CENTER FOR DRUG EVALUATION AND RESEARCH

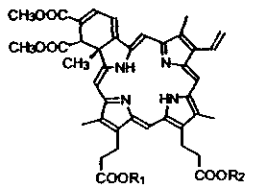
APPLICATION NUMBER:

21-119 /S-004

CHEMISTRY REVIEW(S)

Chemistry Review Review #1	1. Division HFD-550	2. NDA Number #21-119
3. Name and Address of Applicant QLT Inc. 887 Great Northern Way Vancouver, BC Canada V5T 4T5		4. Supplement Number Date SCM-004 31-JAN-02
5. Name of Drug: VISUDYNE™ (verteporfin for injection)	6. Nonproprietary Name: Verteporfin	
7. Supplement Provides for: Alternate manufacturing site for drug product		8. Amendment(s) 15-MAR-02/BC 12-APR-02/BC 04-APR-02/BC 30-APR-02/BC 09-APR-02/BL
9. Pharmacological Category: Photodynamic therapy for age-related macular degeneration	10. How Dispensed Rx	11. Related Documents
12. Dosage Form: Sterile, lyophilized powder for i.v. injection	13. Potency(ies) 15 mg verteporfin per vial	

14. Chemical Name and Structure see USAN



BPD-MA$_C$: $R_1 = CH_3$, $R_2 = H$

BPD-MA$_D$: $R_1 = H$, $R_2 = CH_3$

$C_{41}H_{42}N_4O_8$

M.W.: 718.81

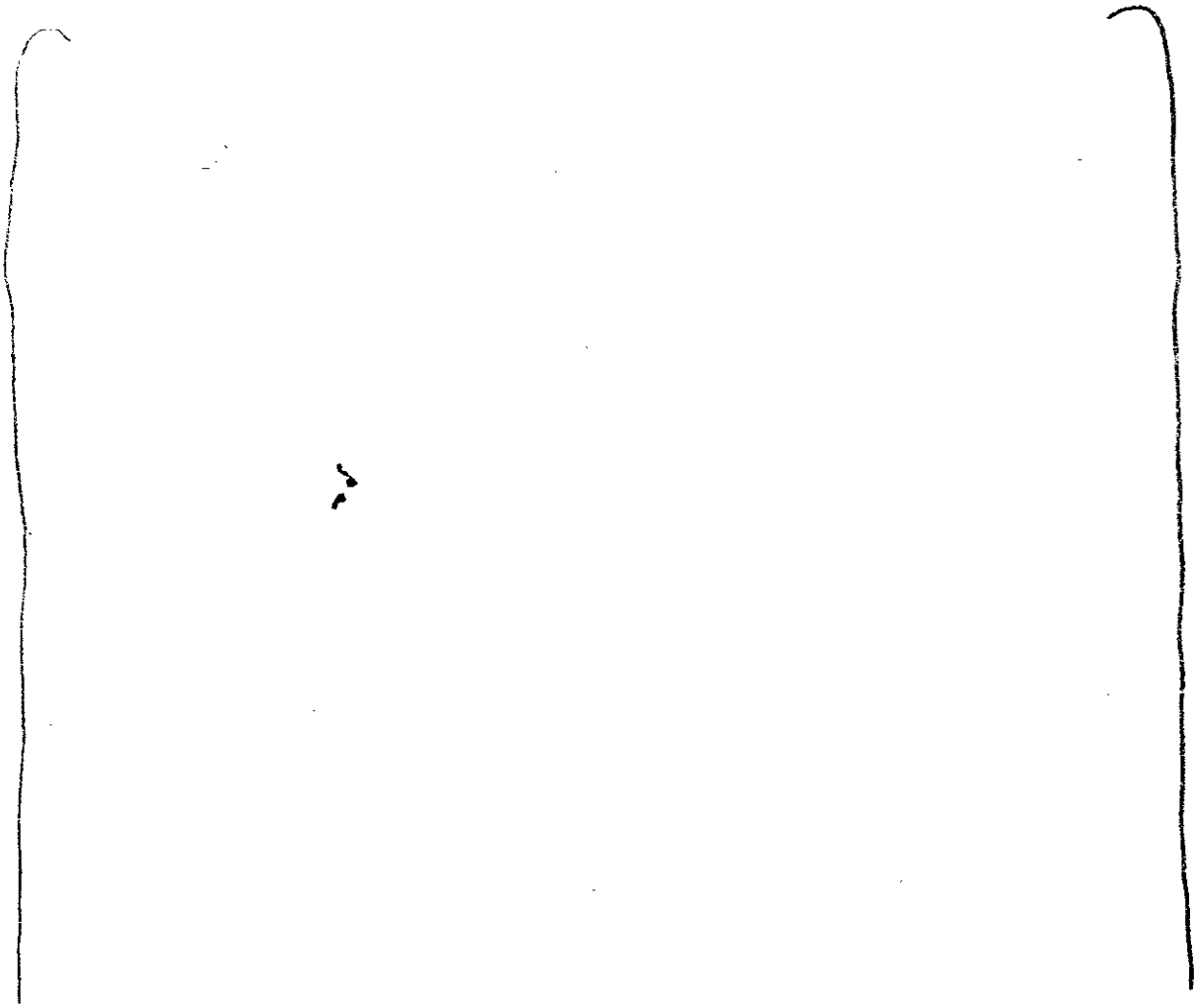
9-Methyl and 13-Methyl trans-(±)-18-ethenyl-4,4a-dihydro-3,4- bis(methoxycarbonyl)--4a,8,14,19-tetramethyl-23*H*,25*H*- benzo[*b*]porphine-9,13-dipropanoate OR 23*H*,25*H*-Benzo[*b*]porphine-9,13-dipropanoic acid, 18-ethenyl-4,4a- dihydro-3,4-bis(methoxycarbonyl)-4a,8,14,19-tetramethyl-, monomethyl ester, *trans*-

