CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 74-655

ADMINISTRATIVE DOCUMENTS

[redacted]

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

MEMORANDUM

DATE: June 16, 1997

FROM: Sriram Subramaniam, Ph.D.
Pharmacologist
Division of Scientific Investigations (HFD-345)

THROUGH: C. T. Viswanathan, Ph.D. CTV 6/16/97
Associate Director
Division of Scientific Investigations (HFD-34

SUBJECT: Review of a EIR Covering ANDA 74-655,
Ranitidine HCl Capsules (300 mg), sponsor
Geneva Pharmaceuticals, Broomfield, CO.

TO: Nicholas M. Fleischer, Ph.D.
Director, Division of Bioequivalence (HFD-65
Division of Sc

As requested by HFD-650, the Division of
Investigations initiated an audit of the
study:

Study 941143: Comparativ
2-Way Crossover Bioava
Glaxo (Zantac® 300) R
Healthy Adult Males

The study compared the bioavai
300 mg capsules to the curren
capsules. Both the clinica
udy were conducted at

the inspecti
tional find

for rejecting standards, Run CTE 25 (containing samples from Subject #23) would be rejected. Statistical analysis conducted after excluding data from Subject #23 did not change the conclusion of the study.

2) **Temperature recording charts for the walk-in freezers show numerous long term deviations from nominal temperature for storage of study samples awaiting analysis.**

Incorrect charts for the recorders were used. Calibration records coupled with the consistency of recorder tracing indicated that storage temperatures remained within acceptable limits during the time periods in question.

3) **Injection numbers and corresponding data were reversed for two injections in Run CTE 14. As a result, both determined values were identified as outliers and not reported. Normal review processes did not detect this error. There is no established requirement for investigation of such outliers.**

Had this error been caught on review of the data, both results would have been acceptable. This is particularly noteworthy because one of the wrongly identified value was potentially the Cmax value for Subject #11 in period 2.

4) **No established upper limit for allowable variation of internal standard response within a run.**

The above findings are not likely to affect the results of the study. We recommend that the study data be accepted for Agency review.

Following your review, please append this transmittal memo to the original ANDA submission.

Sriram Subramaniam, Ph.D.

CDER Establishment Evaluation Report
for October 20, 1997

Application: **ANDA 74655/000**
Stamp: **03-APR-1995** Regulatory Due:
Applicant: **GENEVA PHARMS**
2555 WEST MIDWAY BLVD
BROOMFIELD, CO 80038

Priority:
Action Goal:
Brand Name:
Established Name: **RANITIDINE**
Generic Name:
Dosage Form: **CAP (CAPSULE)**
Strength: **150 MG, 300 MG**

Org Code: **600**
District Goal:

FDA Contacts:

Overall Recommendation:

ACCEPTABLE on 31-JAN-1997 by S. FERGUSON (HFD-324) 301-827-0062

Establishment: **1717759**
GENEVA PHARMACEUTICALS INC
2555 WEST MIDWAY BLVD
BROOMFIELD, CO 80038

DMF No:

AADA No:

Profile: **CSG** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDAT 31-JAN-1997**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities:

Establishment:

DMF No:

AADA No:

Profile: **CSG** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDAT 12-DEC-1995**
Decision: **ACCEPTABLE**
Reason:

Responsibilities:

CDER Establishment Evaluation Report
for July 14, 1997

Application: **ANDA 74655/000**
Stamp: **03-APR-1995** Regulatory Due:
Applicant: **GENEVA PHARMS**
2555 WEST MIDWAY BLVD
BROOMFIELD, CO 80038

Priority:
Org Code: **600**
Action Goal:
District Goal:
Brand Name:
Established Name: **RANITIDINE**
Generic Name:
Dosage Form: **CAP (CAPSULE)**
Strength: **150 MG, 300 MG**

FDA Contacts:

Overall Recommendation:

ACCEPTABLE on 31-JAN-1997 by S. FERGUSON (HFD-324) 301-827-0062

Establishment: **1717759**
GENEVA PHARMACEUTICALS INC
2555 WEST MIDWAY BLVD
BROOMFIELD, CO 80038

DMF No:
AADA No:

Profile: **CSG** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDAT 31-JAN-1997**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities:

Establishment:

DMF Nc
AADA No:

Profile: **CSG** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDAT 12-DEC-1995**
Decision: **ACCEPTABLE**
Reason:

Responsibilities:

First Generic (capsule form) / Approval Summary

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

ANDA Number: 74-655 Date of Submission: March 25, 1997

Applicant's Name: **Geneva Pharmaceuticals, Inc.**

Established Name: **Ranitidine Capsules, 150 mg and 300 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 & No
If no, list why: Latest submission only has 9 copies of FPL insert and 500s container label (150 mg and 300 mg) in the archival jacket. 12 FPL for containers 30s, 60s, & 90s (150 mg and 300 mg) are present.

1. Container Labels

   a. 30s, 60s, and 90s (150 mg and 300 mg)

      Satisfactory on February 5, 1996.

   b. 500s (150 mg and 300 mg)

      Satisfactory on March 25, 1997.

