CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40378

ADMINISTRATIVE DOCUMENTS

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 40-378 **Date of Submission: July 19, 1999**
Applicant's Name: Upsher-Smith Laboratories, Inc.
Established Name: Niacin Tablets USP, 500 mg

Labeling Deficiencies:

1. CONTAINER (100's)

   Satisfactory in draft.

2. AUXILIARY STICKER

   Satisfactory in draft. [NOTE: This auxiliary sticker should be used only for the first 6 months the product is marketed.]

3. INSERT

   a. TITLE

      We encourage the inclusion of "Rx only" in this section. Relocate "Rx only" from the HOW SUPPLIED SECTION.

Please revise your insert labeling, as instructed above, and submit 12 copies of final printed container labels, along with 12 copies of final printed auxiliary sticker and insert labeling.

Prior to approval, it may be necessary to further revise your labeling subsequent to approved changes for the reference listed drug. We suggest that you routinely monitor the following website for any approved changes-
http://www.fda.gov/cder/ogd/rld/labeling_review_branch.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

/S/

Robert L. West, M.S., R.Ph.
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval): Do you have 12 Final Printed Labels and Labeling? Yes

Container Labels: (100's)

Professional Package Insert Labeling:

Revisions needed post-approval:

BASIS OF APPROVAL:
Was this approval based upon a petition? No

What is the RLD on the 356(h) form: NICOLAR®

NDA Number: 83-823/S-010
NDA Drug Name: Niacin Tablets USP, 500 mg
NDA Firm: Rhone-Poulenc Rorer

Date of Approval of NDA Insert and supplement #: May 27, 1993
Has this been verified by the MIS system for the NDA? Yes
Was this approval based upon an OGD labeling guidance? Yes. July 92.

Basis of Approval for the Container Labels: Side-by-side comparison with innovator labels in jacket.

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		X	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 23	X		
Is this name different than that used in the Orange Book?		X	
If not USP, has the product name been proposed in the PF?			X
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection. NIACOR	X		
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?	X		
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?	X		
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		X	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		X	
Does the package proposed have any safety and/or regulatory concerns?		X	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?		X	
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		X	
Are there any other safety concerns?		X	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		X	
Has applicant failed to clearly differentiate multiple product strengths?		X	
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Labeling (continued)	**Yes**	**No**	**N.A.**
Does KLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?		X	

Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.		X	
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		X	
Do any of the inactives differ in concentration for this route of administration?		X	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		X	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		X	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?		X	
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?		X	
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)		X	
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		X	
Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		X	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.		X	
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		X	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		X	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.		X	

NOTES/QUESTIONS TO THE CHEMIST:

FOR THE RECORD:

1. The reference listed drug for this product is NICOLAR®(Rhone-Poulenc Rorer; ANDA#83-823/S-010); approved May 27, 1993. And the July 1992 labeling guidance.

2. The firm certifies there are no patents/exclusivities in effect for this product. See Vol. 1.1., page 7.

3. The product will be manufactured by Upsher-Smith Laboratories, Inc., 14905 23rd Avenue North, Minneapolis, MN 55447. See Vol. 1.1, page 259.

4. Outside firms are utilized for testing only. See Vol. 1.1, page 282.

5. Container/Closure

The applicant's product is packaged in 150 cc white, round HDPE bottles. The closures are 38 mm child-resistant caps with foil induction seals. Rayon is used as the filler. See Vol. 1.2, page 385.

6. Finished product

A water-soluble B-complex vitamin and antihyperlipidemic agent. It is a white crystalline powder, sparingly soluble in water. See Vol. 1.1, page 37.

7. Product Line

A white, capsule-shaped, scored, uncoated tablet, debossed "US" to the left and "67" to the right of the score, with "500" strength on the unscored side. See Vol. 1.1, page 37.

8. Components/Composition.

Innovator:
Active:
Inactive:

Applicant:
Active: Niacin USP, 500 mg
Inactive Croscarmellose Sodium, NF
Hydrogenated Vegetable Oil, NF
Magnesium Stearate, NF
Microcrystalline Cellulose, NF

See Vol. 1.1, page 81.

9. Storage/Dispensing

NDA:

ANDA: Dispense in a tight container as defined in the USP, with a child-resistant closure. Store at controlled room temperature, 15-30°C (59-86°F).

USP: Preserve in well-closed containers.

