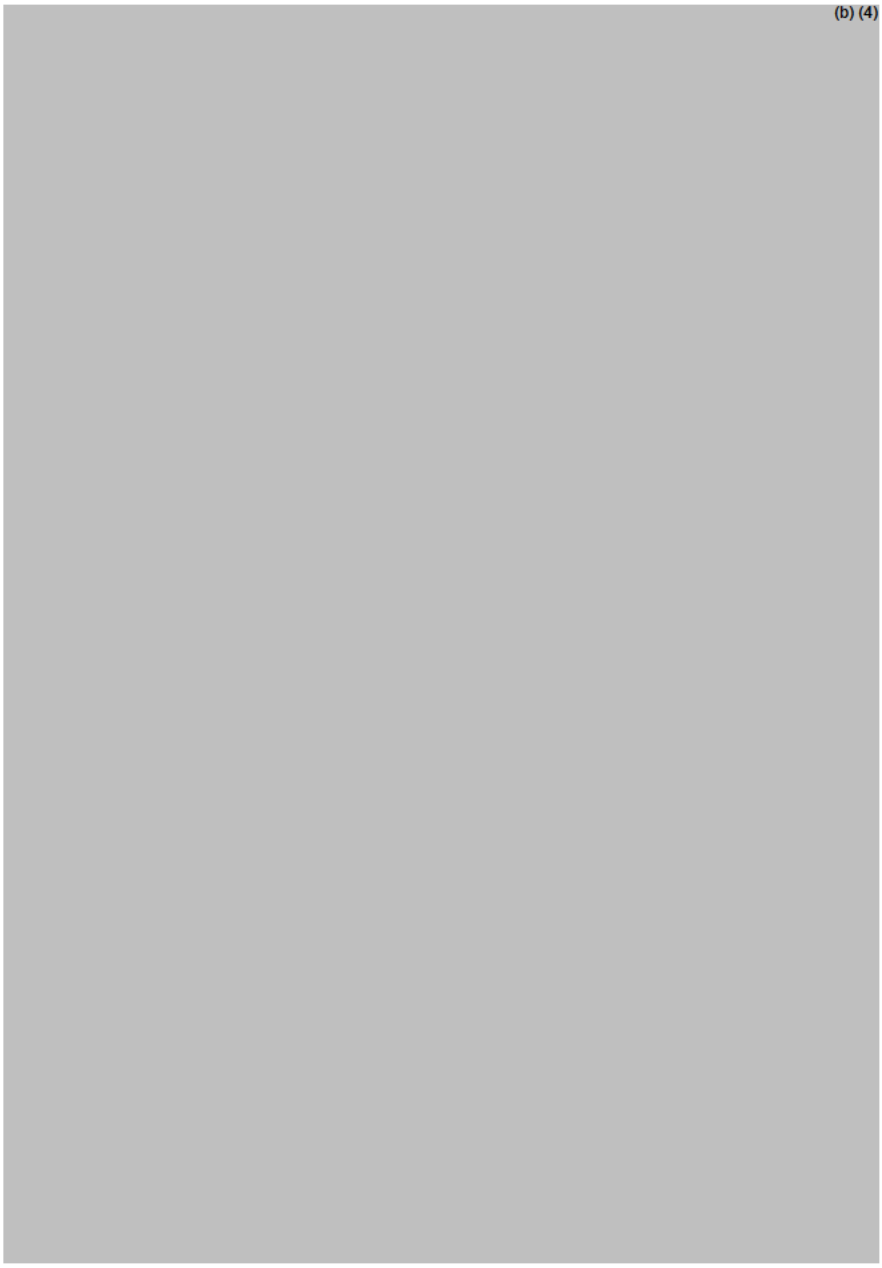
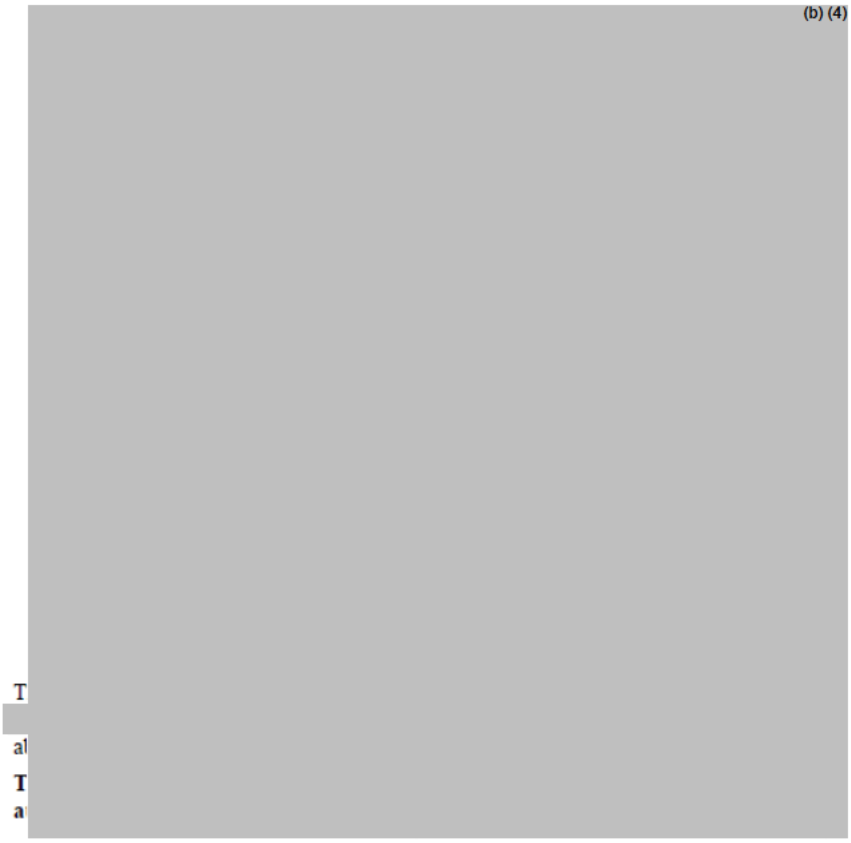
LABEL FOR NDA 210850

