CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

211488Orig1s000

OTHER REVIEW(S)

MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING
Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	May 7, 2021
Requesting Office or Division:	Division of Oncology 1 (DO1)
Application Type and Number:	NDA 211488
Product Name and Strength:	Camcevi (leuprolide) injectable emulsion, 42 mg
Applicant/Sponsor Name:	Foresee Pharmaceuticals Co LTD (Foresee)
OSE RCM #:	2019-734-3
DMEPA Safety Evaluator:	Sarah Thomas, PharmD
DMEPA Team Leader:	Ashleigh Lowery, PharmD, BCCCP

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised carton labeling received on May 6, 2021 for Camcevi. The Division of Oncology 1 (DO1) requested that we review the revised carton labeling for Camcevi (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.[a]

2 CONCLUSION

The Applicant implemented all of our recommendations, and we have no additional recommendations at this time.

3 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

[a] Thomas S. Label and Labeling Review for Camcevi (NDA 211488). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 MAY 3. RCM No.: 2019-734-2.

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/s/

SARAH E THOMAS
05/07/2021 01:47:51 PM

ASHLEIGH V LOWERY
05/11/2021 01:10:08 PM

FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion

****Pre-decisional Agency Information****

Memorandum

Date: May 11, 2021

To: Amy Tilley, Regulatory Project Manager
Division of Oncology 1 (DO1)

William Pierce, PharmD, Associate Director for Labeling, DO1

From: Lynn Panholzer, PharmD, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Aline Moukhtara, RN, MPH, Team Leader, OPDP

Subject: OPDP Labeling Comments for CAMCEVI (leuprolide) injectable emulsion, for subcutaneous use

NDA: 211488

In response to DO1's consult request dated August 11, 2020, OPDP has reviewed the proposed product labeling (PI) and carton and container labels for the original NDA submission for CAMCEVI (leuprolide) injectable emulsion, for subcutaneous use.

Labeling: OPDP's comments on the proposed PI are based on the draft PI obtained from Sharepoint on May 7, 2021, and are provided below.

Carton and Container Labels: OPDP has reviewed the attached proposed carton and container labels submitted by the Applicant to the electronic document room on April 28, 2021, and we do not have any comments.

Thank you for your consult. If you have any questions, please contact Lynn Panholzer at (301) 796-0616 or lynn.panholzer@fda.hhs.gov.

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/s/

LYNN M PANHOLZER
05/11/2021 09:53:19 AM

MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING
Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	May 3, 2021
Requesting Office or Division:	Division of Oncology 1 (DO1)
Application Type and Number:	NDA 211488
Product Name and Strength:	Camcevi (leuprolide) injectable emulsion, 42 mg
Applicant/Sponsor Name:	Foresee Pharmaceuticals Co LTD (Foresee)
OSE RCM #:	2019-734-2
DMEPA Safety Evaluator:	Sarah Thomas, PharmD
DMEPA Team Leader:	Ashleigh Lowery, PharmD, BCCCP

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container label, carton labeling, prescribing information (PI), and instructions for use (IFU) received on April 28, 2021 for Camcevi. The Division of Oncology 1 (DO1) requested that we review the revised container label, carton labeling, PI, and IFU for Camcevi (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during previous label and labeling reviews.[a,b]

2 CONCLUSION

Upon review of the container label, carton labeling, PI, and IFU, we note that the Applicant implemented most of our recommendations except for adding color to the gray syringe cap in the diagrams showing syringe assembly and administration. Foresee's vendor was not able to add color to the syringe cap (b) (4) We find their rationale for not implementing this recommendation reasonable. However, we have additional edits and recommendations provided below in Sections 3 and 4 to further improve the labeling and ensure safe medication use.

[a]Thomas S. Label and Labeling Review for Camcevi (NDA 211488). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 MARCH 16. RCM No.: 2019-734.
[b] Thomas S. Label and Labeling Review Memo for Camcevi (NDA 211488). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 APRIL 20. RCM No.: 2019-734-1.

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/s/

SARAH E THOMAS
05/03/2021 06:40:31 PM

ASHLEIGH V LOWERY
05/05/2021 09:54:54 AM

OFFICE OF PRODUCT EVALUATION AND QUALITY
OFFICE OF HEALTH TECHNOLOGY 3

DIVISION OF DRUG DELIVERY, GENERAL HOSPITAL & HUMAN FACTORS
INTERCENTER CONSULT MEMORANDUM – PRE-FILLED SYRINGES

Date	4/30/2021		
To:	Amy Tilley, CDER/OND/ORO/DROOD		
Requesting Center/Office	CDER/OND	**Clinical Review Division**	Other
From	Florencia Wilson OPEQ/OHT3/DHT3C		
Through (Team)	Courtney Evans, Acting Team Lead, Injection Team OPEQ/OHT3/DHT3C		
Through (Division) *Optional	Rumi Young, MS, RAC, Acting Assistant Director OPEQ/OHT3/DHT3C		
Subject	NDA 211488, Leuprolide mesylate injectable suspension ICC2000742 Case 00026686		
Recommendation	**Filing Recommendation Date: 9/9/2020** ☐ CDRH did not provide a Filing Recommendation ☑ Device Constituent Parts of the Combination Product are acceptable for Filing. ☐ Device Constituents Parts of the Combination Product are Acceptable for Filing with Information requests for the 74-Day Letter, See Appendix A ☐ Device Constituents Parts of the Combination Product are Not Acceptable for Filing - See Section 5 for Deficiencies		
	Mid-Cycle Recommendation Date: 12/3/2020 ☐ CDRH did not provide a Mid-Cycle Recommendation ☐ CDRH has no approvability issues at this time. ☑ CDRH has additional Information Requests, See Appendix A ☐ CDRH has Major Deficiencies that may present an approvability issue, See Appendix A.		
	Final Recommendation Date: 4/14/2021 ☑ Device Constituent Parts of the Combination Product are Approvable. ☐ Device Constituent Parts of the Combination Product are Approvable with Post-Market Requirements/Commitments, See Section 2.3 ☐ Device Constituent Parts of the Combination Product are Not Approvable - See Section 2.2 for Complete Response Deficiencies		

Digital Signature Concurrence Table		
Reviewer	**Team Lead (TL)**	**Division (*Optional)**

Of Note: words in red are additional information received on April 30, 2021 related to the change in dose accuracy (deliverable weight) specifications

1. SUBMISSION OVERVIEW

Submission Information

Submission Number	NDA 211488
Sponsor	FORESEE PHARMACEUTICALS CO LTD
Drug/Biologic	Leuprolide mesylate injectable suspension
Indications for Use	Palliative treatment of advanced prostate cancer
Device Constituent	Pre-Filled Syringe
Related Files	ICC1900343/Case 00010489

Important Dates	
Filing	9/9/2020
74-Day Letter	
Midcycle Meeting/IRs due	12/3/2020
Final Lead Device Review Memo Due	4/27/2021
PDUFA Date	5/27/2021

2. EXECUTIVE SUMMARY AND RECOMMENDATION

CDRH recommends the combination product is:
☑ Approvable – the device constituent of the combination product is approvable for the proposed indication.
☐ Approvable with PMC or PMR, See Section 2.3
☐ Not Acceptable – the device constituent of the combination product is not approvable for the proposed indication. We have Major Deficiencies to convey, see Section 2.2.

