

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

76175

ADMINISTRATIVE DOCUMENTS

APPROVAL SUMMARY

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

ANDA Number: 76-175
Dates of Submission: October 26, 2001 (Amendment)
November 5, 2001 (Amendment)
Applicant's Name: Geneva Pharmaceuticals Technology Corporation
Established Name: Mefloquine Hydrochloride Tablets, 250 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

- 1. UNIT-OF-USE BLISTER (5 x 5)**
Satisfactory as of November 5, 2001 submission (Vol. A2.1, Pages 000005 - 000015)
- 2. CARTON: (25 Tablets)**
Satisfactory as of November 5, 2001 submission (Vol. A2.1, Pages 000018 - 000028)
- 3. INSERT (Code #L-1709; MF#1709-02; Revised October 2001):**
Satisfactory as of November 5, 2001 submission (Vol. A2.1, Pages 000030 - 000032)

Revisions needed post-approval:

Insert (Description) - Revise the molecular formula to read: $C_{17}H_{16}F_6N_2O \cdot H_2O$

BASIS OF APPROVAL:

Patent/Exclusivity Issues --

Patent Data – NDA 19-591

No	Expiration	Use Code	Use	File
4579855	October 1, 2004			P-IV

Exclusivity Data For NDA 19-591

Code/sup	Expiration	Use Code	Description	Labeling Impact
			There is no unexpired exclusivity for this product	

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Lariam

NDA Number: 19-591

NDA Drug Name: Mefloquine Hydrochloride Tablets

NDA Firm: Hoffman-La Roche, Inc.

Date of Approval of NDA Insert and supplement #010: August 2, 1999

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

Was this approval based upon an OGD labeling guidance? No

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

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 24		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?			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	
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.			
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?		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	
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	
Because of proposed packaging configuration or for any other reason, does this applicant fail to meet all of the unprotected conditions of use of referenced by the RLD?		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.			
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: None

FOR THE RECORD:

1. MODEL LABELING

This review was based on the labeling of Lariam® Tablets (mefloquine hydrochloride) by Hoffman-La Roche, Inc. (NDA 19-591/S-010, 012), revised April 1999; approved in draft August 2, 1999.

2. PATENT/EXCLUSIVITIES

Patent Data – NDA 19-591

No	Expiration	Use Code	Use	File
4579855	October 1, 2004			P-IV

Exclusivity Data For NDA 19-591

Code/sup	Expiration	Use Code	Description	Labeling Impact
			There is no unexpired exclusivity for this product	

3. MANUFACTURING FACILITY OF FINISHED DOSAGE FORM

Geneva Pharmaceuticals Technology Corporation
2400 Route 130
Dayton, NJ 08810 (Vol. B1.1, Section IX, Page 4710)

4. CONTAINER/CLOSURE (Vol. B 1.1, Section XIV, Page 4989)

5 x 5 tablet blister cards of child resistant laminate over blister foil in a SBS folding carton.

5. INACTIVE INGREDIENTS (Vol. B 1.1, Section VII, Page 4563)

There does not appear to be a discrepancy between the listing of inactive in the DESCRIPTION and Components and Composition Statements.

6. PRODUCT DESCRIPTION

RLD: white, scored, round tablets imprinted with LARIAM 250 ROCHE.

ANDA: white, round, compressed tablets engraved GP above and 118 below the bisect on one side and plain on opposite side.

7. PACKAGING CONFIGURATIONS (Vol. B 1.1, Section XIV, Page 4563)

RLD: Unit dose packages of 25 tablets

ANDA: 5 x 5 Unit of use packs of 25 tablets

8. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

RLD: Tablets should be stored at 15° to 30° C (59° to 86°F).

ANDA: Store at controlled room temperature 15 and 30°C (59 and 86°F).

9. DISPENSING RECOMMENDATIONS

RLD: Tel-E-Dose® packaging is intended for institutional in-patient use. If dispensing this drug for out-patient use, and appropriate child-resistant package should be provided. (Found on carton only)

ANDA: None provided, however tablets are covered with child resistant laminate.