I. PI

1. Highlights of Prescribing Information





Revised: October 2017

Item	Information Provided in NDA	Reviewer's Assessment
Product Title (Labeling Review Tool and 21 CFR 201.57(a)(2))		
Proprietary name and established name	SINCALIDE For Injection, for intravenous use	**No proprietary name is proposed. The established name is sincalide which is the same as the listed drug** ***Adequate***
Dosage form, route of administration	For Injection, for intravenous use	**Since the proposed drug is proposed to be reconstituted for intravenous** (b) (4) **therefore** (b) (4) **should be reflected in the product title.** ***Not Adequate***
Controlled drug substance symbol (if applicable)	N/A	

Dosage Forms and Strengths (Labeling Review Tool and 21 CFR 201.57(a)(8))		
Summary of the dosage form and strength	Injection: single-dose vial containing 5 mcg of sincalide, for reconstitution	**Adequate**

Deficiencies

- [redacted] (b) (4) **will be added into the title if the administration route is approved**

2. *Section 2 Dosage and Administration*

[redacted] (b) (4)

(b) (4)

Item	Information Provided in NDA	Reviewer's Assessment
(Refer to Labeling Review Tool and 21 CFR 201.57(c)(12))		
Special instructions for product preparation (e.g., reconstitution, mixing with food, diluting with compatible diluents)	(b) (4) To reconstitute, aseptically add 5 mL of Sterile Water for Injection USP to the vial. This solution may be kept at room temperature and should be used within 8 hours of reconstitution, after which time any unused portion should be discarded. (b) (4) inspected visually for particulate matter and discoloration prior to administration, (b) (4)	**Adequate**

3. *Section 3 Dosage Forms and Strengths*

(b) (4)

Item	Information Provided in NDA	Reviewer's Assessment
(Refer to Labeling Review Tool and 21 CFR 201.57(c)(4))		
Available dosage forms	For injection as a single dose vial	**Adequate**
Strengths: in metric system	5 mcg sincalide per vial	**Adequate**
Active moiety expression of strength with equivalence statement (if applicable)	N/A	
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, and imprinting, when applicable.	None	**Not Adequate** **Add "a lyophilized white powder"**

4. ***Section 11 Description***

(b) (4)

