

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**203255Orig1s000**

**MICROBIOLOGY / VIROLOGY REVIEW(S)**

# Product Quality Microbiology Review

August 15, 2014

**NDA:** 203255

**Drug Product Name**

**Proprietary:** SIGNIFOR® LAR  
**Non-proprietary:** Pasireotide injection

**Review Number:** 1

**Dates of Submission(s) Covered by this Review**

<u>Submit</u>	<u>Received</u>	<u>Review Request</u>	<u>Assigned to Reviewer</u>
November 15, 2013	November 15, 2013	November 15, 2013	November 20, 2013

**Submission History (for 2<sup>nd</sup> Reviews or higher) – N/A**

**Applicant/Sponsor**

**Name:** Novartis Pharmaceutical Corporation  
**Address:** One Health Plaza, East Hanover, NJ 07936-1080

**Representative:** Rose Gao, Director, Regulatory Affairs  
Tel: 862-778-6795, email: [rose.gao@novartis.com](mailto:rose.gao@novartis.com)

**Name of Reviewer:** Vinayak B. Pawar, Ph.D.

**Conclusion:** Recommend Approval

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## Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUBMISSION:** Original NDA
  2. **SUBMISSION PROVIDES FOR:** An original NDA in accordance with 505(b) (1).
  3. **MANUFACTURING SITE:**  
Bulk Powder is manufactured at Novartis Pharma AG, Basel, Switzerland.  
 (b) (4)
  4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** 20mg, 40mg & 60mg powder for suspension for injection presentations in 6mL glass vial. Vehicle, 2 mL suspension in a 3mL pre-filled syringe.
  5. **METHOD(S) OF STERILIZATION:** Powder for suspension is  
 (b) (4)
  6. **PHARMACOLOGICAL CATEGORY:** Somatostatin analog.
- B. **SUPPORTING/RELATED DOCUMENTS:** None.
- C. **REMARKS:** This electronic submission is for an original NDA 203255, for Signifor® LAR powder to be suspended in an aqueous diluent (vehicle) for intramuscular injection. The drug product will be available in the form of a kit consisting of: 1 glass vial consisting of the drug product in 20mg, 40mg or 60mg presentation; 1 glass pre-filled syringe with the diluent; 1 plunger rod; 1 vial adapter; and 1 20G safety injection needle.

**filename:** N203255R1

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**Executive Summary****I. Recommendations**

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

**II. Summary of Microbiology Assessments**

- A. **Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology** – (b)(4)



- B. **Brief Description of Microbiology Deficiencies** – None.
- C. **Assessment of Risk Due to Microbiology Deficiencies** – N/A
- D. **Contains Potential Precedent Decision(s)** -  Yes  No

**III. Administrative**

- A. **Reviewer's Signature** \_\_\_\_\_  
Vinayak B. Pawar, Ph.D., Sr. Review Microbiologist, OPS/CDER
- B. **Endorsement Block** \_\_\_\_\_  
Stephen E. Langille, Ph.D., Sr. Review Microbiologist,  
OPS/CDER
- C. **CC Block**  
N/A

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

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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VINAYAK B PAWAR  
08/21/2014

STEPHEN E LANGILLE  
08/21/2014

# PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

**NDA Number:** 203255

**Applicant:** Novartis  
Pharmaceuticals Corporation

**Letter Date:** November 15,  
2013

**Drug Name:** SIGNIFOR® LAR **NDA Type:** Original NDA  
(pasireotide) injection

**Stamp Date:** November 15,  
2013

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

	Content Parameter	Yes	No	Comments
1	Is the product quality microbiology information described in the NDA and organized in a manner to allow substantive review to begin? Is it legible, indexed, and/or paginated adequately?	X		
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	X		DP powder & Vehicle: Documents 7006571_P33_M_975_2 & 7006364_23P_M_840_2.
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	X		
4	Are any study reports or published articles in a foreign language? If yes, has the translated version been included in the submission for review?		X	N/A
5	Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies?			(b) (4)
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	X		DP Specifications: Doc. PP7006364_A_R_1.
7	Has the applicant submitted the results of analytical method verification studies?			Bacterial Endotoxins Test per USP <85>, Ph.Eur. 2.6.14. Limits at (b) (4) [Validation Doc: LVD 5-23-125] Sterility Test per USP <71>, Ph.Eur. 2.6.1, [Validation Doc: LVD 5-23-159]
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?		X	N/A
9	If sterile, are extended post-constitution and/or post-dilution hold times in the draft labeling supported by microbiological data?		X	Extended Post constitution is not required.
10	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: The Drug Product solution component is (b) (4)

\_\_\_\_\_  
**Vinayak B. Pawar, Ph.D., Senior Review Microbiologist**                      **Date**

\_\_\_\_\_  
**John W. Metcalfe, Ph.D., Senior Review Microbiologist**                      **Date**

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/s/  
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VINAYAK B PAWAR  
12/03/2013

JOHN W METCALFE  
12/03/2013  
I concur.