2.1. Comments to the Review Team

☑ CDRH does not have any further comments to convey to the review team.
☐ CDRH has the following comments to convey to the review team:

2.2. Complete Response Deficiencies

☑ There are no outstanding unresolved information requests, therefore CDRH does not have any outstanding deficiencies.
☐ The following outstanding unresolved information requests should be communicated to the Sponsor as part of the CR Letter:

2.3. Recommended Post-Market Commitments/Requirements

CDRH has Post-Market Commitments or Requirements	☐
CDRH does not have Post-Market Commitments or Requirements	☑

3. PURPOSE/BACKGROUND

3.1. Scope

FORESEE PHARMACEUTICALS CO LTD is requesting approval of Leuprolide mesylate injectable suspension . The device constituent of the combination product is a Pre-Filled Syringe.

CDER/OND has requested the following consult for review of the device constituent of the combination product:

DO1 is requesting CDRH to provide consultative review of the device component to this pre-filled syringe combination product regarding this 505b2 NDA Resubmission after Refuse to File (RTF due to CDRH issues) for leuprolide mesylate injectable suspension, for prostate cancer.

The goal of this memo is to provide a recommendation of the approvability of the device constituent of the combination product. This review will cover the following review areas:

☒ Device performance
☐ Biocompatibility of the patient contacting components
☐ Sterility
☒ Stability – device performance on stability
☒ Essential Performance Requirements (EPR) Control strategy
☒ Quality Systems Assessment

This review will not cover the following review areas:

- Compatibility of the drug with the device materials (deferred to CDER)
- Biocompatibility of the primary container closure, including needle (deferred to CDER)
- Sterility (primary container closure sterility deferred to CDER)
- Human Factors (deferred to DMEPA)

The original review division will be responsible for the decision regarding the overall safety and effectiveness for approvability of the combination product.

3.2. Prior Interactions

CDRH was consulted initially under ICC1900343/Case 00010489. However, the device constituent parts of the combination product was not accepted for filing because, *"Design verification of the Essential Performance Requirements (EPR) was not provided for the subject device. Test reports and results for EPRs was requested interactively; however, the sponsor's interactive response indicated that device design verification was not performed for the proposed combination product. The proposed justification for not conducting design verification was not adequate. The submission does not include necessary elements for filing. Please refer to Section 5.3 for the complete interactive review and detailed consultant comments."*

3.2.1. Related Files

3.3. Indications for Use

Combination Product	Indications for Use
Leuprolide mesylate injectable suspension	Palliative treatment of advanced prostate cancer
Pre-Filled Syringe	Delivery of the Drug Product
needle	(b) (4), 18G x 5/8"
Point-Lok® needle Protection Device	red plastic stand alone upright needle protection device.

	(b) (4)

3.4. Materials Reviewed

Materials Reviewed	
Sequence	**Module(s)**
007	Modules 1, 3
0028	Modules 1, 3

4. DEVICE DESCRIPTION

4.1. Device Description

Figure 25: Pre-Fillable Syringe Diagram (Fully Assembled)

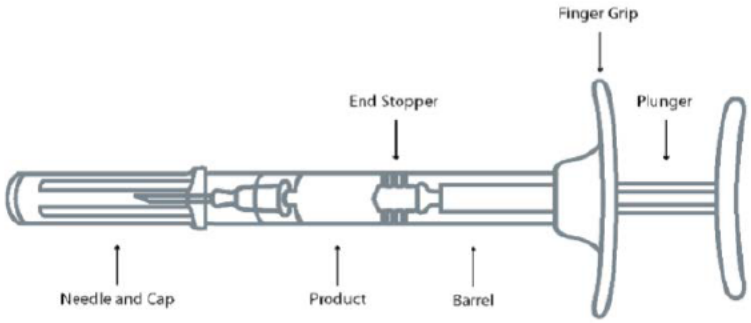

Figure 26: Point-Lok Needle Protection Device Diagram

(b) (4)

Refer to Table 75 for description of the container closure system components and co-packed devices.

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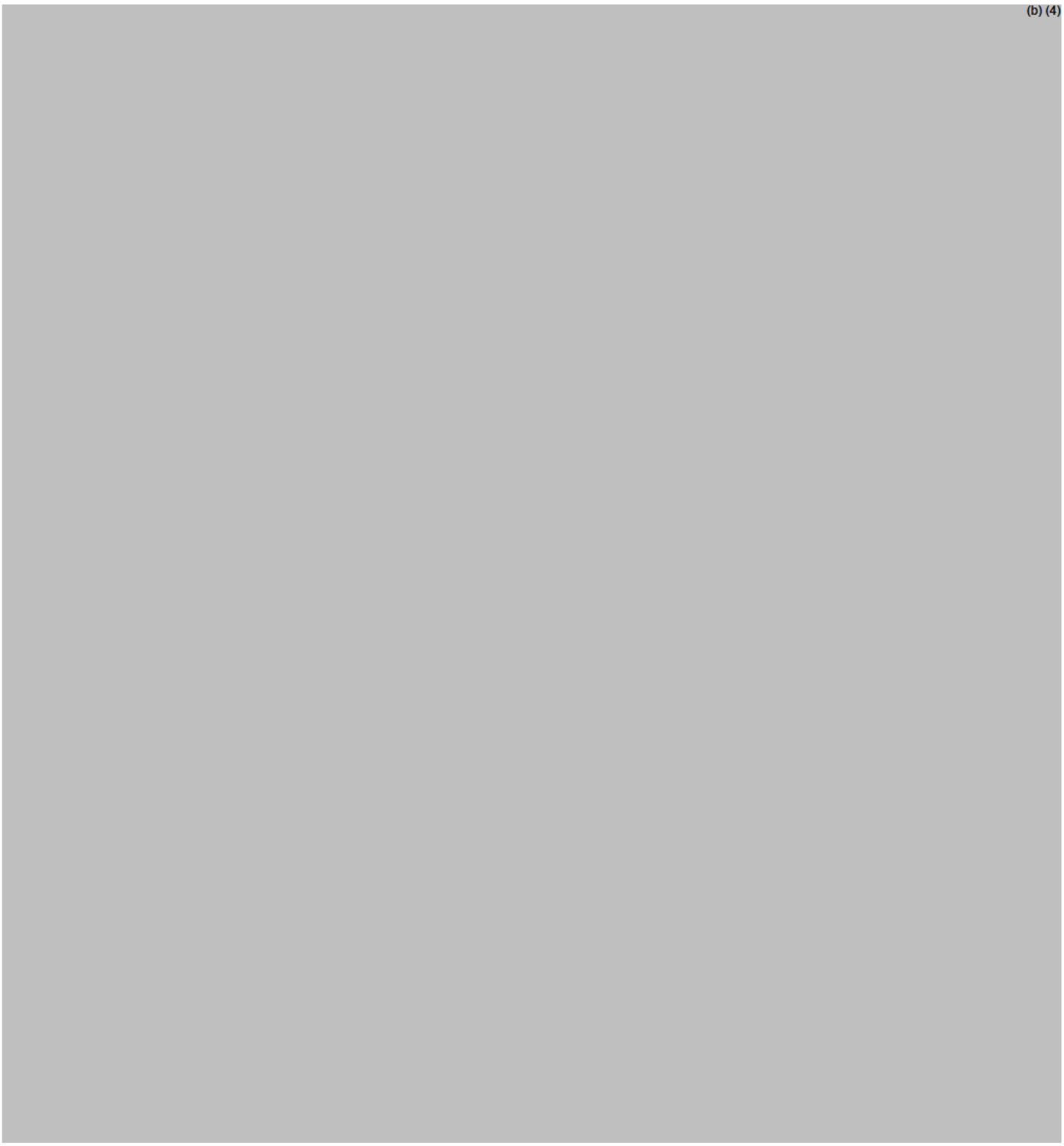

4.2. Design Requirements

Basic Syringe Description/Requirements

Requirement	Reviewer Comment
Intended user (e.g., self-administration, professional use, user characteristics and / or disease state that impact device use)	Health care professionals (HCP)