Item	Information Provided in NDA	Reviewer's Assessment
(Refer to Labeling Review Tool and 21 CFR 201.57(c)(12), 21 CFR 201.100(b)(5)(iii), 21 CFR 314.94(a)(9)(iii), and 21 CFR 314.94(a)(9)(iv))		
Proprietary name and established name	Sincalide for Injection	**Adequate**
Dosage form and route of administration	For injection	**Adequate**
Active moiety expression of strength with equivalence statement (if applicable)	N/A	
For parenteral, otic, and ophthalmic dosage forms, include the quantities of all inactive ingredients [see 21 CFR 201.100(b)(5)(iii), 21 CFR 314.94(a)(9)(iii), and 21 CFR 314.94(a)(9)(iv)], listed by USP/NF names (if any) in alphabetical order (USP <1091>)	All inactive ingredients are listed, but not in alphabetic order	**Not Adequate** **The inactive ingredients will need to be listed in alphabetic order**
Statement of being sterile (if applicable)	stated	**Adequate**
Pharmacological/ therapeutic class	A cholecystopancreatic-gastrointestinal hormone peptide	**Adequate**
Chemical name, structural formula, molecular weight	Provided	**Adequate**
If radioactive, statement of important nuclear characteristics.	N/A	
Other important chemical or physical properties (such as pKa or pH)	…a sterile nonpyrogenic lyophillized white powder… The pH is adjusted to 6.5 to 7.5 with hydrochloric acid and/or sodium hydroxide prior to lyophilization	**Adequate**

5. ***Section 16 How Supplied/Storage and Handling***

Item	Information Provided in NDA	Reviewer's Assessment
(Refer to Labeling Review Tool and 21 CFR 201.57(c)(17))		
Strength of dosage form	5 mcg sincalide per vial	**Adequate**
Available units (e.g., bottles of 100 tablets)	Packages of 10 vials containing 5 mcg of sincalide per vial	**Adequate**
Identification of dosage forms, e.g., shape, color, coating, scoring, imprinting, NDC number	For injection, NDC number included	**Adequate**
Special handling (e.g., Dispense in tight and light resistant container as defined in USP)	N/A	**Adequate**
Storage conditions	Store at 25°C (77°F), excursions permitted from 15°C to 30°C (59°F-86°F) [see USP Controlled Room Temperature]	**Adequate**
Manufacturer/distributor name (21 CFR 201.1(h)(5))	Not included	**Inadequate** **Manufacturer/distributor name and contact information should be included**

Deficiency:

- The Highlight section should include all the approved Administration route, add (b) (4) in the Title
- The section 3 should include a description of "lyophilized white powder"
- The section 11 will need to be rearranged for the inactive ingredients in an alphabetic order

- The section 16 should include Manufacturer/distributor name and contact information should be included.

II. Labels:

1. **Immediate Container Label**

Item	Information Provided in NDA	Reviewer's Assessment
Proprietary name, established name (font size and prominence (21 CFR 201.10(g)(2))	Sincalide for injection	**Adequate**
Dosage strength Active moiety expression of strength with equivalence statement (if applicable), if space is available	5 mcg	**Adequate**
Net contents	single dose vial, 5 mcg	**Adequate**
"Rx only" displayed prominently on the main panel	Provided	**Adequate**
NDC number (21 CFR 207.35(b)(3)(i))	Provided	**Adequate**
Lot number and expiration date (21 CFR 201.17)	it is indicated that "batch details (to be printed online)	**Adequate Clarify that the batch detail includes Lot Number and Expiration Date**
Storage conditions Special handling, e.g., "Dispense in tight and light resistant container as defined in USP".	**Store at 25° C (77° F) See insert**	**Adequate Due to the congested space in a small vial, use of "see insert" is acceptable in the place of excursion storage condition**
Bar code (21CFR 201.25)	Provided	**Adequate**
Name of manufacturer/distributor	Provided	**Adequate**
And others, if space is available	Intravenous • Vial contains a sterile, lyophilized powder providing 5 mcg sincalide (see insert for inactive ingredients); pH adjusted to 6.5 - 7.5 with hydrochloric acid and/or sodium hydroxide. Usual dose: See insert	**Adequate Due to the congested space in a small vial, use of "see insert" is acceptable for the inactive ingredients**

