CIRCA PHARMACEUTICALS, INC.
33 RALPH AVENUE P.O. BOX 30 COPIAGUE, NY 11726-0030
(516) 842-8383 FAX (516) 842-8630

August 15, 1996

Noted:
To Labeling
Via Anderson
1/21/97

Archival Copy

Mr. Douglas Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research
FOOD AND DRUG ADMINISTRATION
Document Control Room
HFD-600, Room 150
Metro Park North II
7500 Standish Place
Rockville, MD 20855-2773

NEW CORRESP

RECEIVED
AUG 19 1996
GENERIC DRUGS

RE: NICOTINE POLACRILEX GUM, 2 MG, ANDA 74-507
NEW CORRESPONDENCE

Dear Mr. Sporn:

Reference is made to our Abbreviated New Drug Application dated June 16, 1994, submitted pursuant to Section 505(j) of the Food, Drug and Cosmetic Act for Nicotine Polacrilex Gum, 2 mg. At this time, it is necessary for Circa to begin the process of proposing tradenames that will be used for the final marketed product. Therefore, as part of our on-going review and approval of this application, we would like to submit six trade names for consideration by the Nomenclature Committee. They are as follows:

a) ion
b)
c)
d)
e)
f)

Thank you for your attention. Should you require any additional information, please do not hesitate to contact us.

Pursuant to 21 CFR 314.96(b), we certify that a field copy of this new correspondence has been sent by overnight courier to Mr. Edward T. Warner, District Director, Food and Drug Administration (NYK-DO), 850 Third Avenue, Brooklyn, New York 11232-1593

Sincerely,
CIRCA PHARMACEUTICALS, INC.

Joyce Anne DelGaudio

Joyce Anne DelGaudio
Director, Regulatory Affairs

DEPARTMENT OF HEALTH AND HUMAN SERVICES **Public Health Service**

Center for Drug Evaluation and Research
Office of Training and Communication
Freedom of Information Staff HFD-205
5600 Fishers Lane 12 B 05
Rockville, Maryland 20857

August 18, 1999

In Response Refer to File : F99-01925
F99-06715

Natasha Leskovsek
Fox Bennett & Turner
750 17th Street N.W.
Suite 1100
Washington DC 20006

Dear Ms. Leskovsek:

This is in response to your requests of January 25, 1999 and March 18, 1999 , in which you requested ANDA 74-507 and all correspondence between Circa Pharmaceuticals or Watson Pharmaceuticals and FDA regarding Nicotine products. Your request was received in the Centers for Drug Evaluation and Research on January 29, 1999 and March 23, 1999 respectively.

The documents you have requested are enclosed.

"In order to help reduce processing time and costs, certain material has been deleted from the record(s) furnished to you because a preliminary review of the record(s) indicated that the deleted information is not required to be publicly disclosed. If, however, you desire to review the deleted material, please make an additional request at the following address:

Food and Drug Administration
Freedom of Information Staff, HFI-35
5600 Fishers Lane
Rockville, MD 20857

Should the Agency then deny this information, you would have the right to appeal such denial. Any letter of denial will explain how to make this appeal." SMG 2460.7(3)

Charges of $306.20 (Search $58.00, Review $232.00, Reproduction $16.20, Computer time will be included in a monthly invoice. **DO NOT SEND ANY PAYMENT UNTIL YOU RECEIVE AN INVOICE.**

If there are any problems with this response, please notify us in writing of your specific problem(s). Please reference the above file number.

This concludes the response for the Center for Drug Evaluation and Research.

Sincerely,

David Krawetz
FOI Officer
Office of Training and Communications
Freedom of Information Staff HFD-205

enclosures
ANDA 74-507

7-SP96

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

ANDA Number: 74-507 **Date of Submission:** August 14, 1997

Applicant's Name [as seen on 356(h)]: Circa Pharmaceuticals Inc.

Established Name: Nicotine Polacrilex Gum USP, 2 mg

LABELING DEFICIENCIES:

1. GENERAL COMMENT

   We acknowledge your comment to differentiate your two product strengths by the use of contrasting colors.

2. CONTAINER (Blister Pack)

   a. We note your comments concerning the child-resistant nature of your container.

   b. We encourage the inclusion of "USP" in the established name.

3. CARTON (Starter and Refill)

   a. We acknowledge your commitments to make the revisions as stated in our letter of March 6, 1997.

   b. Front Panel - Add the statement "**IF YOU SMOKE MORE: try Nicotine Polacrilex Gum USP, 4 mg**" at the bottom immediately beneath the statement "**FOR SMOKERS <u>UNDER</u> 25 CIGARETTES A DAY**" and on the same line as "108 chewing pieces".

   c. Bottom Panel - Please submit pictorials as seen on Nicorette's bottom panel.

   d. Back Panel - See comment 4(c) below.

4. USER'S GUIDE

a. Will your User's Guide have pictures?

b. Stickers - Please state (below the stickers) where the stickers are to be placed on the calendar as does the reference listed drug.

c. We acknowledge your comments regarding the page numbers and telephone numbers and that you are in the process of developing a support system. Please note that this information should also appear on the back panel of the carton labeling - See comment 3(d) above.

