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

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. 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

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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
Stephen E. Langille, Ph.D.
Peter Cooney, Ph.D.

C. CC Block
In DFS

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3

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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

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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