2. Carton Label

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Item	Information Provided in NDA	Reviewer's Assessment
Proprietary name, established name (font size, prominence)	Sincalide for Injection	**Adequate** No proprietary name is proposed
Dosage strength Active moiety expression of strength with equivalence statement (if applicable) in the side panel.	5 mcg/vial	**Adequate**
Net quantity of dosage form	10 vial, 5 mcg/vial	**Adequate**
"Rx only" displayed prominently on the main panel	provided	**Adequate**
Lot number and expiration date	Space provided as shown below Un varnish area for Batch details & 2D barcode (To be printed online) 50 x 35 mm	**Adequate Clarify that the batch detail includes Lot Number and Expiration Date**
Storage conditions Special handling, e.g., "Dispense in tight and light resistant container as defined in USP".	Provided as shown below (b) (4)	**Inadequate Include "**excursions permitted from 15°C to 30°C (59°F-86°F) [see USP Controlled Room Temperature]"
Bar code (21CFR 201.25)	Space for 2D barcode is provided	**Adequate**
NDC number (21 CFR 207.35(b)(3)(i))	Provided	**Adequate**
Manufacturer/distributor's name	Provided	**Adequate**
Quantitative ingredient information (injectables)	Each vial contains a sterile, lyophilized powder providing 5 mcg sincalide with 170 mg mannitol, 30 mg arginine hydrochloride, 15 mg lysine hydrochloride, 4 mg methionine, 2 mg pentetic acid and 0.04 mg sodium metabisulfite. pH adjusted to 6.5 - 7.5 with hydrochloric acid and/or sodium hydroxide. When reconstituted with 5 mL of Sterile Water for Injection USP, each mL contains 1 mcg sincalide.	**Adequate**
Statement of being sterile (if applicable)	Each vial contains a sterile, lyophilized powder…	**Adequate**
"See package insert for dosage information"	Usual dose: See insert	**Adequate**
"Keep out of reach of children" (Required for OTC in CFR. Optional for Rx drugs)	Not provided	**Acceptable for the Rx drugs**

Deficiencies:

1. Clarify that batch details to be printed on the container and carton labels include Lot No and expiration date.
2. Include "excursions permitted from 15°C to 30°C (59°F-86°F) [see USP Controlled Room Temperature]" for the storage condition in the carton label
3. List inactive ingredients in an alphabetic order

List of Deficiencies:

For the Labeling insert

1. The Highlight section should include (b) (4) including (b) (4) in the Title
2. The section 3 should include a description of "lyophilized white powder"
3. The section 11 should be rearranged for the inactive ingredients in an alphabetic order.
4. The section 16 should include Manufacturer/distributor name and contact information.

For the Carton and Container Labels:

1. Clarify that "batch details" to be printed on the container and carton labels includes Lot No and expiration date.
2. Include "excursions permitted from 15°C to 30°C (59°F-86°F) [see USP Controlled Room Temperature]" for the storage condition in the carton label
3. List the inactive ingredients in alphabetic order on the carton label

Overall Assessment and Recommendation:

The labels and labeling are not acceptable until the above deficiencies are adequately addressed.

Primary Labeling Reviewer Name and Date:

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

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

I agree with Dr. Ge's assessment on the labeling and labels that they are not ready for approval as they are until the deficiencies delineated in the **List of Deficiencies** are satisfactorily resolved.

Moo-Jhong Rhee, Ph. D.
Branch Chief, BRANCH V/DIVISION II
OFFICE OF NEW DRUG PRODUCT

Zhengfang Ge

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Moo Jhong Rhee

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BIOPHARMACEUTICS

Product Background:

NDA: 210850

Drug Product Name / Strength: Sincalide for Injection, 5 mcg/vial

Route of Administration: Intravenous (b) (4) proposed

Applicant Name: MAIA Pharmaceuticals

Review Summary:

MAIA's NDA 210850 is a 505(b)(2) submission seeking approval for Sincalide for Injection, 5 mcg/vial. The proposed generic drug product contains 5 mcg/vial of Sincalide, a cholecystokinetic agent (in an injectable dosage form), referencing the Listed Drug (LD), Kinevac, (Sincalide for Injection, 5 mcg/vial), under NDA 017697, which was approved on 07/21/1976. It is indicated (1) to stimulate gallbladder contraction, (2) to stimulate pancreatic secretion, and (3) to accelerate the transit of a barium meal through the small bowel.

