CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
21-670

MICROBIOLOGY REVIEW(S)
Product Quality Microbiology Review
Review for HFD 550
1-October-2004

NDA: 21-670/N-000(BL)

Drug Product Name
Proprietary: Vision Blue®
Non-proprietary: Trypan Blue

Drug Product Classification:

Review Number: 3

Subject of this Review
Submission Date: August 13, 2004
Receipt Date: August 19, 2004
Consult Date: September 20, 2004
Date Assigned for Review: September 21, 2004

Submission History (for amendments only)
Date(s) of Previous Submission(s): October 27, 2003, June 11, 2004
Date(s) of Previous Micro Review(s): April 5, 2004, August 22, 2004

Applicant/Sponsor
Name: D.O.R.C
Address: Scheijdelveweg 2
NL-3214 VN Zuidland
P.O. Box 43
NL-3214 ZG Zuidland
The Netherlands

Representative: Frank Ruseler
Telephone: (+31) (0)181 45 80 80
Name of Reviewer: Stephen E. Langille, Ph.D.

Conclusion: Recommended for approval
Product Quality Microbiology Data Sheet

A.  
1. TYPE OF SUPPLEMENT: Not applicable
2. SUPPLEMENT PROVIDES FOR: Not applicable
3. MANUFACTURING SITE: 

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:
   - 0.6% solution
   - intraocular injection
   - Syringe

5. METHOD(S) OF STERILIZATION: —

6. PHARMACOLOGICAL CATEGORY: Ophthalmic Diagnostic Agent

B. SUPPORTING/RELATED DOCUMENTS: Not applicable

C. REMARKS: The first review of NDA 21-670 was completed by Dr. Paul Stinavage on April 5, 2004. A teleconference was held with the sponsor on June 28, 2004 to discuss the June 11th submission. A review of the June 11, 2004 submission was completed on August 22. A response to the deficiencies discussed during the June 28, 2004 teleconference and in the August 22, 2004 review was provided on August 13, 2004.

filename: C:/reviews/N021670R3.DOC
Executive Summary

I. Recommendations

A. Recommendation on Approvability -
   NDA 21-670/N-000(BZ) is recommended for approval from the standpoint of product quality microbiology.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable -
   Not applicable

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology -
   The drug product is packaged in pre-filled syringes and

B. Brief Description of Microbiology Deficiencies -
   No deficiencies were identified based upon the information provided.

C. Assessment of Risk Due to Microbiology Deficiencies -
   Not applicable

III. Administrative

A. Reviewer's Signature

B. Endorsement Block
   Stephen E. Langille, Ph.D.
   Supervisor

C. CC Block
   In DFS
Withheld

2

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/s/
Stephen Langille
10/1/04 11:07:33 AM
MICROBIOLOGIST

David Hussong
10/1/04 01:47:25 PM
MICROBIOLOGIST
Product Quality Microbiology Review
Review for HFD 550

27-July-2004

NDA: 21-670/N-000(BZ)

Drug Product Name
Proprietary: Vision Blue®
Non-proprietary: Trypan Blue

Drug Product Classification:

Review Number: 2

Subject of this Review
Submission Date: June 11, 2004
Receipt Date: June 16, 2004
Consult Date: June 24, 2004
Date Assigned for Review: June 25, 2004

Submission History (for amendments only)
Date(s) of Previous Submission(s): October 27, 2003
Date(s) of Previous Micro Review(s): April 5, 2004

Applicant/Sponsor
Name: D.O.R.C
Address: Scheijdelveweg 2
NL-3214 VN Zuidland
P.O. Box 43
NL-3214 ZG Zuidland
The Netherlands

Representative: Frank Ruseler
Telephone: (+31) (0)181 45 80 80

Name of Reviewer: Stephen E. Langille, Ph.D.
Conclusion: Approvable Pending Revision

APPEARS THIS WAY
ON ORIGINAL
Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUPPLEMENT: Not applicable
2. SUPPLEMENT PROVIDES FOR: Not applicable
3. MANUFACTURING SITE: /