2. Professional Package Insert Labeling - "Rev. 97-3M"

   Satisfactory on March 25, 1997.

Revisions needed post-approval: None noted.

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Zantac GELdose Capsules

NDA Number: NDA 20-095

NDA Drug Name: Zantac GELdose Capsules

NDA Firm: Glaxo Wellcome, Inc.

Date of Approval of NDA Insert and supplement #:
20-095/SLR-006 approved in draft 11-27-96 (also see FTR, item 1)

Has this been verified by the MIS system for the NDA? Yes

Was this approval based upon an OGD labeling guidance? Yes
If yes, give date of labeling guidance: Revised 2/97

Basis of Approval for the Container Labels: Side-by-side, CFR

Other Comments: None

REVIEW OF PROFESSIONAL LABELING CHECKLIST

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.		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?			
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?			
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?			X
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?: FYR: 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: (Portions carried over from previous review.)

1. MODEL LABELING - Zantac®; Glaxo Wellcome, Inc.; Approved (in draft) 11-27-96; Revised December 1995; and labeling guidance revised 2/97. This new RLD insert labeling is still combined for all of innovator's oral dosage forms. The referenced listed drug is NDA 20-095, the "GELdose™" Capsule.

2. PATENTS/EXCLUSIVITIES
   a. GATT extensions affected these patents. The patent for the Zantac® gelatin capsule formulation (5028432) was noted as expiring on July 2, 2008, per last review. A double check reveals in the O Book, 16th Edition, that this patent's expiration is now February 22, 2010. Nonetheless, this firm is challenging this patent and plans to market the drug product after the expiration of the Form I patent, which expires July 25, 1997. The formulation differs from the RLD because it does not use fatty acid glyceride and mineral oil or paraffin matrix.

   b. Patent 4128658 for Form I expires July 25, 1997. The firm plans to market the drug product after the expiration of this patent.

   c. D-25 - Treatment of Endoscopically Diagnosed Erosive Esophagitis - Expired May 19, 1995. Included in the labeling.

   d. D-21 - Alternative Dosage of 300 mg Once Daily After the Evening Meal - Expires February 28, 1997. Requested firm to add due to expiration prior to "Form I" in July 1997.

   e. I-116 - Maintenance of Healing of Erosive Esophagitis - Expires November 3, 1997. Not to be contained in labeling. (It is only listed for the oral tablet in the Orange book, but upon consultation with Don Hare, it was agreed that it should not be included for the

capsule because this would "retard innovativeness.")

f. I-120 - Maintenance Therapy For Gastric Ulcer Patients At Reduced Dosage After Healing Acute Ulcers - Expires March 29, 1998. Not included in labeling.

3. INACTIVE INGREDIENTS - This firm has accurately listed all inactive ingredients in the DESCRIPTION section of the package insert. See Components/Composition statement on page 30c of Vol. 1.1 in section 5.

4. This is a potential first generic on the ranitidine capsule formulation.

5. NOT USP - This is not a USP product.

6. This dosage formulation is Form I - see page 95, vol. 1.1.

7. STORAGE TEMPERATURE RECOMMENDATIONS/DISPENSING STATEMENTS COMPARISON
USP: This dosage form is not the subject of a USP monograph.

NDA: Store between 2º and 25ºC (36ºand 77ºF) in a dry place. Protect from light. Replace cap securely after each opening. No dispensing statement.

ANDA: Store between 2º-25ºC (36º-77ºF) in a dry place. Protect from light. Replace cap securely after opening. Dispense in T, L-R container. (Appears in insert, omitted on labels - to be a future revision.)

8. BIOEQUIVALENCE - Still pending.

9. PACKAGING CONFIGURATIONS
ANDA - The firm intends to package both strengths of this product in HDPE white opaque bottles with CRC closures on the 30's, 60's and 90's. The 500's will have a screw top. See pages 390 and 391 of Vol. 1.2.

RLD - 150 mg: 60s and UD 60s. 300 mg: 30s and UD 30s.

10. The capsule imprints have been accurately described in the HOW SUPPLIED section as required by 21 CFR 206, et al.

Date of Review: 4/3/97 Date of Submission: 3/25/97

Primary Reviewer: /S/ Date: 4-3-97

Secondary Reviewer: Date: 4-3-97

Team Leader: /S/ Date: 4/3/97

/S/

cc:

MAR 14 1997

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

ANDA Number: 74-655 Date of Submission: January 16, 1997

Applicant's Name: **Geneva Pharmaceuticals, Inc.**

Established Name: **Ranitidine Capsules, 150 mg and 300 mg**

Labeling Deficiencies:

1. CONTAINER - 500s

   Upon further review, since this is not a unit-of-use container, revise your container label to include the following "Dispense in" statement. We refer you to 21 CFR 201.100(b)(7) for further guidance.

   Dispense in a tight, light-resistant container.