Injection Site	Abdomen that has not been used
Injection tissue and depth of injection	subcutaneous
Type of Use (e.g. single use, disposable, reusable, other)	Single use
Environments of use (e.g. home, clinic)	Health care facilities
Storage conditions and expiry	24 months expiry
Needle connection (e.g. luer, slip tip, staked)	luer
Syringe Volume	1 mL
Device materials including lubricant	**Syringe barrel**: (b) (4) **Stainless steel needle**, (b) (4) **Plunger rod and stopper**: (b) (4) **Backstop (finger grip)**: (b) (4) **Syringe tip caps**: (b) (4) . **Point-Lok® needle Protection Device**: red plastic stand alone upright needle protection device (b) (4)

Additional Syringe Description/Requirements

Requirement	Reviewer Comment
Hypodermic Needle: length, gauge, and configuration of the tip.	(b) (4) Needle, 18G x 5/8”
Markings (graduated scale, position of scale, length of scale, numbering of scale, and legibility criteria (for insulin syringes). Insulin Syringes: The scale on the barrel should be in units of insulin.	It is filled by weight (specification (b) (4)) *see Additional Information in Section 4.3 below
Reuse Durability (for reusable piston syringes): number of times the device can be sterilized and still meet specifications (using sterilization method indicated in the labeling).	N/A
Safety Features (e.g. Needle safety component/device)	The kit comes with a point lok needle protection device by (b) (4). It is not part of the PFS

Automated Functions	N/A
Sterilization method	(b) (4)

*See Design Verification Section for verification of design requirements

4.3. Device Description Conclusion

DEVICE DESCRIPTION REVIEW CONCLUSION

Filing Deficiencies:	Mid-Cycle Deficiencies:	Final Deficiencies:
☐ Yes ☑ No ☐ N/A	☐ Yes ☑ No ☐ N/A	☐ Yes ☑ No ☐ N/A

Reviewer Comments

The device constituent part of the combination product is the typical PFS consisting of the syringe, plunger rod, finger grip, stopper, tip cap, and co-packaged with two 510(k) cleared devices (needle with tip cap and patient-lok needle protection device). The needle protection device is used after the administration of the drug product. The sponsor provided an adequate device description.

*Additional Information:
Please note that on April 30, 2021, the Drug Product team received confirmation of the updated specification for dose accuracy (deliverable weight). The update specification is below:

Average of 5 syringes: (b) (4) mg
Each syringe: NLT (b) (4) mg

The data previously provided for release, stability, and shipping validation meets the updated specification or acceptance criteria.

CDRH sent Device Description Deficiencies or Interactive Review Questions to the Sponsor: ☐ Yes ☑ No

5. FILING REVIEW

CDRH performed Filing Review	☑
CDRH was not consulted prior to the Filing Date; therefore CDRH did not perform a Filing Review	☐

5.1. Filing Review Checklist

Filing Review Checklist				
Description		**Present**		
		Yes	**No**	**N/A**
Description of Device Constituent		X		
Device Constituent Labeling		X		
Letters of Authorization		X		
Essential Performance Requirements defined by the application Sponsor		X		
Design Requirements Specifications included in the NDA / BLA by the application Sponsor		X		
Design Verification Data included in the NDA / BLA or adequately cross-referenced to a master file.		X		
Risk Analysis supplied in the NDA / BLA by the application Sponsor		X		
Traceability between Design Requirements, Risk Control Measures and V&V Activities		X		
Verification/ Validation Check	Full Test Reports for Verification and Validation Testing	X		
	Reliability			X
	Biocompatibility			X

	Sterility			X
	Shelf Life, Aging and Transportation of EPRs	X		
Quality Systems/ Manufacturing Controls Check	Description of Quality Systems	X		
	Control Strategy provided for EPRs	X		

5.2. Facilities & Quality Systems Triage Inspection Recommendation Information

CDRH completed a **review** of the Facilities	☐ Yes ☐ No ☑ N/A
Inspection Recommendation	☐ Pre-Approval Inspection (PAI) ☐ Post-Approval Inspection ☐ Routine Surveillance ☑ No Inspection Needed ☐ N/A
CDRH completed a **review** of the Quality Systems	☐ Yes ☐ No ☑ N/A

*If a Facilities and/or Quality Systems Review is completed, the review is located in Appendix B

3.2.P.3.1. Manufacturers

Leuprolide Mesylate Injectable Suspension 50 mg drug product is manufactured according to current good manufacturing practices by (b) (4) Refer to Table 1 for information on the facilities involved in the manufacture, packaging, and control of the drug product.

Table 1: Facilities and Functions

Facility Information FEI/DUNS	Contact (name/phone/email)	Function/Responsibility
(b) (4)		

Facility Information FEI/DUNS	Contact (name/phone/email)	Function/Responsibility
		(b) (4)

5.3. Filing Recommendation

FILING REVIEW CONCLUSION

Acceptable for Filing: ☑ Yes ☐ No (Convert to a RTF Memo) ☐ N/A

Facilities Inspection Recommendation:

☐ (PAI) Pre-Approval Inspection ☐ Post-Approval Inspection ☐ Routine Surveillance
☑ No Inspection ☐ N/A

Site(s) needing inspection:

Reviewer Comments

The Sponsor provided a list of sites responsible for designing, fabricating, assembling, labeling, packaging, holding, and storing the finished combination product above. In addition, no inspection and Quality System Review needed because of the reasons below:

- the needle included in the co-packaged convenience kit is a 510(k) cleared device. Therefore, CDRH OPEQ does not need a consult to review combination products utilizing 510(k) cleared devices as long as the NDA does not introduce a change to the 510(k) cleared labeling or indications for use.
- For products that do not treat high risk conditions, and where the products have no known quality issues, CDRH OPEQ does not need to perform a 21 CFR 820 review or provide a facilities review. This type of device constituent part is a well understood device and is typically sourced from a limited number of manufacturers (b) (4). In the clinic environment, if one product fails, there is likely another unit

readily available. This type of device constituent part also has basic technology and has a low risk of device-related injuries or malfunctions.
Refuse to File Deficiencies: ☐ Yes ☐ No ☑ N/A
74-Day Letter Deficiencies: ☐ Yes ☑ No ☐ N/A

6. DEVICE PERFORMANCE REVIEW

6.1. Design Verification/Validation

6.1.1. Device Specification Standards and Guidance Documents

Syringe		**Data Adequate**		
		Yes	**No**	**N/A**
Pre-filled Syringe	ISO 11040-8, Prefilled syringes – Part 8: Requirements and test methods for prefilled syringes	☐	☐	☑
Co-packaged Syringe	ISO 7886-1, Sterile Hypodermic Syringes for Single Use—Part 1: Syringes for Manual Use	☐	☐	☑
Insulin Syringe	ISO 8537, Sterile single-use syringes, with or without needle, for insulin	☐	☐	☑
Needle/Sharps		**Data Adequate**		
		Yes	**No**	**N/A**
Needle	ISO 7864, Sterile Hypodermic Needles for Single Use	☑	☐	☐
Needle	ISO 6009, Hypodermic needles for single use – Color coding for identification	☑	☐	☐
Sharps Injury Prevention Feature	ISO 23908 - Sharps injury protection - Requirements and test methods - Sharps protection features for single-use hypodermic needles, introducers for catheters and needles used for blood sampling	☐	☐	☑
Luer Lock		**Data Adequate**		
		Yes	**No**	**N/A**
Connection	ISO 594-1, Conical fittings with a 6 % (Luer) taper for syringes, needles and certain other medical equipment - - Part 1: General requirements ISO 594-2, Conical fittings with 6 % (Luer) taper for syringes, needles and certain other medical equipment - - Part 2: Lock fittings	☑	☐	☐
Other		**Data Adequate**		
		Yes	**No**	**N/A**
[Other]	[Other]	☐	☐	☑

Reviewer Comment

The primary container closure is a syringe system filed with the FDA under DMF# (b) (4). The Sponsor provided an LoA and certificate of Compliance for the syringe system. In addition, this device is widely used as the container closure for other approved drug products, therefore, has been reviewed widely as well by our group.