The proposed dosage form (injectable), strength (5 mcg/vial), and indications for MAIA's proposed generic drug product are the same as the currently approved LD. The proposed MAIA's product seeks route of administration for (b) (4) intravenous (IV) (b) (4) (b) (4)

Of note, when Kinevac was initially approved in 1976, only the IV route was approved. However, there is a sentence under "Dosage and Administration" in the current Kinevac labeling which states (p.8):

(b) (4)

Two issues were then raised for Kinevac:

1 (b) (4)
2

The generic formulation of MAIA's proposed drug product is not identical to the currently approved LD. As discussed in a Pre-IND meeting, MAIA's proposed DP does not contain potassium phosphate dibasic, a (b) (4) or polysorbate 20, a (b) (4) as those in the current LD. Thus, MAIA product has different inactive ingredients than the Listed Drug (b) (4)

The differences between MAIA's proposed drug product and the current LD do not support an application under Section 505(j) (or an Abbreviated New Drug Application). Therefore, it is concluded by OGD that MAIA's proposed DP is not eligible for submission of an ANDA under 505(j).

MAIA's proposed Sincalide 5 mcg/ml formulation (NDA 210850) was then submitted under 505(b)(2). A comparison of inactive ingredients between the MAIA's proposed DP and current LD is given in Table 1.

Table 1: Comparison of Inactive Ingredients: Listed Drug versus MAIA Product

Listed Drug (KINEVAC (sincalide) for Injection, 5 mcg/vial)		MAIA Product (Sincalide for Injection, 5 mcg/vial)	
Ingredient	**Amount/vial**	**Ingredient**	**Amount**
Mannitol	170 mg	Mannitol USP	170 mg
Arginine hydrochloride	30 mg	Arginine hydrochloride USP	30 mg
Lysine hydrochloride	15 mg	Lysine hydrochloride USP	15 mg
Potassium phosphate dibasic	9 mg		
Methionine	4 mg	Methionine USP	4 mg
Pentetic acid	2 mg	Pentetic acid USP	2 mg
Sodium metabisulfite	0.04 mg	Sodium metabisulfite USP	0.04 mg
Polysorbate 20	0.005 mcg		
Sodium hydroxide/ Hydrochloric acid	Q.S to pH 6.0 to 8.0	Sodium hydroxide NF/ Hydrochloric acid NF	**Q.S to pH 6.5 to 7.5**

There are only three changes between the proposed MAIA product and the current LD, i.e., the absence of dibasic potassium phosphate, the absence of polysorbate 20, and tighter pH control with sodium hydroxide and hydrochloric acid.

The applicant, MAIA, submitted a request for waiver for in vivo bioavailability studies for both routes of administration, intravenous (IV) and (b) (4) In the request, the applicant stated that the active pharmaceutical ingredient (API) is at the same strength as that of the LD, (b) (4) (b) (4) The applicant cited 21 CFR 320.24(b)(6), which states that the FDA can rely on "any other approach deemed adequate by FD to measure bioavailability or establish bioequivalence" for the IV route of administration.

The Agency clarified in the final meeting minutes of the pre-IND meeting that "the Sponsor will provide additional comparative solubility data of Sincalide in the formulations to support the (b) (4) (b) (4) of administration".
The applicant submitted a justification for a biowaiver for the (b) (4) of administration, dated November 10, 2017. In it, the applicant also noted that the Agency has confirmed that

comparison of physicochemical properties such as pH and osmolality has been used as an appropriate justification for a biowaiver for (b) (4) PIND (b) (4). The applicant provided physicochemical data as shown in the following table.

Table 12: Physicochemical Comparison of Listed Drug and MAIA's Sincalide for Injection after Reconstitution

Product	Batch Number (Expiry Date)	pH	Osmolality (mOsmol/kg)
Listed Drug: Kinevac (Sincalide for Injection), 5 mcg/vial	C1400177 (Test Date: 12/14; Expiry:10/15)	7.1	309
	C1500115 (Test Date: 02/16; Expiry: 08/16)	7.0	306
	C1500132 (Test Date: 02/16; Expiry: 09/16)	7.0	310
MAIA's Sincalide for Injection, 5 mcg/vial, Registration batches	AKA601	7.0	293
	AKA602	7.0	299
	AKA603	7.0	301

In addition, the applicant noted that Kinevac and the proposed product form true solutions. Current Kinevac drug product contains polysorbate 20 at (b) (4) mcg/mL, a concentration well below the critical micellar concentration (CMC) (b) (4) mM, or about (b) (4) mcg/mL). Absence of micelles in the currently Listed Drug and the MAIA proposed product was further confirmed by dynamic light scattering (DLS) studies and summarized in the following table.