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:
   - 0.6% solution
   - intraocular injection
   - Syringe

5. METHOD(S) OF STERILIZATION: -

6. PHARMACOLOGICAL CATEGORY: Ophthalmic Diagnostic Agent

B. SUPPORTING/RELATED DOCUMENTS: Not applicable

C. REMARKS: The first review of NDA 21-670 was completed by Dr. Paul Stinavage on April 5, 2004. A teleconference was held with the sponsor on June 28, 2004 to discuss the June 11th submission.

filename: C:/reviews/21-670r1
Executive Summary

I. Recommendations

A. Recommendation on Approvability -
NDA 21-670/N-000(BZ) is approvable pending the resolution of product quality microbiology issues.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable -
Not applicable

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology -
The drug product is in syringes.

B. Brief Description of Microbiology Deficiencies –
The Applicant failed to provide adequate information regarding container closure integrity testing and endotoxin testing.

C. Assessment of Risk Due to Microbiology Deficiencies -
Failure to address the microbiology deficiencies could result in an increased risk of microbial and/or endotoxin contamination of the drug product.

III. Administrative

A. Reviewer's Signature

B. Endorsement Block
Stephan E. Langille, Ph.D.
Peter Cooney, Ph.D.

C. CC Block
In DFS
Withheld

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/s/

Stephen Langille
8/24/04 10:00:59 AM
MICROBIOLOGIST

Peter Cooney
8/24/04 10:06:44 AM
MICROBIOLOGIST
Product Quality Microbiology Review
Review for HFD-180
05 April 2004

NDA: 21-670

Drug Product Name
Proprietary: Vision Blue
Non-proprietary: Trypan Blue
Drug Product Classification: Diagnostic agent: dye

Review Number: 1

Subject of this Review
Submission Date: 27 October 2003
Receipt Date: 29 October 2003
Consult Date: 5 November 2003
Date Assigned for Review: 21 November 2003

Submission History (for amendments only)
Date(s) of Previous Submission(s): 18 February 2004
Date(s) of Previous Micro Review(s): none

Applicant/Sponsor
Name: Dutch Ophthalmic Research Center International
Address: Scheijdelveweg 2, NL-3214 VN Zuidland, P.O. Box 43, NL-3214 ZG Zuidland, The Netherlands
Representative: Frank Ruseler
Telephone: (+31) (0)181 45 80 80

Name of Reviewer: Paul Stinavage, Ph.D.

Conclusion: The application is approvable pending resolution of product quality microbiology concerns.
Product Quality Microbiology Data Sheet

A.  1. TYPE OF SUPPLEMENT: N/A
    2. SUPPLEMENT PROVIDES FOR: N/A
    3. MANUFACTURING SITE: 
    4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: 0.06%
    5. STERILIZATION METHOD(S): 
    6. PHARMACOLOGICAL CATEGORY: Diagnostic Agent: Dye

B. SUPPORTING/RELATED DOCUMENTS: N/A

C. REMARKS: The original submission was assigned for review on 21 November 2003 and was assessed for fileability. The fileability assessment noted that no sterilization validation information was included in the submission, however the application was filed. Sterilization validation information was submitted in an amendment dated 24 February 2004.

filename: n21670.doc
Executive Summary

I. Recommendations

A. Recommendation on Approvability – The application is approvable pending resolution of product quality microbiology concerns.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable – N/A

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology – The product is — in syringes.

B. Brief Description of Microbiology Deficiencies – None

C. Assessment of Risk Due to Microbiology Deficiencies – N/A

III. Administrative

A. Reviewer's Signature ____________________________

B. Endorsement Block
   P. Stinavage
   P. Cooney

C. CC Block
   cc:
   Original NDA 21-670
   HFD-550/Division File/NDA 21-670/N. Halonen/L. Ng
Withheld

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/s/

Paul Stinavage
4/5/04 10:17:41 AM
MICROBIOLOGIST
Manufacture in . Four deficiencies.

Peter Cooney
4/5/04 10:38:50 AM
MICROBIOLOGIST