CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 75-086

MICROBIOLOGY REVIEW(S)

OFFICE OF GENERIC DRUGS, HFD-640
Microbiologist's Review #3
February 9, 1998

A. 1. ANDA 75-086

APPLICANT Taylor Pharmaceuticals

2. PRODUCT NAMES: Diltiazem Hydrochloride Injection

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: 5 mg/mL, 5 mL and 10 mL Single Dose Vials, Intravenous

4. METHOD(S) OF STERILIZATION:

5. PHARMACOLOGICAL CATEGORY: Vasodilator

B. 1. DATE OF INITIAL SUBMISSION: February 28, 1997 (Received, March 4, 1997)

2. DATE OF AMENDMENT: January 30, 1998 **Subject of this Review** (Received, February 3, 1998)

3. RELATED DOCUMENTS: None

4. ASSIGNED FOR REVIEW: 12/2/97

C. REMARKS: The amendment is in response to the microbiology deficiencies presented in the letter dated December 30, 1997 for the subject drug product.

D. CONCLUSIONS: The submission is recommended for approval on the basis of sterility assurance. Specific comments regarding the process provided in "E. Review Notes".

Andrea S. High 2/9/98

Andrea S. High, Ph. D.

cc:

2/3

2/9/98

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Commercial/Confidential

Information and are not

releasable.

2/1/95

#3 Micro review notes

Microbiology Comments to be Provided to the Applicant

ANDA: 75-086 APPLICANT: Taylor Pharmaceuticals

DRUG PRODUCT: Diltiazem Hydrochloride Injection, 5 mg/mL

A. Microbiology Deficiencies:

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releasable.

micro Review #2

You should consider confirming the population and values given by the vendor.

Please clearly identify your amendment to this facsimile as "RESPONSE TO MICROBIOLOGY DEFICIENCIES". The "RESPONSE TO MICROBIOLOGY DEFICIENCIES" should also be noted in your cover page/letter.

Sincerely yours,

Frank O. Holcombe, Jr., Ph.D.
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

OFFICE OF GENERIC DRUGS, HFD-640
Microbiologist's Review #2
December 4, 1997

A. 1. ANDA 75-086

APPLICANT Taylor Pharmaceuticals

2. PRODUCT NAMES: Diltiazem Hydrochloride Injection

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: 5 mg/mL, 5 mL and 10 mL Single Dose Vials, Intravenous

4. METHOD(S) OF STERILIZATION:

5. PHARMACOLOGICAL CATEGORY: Vasodilator

B. 1. DATE OF INITIAL SUBMISSION: February 28, 1997 (Received, March 4, 1997)

2. DATE OF FAX AMENDMENT: November 14, 1997 **Subject of this Review**

DATE OF FAX AMENDMENT to Document Room: 11/14/97 **Subject of this Review** (Received November 17, 1997)

3. RELATED DOCUMENTS: None

4. ASSIGNED FOR REVIEW: 12/2/97

C. REMARKS: The FAX amendment is in response to the microbiology deficiencies presented in the letter dated October 17, 1997 for the subject drug product.

D. CONCLUSIONS: The submission is not recommended for approval on the basis of sterility assurance. Specific comments regarding the filling process provided in "E. Review Notes" and "Microbiology Comments to be Provided to the Applicant".

S

12/5/97

Andrea S. High, Ph. D.

cc:

12/5/97

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releasable.

12/4/97

Micro Review # 2

Microbiology Comments to be Provided to the Applicant

ANDA: 75-086 APPLICANT: Taylor Pharmaceuticals

DRUG PRODUCT: Diltiazem Hydrochloride Injection, 5 mg/mL

A. Microbiology Deficiencies:

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Information and are not

releasable.

Micro Review #1

Please clearly identify your amendment to this facsimile as "RESPONSE TO MICROBIOLOGY DEFICIENCIES".

Sincerely yours,

Frank O. Holcombe, Jr., Ph.D.
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

OFFICE OF GENERIC DRUGS, HFD-640
Microbiologist's Review #1
June 25, 1997

A. 1. ANDA 75-086

APPLICANT Taylor Pharmaceuticals

2. PRODUCT NAMES: Diltiazem Hydrochloride Injection

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: 5 mg/mL, 5 mL and 10 mL Single Dose Vials, Intravenous

4. METHOD(S) OF STERILIZATION:

5. PHARMACOLOGICAL CATEGORY: Vasodilator

B. 1. DATE OF INITIAL SUBMISSION: February 28, 1997
Subject of this Review (Received, March 4, 1997)

2. DATE OF AMENDMENT: May 15, 1997
Subject of this Review (Received, May 16, 1997)

3. RELATED DOCUMENTS:

4. ASSIGNED FOR REVIEW: 6/11/97

C. REMARKS: The subject drug product is filled at the
MD and distributed by Taylor Pharmaceuticals,

D. CONCLUSIONS: The submission is not recommended for approval on the basis of sterility assurance. Specific comments regarding the aseptic filling process provided in "E. Review Notes" and "Microbiology Comments to be Provided to the Applicant"

/S/ 6/26/97
Andrea S. High, Ph. D.

cc:

6/26/97

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releasable.

Micro Review #1

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. You are using the 0.1% statistic that has been accepted by the industry for several years; however, with current technology and larger fills, the level of contamination should be closer to "0".

2. Please note that not all versions of the master batch records reflect the change in the endotoxin limit.

Please clearly identify your amendment to this facsimile as "RESPONSE TO MICROBIOLOGY DEFICIENCIES".

Sincerely yours,

Frank O. Holcombe, Jr., Ph.D.
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research