The needle used for the co-packaged combination product is a 510(k) cleared device (b) (4) and conformed to the appropriate needle standards.

The luer connections for the syringe and needle both conforms to ISO 594-1 and ISO 594-2. The verification testing for the EPRs (deliverable weight, break loose, and glide force) were performed with the needle attached to the primary container closure. The sample size is n=60 for each batch use to perform the EPR testing.

This is acceptable.

6.1.2. Device Performance Evaluation

The application initially was placed on Refuse to File (RTF). Below is a list of deficiencies sent to the Sponsor to provide for this re-submission:

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Table 80: Results of Break Loose Force, Glide Force and Deliverable Weight in Container[1] for LMIS 50 mg

Syringe Number	Deliverable Weight (mg)	Break Loose Force (N)	Glide Force (N)
Min	373.2	1.9	2.1
Max	390.2	5.2	3.1
Average	381.8	3.6	2.5

[1] Refer to Module 3.2.P.5.2 for method description

Essential Performance Requirement	Specification
Dose Accuracy	(b) (4)
Break loose Force	
Glide Force	

Conclusions: All the individual results obtained on the statistically valid sample (60 syringes) fulfilled the acceptance criteria for deliverable weight in container, break loose force and glide force specified in Module 3.2.P.5.1. These design verification results confirm that LMIS 50 mg drug-device combination product performs correctly to achieve final user needs in terms of dose accuracy, break loose force and glide force.

The following are taken from Module 3.2.P.5.1:
Please note that the table below is the revised release specifications provided from the IR Response on April 30, 2021:

Test	Method	Analytical Reference	Specification for Release	Specifications for Shelf-Life
Deliverable weight in container	Analytical		(b) (4)	
Break Loose Force (N)	In-house			
Glide Force (N)	In-house			

Essential Performance Requirement	Specification	Verification Method Acceptable (Y/N)	Validation (Y/N)	Aging / Stability (Y/N)	Shipping/ Transportation (Y/N)
Dose Accuracy (deliverable weight)	(b) (4)	(b) (4) Y (attribute with n=60)	Y	Y	FP01N-21-001 Y
Break loose Force		(b) (4) Y (attribute with n=60)	Y	Y	FP01N-21-001 Y
Glide Force		(b) (4) Y (attribute with n=60)	Y	Y	FP01N-21-001 Y
Cap Removal Force				n/a	n/a
Other					

Reviewer Comment

The verification study were performed using 60 syringes at release which met the specified requirements for the essential performance (dose accuracy (deliverable weight), break loose/glide force of the PFS. Acceptable.

The validation study was performed by comparing the drug product to a similar approved combination product, Eligard 45 mg syringe system. This is in lieu of formal user studies and human factor analysis. In addition, the Sponsor also analyze data from the review of clinical Phase III data that demonstrated the drug product PFS can be used safely and effectively to satisfy the User Requirements. It is also noted that the combination product does not have any novel feature and that it is given by healthcare providers, who are familiar with drug administration with PFS. Therefore, it is acceptable.

Additional Information (4/30/2021):

After CDRH review was performed, additional information from CDER OPQ, Drug Product was received. The dose accuracy (deliverable weight) specification has been changed (see table above). Per the Clinical team, the dose accuracy parameter average (b) (4) mg) and that each syringe is NLT (b) (4) mg is a safe range/dose for the intended population. Despite the dose accuracy change, the Sponsor's data provided at release, stability, and shipping meets the updated dose accuracy performance specifications. This is acceptable.

6.1.3. Stability Review Summary

Shelf-life:	24 months
Storage **conditions**:	35 (b) (4)–46 (b) (4) F (2–8°C)
Time period and storage conditions provided for accelerated aging:	25 ±2 °C/60%RH
Time period and storage conditions provided for real-time aging:	5 ±3 °C

*Endpoint evaluation is provided in section 6.1.2.

The following summary are taken from 3.2.P.2. Pharmaceutical development:

Table 81: Results of Break Loose Force, Glide Force and Deliverable Weight in Container[1] at 5±3°C

Batch Number / Testing Time Point	T=0	T=1	T=3	T=6	T=9	T=12	T=18	T=24
Break Loose Force in N (Specification: (b) (4)								
CC0442	6.7	5.9	NT	NT	NT	NT	NT	NT
P99999	7.3	7.2	5.8	5.8	6.4	5.9	5.2	8.2
CL0080	6.3	NT	6.3	6.6	6.4	7.9	7.5	7.7
P99997	4.7	6.0	4.7	5.1	4.5	6.9	7.0	Pending
P99996	4.9[2]	NT	7.0	5.6	5.5	5.4	Pending	Pending
P00001	4.0	NT	4.0	4.0	Pending	Pending	Pending	Pending
Glide Force in N (Specification: (b) (4)								
CC0442	3.4	2.5	NT	NT	NT	NT	NT	NT
P99999	3.2	3.0	3.0	3.4	4.1	3.4	3.4	2.9
CL0080	2.6	NT	2.8	2.4	2.7	2.5	2.1	2.2
P99997	2.4	3.5	2.9	3.1	2.3	2.9	2.6	Pending
P99996	2.4	NT	3.0	2.6	2.6	2.5	Pending	Pending
P00001	3.0	NT	2.0	3.0	Pending	Pending	Pending	Pending
Deliverable Weight in Container in mg (Specification: (b) (4)								
CC0442	Average: 362 Min: 356	NT	NT	NT	NT	NT	NT	NT
P99999	Average: 376 Min: 372	NT	NT	NT	NT	NT	NT	NT
CL0080	Average: 380 Min: 377	NT	NT	NT	NT	NT	NT	NT
P99997	Average: 379 Min: 377	NT	NT	NT	NT	386 379	380 376	Pending
P99996	Average: 385 Min: 374	NT	NT	NT	NT	380 371	Pending	Pending
P00001	Average: 380 Min: 377	NT	392 385	390 385	Pending	Pending	Pending	Pending

Table 82: Results of Break Loose Force, Glide Force and Deliverable Weight in Container[1] at 25±2°C/60±5%RH

Batch Number / Testing Time Point	T=0	T=1	T=3	T=6
Break Loose Force in N (Specification: (b) (4)				
CC0442	6.7	7.1	NT	NT
P99999	7.3	7.7	7.8	7.3
CL0080	6.3	6.8	6.0	6.3
P99997	4.7	6.5	6.7	7.7
P99996	4.9[2]	4.1	6.0	6.6
P00001	4.0	NT	2.0	5.0
Glide Force in N (Specification: (b) (4)				
CC0442	3.4	2.5	NT	NT
P99999	3.2	3.7	3.3	3.1
CL0080	2.6	2.8	2.7	2.2
P99997	2.4	3.2	3.1	2.7
P99996	2.4	2.8	2.7	2.3
P00001	3.0	NT	3.0	2.0
Deliverable Weight in Container (Specification: (b) (4)				
CC0442	Average: 362 Min: 356	NT	NT	NT
P99999	Average: 376 Min: 372	NT	NT	NT
CL0080	Average: 380 Min: 377	NT	NT	NT
P99997	Average: 379 Min: 377	NT	NT	381 372
P99996	Average: 385 Min: 374	NT	NT	384 378
P00001	Average: 380 Min: 377	NT	394 387	394 391

[1] Refer to Module 3.2.P.5.2 for method description
[2] Test performed on 9 syringes
NT = not tested, NMT = not more than, NLT = not less than

Conclusion: The results of deliverable weight in container, break loose force and glide force obtained during drug product development show that device constituents deliver intended dose in reproducible and accurate manner and functionality of LMIS mg is maintained throughout drug product shelf-life.

