CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40136

MICROBIOLOGY REVIEW

DIVISION OF CHEMISTRY I
OFFICE OF GENERIC DRUGS

Microbiologist's Review #4

April 7, 1997

A. 1. ANDA: **40-136**

APPLICANT: Luitpold Pharmaceuticals, Inc.
Attention: Robert J. Anderson
One Luitpold Drive
Shirley, New York 11967

2. PRODUCT NAME: **Hydralazine Hydrochloride Injection USP**

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: **20 mg/mL**
Sterile solution for intramuscular or intravenous administration; packaged as 1 mL fill in 2 mL single dose glass vials

4. METHOD OF STERILIZATION:

5. PRINCIPLE INDICATIONS: Severe essential hypertension when the drug cannot be given orally or when there is an urgent need to lower blood pressure

6. PHARMACOLOGICAL CATEGORY: Antihypertensive

B. 1. DATE OF INITIAL SUBMISSION: **February 17, 1995**

2. DATES OF AMENDMENTS:

June 21, 1996
January 22, 1997

March 6, 1997 (Received by OGD on 3/7/97)
Telephone Minor Amendment - Subject of this Review
Sent in response to the FDA telephone contact of 2/13/97
- Provided revised Post Approval Stability Commitment

3. RELATED DOCUMENTS:

DMF
DMF
for the active ingredient, Hydralazine Hydrochloride

4. ASSIGNED FOR REVIEW: April 3, 1997

C. REMARKS: The information provided in the amendment was sufficient to determine that the applicant is taking the necessary steps to ensure the sterility of the subject drug product (Hydralazine HCl Injection, USP) over its shelf life.

D. CONCLUSIONS: The submissions are therefore recommended for approval on the basis of sterility assurance. Specific comments are provided in "E. Review Notes."

/S/ 4/7/97.
Kenneth H. Muhvich, Ph.D.

HFD-620 initialed by RPatel
drafted by: KHMuhvich, 4/7/97

Rec'd 4/9/97

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Original **ANDA 40-136**
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DIVISION OF CHEMISTRY I
OFFICE OF GENERIC DRUGS

Microbiologist's Review #3

February 4, 1997

A. 1. ANDA: **40-136**

APPLICANT: Luitpold Pharmaceuticals, Inc.
Attention: Audrey L. Bialeski
One Luitpold Drive
Shirley, New York 11967

2. PRODUCT NAMES: **Hydralazine Hydrochloride Injection USP**

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: **20 mg/mL**
Sterile solution for intramuscular or intravenous administration; packaged as a 1 mL fill in 2 mL single dose glass vials

4. METHOD(S) OF STERILIZATION:

5. PRINCIPLE INDICATIONS: Severe essential hypertension when the drug cannot be given orally or when there is an urgent need to lower blood pressure

6. PHARMACOLOGICAL CATEGORY: Antihypertensive

B. 1. DATE OF INITIAL SUBMISSION: **February 17, 1995**

2. DATE OF AMENDMENT:

June 21, 1996 (Received by OGD on 6/24/96)
Sent in response to the Office's letter dated 4/18/96

January 22, 1997 (Received by OGD on 1/24/97)
- Subject of this Review
Sent in response to the Office's letter dated 12/4/96

3. RELATED DOCUMENTS:

DMF
DMF
for
the active ingredient, Hydralazine Hydrochloride

4. ASSIGNED FOR REVIEW: August 5, 1996

C. REMARKS: The information contained in the amendment was sufficient to determine that the applicant is now taking the necessary steps to ensure the sterility of the subject drug product (Hydralazine Hydrochloride Injection USP) over its shelf life.

D. CONCLUSIONS: The submissions are therefore recommended for approval on the basis of sterility assurance. Specific comments are provided in "E. Review Notes."

/S/ 2/4/97

Kenneth H. Muhvich, Ph.D.