2. INSERT

   a. GENERAL COMMENTS

      Due to recent changes in the approved labeling of the reference listed drug, Zantac®; (Glaxo Wellcome, Inc.; Approved November 27, 1996; Revised December 1995), we request you make the following revisions to your insert labeling.

   b. CLINICAL PHARMACOLOGY

      Clinical Trials

      i. Active Duodenal Ulcer, last paragraph - Delete the last sentence "There have been ... alters recurrence rates."

      ii. Gastroesophageal Reflux Disease (GERD) - Add the following text as the last paragraph:

      In two additional U.S. multicenter, double-blind, placebo-controlled, 2-week trials, ranitidine 150 mg b.i.d. was shown to provide relief of heartburn pain within 24 hours of initiating therapy and a reduction in the frequency and severity of heartburn.

c. INDICATIONS AND USAGE

Item 5. Treatment of GERD - Revise to read "... occurs within 24 hours after starting ..." ["24 hours" rather than "1 or 2 weeks"].

d. ADVERSE REACTIONS

Integumentary - Revise to read "... rare cases of erythema multiforme ..." [Delete "suggestive" and "mild"].

e. DOSAGE AND ADMINISTRATION

i. Active Duodenal Ulcer

A). Sentence 2 - "alternative" rather than "alternate".

B). Sentence 3 - Revise to read "... (see CLINICAL PHARMACOLOGY, Clinical Trials: *Active* ..."

ii. Maintenance Therapy - Revise this subsection heading to read "Maintenance of Healing of Duodenal Ulcers."

Please revise your container (500s) label and insert labeling, as instructed above, and submit final printed container labels and package insert labeling. Please note that final printed insert labeling is not required for tentative approval of an application if it is granted with more than 90 days remaining from the date when full approval can be considered. Alternatively, you may submit "printer's proof" if your prefer.

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

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/

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

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

ANDA Number: 74-655 Date of Submission: January 16, 1997

Applicant's Name: **Geneva Pharmaceuticals, Inc.**

Established Name: **Ranitidine Capsules, 150 mg and 300 mg**

Labeling Deficiencies:

1. CONTAINER - 500s

   Upon further review, since this is not a unit-of-use container, revise your container label to include the following "Dispense in" statement. We refer you to 21 CFR 201.100(b)(7) for further guidance.

   Dispense in a tight, light-resistant container.

2. INSERT

   a. GENERAL COMMENTS

      Due to recent changes in the approved labeling of the reference listed drug, Zantac®; (Glaxo Wellcome, Inc.; Approved November 27, 1996; Revised December 1995), we request you make the following revisions to your insert labeling. (DK 3/13/97)

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      Clinical Trials

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B). Sentence 3 - Revise to read "... (see CLINICAL PHARMACOLOGY, Clinical Trials: *Active* ..."

ii. Maintenance Therapy - Revise this subsection heading to read "Maintenance of Healing of Duodenal Ulcers."

Please revise your container (500s) label and insert labeling, as instructed above, and submit final printed container labels and package insert labeling. Please note that final printed insert labeling is not required for tentative approval of an application if it is granted with more than 90 days remaining from the date when full approval can be considered. Alternatively, you may submit "printer's proof" if your prefer.

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

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.

REVIEW OF PROFESSIONAL LABELING CHECKLIST

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.		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?			
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?			
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 inconsistant 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?			X
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: (Portions carried over from previous review.)

1. MODEL LABELING - Zantac®; Glaxo Wellcome, Inc.; Approved (in draft) 11-27-96; Revised December 1995; and labeling guidance revised 9/96. The new RLD insert labeling (still combined for all of innovator's oral dosage forms) primarily prompts the request for revised FPL amendment.
The referenced listed drug is NDA 20-095, the "GELdose™" Capsule.

2. PATENTS/EXCLUSIVITIES
   a. GATT extensions affected these patents. The patent for the Zantac® gelatin capsule formulation (5028432) was noted as expirin er last review. A double check rev 16th Edition, that this patent's ex uary 22, 2010. Nonetheless, thi g this patent and plans to market er the expiration of the Form I pa uly 25, 1997. The formulation diff ause it does not use fatty acid g oil or paraffin matrix.

   I think they all looks for full approval

   b. Patent 4128658 for Form I expires July 25, 1997. The firm plans to market the drug product after the expiration of this patent.

   c. I-75 - Treatment of Endoscopically Diagnosed Erosive Esophagitis - Expired May 19, 1995. Included in the labeling.

   d. D-21 - Alternative Dosage of 300 mg Once Daily After the Evening Meal - Expires February 28, 1997. Requested firm to add due to expiration prior to "Form I" in July 1997.

   e. I-116 - Maintenance of Healing of Erosive Esophagitis - Expires November 3, 1997. Not to be contained in labeling. (It is only listed for the oral tablet in the Orange book, but upon consultation with Don Hare, it was agreed that it should not be included for the capsule because this would "retard innovativeness.")

   f. I-120 - Maintenance Therapy For Gastric Ulcer Patients At Reduced Dosage After Healing Acute Ulcers - Expires March 29, 1998. Not included in labeling.

