CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

206627Orig1s000

MICROBIOLOGY / VIROLOGY REVIEW(S)

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: 30 July 2014

TO: NDA 206627

FROM: John W. Metcalfe, Ph.D.
Senior Review Microbiologist
CDER/OPS/New Drug Microbiology Staff

THROUGH: Bryan S. Riley, Ph.D.
Team Leader (Acting)
CDER/OPS/New Drug Microbiology Staff

cc: Dominic Chiapperino
Senior Regulatory Health Project Manager
CDER/OND/ODEII/DAAAP

SUBJECT: Product Quality Microbiology assessment of Microbial Limits for Hysingla ER [Submission Date: 26 April 2014 & Amendment Date: 18 July 2014]

The NDA for Hysingla does not include a Microbial Limits release specification for drug product release or stability; however, the applicant provides a suitable rationale for the exclusion of this testing. Therefore, this submission is recommended for approval from the standpoint of product quality microbiology.

The proposed drug product is a film-coated tablet for oral administration.

The applicant presents a rationale for waiving Microbial Limits testing for product release and stability, stating that a risk assessment was performed on the product and process. The assessment included a review of the following:

- Microbiological quality of raw materials (microcrystalline cellulose, magnesium stearate and (b) (4) are all tested for microbial enumeration; the applicant provided a rationale for why the remaining components are not tested for microbial enumeration)
- Microbiological qualification of the (b) (4)
- (b) (4)
- Microbial enumeration data of the primary stability batches

ADEQUATE

Reviewer Comments – The applicant's proposal to waive microbial limits testing for product release and stability is acceptable.

END

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

/s/

JOHN W METCALFE
07/30/2014

BRYAN S RILEY
07/30/2014
I concur.

PRODUCT QUALITY MICROBIOLOGY NON-STERILE

DRUG PRODUCT FILING CHECKLIST

NDA Number: 206627 **Applicant:** Purdue Pharma L.P. **Letter Date:** 26 April 2014

Drug Name: Hydrocodone Bitartrate **NDA Type:** 505 (b)(2) **Stamp Date:** 28 April 2014

Dosage Form: Tablet **Reviewer:** John W. Metcalfe, Ph.D.

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

	Content Parameter	Yes	No	Comments
1	Is the product quality microbiology information described in the NDA and organized in a manner to allow substantive review to begin? Is it legible, indexed, and/or paginated adequately?	X		
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	X		
3	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?		X	See Microbiology Information Request on page 2.
4	Has the applicant submitted the results of analytical method verification studies?		X	
5	Has the applicant submitted preservative effectiveness studies (if applicable)?			Not applicable.
6	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: Please forward the Microbiology Information Request (page 2) to the applicant.

16 May 2014

John W. Metcalfe, Ph.D. Date
Senior Microbiology Reviewer, CDER/OPS/NDMS

16 May 2014

Bryan S. Riley, Ph.D. Date
Team Leader (Acting), CDER/OPS/NDMS

Microbiology Information Request to be Forwarded to Applicant

You propose waiving microbial enumeration release testing for your drug product. This proposal may be acceptable provided adequate upstream controls are established and documented. We acknowledge your summary of both (b) (4) and microbial limits testing data in module 3.2.P.2. However, a release program that does not include microbial enumeration testing necessitates adequate microbiological controls of both incoming raw materials and the manufacturing process, in addition to the product's (b) (4) . More information on your process is needed. Address the following points.

1. Identify and justify critical control points in the manufacturing process that could affect microbial load of the drug product.

(b) (4)

2. Describe microbiological monitoring and acceptance criteria for the critical control points that you have identified. Verify the suitability of your testing methods for your drug product. Conformance to the acceptance criteria established for each critical control point should be documented in the batch record in accordance with 21 CFR 211.188.

3. Describe activities taken when microbiological acceptance criteria are not met at control points.

In addition to these points, address the following:

1. You should minimally perform microbial limits testing at the initial stability testing time point. Provide an updated stability schedule to reflect this testing.

In lieu of providing this information, amend the drug product release and stability specifications with microbial enumeration testing of every batch.

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

/s/

JOHN W METCALFE
05/16/2014

BRYAN S RILEY
05/16/2014
I concur.