9. BIOAVAILABILITY/BIOEQUIVALENCE - Deemed acceptable July 31, 2001

Date of Review:
February 6, 2002

Date of Submission:
October 26, 2001 (Amendment)
November 5, 2001 (Amendment)

Primary Reviewer:

Date:

Team Leader:

Date:

cc: ANDA: 76-175
DUP/DIVISION FILE
HFD-613/LGolson/JGrace (no cc)

Review

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

A 1.1
Ramesh Sood
1/23/01

ANDA Number: 76-175
Date of Submission: May 23, 2001 (Original draft)
Applicant's Name: Geneva Pharmaceuticals Technology Corporation
Established Name: Mefloquine Hydrochloride Tablets, 250 mg

Labeling Deficiencies:

1. UNIT-OF-USE BLISTER (5 x 5)

Revise each blister to read "Mefloquine Hydrochloride Tablet, 250 mg". (singular rather than plural)

2. CARTON: (25 Tablets) - Satisfactory in draft

3. INSERT:

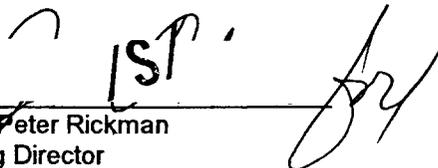
Due to changes in the insert labeling for the reference listed drug, (Lariam - Hoffman-La Roche, Inc.; revised April 1999; approved in draft August 2, 1999), please revise your labeling to be in accord with the attached labeling.

Please revise your labeling, as instructed above, and submit four 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.

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 the attached labeling with all differences annotated and explained.


Wm. Peter Rickman
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

Attachment: Lariam's insert labeling.

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 24		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?			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	
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Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	
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NOTES/QUESTIONS TO THE CHEMIST: None

FOR THE RECORD:

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2. PATENT/EXCLUSIVITIES

Patent Data – NDA 19-591

No	Expiration	Use Code	Use	File
4579855	October 1, 2004			P-III

Amended to P-10

6-7-2001

Exclusivity Data For NDA 19-591

Code/sup	Expiration	Use Code	Description	Labeling Impact
			There is no unexpired exclusivity for this product	

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Dayton, NJ 08810 (Vol. B1.1, Section IX, Page 4710)

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ANDA: None provided, however tablets are covered with child resistant laminate.

9. BIOAVAILABILITY/BIOEQUIVALENCE

Pending

Date of Review:
October 26, 2001

Date of Submission:
May 23, 2001 (Original draft)

Primary Reviewer:

Date:

ISI
Team Leader:

10/26/01
Date:

ISI

10/26/2001

cc: ANDA: 76-175
DUP/DIVISION FILE
HFD-613/LGolson/JGrace (no cc)

Review

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 : May 29, 2001

TO : Director
Division of Bioequivalence (HFD-650)

FROM : Chief, Regulatory Support Branch
Office of Generic Drugs (HFD-615)

TS/

30-MAY-2001

SUBJECT: Examination of the bioequivalence study submitted with an ANDA for Mefloquine Hydrochloride Tablets, 250 mg to determine if the application is substantially complete for filing.

Geneva Pharmaceuticals Technology Corp. has submitted ANDA 76-175 for Mefloquine Hydrochloride Tablets, 250 mg. The ANDA contains a first generic. In order to accept an ANDA that contains a first generic, the Agency must formally review and 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 request for study submitted by Geneva on May 23, 2001 for its Mefloquine Hydrochloride product satisfies the statutory requirements of "completeness" so that the ANDA may be filed.

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:

- Study meets statutory requirements
 Study does **NOT** meet statutory requirements

Reason:

- N/A Waiver meets statutory requirements
 Waiver does **NOT** meet statutory requirements

Reason:

Mohd H. Mallary 5/30/01

*CAK:cur
ISI
5/31/01*

ISI

Director, Division of Bioequivalence

6/5/01
Date

Patent and Exclusivity Search Results from query on 019591 001.

Patent Data

	Appl	Prod	Patent	Patent	Use
	No	No	No	Expiration	Code
# IV	019591	001	4579855	OCT 01,2004	

Exclusivity Data

There is no unexpired exclusivity for this product.

Thank you for searching the Electronic Orange Book

Patent and Exclusivity Terms

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*Verified
2/19/02
raw*

Search results from the "Rx" table for query on "019591."

Active Ingredient:	MEFLOQUINE HYDROCHLORIDE
Dosage Form,Route:	Tablet; Oral
Proprietary Name	LARIAM
Applicant:	ROCHE
Strength:	250MG
Application Number:	019591
Product Number:	001
Approval Date:	MAY 02, 1989
Reference Listed Drug:	Yes
RX/OTC/DISCN:	RX
TE Code:	
Patent and Exclusivity Info for this product:	Click Here

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