3. INACTIVE INGREDIENTS - This firm has accurately listed all inactive ingredients in the DESCRIPTION section of the package insert. See Components/Composition statement on page 30c of Vol. 1.1 in section 5.

4. This is a potential first generic on the ranitidine capsule formulation.

5. NOT USP - This is not a USP product.

6. This dosage formulation is Form I - see page 95, vol. 1.1.

7. STORAGE TEMPERATURE RECOMMENDATIONS/DISPENSING STATEMENTS COMPARISON
USP: This dosage form is not the subject of a USP monograph.

NDA: Store between 2° and 25°C (36°and 77°F) in a dry place. Protect from light. Replace cap securely after each opening. No dispensing statement.

ANDA: Store between 2°-25°C (36°-77°F) in a dry place. Protect from light. Replace cap securely after opening. Dispense in T, L-R container. (Appears in insert, omitted on labels - to be a future revision.)

8. BIOEQUIVALENCE - Pending.

9. PACKAGING CONFIGURATIONS
The firm intends to package both strengths of this product in HDPE white opaque bottles with CRC closures on the 30's; 60's and 90's. The 500's will have a screw top. See pages 390 and 391 of Vol. 1.2.

10. The capsule imprints have been accurately described in the HOW SUPPLIED section as required by 21 CFR 206,et al.

11. ALL CONTAINER LABELS were deemed satisfactory in FPL as of 2/5/96 submission. (30s, 60s, 90s and 500s - 150 mg and 300 mg). Future revision noted was "Include container specifications for dispensing." Per 21 CFR 201.100(b)(7), the "Dispense in" statement is required for non unit-of-use containers. Since the 30s, 60s, and 90s, have a CRC the regulation allows them to not bear the statment. Comment made to revise the 500s label to add the statement.

Date of Review: 2-3-97 Date of Submission: 1-16-97

Primary Reviewer: Date: 2/6/97

Secondary Reviewer Date: 2/6/97

Team Leader: Date: 2/6/97

cc:

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Public Health Service
FOOD AND DRUG ADMINISTRATION

ESTABLISHMENT EVALUATION REQUEST

.ST TYPE *(Check One)* Original X FollowUp ☐ FUR	DATE May 17, 1996	PHONE NO. 594-1300
REQUESTORS NAME:E.Ramos/K.Sherrod	DIVISION: Office of Generic Drugs	MAIL CODE: HFD-645
APPLICATION AND SUPPLEMENT NUMBER: ANDA 74-655		
BRAND NAME:	ESTABLISHED NAME: Ranitidine Hydrochloride	
DOSAGE STRENGTH: 150 mg and 300 mg Capsules		STERILE ☐Yes ☒ No
PROFILE CLASS:: CSG	PRIORITY CLASSIFICATION *(See SMG CDER-4820.3)*	
APPLICANT'S NAME: Geneva Pharmaceuticals, Inc.		
APPLICANT'S ADDRESS: 2555 W. Midway Blvd. Broomfield, CO 80038-0446		
COMMENTS :		

FACILITIES TO BE EVALUATED

(Name and Complete Address)	RESPONSIBILITY	DMF NUMBER/ PROFILE CODE	FKEY CIRTS ID
1.	Manufacturer c NDS		
		ccs	
	Manufacturing and testing facility		
		csg	
3.			
4.			
5.			

[redacted]

FORM FDA 3274 (8/92) Distribution: Original and Yellow Copy: HFD-324.

x:\wpfile\eerforms\74655

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

Date of Review: April 23, 1996

Date of Submission: February 5, 1996

Primary Reviewer: Carol Zimmermann

Secondary Reviewer: John Grace

ANDA Number: 74-655 **Review Cycle:** 2 - FPL

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

Manufacturer's Name (If different than applicant):

Established Name: Ranitidine Capsules, 150 mg and 300 mg

LABELING DEFICIENCIES, WHICH ARE TO BE INCORPORATED WITH THE CHEMISTRY COMMENTS TO THE FIRM:

B. LABELING DEFICIENCIES

1. GENERAL COMMENT

   Due to [redacted] patent extensions the DOSAGE AND [redacted] section of your insert labeling should be revised as indicated below. In addition, you should amend your application as appropriate.

2. CONTAINER [redacted] 30's, 60's, 90's and 500's

   Satisfactory in final print.

3. INSERT

   a. After further review we request that you revise to read "ranitidine" rather than "ranitidine

hydrochloride" throughout the text of the insert except in the DESCRIPTION section.

b. INDICATIONS AND USAGE

Revise indication number six to read as follows:

...ranitidine 150 mg q.i.d.

[NOTE: "150 mg" rather than "50 mg"]

c. DOSAGE AND ADMINISTRATION

Active Duodenal Ulcer - Revise the second sentence of paragraph one to read as follows:

...daily after the evening meal or at bedtime...

Please revise your insert labeling, as instructed above, and submit final printed labeling. 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 labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

Do [redacted] Labeling? Yes

Cont[redacted] February 5, 1996 (30s, 60s, 90s and 500s - IS[redacted] mg).

