

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**204223Orig1s000**

**MICROBIOLOGY / VIROLOGY REVIEW(S)**

# Product Quality Microbiology Review

November 15, 2012

**NDA:** 204223

**Drug Product Name**

**Proprietary:**

**Non-proprietary:** Morphine Sulfate Injection, USP

**Review Number:** 1

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

<b>Submit</b>	<b>Received</b>	<b>Review Request</b>	<b>Assigned to Reviewer</b>
5/31/2011	6/01/2011	6/18/2012	6/21/2012
10/31/2012	11/01/2012	N/A	N/A

**Submission History (for amendments only):**

None

**Applicant/Sponsor**

**Name:** Becton Dickenson and Co.

**Address:** 1 Becton Dr., MC 241, Franklin Lakes, NJ 07417

**Representative:** Edward Eichmann

**Telephone:** 201-847-5057

**Name of Reviewer:** Steven P. Donald, M.S.

**Conclusion:** Approval Recommended

## Product Quality Microbiology Data Sheet

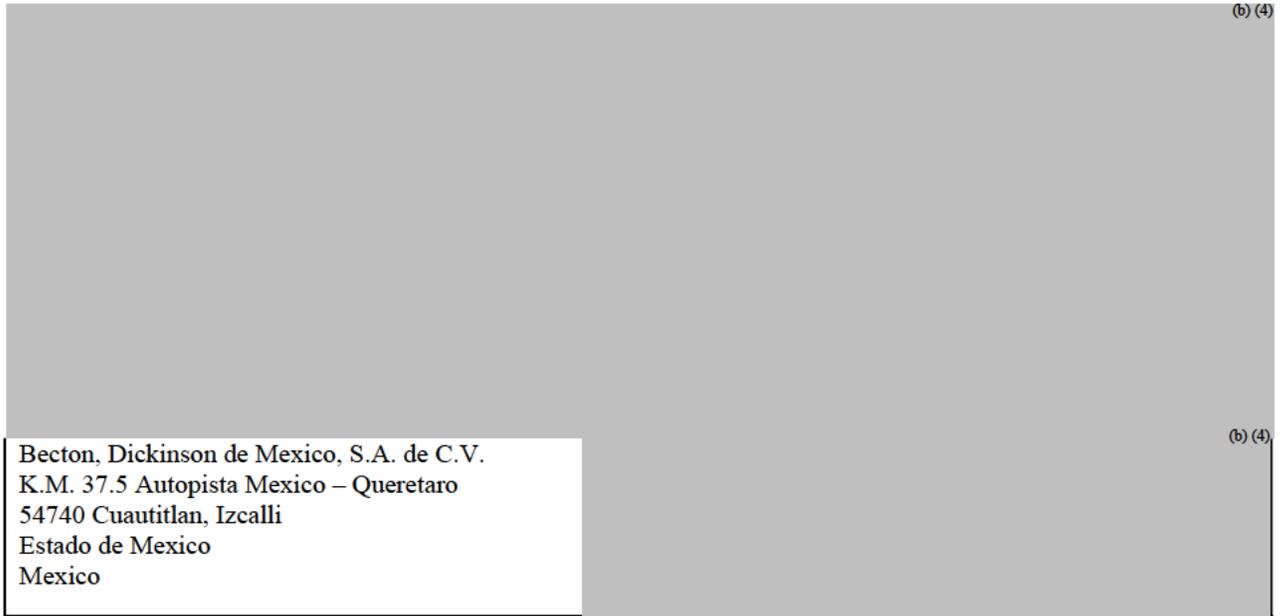
- A. 1. TYPE OF SUBMISSION:** Original NDA
- 2. SUBMISSION PROVIDES FOR:** Manufacture and marketing of a sterile drug product.
- 3. MANUFACTURING SITE:**  
 Becton, Dickinson and Co.  
 5200 Corporate Parkway West  
 Wilson, North Carolina, 27893
- 4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Sterile solution for IV or IM injection; 2 mg/ml, 4 mg/ml, 5 mg/ml, 8 mg/ml and 10 mg/ml in prefilled, glass syringes; single use.
- 5. METHOD(S) OF STERILIZATION:** (b) (4) sterilization (b) (4).
- 6. PHARMACOLOGICAL CATEGORY:** Narcotic analgesic

**B. SUPPORTING/RELATED DOCUMENTS:**

DMF (b) (4)



Establishment and Address	Component	DMF Number
Becton, Dickinson de Mexico, S.A. de C.V. K.M. 37.5 Autopista Mexico – Queretaro 54740 Cuautitlan, Izcalli Estado de Mexico Mexico  BD Medical – Pharmaceutical Systems 11, rue Aristide Berges, BP4 38800 Le Ponte de Claix France	(b) (4)	DMF # (b) (4)  September 12, 2011 submission to the DMF; Vol. 43.2



(letters-of-authorization.pdf, Section 1.4.1)

- C. **REMARKS:** The LOA table provided by the applicant identifies the Mexico site and the France site as locations for syringe assembly sterilization, however the LOA identifies the Mexico site for sterilization of the syringe assemblies and the France site as the location for stopper/plunger sterilization. The France location has been reviewed previously for the syringe assembly sterilization and has been found to be adequate. Depyrogenation of the elastomeric tip cap, as described in DMF (b) (4) is not deemed critical (b) (4) syringe assembly is monitored and controlled by acceptance criteria, before filling. Depyrogenation of the stopper/plunger as described in DMF (b) (4) is not deemed critical as the (b) (4)

A Comparability Protocol has been included in this submission. See Section 3.2.R.3 of this review.

A response to the 9/19/2012 information request was dated 10/31/2012 and was received on 11/01/2012. The deficiencies and responses are included below each comment section in relevant sections of this review.

**filename:** N204223r1.doc

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## **Executive Summary**

### **I. Recommendations**

- A. Recommendation on Approvability –**  
NDA 204223 is recommended for approval from the standpoint of product quality microbiology.
- 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 –**the compounded drug substance is sterile (b)(4) filled into presterilized syringes and fitted with sterile tip caps and sterile plunger stoppers. Filled and sealed syringes are (b)(4) packaged.
- B. Brief Description of Microbiology Deficiencies –** No product quality microbiology deficiencies were identified based upon the information provided.
- C. Assessment of Risk Due to Microbiology Deficiencies – N/A**

### **III. Administrative**

- A. Reviewer's Signature** \_\_\_\_\_  
Steven P. Donald, M.S.
- B. Endorsement Block**  
Team Leader: Bryan Riley, Ph.D.
- C. CC Block**  
N/A

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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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STEVEN P DONALD  
11/19/2012

BRYAN S RILEY  
11/20/2012  
I concur.