CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40378

CHEMISTRY REVIEW(S)

Office of Generic Drugs

Chemistry, Manufacturing and Controls Review

1. **CHEMIST'S REVIEW NO.:** No. 1

2. **ANDA #** 40-378

3. **NAME AND ADDRESS OF APPLICANT:**

Upsher-Smith Laboratories, Inc.
Attn: Mark S. Robbins
14905 23rd Avenue North
Minneapolis, MN 55447

Telephone: (612) 473-4412

4. **LEGAL BASIS FOR ANDA SUBMISSION:** 505 j

5. **Supplement(s):** N/A

6. **PROPRIETARY NAME:** N/A

7. **NONPROPRIETARY NAME:** Niacin Tablets, USP

8. **SUPPLEMENT(S) PROVIDE(S) FOR:** N/A

9. **AMENDMENTS AND OTHER DATES:**

Upsher-Smith:

07/19/99-	Submission of ANDA (received on 07/20/99)

FDA:

08/17/99	Acknowledgment (accept for filling: 07/19/99)
08/17/99	EERs were issued.
08/26/99	Labeling review (1st round), w/ deficiencies.
08/31/99	Bio waiver is granted.

10. **PHARMACOLOGICAL CATEGORY:**
Reduction of cholesterol; Treatment of high serum.

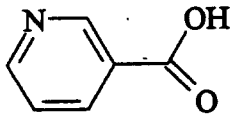
11. **Rx or OTC:** Rx

12. **RELATED IND/NDA/DMF(s):**
Niacor®; Innovator: Phone-Poulenc Rorer Pharmaceuticals
DMF:

13. **DOSAGE FORM:** Tablet

14. **POTENCY:** 500 mg

15. **CHEMICAL NAME AND STRUCTURE:**



3-Pyridinecarboxylic acid;
C6H5NO2;

MW 123.11;
[59-67-6]

16. **RECORDS AND REPORTS:** N/A

17. **COMMENTS:**

- Bio/stability Batch#: LOT 64892
- EERs (issued on 08/17/99): Pending.
- DMF: Inadequate (01/07/00)
- Labeling review: 1st round–Deficiencies (08/26/99)
- Bio-review: Waiver granted (08/31/99).
- Micro: N/A
- MV: Not required (USP DS/DP)
- Minor CMC deficiencies could be found in item 38.

18. **CONCLUSIONS AND RECOMMENDATIONS:**
Not approvable (MINOR Amendment).

19. **REVIEWER:**	**DATE COMPLETED:**	**DATE REVISED:**
Bing Cai, Ph.D.	01/12/00	01/27/00

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Chem Review #2

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38. Chemistry Comments to be Provided to the Applicant:

ANDA: 40-378
APPLICANT: Upsher-Smith Laboratories, Inc.
DRUG PRODUCT: Niacin Tablets USP, 500 mg

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. The DMF for the drug substance, Niacin USP is found deficient and the DMF holder has been informed. Please confirm a response.

2. Please clarify if you will use any of the proposed contract laboratories to test drug substance or drug product (chemical or microbial tests).

3. Your sample preparation procedure for IR (ID test) for the drug product, Niacin Tablets USP is different from the compendial test method. Please demonstrate that there would be no matrix interference in the IR "fingerprint" region, which may be caused by those excipients used in your formulation.

4. Please acknowledge that you will provide at least three batches of adequate stability data before you extend your expiration dating period in an Annual Report.

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

1. The CGMP status of the firms referenced in the ANDA are currently being evaluated by our Office of Compliance. A satisfactory evaluation is required for approval.

2. Your response must also address the labeling deficiencies.

3. Please provide any additional long term stability data that is available.

4. The USP analytical methods, as written, are considered regulatory and shall rule in the event of a dispute.

Sincerely yours,

/S/

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center of Drug Evaluation and Research

Office of Generic Drugs

Chemistry, Manufacturing and Controls Review

1. **CHEMIST'S REVIEW NO.:** No. 3

2. **ANDA #** 40-378

3. **NAME AND ADDRESS OF APPLICANT:**

Upsher-Smith Laboratories, Inc.
Attn: Mark S. Robbins
14905 23rd Avenue North
Minneapolis, MN 55447

Telephone: (612) 473-4412

4. **LEGAL BASIS FOR ANDA SUBMISSION:** 505 j

5. **Supplement(s):** N/A

6. **PROPRIETARY NAME:** N/A

7. **NONPROPRIETARY NAME:** Niacin Tablets, USP

8. **SUPPLEMENT(S) PROVIDE(S) FOR:** N/A

9. **AMENDMENTS AND OTHER DATES:**

Upsher-Smith:

07/19/99	Submission of ANDA (received on 07/20/99)
03/03/00	Minor Amendment (CMC and Labeling)
04/11/00	Minor Amendment

FDA:

08/17/99	Acknowledgment (accept for filling: 07/19/99)
08/17/99	EERs were issued.
08/26/99	Labeling review (1st round), w/ deficiencies.
08/31/99	Bio waiver is granted.
01/31/00	CMC review/NA minor.
03/08/00	Labeling review: Accepted.
03/17/00	CMC review/NA minor (DMF)

10. **PHARMACOLOGICAL CATEGORY:**
Reduction of cholesterol; Treatment of high serum.

