CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75411

ADMINISTRATIVE DOCUMENTS

APPROVAL SUMMARY

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

ANDA Number: 75-411 (0.25% base)
75-412 (0.5% base)

Date of Submission:
April 14, 2000 (Amendment)

Applicant's Name: Novex Pharma

Established Name: Timolol Maleate Ophthalmic Solution, USP

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

Do you have 12 Final Printed Labels and Labeling? Yes

Container Labels: (10 mL and 15 mL) – Satisfactory as of April 14, 2000 submission

Carton Labeling: (10 mL and 15 mL) – Satisfactory as of ~~April 14, 2000~~ March 16, 2000 submission

Professional Package Insert Labeling: Satisfactory as of March 16, 2000 submission

BASIS OF APPROVAL:

Was this approval based upon a petition? No

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

NDA Number: 18-086

NDA Drug Name: Timolol Maleate Ophthalmic Solution

NDA Firm: Merck & Co., Inc.

Date of Approval of NDA Insert and supplement #052: March 18, 1998

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

Basis of Approval for the Carton Labeling: 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 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?			x
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			x
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		x	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		x	
Does the package proposed have any safety and/or regulatory concerns?		x	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			x
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		x	
Is the strength and/or concentration of the product unsupported by the insert labeling?		x	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?		x	
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?	x		
Are there any other safety concerns?		x	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		x	
Has applicant failed to clearly differentiate multiple product strengths?		X	
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Labeling(continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	

Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			x
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			
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	
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.			

FOR THE RECORD:

1. Labeling review based on the reference listed drug, (Timoptic™ - Merck & Co., Inc.; approved March 18,1998).

2. Packaging
The RLD packages its product in white, opaque, plastic OCUMETER® ophthalmic dispensers with controlled drop tips in 2.5 mL, 5 mL, 10 mL, and 15 mL. The 0.25% product has blue caps. The 0.5% product has yellow caps.

The applicant proposes to package its products in 10 mL and 15 mL white, LDPE, opaque bottles with white, opaque ophthalmic caps with sealing tape. The opacity of the bottles should adequately protect the product from light.

3. Labeling
Firm re-submitted container labels because included a % depiction on the same page as the printer's proof which was not FOIable.

4. Inactive Ingredients
There does not appear to be a discrepancy in the listing of inactives between the DESCRIPTION section of the insert labeling and the Components and Composition Statements.

5. USP Issues
USP - Preserve in tight, light-resistant containers.
RLD - Store at RT, 15-30°C (59-86°F). Protect from freezing. Protect from light.
ANDA - same as RLD.

6. Bioequivalence Issues - Waiver granted 10/19/98.

7. Microbiology Issues - pending

8. Patent/Exclusivity Issues - None pending

Date of Review:
April 19, 2000

Date of Submission:
April 14, 2000 (Amendment)

Primary Reviewer:
/S/

Date:
4/19/00

Secondary Reviewer:

Date:

Team Leader:
/S/

Date:
4/20/2000

cc:
ANDA: 75-411 and 75-412
DUP/DIVISION FILE
HFD-613/LGolson/JGrace (no cc)
V:\FIRMSNZ\NOVEX\LTRS&REV\75411ap.l and 75412ap.l
Review

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

ANDA Number: 75-411 (0.25% base)
75-412 (0.5% base)

Date of Submission:
March 31, 2000 (Amendment)

Applicant's Name: Novex Pharma

Established Name: Timolol Maleate Ophthalmic Solution, USP

Labeling Deficiencies:

CONTAINER (10 mL and 15 mL)

In order to assure that the requirements of section 502(c) and 21 CFR 201.15 are met, final printed labeling must be of actual size, color, and clarity. The submitted container labels fail to meet these requirements.

Please revise your labels, as instructed above, and submit in final print.

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 following web site 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 enclosed labeling with all differences annotated and explained.

/S/

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

REVIEW OF PROFESSIONAL LABELING CHECK LIST

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

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	
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.			

FOR THE RECORD:

1. Labeling review based on the reference listed drug, (Timoptic™ - Merck & Co., Inc.; approved March 18,1998).

2. Packaging
   The RLD packages its product in white, opaque, plastic OCUMETER® ophthalmic dispensers with controlled drop tips in 2.5 mL, 5 mL, 10 mL, and 15 mL. The 0.25% product has blue caps. The 0.5% product has yellow caps.

   The applicant proposes to package its products in 10 mL and 15 mL white, LDPE, opaque bottles with white, opaque ophthalmic caps with sealing tape. The opacity of the bottles should adequately protect the product from light.

3. Labeling
   Firm has been asked to re-submit container labels because they do not appear clear.

4. Inactive Ingredients
There does not appear to be a discrepancy in the listing of inactives between the DESCRIPTION section of the insert labeling and the Components and Composition Statements.

5. USP Issues
USP - Preserve in tight, light-resistant containers.
RLD - Store at RT, 15-30°C (59-86°F). Protect from freezing. Protect from light.
ANDA - same as RLD.