Professional Package Insert [redacted]

Revisions needed post-approval: Container[redacted] Include container specifications for [redacted]

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Zantac Geldose Capsules

NDA Number: 74-655

NDA Drug Name: Zantac Geldose Capsules

NDA Firm: Glaxo Pharmaceuticals, Inc.

Date of Approval of NDA Insert and supplement #: March 29, 1995/S-005.

Has this been verified by the MIS system for the NDA?
Yes

Was this approval based upon an OGD labeling guidance?
Yes

If yes, give date of labeling guidance: December 1995

Basis of Approval for the Container Labels: Ranitidine Labels in file folder.

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 in the [redacted] supplement in which verification was assured?		X	
Is this name different than that used in the Orange Book?		X	
If not USP, has the proposed name been proposed in the PF?		X	
Error Prevention Analysis			
PROPRIETARY NAME			
Has the firm proposed a proprietary name? If yes, complete this subsection.		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?			
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?			

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	
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	
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/Distributed statement incorrect or falsely inconsistent between labels and labeling? "Manufactured by...", statement needed?		X	
Failed to [redacted] identifying markings in HOW SUPPLIED?		X	
Has this firm [redacted] compatibility or stability claims which appear in the insert labeling? [redacted] confirm the data has been adequately supported.		X	
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			X
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 bioeqivalency 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.			

NOTE TO THE CHIEF:

Please confirm this is FORM 1 of ranitidine. OK EAP 5/16/96

FOR THE RECORD:

1. This review was based on the labeling guidance for ranitidine tablets (Rev. November 1993 and December 1995 [not signed off yet]) and the labeling of the listed drug ZANTAC® (Approved March 29, 1995; Revised March 1995).

2. Storage/Dispensing Recommendations

USP: This dosage form is not the subject of a USP monograph.

NDA: Store between 2° and 25°C(36°and 77°F)in a dry place. Protect from light. Replace cap securely after each opening.

ANDA: Store between 2°-25°C (36°-77°F) in a dry place. Protect from light. Replace cap securely after opening.

3. Patents/Exclusivity

a. Patent for the gelatin cap formulation (5028432) expires on July 2, 2008. This firm is challenging this patent and plans to market the drug product after December 5, 1995. This patent was extended by GATT until July 25, 1997. The formulation differs from the RLD because it does not use fatty acid glyceride and mineral oil or paraffin matrix.

b. Patent 4128658 for Form I expires July 25, 1997 (extended by GATT from December 5, 1995). The firm plans to market the drug product after the expiration of this patent.

c. I-75 - Treatment of Endoscopically Diagnosed Erosive Esophagitis - Expires May 19, 1995. In labeling.

d. D-21[illegible] Alternative Dosage of 30[illegible] mg Once Daily After the Evening Meal - Expires February 28, 199[illegible] Requested firm to add due to expiration [illegible] Form I" in July 1997.

[illegible] Maintenance of Healing of Erosive [illegible]itis - Expires November 3, 1997. Not [illegible]ed in labeling. It is only listed for the oral tablet in the Orange book. Confirmation request forwarded to M. Holovac if can be included.

f. I-120 - Maintenance Therapy For Gastric Ulcer Patients At Reduced Dosage After Healing Acute Ulcers - Expires March 29, 1998. Not included in labeling.

4. Components/Composition

This firm has accurately listed all inactive ingredients in the DESCRIPTION section of the package insert. See Components/Composition statement on page 30c of Vol. 1.1 in section 5.

5. Container/Closure

The firm intends to package both strengths of this product in 1 bottles with CRC closures on the 30's, 60's and 90's. The 500's will have a screw top. See pages 390 and 391 of Vol. 1.2.

6. The HOW SUPPLIED section is consistent with the master manufacturing formula. See pages 184 and 159 in Vol. 1.2.

7. The only outside contracting facility is being utilized for resin testing for the s. (See pages 152 and 153 of Vol. 1.2) All manufacturing will be completed by Geneva. (See page 150, Vol. 1.2).

8. This dosage formulation is Form I - see page 95, vol. 1.1.

9. Bioequivalence - Pending.

Primary /S/ Reviewer — Date 4/30/96

/S/ Acting Ch[illegible] Rev. Branch — Date 4/30/96

cc:

I am in favor
Sup

REVIEW OF PROFESSIONAL LABELING #1

ANDA

DRAFT

DATE OF REVIEW: June 12, 1995

ANDA #: 74-655

NAME OF FIRM: Geneva Pharmaceuticals, Inc.

NAME OF DRUG: Ranitidine Capsules, 150 mg and 300 mg

DATE OF SUBMISSION: March 31, 1995

COMMENTS:

CONTAINER: 30's, 60's, 90's and 500's

1. Increase the prominence of the established name and strength.

2. Revise the "Each tablet contains" statement to read as follows:

   Each capsule contains ranitidine hydrochloride equivalent to ...mg of ranitidine.