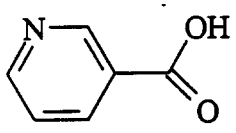
11. **Rx or OTC:** Rx

12. **RELATED IND/NDA/DMF(s):**
Niacor®; Innovator: Phone-Poulenc Rorer Pharmaceuticals
DMF: See DMF check list

13. **DOSAGE FORM:** Tablet

14. **POTENCY:** 500 mg

15. **CHEMICAL NAME AND STRUCTURE:**



3-Pyridinecarboxylic acid;
C6H5NO2;

MW 123.11;
[59-67-6]

16. **RECORDS AND REPORTS:** N/A

17. **COMMENTS:**

- Bio/stability Batch#: LOT 64892
- EERs (issued on 08/17/99): Acceptable per 04/12/00
- DMF: Adequate per 04/19/00
- Labeling review: Accepted (03/08/00)
- Bio-review: Waiver Granted (08/31/99).
- Micro: N/A
- MV: Not required (USP DS/DP)
- CMC: Approvable.

19. **REVIEWER:** Bing Cai, Ph.D. **DATE COMPLETED:** 04/20/00 **DATE REVISED:**

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Chem Review #3

Office of Generic Drugs

Chemistry, Manufacturing and Controls Review

1. **CHEMIST'S REVIEW NO.:** No. 2

2. **ANDA #** 40-378

3. **NAME AND ADDRESS OF APPLICANT:**

Upsher-Smith Laboratories, Inc.
Attn: Mark S. Robbins
14905 23rd Avenue North
Minneapolis, MN 55447

Telephone: (612) 473-4412

4. **LEGAL BASIS FOR ANDA SUBMISSION:** 505 j

5. **Supplement(s):** N/A

6. **PROPRIETARY NAME:** N/A

7. **NONPROPRIETARY NAME:** Niacin Tablets, USP

8. **SUPPLEMENT(S) PROVIDE(S) FOR:** N/A

9. **AMENDMENTS AND OTHER DATES:**

Upsher-Smith:

07/19/99	Submission of ANDA (received on 07/20/99)
03/03/00	Minor Amendment (CMC and Labeling)

FDA:

08/17/99	Acknowledgment (accept for filling: 07/19/99)
08/17/99	EERs were issued.
08/26/99	Labeling review (1st round), w/ deficiencies.
08/31/99	Bio waiver is granted.
01/31/00	CMC review/NA minor.
03/08/00	Labeling review: Accepted.

10. **PHARMACOLOGICAL CATEGORY:**
Reduction of cholesterol; Treatment of high serum.

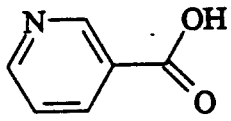
11. **Rx or OTC:** Rx

12. **RELATED IND/NDA/DMF(s):**
Niacor®; Innovator: Phone-Poulenc Rorer Pharmaceuticals
DMF: See DMF check list

13. **DOSAGE FORM:** Tablet

14. **POTENCY:** 500 mg

15. **CHEMICAL NAME AND STRUCTURE:**



3-Pyridinecarboxylic acid;
C6H5NO2;

MW 123.11;
[59-67-6]

16. **RECORDS AND REPORTS:** N/A

17. **COMMENTS:**

- Bio/stability Batch#: LOT 64892
- EERs (issued on 08/17/99): **Pending**
- **DMF update information not available.**
- Labeling review: Accepted (03/08/00)
- Bio-review: Waiver granted (08/31/99).
- Micro: N/A
- MV: Not required (USP DS/DP)
- NA (Minor). NEED DMF UPDATE.

19. **REVIEWER:** Bing Cai, Ph.D. **DATE COMPLETED:** 03/13/00 **DATE REVISED:**

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Chem Review #2

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38. Chemistry Comments to be Provided to the Applicant:

ANDA: 40-378
APPLICANT: Upsher-Smith Laboratories, Inc.
DRUG PRODUCT: Niacin Tablets USP, 500 mg

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

DMF remains deficient. Please confirm a response to our recent letter before amending this ANDA.

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

A satisfactory compliance evaluation is necessary for approval. We are awaiting the report from the Office of Compliance.

Sincerely yours,

/S/

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center of Drug Evaluation and Research