Table 13: Volume-Based Particle Size Distribution by DLS in Simulated Kinevac and MAIA's Sincalide for Injection

Sample	Volume-Based Particle Size (Diameter) Distribution* (nm)		
	D_V 10	D_V 50	D_V 90
Positive Control: 1 mg/mL polysorbate 20	(b) (4)		
MAIA Sincalide for Injection, Batch No. SCL-05-183*			
Simulated Kinevac† Placebo, Batch No. SCL-04-120*			
Simulated Kinevac†, Batch No. SCL-04-146*			

* After reconstitution in 5 mL of Water for Injection

† Simulated formulation of Kinevac was used due to shortage of the Listed Drug at the time of the study

The applicant also provided the results of a solubility study with and without polysorbate 20, as shown in the following table.

Table 14: Results of Solubility Study of Sincalide with and without Polysorbate 20

S. No.	Excipient Solution	Solubility
1	*Proposed formulation without polysorbate 20* Excipient solution at the bulk concentration level (b) (4) mg/mL Mannitol mg/mL Arginine Hydrochloride mg/mL Lysine Hydrochloride m/mL Methionine (b) (4) mg/mL Pentetic acid (b) (4) mg/mL Sodium metabisulfite Sodium hydroxide, Q.S to pH 7.0 Water for Injection	>100 mcg/mL (100-fold greater than the 1 mcg/mL reconstituted concentration)
2	*Proposed formulation with polysorbate 20* All of the above excipients, and additionally (b) (4) mcg/mL Polysorbate 20 (corresponding to Listed Drug bulk concentration)	>100 mcg/mL

MAIA reported that the above data/results show that neither potassium phosphate dibasic nor polysorbate 20 is required (b) (4) the active ingredient, and therefore their absence is unlikely to affect bioavailability.

Finally, the applicant noted that the original formulation of Kinevac approved in 1976 (which contained only (b) (4) mcg sincalide and (b) (4) mg of (b) (4) with sodium hydroxide/hydrochloric acid to adjust to a pH of (b) (4) and marketed until 2002 for over 25 years without potassium phosphate dibasic or polysorbate 20 in the formulation.

Based on the submitted information and justification, the applicant's request for granting a waiver for conducting a bioavailability (BA)/bioequivalence (BE) study for the true solution of sincalide via the intravenous route can be granted from biopharmaceutics perspective.

(b) (4)

(b) (4)

List Submissions being reviewed (table):

08/25/2017	NDA 210850/0000/Original submission
11/17/2017	NDA 210850/0003/Response to Information Requests Dated October 25, 2017, November 7, 2017 and November 8, 2017

Highlight Key Outstanding Issues from Last Cycle: N/A

Concise Description Outstanding Issues Remaining: The Applicant's request for a waiver for the intravenous route is reviewed and found adequate which has been justified via a biobridge pathway under 21 CFR 320.24(b)(6).

However, the request for a waiver for the (b) (4) was found inadequate which requires further justification. Please see the Live Cycle Management Consideration on p.7 for details.

BCS Designation

Reviewer's Assessment: N/A

Solubility: see Biopharm review above

Permeability: N/A

Dissolution: N/A

Dissolution Method and Acceptance Criteria

Reviewer's Assessment: N/A

{Assess method development, method robustness, and criteria; modeling approach}

Clinical relevance of dissolution method & acceptance criteria (e.g., IVIVR, IVIVC, In Silico Modeling, small scale in vivo)