5. AUDIO TAPE

The text for your proposed audio is not the same as that for the reference listed drug, Nicorette®. Please note that the text of the audio tape for Nicorette® was reviewed and approved by the medical review officer in the appropriate review division. 21 CFR 314.94(a)(8)(iv) requires that your labeling be the same as the labeling approved for the reference listed drug except for the differences cited therein. Please revise your tape text to be in accord with that of Nicorette®.

Please revise your labels and labeling, as instructed above, and submit 4 draft copies for a tentative approval or 12 final printed copies for a full approval of this application. If draft labeling is provided, please be advised that you will be required to submit 12 final printed copies of all labels and labeling at least 60 days prior to full approval of this application. In addition, you should be aware that color and other factors (print size, prominence, etc.) in final printed labeling could be found unacceptable and that further changes might be requested prior to approval. Also submit a draft copy of the revised text for your audio tape.

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.

Please note that we reserve the right to request further changes in your labels and/or labeling based upon further changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

APPLICATION REASSIGNMENT AUTHORIZATION FORM

OFFICE OF GENERIC DRUGS

ANDA	DRUG	FIRM
74-507	Nicotine Polacrilex Tabs	Circa

1. REASSIGN FROM: Random 6

DATE OF ORIGINAL ASSIGNMENT: 15-Aug-1997

2. ASSIGN TO: Radika Rajagopalan/Branch 5

DATE OF ASSIGNMENT: 29-Jan-1998

REASON FOR REASSIGNMENT: Work Load Equalization

Please reassign the labeling review to Julia Johnson

BRANCH SUPERVISOR (SIGNATURE) 1/29/98 DATE

CONCUR: ✓ NOT CONCUR: ____

CHEMISTRY/BIOEQUIVALENCE

DIVISION DIRECTOR (SIGNATURE) DATE: 1/29/98

A COPY OF THIS FORM SHOULD BE PLACED IN EACH APPLICATION AND IN THE DIVISION FILE

+ phone
1.30.98
by

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

ANDA Number: 74-507 **Date of Submission:** March 09, 1999

Applicant's Name [as seen on 356(h)]: Circa Pharmaceuticals Inc.

Established Name: Nicotine Polacrilex Gum USP, 2 mg (Nicotine)

APPROVAL SUMMARY:

Do you have 12 Final Printed Labels and Labeling? Yes

Carton Labeling (Starter): 108s
Satisfactory as of March 9, 1999 submission.

Carton Labeling (Refill): 48s
Satisfactory as of March 9, 1999 submission.

Unit Dose Blister Label:
Satisfactory as of January 8, 1999 submission.

User's Guide:
Satisfactory as of March 9, 1999 submission.

Audio Tape Transcript:
Satisfactory as of May 5, 1998 submission.

Audio Tape (2 copies):
Satisfactory as of January 8, 1999 submission.

Revisions needed after approval:

Use triangular sign for "Read the label", consistent with innovator labeling.

Increase prominence of the statement, "Blister packaged for your protection. Do not use if individual seals are broken.".

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Nicorette® Gum
NDA Number: 18-612

NDA Drug Name: Nicorette® (Nicotine Polacrilex) Gum

NDA Firm: SmithKline Beecham

Date of Approval of NDA Insert and supplement #: 2/9/96 (S-022)

Has this been verified by the MIS system for the NDA? S-022 is not in the MIS system.

Was this approval based upon an OGD labeling guidance? No

Basis of Approval for the Unit Dose Blister Labels: labels on file

Basis of Approval for the Carton Labeling: labeling on file

Basis of Approval for the User's Guide: labeling on file

Basis of Approval for the Audio Tape: script of tape on file

Other Comments:

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Applicant's 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.	X		
Is this name different than that used in the Orange Book?	X		
Error Prevention Analysis			
PROPRIETARY NAME - None proposed		X	
PACKAGING -See applicant's packaging configuration in FTR			
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	
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	
Error Prevention Analysis: *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	
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	
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.			

FOR THE RECORD:

1. Container labels, carton and User's Guide labeling were reviewed against the labeling of Nicorette®, NDA 18-612/S-022, approved February 9, 1996. Efficacy Supplement 007, approved on 12/23/98 is for the mint flavoring.

2. This is a first generic product.

3. There is a new product exclusivity for the OTC drug product listed in the 18th edition of the Orange Book which expires February 9, 1999.

4. This is a USP item. The monograph appears in the 1st supplement to USP 23.

5. The User's Guide Nicorette® does not have the statements regarding the sale of the product to those under 18. The approval letter dated 2/9/96 states that these statements should appear in all the labeling for the product. The applicant has included the statements on the inside of the front cover for the User's Guide.

6. The firm has developed support and surveillance initiatives found acceptable by HFD-170 and HFD-560. The firm also included a "800" telephone number with this submission.

   The firm neglected to place "(nicotine)" after "2 mg" in the title of the User's Guide". Firm notified of this 8-3-98 via telephone call [AEV to Joyce DelGaudio] and has made this revision in this submission.