6. Bioequivalence Issues - Waiver granted 10/19/98.

7. Microbiology Issues - pending

8. Patent/Exclusivity Issues - None pending

9. Firm will be telephoned with comments.

Date of Review:
April 6, 2000

Date of Submission:
March 31, 2000 (Amendment)

Primary Reviewer:
/S/

Date:
4/6/00

Team Leader:
/S/

Date:
4/7/2000

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cc:

ANDA: 75-411 and 75-412
DUP/DIVISION FILE
HFD-613/LGolson/JGrace (no cc)

Review

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

ANDA Number: 75-411 (0.25% base)
75-412 (0.5% base)

Date of Submission:
March 6, 2000 (Amendment)

Applicant's Name: Novex Pharma

Established Name: Timolol Maleate Ophthalmic Solution, USP

Labeling Deficiencies:

CONTAINER (10 mL and 15 mL)

Revise to submit only the label depicting the "true size". Delete the % representation.

Please revise your labels, as instructed above, and submit in final print.

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 following web site 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 enclosed labeling with all differences annotated and explained.

/S/

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

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	
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.			

FOR THE RECORD:

1. Labeling review based on the reference listed drug, (Timoptic™ - Merck & Co., Inc.; approved March 18,1998).

2. Packaging
The RLD packages its product in white, opaque, plastic OCUMETER® ophthalmic dispensers with controlled drop tips in 2.5 mL, 5 mL, 10 mL, and 15 mL. The 0.25% product has blue caps. The 0.5% product has yellow caps.

The applicant proposes to package its products in 10 mL and 15 mL white, LDPE, opaque bottles with white, opaque ophthalmic caps with sealing tape. The opacity of the bottles should adequately protect the product from light.

3. Labeling
Firm has been asked to re-submit because included a 200% depiction on the same page as the printer's proof which is not FOlable.

REVIEW OF PROFESSIONAL LABELING CHECK LIST

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

4. **Inactive Ingredients**
There does not appear to be a discrepancy in the listing of inactives between the DESCRIPTION section of the insert labeling and the Components and Composition Statements.

5. **USP Issues**
USP - Preserve in tight, light-resistant containers.
RLD - Store at RT, 15-30°C (59-86°F). Protect from freezing. Protect from light.
ANDA - same as RLD.

6. **Bioequivalence Issues - Waiver granted 10/19/98.**

7. **Microbiology Issues - pending**

8. **Patent/Exclusivity Issues - None pending**

9. **Firm will be telephoned with comments.**

Date of Review:
March 27, 2000

Date of Submission:
March 16, 2000 (Amendment)

Primary Reviewer:
/S/

Date:
3/27/00

Team Leader:
/S/

Date:
3/28/2000

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cc:
ANDA: 75-411 and 75-412
DUP/DIVISION FILE
HFD-613/LGolson/JGrace (no cc)

Review

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

ANDA Number: 75-411 (0.25% base)
75-412 (0.5% base)

Date of Submission:
July 26, 1999 (Amendment)

Applicant's Name: Novex Pharma

Established Name: Timolol Maleate Ophthalmic Solution, USP

Labeling Deficiencies:

1. CONTAINER (10 mL and 15 mL)

   Increase the prominence/conspicuousness of the established name on labels. Refer to 21 CFR 201.15 and section 502(c) of the Act for guidance.

2. CARTON (10 mL and 15 mL)

   See CONTAINER comment.

3. INSERT

   a. PRECAUTIONS (Drug Interactions – Quinidine)

      Revise to "CYP2D6" rather than

   b. OVERDOSAGE

      The following should appear as the third paragraph:

      Significant lethality was observed in female rats and female mice after a single dose of 900 and 1190 mg/kg (5310 and 3570 mg/m^2) of timolol, respectively.

Please revise your labels and labeling, as instructed above, and submit in final print.

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 following web site 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 enclosed labeling with all differences annotated and explained.

/S/

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

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

ANDA Number: 75-411 (0.25% base) Date of Submission:
75-412 (0.5% base) July 2, 1998

Applicant's Name: Novex Pharma

Established Name: Timolol Maleate Ophthalmic Solution, USP

Labeling Deficiencies:

1. CONTAINER (10 mL and 15 mL)

   a. We encourage the use of boxing, contrasting colors, or other means to differentiate the strengths of this product.

   b. We encourage you to place the "Rx only" statement prominently on the principal display panel.

   c. Reverse the order of your storage temperature range so that Celsius precedes Fahrenheit.

2. CARTON (10 mL and 15 mL)

   a. See CONTAINER comments (a) and (c).

   b. Revise the listing of inactive ingredients to identify benzalkonium chloride as a preservative. Refer to the innovator labeling for guidance.

3. INSERT

   a. GENERAL COMMENT

      The insert labeling you submitted is based on 1995 labeling for the reference listed drug. However, please revise your labeling to be in accord with the most currently approved labeling for the reference listed drug (Timoptic® Sterile Ophthalmic Solution - Merck & Co., Inc.; approved March 18, 1998), that is mocked-up and enclosed for your convenience.

Additionally,

b. Revise to delete use of the terminal zero (e.g., "5 mg" rather than

c. See CONTAINER comment (c).

Please revise your labels and labeling, as instructed above, and submit in final print or draft if you prefer.

Please note that the Agency reserves 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 the enclosed labeling 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

Enclosure: Mocked-up innovator labeling