3. Storage recommendations - "Store" rather than "Sore".

4. Net quantity; revise to read:

   XXX capsules (rather than "tablets")

INSERT:

1. GENERAL COMMENT

   [redacted]ion headings should be consistent throughout [redacted] the insert. Please revise so that your [redacted] headings have the same prominence and [redacted]

2. [redacted]HARMACOLOGY

   Clinical Trials - Add "hydrochloride" in the following places:

   a. Gastroesophageal Reflux Disease

      i. Paragraph 1, line 3 -
      ...hydrochloride 150 mg bid...

ii. Paragraph 2, line 1 -
...hydrochloride 150 mg bid...

b. Erosive Esophagitis

a. Line 2 - ...hydrochloride 150 mg qid...

b. Table, last column - Place the "+" symbol next to the percentages listed in this column.

3. INDICATIONS AND USAGE

a. Ranitidine capsules are indicated in...

b. Indication #5 - ...ranitidine hydrochloride...

c. Revise indication #6 to read:

...esophagitis. Symptomatic relief of heartburn commonly occurs within 24 hours of therapy initiation with ranitidine hydrochloride 150 mg qid.

4. PRECAUTIONS

Revise the "Pediatric Use" subsection to read as follows:

...in pediatric patients have...

5. OVERDOSAGE

Paragraph 2 - Place "225 mg/kg per day" on the same line.

6. DOSAGE AND ADMINISTRATION

Active Duodenal Ulcer - Delete "hydrochloride" from the [redacted] of the first paragraph.

[redacted]D

[redacted]ve indicated that the 150 mg capsule will be [redacted]nted with GG 615 and the 300 mg capsule will be imprinted with GG 614. However, your master formula indicates that the 150 mg capsule will be imprinted with GG 614 and the 300 mg with GG 615. Please revise accordingly.

b. We encourage the inclusion of your NDC numbers.

RECOMMENDATIONS:

1. Inform the firm of the above comments.

2. Request the firm revise their container labels and package insert labeling, then prepare and submit final printed container labels and draft package insert labeling.

NOTE TO THE CHEMIST:

See comment 7a. Do you concur? Issued 8/2/95

FOR THE RECORD:

1. This review was based on the labeling guidance for ranitidine tablets (Rev. November 1993) and the labeling of the listed drug ZANTAC® (Approved March 29, 1995; Revised March 1995).

2. Storage/Dispensing Recommendations

USP: This dosage form is not the subject of a USP monograph.

NDA: Store between 2° and 25°C (36° and 77°F) in a dry place. Protect from light. Replace cap securely after each opening.

ANDA: Store between 2°-25°C (36°-77°F) in a dry place. Protect from light. Replace cap securely after opening.

3. Patents/Exclusivity

a. Patent for the gelatin cap formulation (5028432) expires on July 2, 2008. This firm is challenging this patent and plans to market the drug product [redacted] December 5, 1995.

[redacted] 4128658 for Form I expires December 5, [redacted] The firm plans to market the drug product [redacted] the expiration of this patent.

[redacted] Treatment of Endoscopically Diagnosed Erosive Esophagitis - Expires May 19, 1995.

d. D-21 - Alternative Dosage of 300 mg Once Daily After the Evening Meal - Expires February 28, 1997.

e. I-116 - Maintenance of Healing of Erosive Esophagitis - Expires November 3, 1997.

f. I-120 - Maintenance Therapy For Gastric Ulcer Patients At Reduced Dosage After Healing Acute Ulcers - Expires March 29, 1998.

All exclusivities will be excluded from the labeling except I-75 because this expires prior to the expiration date on the Form I patent.

4. Components/Composition

This firm has accurately listed all inactive ingredients in the DESCRIPTION section of the package insert. See Components/Composition statement on page 30 of Vol. 1.1.

5. Container/Closure

The firm intends to package both strengths of this product in bottles with CRC closures on the 30's, 60's and 90's. The 500's will have a screw top. See pages 390 and 391 of Vol. 1.2.

6. The HOW SUPPLIED section is not consistent with the master manufacturing formula. The insert states the 150 mg capsule will be imprinted with 615 and the 300 mg with 614. The master formula states the opposite. See comment #7a in review and see pages 184 and 159 in Vol. 1.2.

7. The only outside contracting facility is being utilized for resin testing for the [redacted]. (See pages 152 and 153 of Vol. 1.2) All manufacturing will be completed by Geneva. (See page 150, Vol. 1.2)

8. This dosage formulation is Form I - see page 95, vol. 1.1

cc: [redacted]

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
FOOD AND DRUG ADMINISTRATION