Reviewer Comments

The stability test results of the essential performance requirement (dose accuracy (deliverable weight), break loose/glide force) met the defined specification as seen in the Table 82. It is noted that the real time study results at expiry for the three batches are still pending. However, the accelerated stability study for six month is acceptable and were performed on three batches (P99997, P99996, and P00001). It is noted that during the Type A meeting held on July 29, 2019, CDRH will accept the 6 months accelerated testing for the essential performance requirements of the combination product.

The Sponsor did not provide shipping validation. Therefore an IR will be sent to the Sponsor.

IR sent to the Sponsor – 12/16/2020

On April 13, 2021, the Sponsor provided the shipping validation per ASTM D4169. The protocol and the shipping validation data is reviewed. The test results demonstrated that the EPRs of the device constituents of the combination product met it's specifications. This is acceptable. I do not have further issues with the shipping validation and this IR is resolved.
The stability testing provided is acceptable.

Additional Information (4/30/2021):

Please note of the revised dose accuracy (deliverable weight) discussed above and that despite the revision, the provided data meets the new specification.

Average of 5 syringes: (b) (4) mg
Each syringe: NLT (b) (4) mg

6.1.4. Biocompatibility Evaluation

☐ Biocompatibility was **evaluated** [e.g. co-packaged syringes, co-packaged components outside of primary container closure]
☑ Biocompatibility was not evaluated **because**: it is under the purview of CDER

6.1.5. Sterility Evaluation

☑ Sterility **Evaluated** (e.g. co-packaged syringes, co-packaged components outside of primary container closure)
☐ Sterility not evaluated (syringe, including needle are part of primary container closure, sterility evaluation is under the purview of CDER)

☑ The needle is 510(k) Cleared
☐ The Syringe **is NOT 510(k) Cleared**

510(k) Number: _(b) (4) Needle, 18G x 5/8"			
	Yes	No	N/A
Contact classification of proposed device consistent with cleared 510(k) [if not, please evaluate the following]:	X		
If device is sterilized with EO, review acceptability of EO and ECH **residuals** (gamma radiation)			X
Ensure endotoxin limits are consistent with proposed administration route	X		

Reviewer Comments

The needle included in the co-package is a 510(k) cleared device and is used only during the injection step. The intended use of the needle is not changed when co-packaged with the combination product. It is also noted that the essential performance testing results all met the specifications at release.
This is acceptable.

6.2. Device Performance Review Conclusion

DEVICE PERFORMANCE REVIEW CONCLUSION		
Filing Deficiencies: ☐ Yes ☑ No ☐ N/A	**Mid-Cycle Deficiencies:** ☑ Yes ☐ No ☐ N/A	**Final Deficiencies:** ☐ Yes ☑ No ☐ N/A
Reviewer Comments As stated above, the Sponsor provided the testing for the EPRs of the PFS which met it's specifications. However, the Sponsor did not provide shipping validation. This was requested during the mid-cycle. On April 13, 2021, the Sponsor provided and evaluation of the EPRs after shipping validation per ASTM D4169. The EPRs met its specifications, therefore, the provided IR response is adequate.		
CDRH sent Device Performance Deficiency or Interactive Review Questions to the Sponsor: ☐ Yes ☐ No		

	Date Sent: 12/16/2020	**Date/Sequence Received:** 1/13/2021
Information Request #1	Provide shipping validation per ASTM D4169, "Standard Practice for Performance Testing of Shipping Containers and Systems", for the final finished product to demonstrate that the device Essential Performance Requirements (EPR) specifications are met after shipping. Requested due date: 1/13/2021	
Sponsor Response	*The sponsor requests additional time to submit the Shipping Validation per ASTM D4169 report.* (b) (4) [redacted] (b) (4) [redacted] (b) (4) [redacted] *Foresee will continue to make this requirement a priority and will communicate with FDA on the progress of the studies.*	
Reviewer Comments	Please see the e-mail Interaction with CDER and the follow-up e-mail to the sponsor **Sent:** Thursday, January 14, 2021 9:23 AM Hi Amy,	

	Good Morning, I read the response provided by the Sponsor. If they are projecting the submission of final report for review in May 2021 (they did not say the exact date), this is very close to the PDUFA date of 5/27/2021 and in addition our review due date is 4/27/2021. Based on this, we have the following proposal: • Give the Sponsor a hard deadline of early April 2021, in order for CDRH to meet our device review due date (please see important dates below) • Or extend our due date a couple of days before the PDUFA date, providing that the Sponsor provide the report on the first week of May 2021. Thu 1/14/2021 12:07 PM Per Christy we can extend the clock by 3 months if the CDRH info is submitted in May. I will ask the spon to give us a specific date either late April or early May and if they cannot get it to us by then we either extend the clock with a major amendment or CR this application again since this is an approvability issue.
Response Adequate:	☐ **Yes** ☑ **No, See IR # Sent on 1/14/2021**

Follow-On Deficiency	**Date Sent: 1/14/2021**	**Date/Sequence Received: 4/13/2021**
Information Request #	Please see the e-mail sent to the Sponsor: Thu 1/14/2021 12:19 PM Judith, after reviewing your response to our CDRH IR we note that your projected final report being submitted in May 2021 is close to the PDUFA date. Therefore, we request your final response be submitted **no later than May 3, 2021.** Please confirm that you will provide your response by the May 3rd deadline. Your prompt response to this email is required. Regards. **Amy Tilley** *Regulatory Project Manager*	
Sponsor Response	***4.2. Device Essential Performance Requirement (EPR) test results*** *The packaged 8 boxes, with each box containing 152 units/kits, were inspected before and after the shipping study by* (b) (4). *Visual inspection of carboard box and blister: No surface tear, opening, no impact on syringe and its accessories, and no damage was observed. The temperature range was maintained within 2°C – 8°C.* *Syringes of LMIS 50 mg Lot # P00003 were tested for syringe functionality by* (b) (4) *before and after the mechanical shipping validation study. The results are listed in Table 1 and 2.* ***Table 1:*** *Syringe functionality tests before mechanical shipping study*	

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	(b) (4) [redacted] ***CONCLUSION*** *ASTM-D4169 performance testing showed that the pallet handling was fully possible as there was no damage found. Also, the handling of the* (b) (4) *shippers did not cause any damage to the LMIS 50 mg kits packaged within. The mechanical tests performed before and after the shipping validation study were all compliant. This transportation study demonstrated that the shipping process does not adversely impact the device Essential Performance Requirements and product unit integrity of the LMIS 50 mg finished product.*
Reviewer Comments	After reviewing the data from the provided response, it demonstrated that the device constituent parts of the combination product met its specifications for it EPRs. Therefore, the provided response is adequate. I do not have further issues with this IR.
Response Adequate:	☐ **Yes** ☑ **No, See IR** # **Sent on** Click or tap to enter a date.

7. CONTROL STRATEGY REVIEW

The Sponsor provided the following control strategy information regarding the EPRs of the device constituents:

Essential Performance Requirements Control Strategy Table

** The proposed acceptance criteria for the EPR may be tighter than the design input and should be assessed for adequate quality control)/ Sampling Plan (Sampling plan may be review issue depending on the product (e.g. emergency-use)*

Essential Performance Requirements	Control Strategy Description - The Sponsor provided the following description of how the essential performance requirements of the combination product are controlled through incoming acceptance, in-process control, and/or release testing activities:	Acceptable (Y/N/NA)
Dose Accuracy	(b) (4)	Y
Break loose Force		Y
Glide Force		Y

Reviewer Comments

The Sponsor provided an adequate control strategy for the essential performance requirements, as demonstration in the test reports provided. The testing was performed with a sample size of n=60 with no failure. Therefore, it showing a 95% confidence and 95% reliability.