Date of Review: August 20, 1999
Date of Submission: July 19, 1999

Reviewer: /S/ Date: 8/24/99

Team Leader: /S/ Date: 8/26/1999

cc:
ANDA: 40-378
DUP/DIVISION FILE
HFD-613/TWatkins/JGrace (no cc)

Review

REQUEST FOR TRADEMARK REVIEW

To: Labeling and Nomenclature Committee
Attention: Dan Boring, Chair (HFD-530), 9201 Corporate Blvd, Room N461

From: **Office of Generic Drug** **HFD-613**

Attention: **Phone: (301)827-5846**

Date: 8-20-99

Subject: **Request for Assessment of a Trademark for a Proposed New Drug Product**

Proposed Trademark: NIACOR **ANDA 40-378**

Established name, including dosage form: Niacin Tablets USP, 500 mg

Other trademarks by the same firm for companion products:

Indications for Use (may be a summary if proposed statement is lengthy):
Antihyperlipidemic

Initial Comments from the submitter (concerns, observations, etc.): Sounds very close to the reference listed drug's proprietary name, NICOLAR® (Rhone-Poulenc Rorer; ANDA#83-823)

Note: Meetings of the Committee are scheduled for the 4th Tuesday of the month. Please submit this form at least one week ahead of the meeting. Responses will be as timely as possible.

APPROVAL SUMMARY
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 40-378 **Date of Submission: March 3, 2000**
Applicant's Name: Upsher-Smith Laboratories, Inc.
Established Name: Niacin Tablets USP, 500 mg
APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval): Do you have 12 Final Printed Labels and Labeling? Yes
Container Labels: (100's)- Satisfactory as of March 3, 2000 submission.
Professional Package Insert Labeling: Satisfactory as of March 3, 2000 submission.
BASIS OF APPROVAL:
Was this approval based upon a petition? No
What is the RLD on the 356(h) form: NICOLAR®
NDA Number: 83-823/S-010
NDA Drug Name: Niacin Tablets USP, 500 mg
NDA Firm: Rhone-Poulenc Rorer
Date of Approval of NDA Insert and supplement #: May 27, 1993
Has this been verified by the MIS system for the NDA? Yes
Was this approval based upon an OGD labeling guidance? Yes. July 92.
Basis of Approval for the Container Labels: Side-by-side comparison with innovator labels in jacket.

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		X	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 23	X		
Is this name different than that used in the Orange Book?		X	
If not USP, has the product name been proposed in the PF?			X
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection. NIACOR	X		
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?	X		
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?	X		
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		X	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		X	
Does the package proposed have any safety and/or regulatory concerns?		X	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?		X	
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		X	
Are there any other safety concerns?		X	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		X	
Has applicant failed to clearly differentiate multiple product strengths?		X	
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	

Labeling(continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?		X	
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.		X	
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		X	
Do any of the inactives differ in concentration for this route of administration?		X	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		X	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		X	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?		X	
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?		X	
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)		X	
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		X	
Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		X	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.		X	
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		X	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		X	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.		X	

FOR THE RECORD:

1. The reference listed drug for this product is NICOLAR®(Rhone-Poulenc Rorer; ANDA#83-823/S-010); approved May 27, 1993. And the July 1992 labeling guidance.
2. The firm certifies there are no patents/exclusivities in effect for this product. See Vol. 1.1., page 7.
3. The product will be manufactured by Upsher-Smith Laboratories, Inc., 14905 23rd Avenue North, Minneapolis, MN 55447. See Vol. 1.1, page 259.
4. Outside firms are utilized for testing only. See Vol. 1.1, page 282.
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6. Finished product: A water-soluble B-complex vitamin and antihyperlipidemic agent. It is a white crystalline powder, sparingly soluble in water. See Vol. 1.1, page 37.
7. Product Line: A white, capsule-shaped, scored, uncoated tablet, debossed "US" to the left and "67" to the right of the score, with "500" strength on the unscored side. See Vol. 1.1, page 37.
8. Components/Composition.
   Innovator:
   Active: Niacin USP, 500 mg
   Inactive: microcrystalline cellulose, FD&C Yellow No. 5 (Tartrazine), magnesium stearate, povidone, & colloidal silica.
   Applicant:
   Active: Niacin USP, 500 mg

Inactive Croscarmellose Sodium, NF, Hydrogenated Vegetable Oil, NF, Magnesium Stearate, NF, Microcrystalline Cellulose, NF.See Vol. 1.1, page 81.

9. Storage/Dispensing
NDA: Dispense in a tight container as defined in the USP, with a child-resistant closure. Store at controlled room temperature, 15-30°C (59-86°F).
ANDA: Dispense in a tight container as defined in the USP, with a child-resistant closure. Store at controlled room temperature, 15-30°C (59-86°F).
USP: Preserve in well-closed containers.

Date of Review: March 8, 2000
Date of Submission: March 3, 2000

Reviewer: /S/ **Date:** 3/8/2000
Team Leader: /S/ **Date:** 3/8/2000

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cc:
ANDA: 40-378
DUP/DIVISION FILE
HFD-613/TWatkins/JGrace (no cc)
V:\FIRMSNZ\UPSHER\LTRS&REV\40378.apl
Review

/S/ 3/8/2