ESTABLISHMENT EVALUATION REQUEST

REQUEST TYPE *(Check One)* ☒ Original ☐ FollowUp ☐ FUR	DATE August 2, 1995	PHONE NO. 594-1300	EER ID #
REQUESTORS NAME:E.Ramos/K.Sherrod	DIVISION: Office of Generic Drugs		MAIL CODE: HFD-645
APPLICATION AND SUPPLEMENT NUMBER: ANDA 74-655			
BRAND NAME:	ESTABLISHED NAME: Ranitidine Hydrochloride		
DOSAGE STRENGTH: 150 mg and 300 mg Capsules			STERILE ☐Yes ☒ No
PROFILE CLASS:: CSG	PRIORITY CLASSIFICATION *(See SMG CDER-4820.3)*		
APPLICANT'S NAME: Geneva Pharmaceuticals, Inc.			
APPLICANT'S ADDRESS: 2555 W. Midway Blvd. Broomfield, CO 80038-0446			
COMMENTS :			

FACILITIES TO BE EVALUATED

(Name and Complete Address)

	RESPONSIBILITY	DMF NUMBER/ PROFILE CODE	FKEY CIRTS ID
1.	Manufacturer of NDS	ccs	
2.	Manufacturing and testing facility	csg	
3.			
4.			
5.			

FORM FDA 3274 (8/92) Distribution: Original and Yellow Copy: HFD-324.

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B-95-053

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE : April 7, 1995

TO : Director
Division of Bioequivalence (HFD-650)

FROM : Chief, Regulatory Support Staff 4/7/95
Office of Generic Drugs (HFD-632)

SUBJECT: Examination of the bioequivalence study and waiver request submitted with an ANDA for Ranitidine Capsules to determine if the application is substantially complete for filing and/or granting exclusivity pursuant to USC 355(4)(B)(iv).

Geneva Pharmaceuticals, Inc. has submitted ANDA 74-655 for Ranitidine Capsules, 150 mg and 300 mg. The ANDA contains a certification pursuant to 21 USC 355(j)(2)(A)(vii)(iv) stating that a patent expiring July 2, 2008 will not be infringed by the manufacture or sale of the proposed product. In order to accept an ANDA for filing that contains such a patent certification, the Agency must formally make a determination that the application is substantially complete. Included in this review is a determination that the bioequivalence study is complete, and could establish that the product is bioequivalent.

Please evaluate whether the study submitted by Geneva Pharmaceuticals, Inc. for its Ranitidine products satisfy the statutory requirements of "completeness" so that the ANDA may be filed and that a period of six months of market exclusivity can be granted to the applicant who submitted the first substantially complete ANDA under 21 USC 355(j)(4)(B)(iv).

A "complete" bioavailability or bioequivalence study is defined as one that conforms with an appropriate FDA guidance or is reasonable in design and purports to demonstrate that the proposed drug is bioequivalent to the "listed drug".

In determining whether a bio study is "complete" to satisfy statutory requirements, the following items are examined:

1. Study design

   (a) Appropriate number of subjects
   (b) Description of methodology

2. Study results

   (a) Individual and mean data is provided
   (b) Individual demographic data
   (c) Clinical summary

The issue raised in the current situation revolves around whether the study can purport to demonstrate bioequivalence to the listed drug.

We would appreciate a cursory review and your answers to the above questions as soon as possible so we may take action on this application.

DIVISION OF BIOEQUIVALENCE: Andrew Jackson 4/10/95

✓ Study meets statutory requirements

_____ Study does **NOT** meet statutory requirements

Reason:

✓ Waiver meets statutory requirements

_____ Waiver does not meet statutory requirements

/S/

Director, Division of Bioequivalence

4/10/95

Date

ANDA 74-655

Geneva Pharmaceuticals, Inc.
Attention: Beth Brannan
2555 W. Midway Blvd.
P.O. Box 446
Broomfield, CO 80020-0446

MAY 2 1995

Dear Madam:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

NAME OF DRUG: Ranitidine Capsules, 150 mg and 300 mg

DATE OF APPLICATION: March 31, 1995

DATE OF RECEIPT: April 3, 1995

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Kassandra Sherrod
Consumer Safety Officer
(301) 594-1306

Sincerely yours,

5/2/95

Yana Ruth Nille
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA CHECKLIST FOR COMPLETENESS AND ACCEPTABILITY OF THE APPLICATION

NDA# [illegible]

DRUG NAME [illegible]

DOSAGE FORM [illegible]

SUPERVISORY CHEMIST ( )

RANDOM ASSIGNMENT ( )*

*If high potency, 1 mg/dosage unit or less, assign to Branch 2

Therapeutic Code [illegible] On Cards ✓

Comments [illegible]