Control Strategy Conclusion		
The Sponsor provided adequate information to support the manufacturing control activities for the essential performance requirements of the combination product.	☒Yes	☐No

7.1. Control Strategy Review Conclusion

CONTROL STRATEGY REVIEW CONCLUSION		
Filing Deficiencies: ☐ Yes ☑ No ☐ N/A	**Mid-Cycle Deficiencies:** ☐ Yes ☑ No ☐ N/A	**Final Deficiencies:** ☐ Yes ☑ No ☐ N/A
Reviewer Comments The Sponsor provided adequate information to support the manufacturing control activities for the essential performance requirements of the combination product.		
CDRH sent Control Strategy Deficiency or Interactive Review Questions to the Sponsor: ☐ Yes ☑ No		

<<END OF REVIEW>>

8. APPENDIX A (INFORMATION REQUESTS)

8.1. Filing/74-Day Information Requests

N/A

8.2. Mid-Cycle Information Requests

Sent on 12/16/2020 (see Section 6.2).

8.3. Interactive Information Requests

8.3.1. Interactive Information Requests sent on 12/16/2020

9. APPENDIX B: FACILITIES & QUALITY SYSTEMS REVIEW

9.1. Facility Inspection Report Review

N/A

9.2. Quality Systems Documentation Review

N/A

10. APPENDIX C (CONSULTANT MEMOS)

Clinical Inspection Summary

Date	April 28, 2021
From	Yang-min (Max) Ning, M.D., Ph.D. Min Lu, M.D., M.P.H. Kassa Ayalew, M.D., M.P.H. GCPAB/OSI/CDER/FDA
To	Michael Brave, M.D. Chana Weinstock, M.D. Amy Tilley, RPM DO1/OOD/CDER/FDA
NDA #	211488
Applicant	Foresee Pharmaceuticals Co. Ltd
Drug	Leuprolide mesylate injectable suspension (LMIS)
New Molecular Entity	No
Therapeutic Classification	Gonadotropin-releasing hormone (GnRH) receptor agonist
Proposed Indication	Palliative treatment of advanced prostate cancer
Consultation Request Date	October 5, 2020
Inspection Summary Goal Date	April 16, 2021; Extended to 4/30/2021 per agreement reached on 2/4/2021 with DO1 following extension request of ORA
Action Goal Date	May 27, 2021
PDUFA Date	May 27, 2021

I. OVERALL ASSESSMENT OF INSPECTIONAL FINDINGS AND RECOMMENDATIONS

The clinical data of a single-arm study (FP01C-13-001) were submitted to the Agency in support of a 505(b)(2) New Drug Application (NDA) for LMIS for use in patients with advanced prostate cancer. Three investigators, Dr. Jeffrey Frankel (Site US03), Dr Eliot Horowitz (Site US01), and Dr. Mark Deguenther (Site US07), were selected for clinical inspection.

The inspection of Dr. Frankel found no regulatory violations and the Applicant's submitted data were verifiable with source data at the investigator site.

For Drs. Horowitz and Deguenther, the intended inspections have not been conducted due to the COVID-19 pandemic related travel restriction status at the two investigator sites. This was communicated to the DO1 review team and a decision was made by DO1 to forgo these two inspections for the current submission.

Based on the available inspection results, the clinical data generated from Dr. Frankel appear reliable in support of this 505(b)(2) NDA.

II. BACKGROUND

Leuprolide is a gonadotropin releasing hormone (GnRH) receptor agonist that has been approved for palliative treatment of advanced prostate cancer in the United Sates for three decades.

For this 505(b)(2) application, the Applicant submitted clinical data from a single-arm study [FP01C-13-001] of a 6-month formation of leuprolide mesylate injectable suspension (LMIS) and proposed the same indication as "for the palliative treatment of advanced prostate cancer".

Study FP01C-13-001 [NCT02234115] was an open-label, single-arm trial of LMIS in patients with advanced prostate carcinoma. The study had two parts. Part I was planned to first assess the safety, tolerability and early activity of LMIS in approximately 30 subjects following completion of 28-day assessments. Part 2 was to be initiated to enroll approximately 100 additional subjects if the planned interim analysis for Part 1 showed an acceptable safety profile and a castration rate of ≥ 90% by Day 28 (e.g. castration attained in ≥ 27 of the 30 subjects). For both parts, subjects were required to have: 1) pathologically-confirmed adenocarcinoma of the prostate that was deemed to require androgen ablation therapy by the investigator; 2) a baseline serum testosterone level of >150 ng/dL at screening; 3) no prior chemotherapy, immunotherapy, cryotherapy, radiotherapy, or anti-androgen therapy concomitantly. The primary efficacy measure was the percentage of subjects with castrate levels of testosterone (≤50 ng/dL) from Day 28 through Day 336.

The study product LMIS was administered as a single subcutaneous injection on Day 0 for subjects in both parts. A second dose of LMIS was to be administered on Day 168 for subjects who had tolerated and maintained castrate levels of testosterone. Subjects were to be discontinued from the study secondary to consent withdrawal, lost to follow-up, treatment with the protocol-specified prohibited medications, unacceptable toxicity or adverse event(s), or persistent non-castrate levels or disease progression at the investigator's discretion. For subjects who withdrew from the study due to adverse event(s), follow-up visits were required until resolution and/or stabilization of the event(s).

For the primary efficacy assessment, blood samples for testosterone were collected at the protocol-specified timepoints, including Days 0, 1, 2, 3, 7, 14, 21, 28, 56, 84, 112, 140, 168, 169, 170, 171, 196, 224, 252, 280, 308, and 336. These samples were required to be submitted to the sponsor's designated central laboratory for determination of serum total testosterone levels. For safety assessments, adverse events, vital signs, and the specified hematological and biochemical laboratory tests were collected and documented according to the study protocol. Adverse events were graded by investigators using criteria in the National Cancer Institute Common Terminology Criteria for Adverse Events Version 4.

From 08/12/2014 [first subject enrollment] through 09/02/2016 [completion of the last subject visit], the study enrolled 137 subjects from 21 study sites in 8 countries, with 33 in Part 1 and 104 in Part 2. Of the enrolled, 47% (64/137) were recruited from 8 study sites in the United States. All subjects received at least one dose of study treatment with LMIS and were included

in both efficacy and safety analyses.

The Review Division DO1 and OSI selected the above three domestic clinical investigators for inspections given the adequate numbers of subjects from the United States in this study. Relative to other domestic study sites, these three investigator sites enrolled large numbers of study subjects and were associated with a high castration rate (i.e., a 100% castration rate with Drs. Frankel and Horowitz and a 92% castration rate with Dr. Deguenther).

III. RESULTS

1. **Dr. Jeffrey Frankel, Site US03**
   16259 Sylvester Rd SW Ste 303
   Burien, WA 98166-3059

Dr. Frankel was inspected from October 29 through November 3, 2020 as a data audit for Study FP01C-13-001. For the investigator, this was the first FDA inspection.

The investigator site screened 13 subjects and enrolled 10 subjects into the study, with 7 subjects in Part I and 3 subjects in Part 2. All the subjects received study treatment with LMIS twice (i.e., on Days 0 and 168) and completed the protocol-required assessments. No subjects were discontinued during the study.