CAS-129497-78-5

VERTEPORFIN (a 1:1 mixture of BPD-MA$_C$ and BPD-MA$_D$)

15. Comments. This supplement requests an alternate/additional manufacturing site for the manufacture of the drug product. The site SP Pharmaceuticals Inc. (Albuquerque, NM) is proposed as an alternate to the approved site, Parkedale Pharmaceuticals, Inc. (Rochester, MI). No changes have been made to the manufacturing specifications, test methods or source of the verteporfin active pharmaceutical ingredient, the intermediate (verteporfin presome), or any of the excipients or starting materials. The composition, formula, and regulatory specification (except for the addition of the reconstitution method) for Visudyne are unchanged.

Conclusions and Recommendations (continued)



Based on consideration of chemistry, manufacturing and controls issues, the sponsor's request to include SP Pharmaceuticals as a second site for manufacturing VISUDYNE (verteporfin for injection) from verteporfin presome can be approved, pending final approval by Microbiology and the Office of Compliance.

17. Name	**Signature**	**Date**
Allan Fenselau, Review Chemist		
Concurrence	**Signature**	**Date**
Linda Ng, Team Leader		

cc: NDA #21-119 **Doc ID: n21119s.004**
HFD-550/Division File
HFD-550/CSO/L.Gorski
HFD-550/CHEM/A.Fenselau
HFD-550/CHEM/TeamLdr/L.Ng
HFD-550/Div.Dep.Dir./W.Chambers
HFD-830/Dir.DNDCIII/C-w.Chen

WITHHOLD 26 PAGE(S)

B(4)

Chemistry Review: #2	Division: HFD-550	NDA Number: 21-119

3. Name and Address of Applicant:
QLT Inc.
887 Great Northern Way
Vancouver, BC Canada V5T 4T5

4. Supplement(s):
Number: SCM-004
Date(s): 31-JAN-02

5. Name of Drug:
VISUDYNE™

6. Nonproprietary name:
verteporfin for injection

7. Supplement Provides for: Alternate manufacturing site for drug product

8. Amendment(s): 15-MAR-02/BC
12-APR-02/BC
04-APR-02/BC
30-APR-02/BC
09-APR-02/BL

9. Pharmacological Category:
Photodynamic therapy for age-related macular degeneration

10. How Dispensed:
R_x

11. Related Documents:
N/A

12. Dosage Form: Sterile, lyophilized powder for i.v. injection

13. Potency(es): 15 mg verteporfin per vial

14. Chemical Name and Structure: See USAN
$C_{41}H_{42}N_4O_8$
M.W.: 718.81
9-Methyl and 13-Methyl trans-(±)-18-ethenyl-4,4a-dihydro-3,4- bis(methoxycarbonyl)-
-4a,8,14,19-tetramethyl-*23H,25H-* benzo[b]porphine-9,13-dipropanoate.
CAS-129497-78-5
VERTEPORFIN (a 1:1 mixture of BPD-MAC and BPD-MAD)

15. Comments: This review deals with the results of the microbiology review and the establishment inspection. Dr. Pawar of HFD-160 recommended this supplement for approval "from the microbiological standpoint of [redacted] manufacturing process", on May 9, 2002. The DO recommended the proposed alternate manufacturing site, SP Pharmaceuticals LLC, as acceptable on May 17, 2002 (see attachment).

16. Conclusions and Recommendations: Based on the chemistry approval on review #1 and the recommendations above, from the CMC viewpoint, this supplement is recommended for approval.

17. Name: Libaniel Rodriguez/Review Chemist — Signature: — Date:

18. Concurrence: Linda Ng/ Chemistry Team Leader — Signature: — Date:

ATTACHMENT