	YES	NO
Methods Validation package (3 copies) (✓) Required for Non-USP drugs		
Cover Letter	3/31/95 4/3/95	
Letters of Authorization		
U.S. Agent (If Needed, Countersignature on 356h)		
DMF Referral(s)		
356h Form - Completed/Original Signature	✓	
Table of Contents	✓	
Listed Drug/Firm Zantac Cal Dyne/Genin	✓	
AADA Monograph	✓	
Information to show proposed product is the same as the listed product: (i)(a) indications (ii) active ingredient(s) (iii) (a) route (b) dosage form (c) strength (iv) labeling -- side by side comparison - insert: container: ~~Not Provided~~ see page 21		
Same Formulation? (Ophthalmics/Otics/Externals/Parenterals) prompt sent	✓	
Parenterals: Same Size Container (strength/volume)	✓	
Petition Required	—	
Debarment Certification	—	
List of Convictions	—	
Third Copy Certification DEN-DO 3A 3B	✓	
Patent Certification 6/4/2002 12/5/95 Paragraph III pgs-7	✓	
Use Patent Statement?	4 7/2103	
Exclude Use in labeling/indications? 2/19/95 1-75		
Exclusivity Addressed (If Applicable) 2/28/97 D-21 pg 5	✓	
Five year exclusivity? If yes, cannot be filed until expiration or after 4 years if challenged.		
Labeling: 4 copies of draft ( ) or 12 copies of FPL( )	✓	
Statement re Rx/OTC Status	checked in 356h ✓	
Components & Composition (Unit Composition)	✓	
Manufacturing Controls	✓	
Batch Formulation	—	
Master Production Batch Record for largest batch size intended for production. (No more than 10x pilot batch)	✓	
Certification of GMP.	✓	
Description of Facilities	✓	
Addresses of Manufacturing Site for Production Batches	✓	
Manufacturing Procedures (Batch Records) 6494022/023	✓	
Package entire exhibit bio batch.	✓	
Batch Number(s)/Mfg. Facility		
If Sterile product:		
Aseptic Fill ____ Terminal Sterilization ____	—	

Specifications and Tests for Active Ingredient and Dosage Form	
Source of Active Ingredient	✓
COA from Manufacturer of Active Ingredient	✓
Applicant COA	✓
COA for finished product	✓
Specifications and Tests for Inactive Ingredients	
Source of Inactive Ingredients Identified	✓
COA from Manufacturer of Inactive Ingredient	✓
Applicant COA for Inactive Ingredients	✓
Stability Profile Including Stability Data (Use of Stability Indicating Method)	
3 mo. Accelerated Stability Data	✓
Batch Numbers Listed on Stability Records	✓
Samples Statement Plus Data	✓
Bioavailability/Bioequivalence Study	
In Vivo Study/Waiver Request	✓
Comparative Dissolution Data	✓
Paragraph IV bio study acceptable for filing	✓
Date acceptable for filing	
Environmental Impact Analysis	
Compliance Statement	✓

Reviewing CSO (William Russell)

Date 4/7/95

Recommendation: File Refuse to File

Supervisory Concurrence/Date 4/10/95

Duplicate copy sent to Bio:
(Hold if RF and send when acceptable)

Duplicate copy to HFD- _____ **for consult**
Type of Consult:

Micro Consult: Yes _____ No _____

Revision 10-22-93 bcw/C:\wpfiles\rev.chk

ANDA Assignment Record

Appl Type/Number: N 074655 Status/Date: PN PENDING REVIEW 03-APR-95
Firm: GENEVA PHARMS
Trade Name: USP:
TIDINE

Rx: ✓ OTC: ___ Dosage Form: CAP Strength: 150 MG, 300 MG

Therapeutic Class: 80307006 CP

Doc Set Type: N 000 Amend/Type: ___ Letter Date: 31-MAR-95
Rec-d Date: 03-APR-95 Acknl. Date: __-___-__
Bio Rev Type: To Bio: __-___-__

		Assigned	Completed
Lbl:	CAZ Cimetidine Z	4-25-95	__-___-__
Chm:	RNC Ranitidine TL	4-7-95 CP	__-___-__
Bio:	___	__-___-__	__-___-__
Ins:	___	__-___-__	__-___-__
Col:	___	__-___-__	__-___-__
Co2:	___	__-___-__	__-___-__

DESI Drug: _____ Similar or Related: _____

Applicant Manufacturer: Yes ✓ No ____

If No: Name of Mfg: _____

ANDA #_____ Approved: _____ Pending: _____ Same Formulation: _____

Application Complete: Yes ✓ No ____

Application Acceptable: Yes ✓ No ____

If No: Non-Acceptable Letter to Firm: __-___-__

CSO/~~OSII~~ William Russell Date: 4-7-95

CP 4.7.95

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE

GENEVA PHARMS
2555 WEST MIDWAY BLVD
)OMFIELD CO 80038

ANDA #: N074655

Dear Sir/Madam:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act for the following:

NAME OF DRUG:
RANITIDINE

Dosage Form: CAP Potency: 150 MG, 300 MG USP:

DATE OF APPLICATION: 31-MAR-95

DATE OF RECEIPT: 03-APR-95

We will correspond with you further after we have had the opportunity to review the application.

However, in the interim, please submit three additional copies of the analytical methods and descriptive information needed to perform the tests on the samples (both the bulk active ingredient(s) and finished dosage form) and validate the analytical methods. Please do not send samples unless specifically requested to do so. If samples are required for validation, we will inform you where to send them in a separate communication.

If the above methodology is not submitted, the review of the application will be delayed.

Please identify any communications concerning this application with the ANDA number shown above.

Sincerely yours,

arnuare
Random VI

Roger L. Williams, M.D.
Director
Office of Generic Drugs
Center for Drug Evaluation and Research