All subjects' source documents were reviewed and compared with the Applicant's submitted subject line listings for the site. The reviewed documents or records included the informed consent forms, case medical history, eligibility criteria, enrollment log, subject numbers assigned and treatment administered, blood sampling forms and dates for testosterone and other protocol-required biomarkers, submissions of the blood specimens to the central laboratory per shipment records and documented laboratory values, adverse events and reporting, investigational product accountability, subject case report forms (CRF) and protocol deviations. Regulatory documents and study procedures were also reviewed, including the Institutional Review Board (IRB) approvals for the study and related correspondences, signed FDA 1572s, financial disclosures, training records, subject consenting process, subject data entry into the designated electronic CRF system [OpenClinica EDC system], study monitoring and reporting to the sponsor, and record retention.

The inspection found no regulatory deficiencies. All the subjects met the eligibility criteria for the study and signed the IRB-approved informed consent form before administration of study-related procedures and study treatment. The Applicant's submitted efficacy and safety data were verifiable with source records at the site, with no discrepancies noted. There was no evidence of underreporting of adverse events or protocol deviations.

At the conclusion of this inspection, no Form FDA 483, Inspectional Observations, was

issued to Dr. Frankel.

{See appended electronic signature page}

Yang-min (Max) Ning, M.D., Ph.D.
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CONCURRENCE: {See appended electronic signature page}

Min Lu, M.D., M.P.H.
Team Leader
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CONCURRENCE: {See appended electronic signature page}

Kassa Ayalew, M.D., M.P.H
Branch Chief
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

cc:

Review Division /Division Director
Review Division /Project Manager
Review Division /Clinical Team Lead
Review Division/Medical Officer
OSI/DCCE/GCPAB Reviewer
OSI/Office Director
OSI/DCCE/Division Director
OSI/DCCE/GCPAB Branch Chief
OSI/DCCE/GCPAB Team Lead
OSI/GCP Program Analyst
OSI/Database PM

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/s/

YANGMIN NING
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MIN LU
04/28/2021 02:14:08 PM

KASSA AYALEW
04/28/2021 02:36:11 PM

MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING
Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	April 20, 2021
Requesting Office or Division:	Division of Oncology 1 (DO1)
Application Type and Number:	NDA 211488
Product Name and Strength:	Camcevi (leuprolide) injectable emulsion, 42 mg
Applicant/Sponsor Name:	Foresee Pharmaceuticals Co LTD (Foresee)
OSE RCM #:	2019-734-1
DMEPA Safety Evaluator:	Sarah Thomas, PharmD
DMEPA Team Leader:	Ashleigh Lowery, PharmD, BCCCP

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container label and carton labeling received on March 29, 2021 for Camcevi. The Division of Oncology 1 (DO1) requested that we review the revised container label and carton labeling for Camcevi (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.[a]

2 CONCLUSION

Upon review of the container label and carton labeling, we note that the Applicant implemented most of our recommendations. However, we have additional edits and recommendations provided below in Section 3 to improve the container label and carton labeling and ensure safe medication use.

3 RECOMMENDATIONS FOR FORESEE PHARMACEUTICALS CO LTD (FORESEE)

We recommend the following be implemented prior to approval of this NDA:

A. General Recommendation for All Labels and Labeling

[a]Thomas S. Label and Labeling Review for Camcevi (NDA 211488). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 MARCH 16. RCM No.: 2019-734.

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/s/

SARAH E THOMAS
04/20/2021 04:49:00 PM

ASHLEIGH V LOWERY
04/22/2021 12:34:22 PM

LABEL AND LABELING REVIEW
Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	March 16, 2021
Requesting Office or Division:	Division of Oncology 1 (DO1)
Application Type and Number:	NDA 211488
Product Name, Dosage Form, and Strength:	Camcevi (leuprolide) injectable emulsion, 42 mg
Product Type:	Combination Product (Drug-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Foresee Pharmaceuticals Co LTD (Foresee)
FDA Received Date:	July 27, 2020 and December 22, 2020
OSE RCM #:	2019-734
DMEPA Safety Evaluator:	Sarah Thomas, PharmD
DMEPA Team Leader:	Ashleigh Lowery, PharmD, BCCCP

1 REASON FOR REVIEW

NDA 211488 was resubmitted on July 27, 2020 after it received a Refusal to File determination on May 23, 2019 for the original March 28, 2019 submission. Of note, the proposed leuprolide product is a new leuprolide salt, that of leuprolide mesylate. Also, unlike currently marketed leuprolide products that require reconstitution and/or mixing prior to administration, the proposed Camcevi product will be supplied ready-to-use in a single, sterile, pre-filled syringe.

In response to the August 7, 2020 DO1 consult, this review evaluates the proposed Camcevi container label, carton labeling, Prescribing Information (PI), and Instructions for Use (IFU) to identify areas of vulnerability that could lead to medication errors.

2 MATERIALS REVIEWED

We considered the materials listed in Table 1 for this review. The Appendices provide the methods and results for each material reviewed.

Table 1. Materials Considered for this Review	
Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B
Human Factors Study	C– N/A
ISMP Newsletters*	D – N/A
FDA Adverse Event Reporting System (FAERS)*	E – N/A
Other	F– N/A
Labels and Labeling	G

N/A=not applicable for this review
*We do not typically search FAERS or ISMP Newsletters for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

3 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

We note leuprolide mesylate is a new salt being introduced into the market, with the potential for confusion with the currently marketed leuprolide acetate products (e.g., Eligard). We discussed the risk of medication error with the review team at an October 1, 2020 internal meeting, and how this concern can be mitigated through labeling and designation of the established name, strength, and proprietary name. In terms of the established name and strength designation, the review team plans to align with the USP Salt Policy[a] and designate the established name and strength in terms of the active moiety (e.g., leuprolide, 42 mg). We find this appropriate, and we note the proposed 42 mg strength is slightly different from the 45 mg

[a] Guidance for Industry: Naming of Drug Products Containing Salt Drug Substances. 2013. Available from http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM379753.pdf

strength of the similar, currently marketed Eligard (leuprolide acetate 45 mg subcutaneous every 6 months for injectable suspension) product. Therefore, the new, slightly-different strength may alert the end-user that this is a different salt product. In addition, the proposed 42 mg prefilled syringe packaging configuration will prevent manipulation by the end-user in trying to achieve the leuprolide acetate prefilled syringe 45 mg dose and vice versa. We also support providing the equivalency statement on the label and labeling to display the numerical relationship between the active moiety and leuprolide mesylate salt [e.g., "Each prefilled syringe delivers 42 mg leuprolide (equivalent to approximately 48 mg leuprolide mesylate)"].

In addition, we confirmed with the review team that there is little concern regarding difference in safety and efficacy between Camcevi and the Eligard (leuprolide acetate 45 mg subcutaneous every 6 months for injectable suspension) product if they are confused in clinical practice. Last, the unique proprietary name "Camcevi" will alert the end-user that this is a different product and therefore help to mitigate confusion between the proposed leuprolide mesylate product and the currently marketed leuprolide acetate products.

We reviewed the proposed Camcevi container label, carton labeling, Prescribing Information (PI), and Instructions for Use (IFU) and provide recommendations in Section 4 below to improve readability and ensure safe medication use.

4 CONCLUSION & RECOMMENDATIONS

The proposed Camcevi container label, carton labeling, Prescribing Information (PI), and Instructions for Use (IFU) can be improved to ensure safe medication use. We provide specific recommendations in Section 4.1 and 4.2 below.

4.1 RECOMMENDATIONS FOR DIVISION OF ONCOLOGY 1 (DO1)

(b) (4)

[redacted]

[b] Guidance for Industry: Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use. 2018. Available from https://www.fda.gov/downloads/Drugs/Guidances/UCM468228.pdf.