Reviewer's Assessment: N/A

Application of dissolution/IVIVC in QbD

Reviewer's Assessment: N/A

MODIFIED RELEASE ORAL DRUG PRODUCTS –In-Vitro Alcohol Dose Dumping

Reviewer's Assessment: N/A

In-Vitro Soft-food Interaction Study

Reviewer's Assessment: N/A

In-Vitro Release Testing (IVRT) for Semi-Solid Products

Reviewer's Assessment: N/A

In-Vitro Permeation Testing (IVPT) for Transdermal/Topical Products

Reviewer's Assessment: N/A

In-Vitro Dissolution Testing for Abuse-deterrent Products

Reviewer's Assessment: N/A

In-Vitro BE Evaluation for Pulmonary Products

Reviewer's Assessment: N/A

EXTENDED RELEASE DOSAGE FORMS –Extended Release Claim

Reviewer's Assessment: N/A

Bridging of Formulations

Reviewer's Assessment: N/A

Biowaiver Request

Reviewer's Assessment: Your request for a waiver for the intravenous route is adequate. Your request for a waiver for the (b) (4) however, requires further justification.

R Regional Information

Comparability Protocols

Reviewer's Assessment: N/A

Post-Approval Commitments

Reviewer's Assessment: N/A

Lifecycle Management Considerations:

This drug product is recommended for approval for IV route only from the Biopharmceutics perspective. (b) (4)

1. (b) (4)
2.
3.

List of Deficiencies:

Primary Biopharmaceutics Reviewer Name and Date:

Bryan Ericksen, Ph.D. 11/22/2017

Secondary Reviewer Name and Date (and Secondary Summary, as needed):
Tien-Mien Chen, Ph.D.

I concur. 12/25/17, 01/17/18, 02/07/18

Tien-Mien Chen, Ph.D.
Acting Biopharm. Lead

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MICROBIOLOGY

IQA Review Guide Reference

Product Background

NDA: 210850

Drug Product Name / Strength: Sincalide for Injection, 5 mcg/vial

Route of Administration: IV (b) (4)

Applicant Name: MAIA Pharmaceuticals, Inc.

Manufacturing Site: Gland Pharma Limited
Survey No. 143-148, 150 & 151
Near Gandimaisamma Cross Roads
D.P. Pally, Quthubullapur Mandal
Ranga Reddy District, Dundigal (Post), Hyderabad
500 043, Telengana, India

(FEI # (b) (4)

Method of Sterilization: (b) (4)

Review Recommendation: **The submission is recommended for approval on the basis of sterility assurance.**

List Submissions Being Reviewed: 8/25/17, 11/17/17

Highlight Key Outstanding Issues from Last Cycle: N/A

Remarks: Applicant cover letter requests "Priority Review Designation". The listed drug, KINEVAC (sincalide) for injection is currently listed in the FDA Drug Shortage database. KINEVAC is FDA approved NDA 17697.

Concise Description Outstanding Issues Remaining: N/A. Adequate sterility assurance is demonstrated.

Supporting Documents: DMF (b) (4) **for Rubber Stopper** (b) (4) **is referenced by** (b) (4) **Micro review D** (b) (4) **M33R01.doc dated 2/3/17 by M. Cruz-Fisher reviews the** (b) (4) **data and is adequate. Approved ANDA** (b) (4) **(Y. Chen, 12/19/16) is an** (b) (4)

(b) (4) and lyophilized drug product (b) (4) as this subject drug product.

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

P.1 Description of the Composition of the Drug Product

- **Description of drug product –** Sincalide for Injection is a sterile lyophilized powder. The drug is a 5mcg/vial single dose product packaged in a 5 ml glass vial with a 20 mm stopper.

- **Drug product composition**

Ingredient	Function	Quantity/Vial
Sincalide	Active	5 mcg
Mannitol	(b) (4)	170 mg
L-Arginine HCl	30 mg	(b) (4)
L-Lysine HCl	15 mg	
L-Methionine	4 mg	
Pentetic Acid	2 mg	
Sodium Hydroxide	Q.S for pH	pH
Hydrochloric Acid	Q.S for pH	pH
WFI	(b) (4)	Removed during Lyo
(b) (4)	(b) (4)	Q.S

- **Description of container closure system –**

Configuration	Component	Description	Manufacturer
5 mcg/vial	Glass Vial	(b) (4) 5 ml (b) (4) clear glass vial with 20mm neck (b) (4) (b) (4)	(b) (4)
	Rubber Stopper	20 mm (b) (4) (b) (4) (b) (4)	
	Seal	20mm Cap	

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.

P.2 Pharmaceutical Development

P.2.5 Microbiological Attributes

Container/Closure and Package Integrity
(P.2 page 117/128)

Hitesh Shroff

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