7. A bio waiver was granted January 28, 1998.

Date of Review: 3-10-99 Date of Submission: 3-9-99

Primary Reviewer: Charlie Hoppes Date:

Team Leader: Charlie Hoppes Date

cc:
ANDA 74-507
HFD-613/CHoppes (no cc)
V:\FIRMSAM\CIRCA\LTRS&REV\74507AP1.doc

ANDA 74-507

JAN 18 1995

Circa Pharmaceuticals, Inc.
Attention: Joyce Anne DelGaudio
33 Ralph Avenue
P.O. Box 30
Copiague, NY 11726-0030

Dear Madam:

This is in reference to your abbreviated new drug application dated June 16, 1994, submitted pursuant to Section 505(j) of the Food, Drug, and Cosmetic Act, for Nicotine Polacrilex Gum, 2 mg.

Reference is also made to your amendment dated June 23, 1994.

The application is deficient and, therefore, not approvable under Section 505 of the Act for the following reasons:

Chemistry Deficiencies

5 pgs. redacted in whole.

Chemistry

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

Please note that this a compendial product and the compendial methods are regulatory and will be used in case of dispute.

Frank O. Holcombe, Jr., Ph.D.

Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

MESSAGE CONFIRMATION

03/06/97 10:34
ID=OGD/CDER DOC RM1

DATE	S.R-TIME	DISTANT STATION ID	MODE	PAGES	RESULT	
03/06	04'26"	5168426638	CALLING	07	OK	0000

3/06/97 10:28 OGD/CDER DOC RM1 → 915168426638 NO.193 P01

MAJOR AMENDMENT MAR 6 1997

ANDA/AADA: 74-507

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301) [redacted]

Center for Drug Evaluation and Research
FDA

TO: APPLICANT Circa Pharm, Inc PHONE 516-842-8383
ATTN: Joyce Del Gaudio FAX 516-842-[redacted]6638

FROM: Tim Ames PROJECT MANAGER (301-594-0309)

Dear Sir/Madam:

This facsimile is in reference to your abbreviated new drug/antibiotic application dated 6/16/97, submitted pursuant to Section 505(j)/507 of the Federal Food, Drug, and Cosmetic Act for Nicotine Polacrilex Gum, 2mg.

Reference is also made to your amendments dated 4/23/96 + 8/9/96.

The application is deficient and, therefore not approvable under Section 505/507 of the Act for the reasons provided in the attachments (6 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21

MAJOR AMENDMENT

MAR 6 1997

ANDA/AADA: 74-507

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 ([redacted])

TO: APPLICANT Circa Pharm, Inc PHONE 516-842-8383
ATTN: Joyce Del Gaudio FAX 516-842-[redacted]6638

FROM: Tim Ames PROJECT MANAGER (301-594-0309)

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Reference is also made to your amendments dated 4/23/96 & 8/9/96.

The application is deficient and, therefore not approvable under Section 505/507 of the Act for the reasons provided in the attachments (6 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MAJOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MAJOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If this represents a second or greater occasion upon which significant (MAJOR) deficiencies have been identified, please contact the Project Manager within 30 days for further clarification or assistance.

SPECIAL INSTRUCTIONS:

x:\new\ogdadmin\faxtrak\faxcov.mjr

CIRCA PHARMACEUTICALS, INC.
33 RALPH AVENUE P.O. BOX 30 COPIAGUE, NY 11726-0030
(516) 842-8383 FAX (516) 842-8630

August 4, 1995

ORIGINAL

NDA ORIG AMENDMENT

N/AF

RECEIVED

AUG 07 1995

GENERIC DRUGS

Douglas Sporn
Acting Director
Office of Generic Drugs
Center for Drug Evaluation and Research
FOOD AND DRUG ADMINISTRATION
Metro Park North II
Room 204, HFD 637
7500 Standish Place
Rockville, MD 20855

RE: Nicotine Polacrilex Gum, 2 mg ANDA 74-507
AMENDMENT TO PENDING APPLICATION

Dear Mr. Sporn:

We refer to the June 5, 1995 letter from the Division of Labeling and Program Support providing comments on the labeling in our Abbreviated New Drug Application dated June 16, 1994, submitted pursuant to Section 505(j) of the Food, Drug, and Cosmetic Act, for Nicotine Polacrilex Gum, 2 mg labeling issues. The following is an item-by-item response:

CONTAINER (blister package): *Satisfactory*

Please note that we have enclosed a new draft for the container (blister package) label. This draft has been generated by our contract packager , based on our originally submitted draft. The lot number and expiration date have been moved to the center of the blister pack, as it is 's experience that the patient tends to remove the edge pieces. Therefore, the lot number and expiration date are removed first. Through placement of this information in the center of the blister card, the information is available for a longer period of time. The actual label wording is identical to that submitted in our original ANDA, however, the format has been changed according to their specifications. We have enclosed four copies of this new draft container labeling under Attachment 1.

CARTON:

1. *This product is the subject of a USP monograph. We would encourage the inclusion of USP in the established name.*

2. *"96 chewing pieces" rather than "96 pieces".*

-Continued-