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APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Camcevi received on July 27, 2020 and December 22, 2020 from Foresee Pharmaceuticals Co LTD (Foresee), and the listed drug (LD).[l]

Table 2. Relevant Product Information for Camcevi and the Listed Drug		
Product Name	Camcevi	Lupron[m]
Initial Approval Date	N/A	April 9, 1985
Active Ingredient	leuprolide	leuprolide acetate
Indication	Palliative treatment of advanced prostate cancer	Palliative treatment of advanced prostatic cancer
Route of Administration	subcutaneous	subcutaneous
Dosage Form	injectable emulsion	injection
Strength	42 mg	1 mg/0.2 mL
Dose and Frequency	42 mg subcutaneously every 6 months	1 mg (0.2 mL) administered as a single daily subcutaneous injection
How Supplied	Kit containing a pre-filled, ready-to-use sterile syringe and a sterile 18-gauge needle for subcutaneous injection, NDC 72851-042-01	2.8 mL multiple-dose vial packaged as follows: 14 Day Patient Administration Kit with 14 disposable syringes and 28 alcohol swabs, NDC 0074-3612-30 and six-vial carton, NDC 0074-3612-34
Storage	Store at 35.6–46.4°F (2–8°C). Protect from light by storing in the original package until time of use. Do not freeze or shake.	Store below 77°F (25°C). Do not freeze. Protect from light; store vial in carton until use.
Container Closure	Sterile, ready-to-use single prefilled syringe with depot	Multiple-dose vial

[l] Foresee will rely upon the following information to support product approval:
• Clinical efficacy data from the Sponsor-conducted Phase 3 study.
• Nonclinical and clinical safety information from Sponsor-conducted studies and information in the published literature.
• Nonclinical and safety information supporting the approval of Lupron as reflected in the approved labeling (NDA 019010; Abbvie, Inc.).
The scientific bridge to the nonclinical safety data from the approved Lupron labeling was established through a demonstration of lower exposure to leuprolide from LMIS 50 mg than from daily Lupron 1 mg injections.

[m] Lupron [Prescribing Information]. Drugs@FDA. U.S. Food and Drug Administration. 2020 SEPT 29. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/019010s041lbl.pdf.

	drug formulation filled into a pre-assembled syringe barrel, complete with plunger seal, cap, plunger rod and finger grip (back stop). Labeled and assembled pre-filled and capped syringes are placed in secondary packaging consisting of a thermoformed tray and (b) (4) lid, which compose the blister. A sterile needle is also added to the blister tray, and the blister is sealed (b) (4) with a (b) (4) lid which is imprinted with lot and traceability information. The sealed blister is placed together with a non-sterile Point-Lok needle protection device and package leaflet in a cardboard carton.	

APPENDIX B. PREVIOUS DMEPA REVIEWS

On September 28 and 29, 2020, we searched for previous DMEPA reviews relevant to this current review using the terms, Camcevi, leuprolide, IND# 103206, and NDA# 211488. Our search identified one previous review[n], which was a human factors use-related risk analysis review. In the review, we concluded that our review of the use-related risk analysis and comparative analyses for leuprolide injectable emulsion determined that a human factors validation study is not required to be submitted for Agency review in support of the proposed leuprolide injectable emulsion product.

[n] Stewart, J. Human Factors Use-Related Risk Analysis Review for Leuprolide Mesylate Injectable Suspension, IND 103206. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 AUG 20. RCM No.: 2018-2660.

APPENDIX G. LABELS AND LABELING

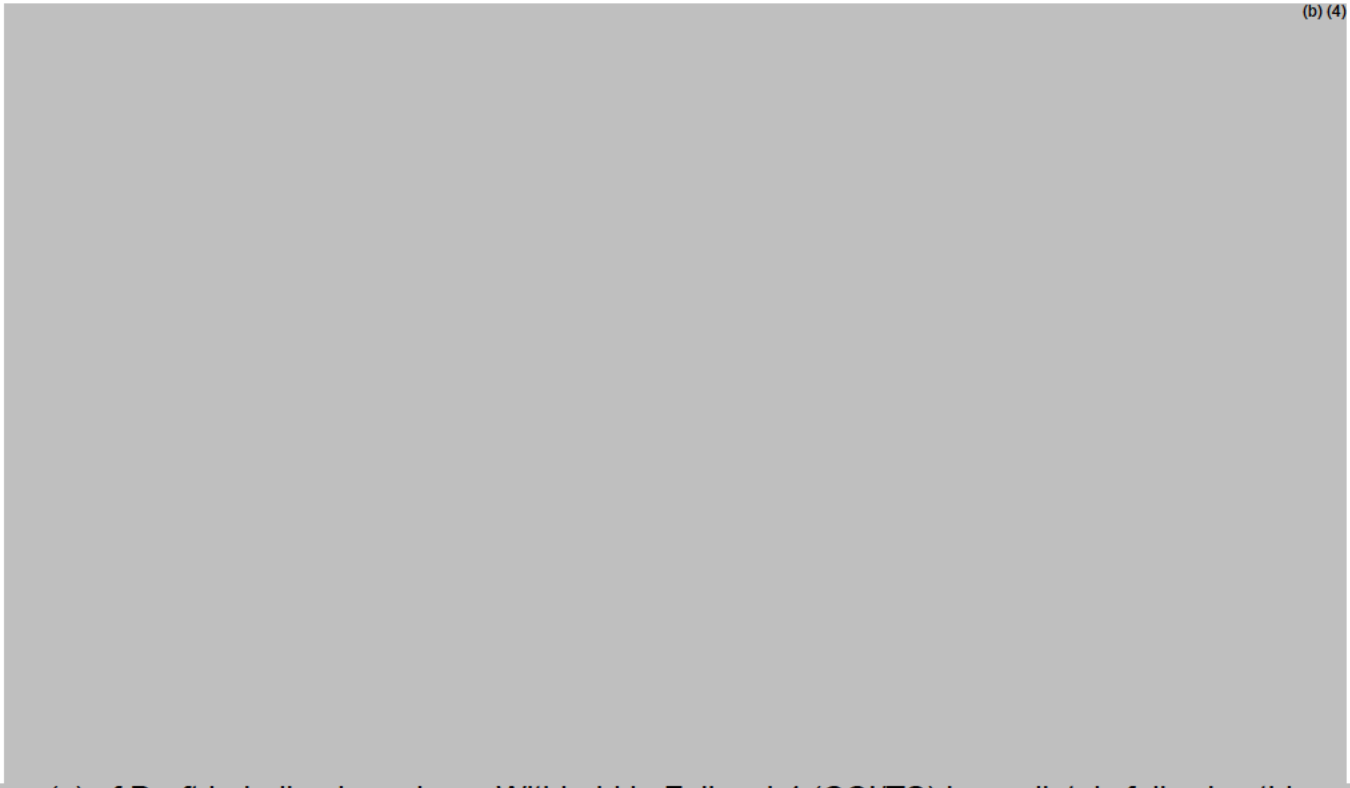
G.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[o] along with postmarket medication error data, we reviewed the following Camcevi label and labeling submitted by Foresee Pharmaceuticals Co LTD (Foresee).

- Container label received on July 27, 2020
- Carton labeling received on July 27, 2020
- Instructions for Use (Image not shown) received on July 27, 2020, available from \\CDSESUB1\evsprod\nda211488\0007\m1\us\114-labeling\draft\labeling\ifu-word-resubmission.docx
- Prescribing Information (Image not shown) received on December 22, 2020, available from \\CDSESUB1\evsprod\nda211488\0018\m1\us\114-labeling\draft\labeling\spl\draft-labeling-track-change-word.docx

G.2 Label and Labeling Images

Prefilled Syringe Container Label



4 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

[o] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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

/s/

SARAH E THOMAS
03/16/2021 04:49:13 PM

ASHLEIGH V LOWERY
03/16/2021 06:58:45 PM