HFD-620/initialed by RPatel
drafted by: KHMuhvich, 2/5/96

Rec'd 2/5/96

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Micro #3

DIVISION OF CHEMISTRY I
OFFICE OF GENERIC DRUGS

Microbiologist's Review #2

August 8, 1996

A. 1. ANDA: **40-136**

APPLICANT: Luitpold Pharmaceuticals, Inc.
Attention: Audrey L. Bialeski
One Luitpold Drive
Shirley, New York 11967

2. PRODUCT NAMES: **Hydralazine Hydrochloride Injection USP**

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: **20 mg/mL**
Sterile solution for intramuscular or intravenous administration; packaged as a 1 mL fill in 2 mL single dose glass vials

4. METHOD(S) OF STERILIZATION:

5. PRINCIPLE INDICATIONS: Severe essential hypertension when the drug cannot be given orally or when there is an urgent need to lower blood pressure

6. PHARMACOLOGICAL CATEGORY: Antihypertensive

B. 1. DATE OF INITIAL SUBMISSION: **February 17, 1995**

2. DATE OF AMENDMENT:

June 21, 1996 (Received by OGD on 6/24/96)
- Subject of this Review
Sent in response to the Office's letter dated 4/18/96

3. RELATED DOCUMENTS:

DMF
DMF /for
the active ingredient, Hydralazine Hydrochloride

4. ASSIGNED FOR REVIEW: August 5, 1996

C. REMARKS: The information contained in the application was insufficient to determine if the applicant is taking the necessary steps to ensure the sterility of the subject drug product (Hydralazine Hydrochloride Injection USP) over its shelf life. Preservative efficacy of the subject drug product is required by the USP, but has not been demonstrated against Aspergillus niger (a fungus).

D. CONCLUSIONS: The submissions are therefore not recommended for approval on the basis of sterility assurance. Specific comments are provided in "E. Review Notes" and "Microbiologist's Draft Letter to the Applicant."

/S/ 8/8/96
Kenneth H. Muhvich, Ph.D.

HFD-620/initialed by RPatel
drafted by: KHMuhvich, 8/8/96

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DIVISION OF CHEMISTRY I
OFFICE OF GENERIC DRUGS

Microbiologist's Review #1

December 28, 1995

A. 1. ANDA: **40-136**

APPLICANT: Luitpold Pharmaceuticals, Inc.
Attention: Audrey L. Bialeski
One Luitpold Drive
Shirley, New York 11967

2. PRODUCT NAMES: **Hydralazine Hydrochloride Injection USP**

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: **20 mg/mL**
Sterile solution for intramuscular or intravenous administration; packaged as a 1 mL fill in 2 mL single dose glass vials

4. METHOD(S) OF STERILIZATION:

5. PRINCIPLE INDICATIONS: Severe essential hypertension when the drug cannot be given orally or when there is an urgent need to lower blood pressure

6. PHARMACOLOGICAL CATEGORY: Antihypertensive

B. 1. DATE OF INITIAL SUBMISSION:

February 17, 1995 (Received by OGD on 2/22/95) - Subject of this Review

2. DATE OF AMENDMENT: N/A, no amendment [illegible] received by the time of this review that contained [illegible] assurance information.

3. RELATED DOCUMENTS:

DMF [illegible]
DMF [illegible] for the active ingredient, Hydralazine Hydrochloride

4. ASSIGNED FOR REVIEW: December 27, 1995

C. REMARKS: The sterility assurance information was submitted in accordance with the FDA's November 1994 Guidance for the "Submission of Documentation for Sterilization Process Validation in Applications for Human and Veterinary Drug Products". Most of the information provided in the application was acceptable. However, a few comments were made by the reviewer to determine if applicant is taking all of the necessary steps to ensure the sterility of the subject drug product (Hydralazine Hydrochloride Injection USP).

D. CONCLUSIONS: The submissions are therefore not recommended for approval on the basis of sterility assurance. Specific comments are provided in "E. Review Notes" and "Microbiologist's Draft of the Letter to the Applicant".

/S/ 12/28/95

Kenneth H. Muhvich, Ph.D.

HFD-620/initialed by RPatel
drafted by: KHMuhvich, 12/28/95

Reviewed 1/2/96

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