CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-119/S-001

CORRESPONDENCE

QLT Inc. 887 Great Northern Way
Vancouver, BC Canada V5T 4T5
t 604.872.7881
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August 14, 2000

Wiley Chambers, MD
Deputy Director
Division of Antiinflammatory, Analgesic and Ophthalmic Drug Products
9201 Corporate Boulevard
Building 2
Rockville, Maryland
USA 20850

NDA NO 21-119 REF NO. 001
NDA SUPPL FOR SE1

Attn: Document Control Room

Subject: Original Supplemental New Drug Application 21-119/S-001 (Efficacy Supplement) for VISUDYNE™ (verteporfin for injection) for a revised indication statement

This is PART I of a multipart submission.

Dear Dr. Chambers:

QLT Inc. [redacted] are submitting a multipart supplemental application for components of a combination product consisting of VISUDYNE™ (verteporfin for injection), a photoactive drug for use in photodynamic therapy (PDT), and specified lasers for use as light sources for the photoactivation of VISUDYNE. These supplements propose a revision to the indication statement and adds treatment of patients with subfoveal choroidal neovascularization secondary to other macular diseases.

The organization and content of this multipart submission are intended to conform to FDA policies and procedures for combination products (drug and device) as described in 21 CFR 3.2(e)(3) and further addressed in the CDRH/CDER Intercenter Agreement (Effective Date – October 31, 1991).

PART I contains the Supplemental New Drug Application (S/NDA) and is to be reviewed by CDER. PARTS II and III are Supplemental Premarket Approval Applications (S/PMAs) to be reviewed by CDRH. Each PART contains a separate cover letter specific for that PART. The multipart submission consists of the following.

PART I – Supplemental New Drug Application for VISUDYNE (verteporfin for injection) NDA 21-119/S-001.

PART II – Supplemental Premarket Approval Application for the [redacted]

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ORIGINAL

PART III – Supplemental Premarket Approval Application for the [redacted]

QLT Inc. hereby submits PART I of this multipart application, which consists of the following:

PART I – Supplemental New Drug Application for VISUDYNE (verteporfin for injection) NDA 21-119/S-001, including complete clinical data.

This supplement contains 128 original volumes. In addition to the normal number of review copies, Ms. Lori Gorski, Project Manager, DAAODP, CDER will receive 15 desk copies of the NDA Summary – Section 2 (Volume 1). As requested, Copy 1 of desk copy Volume 1 will contain a single copy of the two CD-ROMs that contain all electronic documents and data files for this S/NDA. Mr. Richard Felten, Senior Reviewer, ODE1, CDRH will receive a complete desk copy of Volume 1 of this PART.

The required user fee has been submitted, and the assigned User Fee ID Number is 3995.

The applicant, US representative, and contacts for these applications are:

Applicant:

QLT PhotoTherapeutics Inc.[a]
c/o Scott L. Gelband, Attorney
Perkins Coie LLP
1201 Third Avenue, 40th Floor
Seattle, WA 98101-3099

[a] a US subsidiary of QLT Inc. (Vancouver, BC, Canada).

US Representative:

Jonathan Kahan
Hogan & Hartson
555 Thirteenth St., NW
Washington, DC 20004-1109

Tel: (202) 637-5600
Fax: (202) 637-5910

.../3

Direct Sponsor Contacts:

David Mitchell, Senior Manager, Regulatory Affairs
Lawrence D. Mandt, Vice President, Quality and Regulatory Affairs
QLT Inc.
887 Great Northern Way
Vancouver, BC
Canada V5T 4T5

Tel: (604) 872-7881
Fax: (604) 707-7373

The clinical studies included in this NDA were conducted by QLT Inc. [redacted] under [redacted] in accordance with 21 CFR Parts 50, 56, and 312. This S/NDA has been prepared and is being submitted in accordance with 21 CFR 314.

Per the Drug Classification and Priority Review Policy, this drug application meets the definitions for Type 6A therapeutic classification, as an already marketed product of important therapeutic gain. The majority of patients with choroidal neovascularization described herein are not eligible for laser photocoagulation, the only approved alternate therapy. Accordingly, the Sponsor hereby requests a priority review.

QLT hereby requests a waiver from the requirement to perform clinical investigations in pediatric populations due to the fact that age-related macular degeneration and other macular diseases that are the subject of this application occur only in adult or elderly populations.

The existence of this multipart submission and the data and other information that it contains are confidential, and the protection afforded to such confidential information by 18 USC 1905, 21 USC 331(j), 5 USC 552, and other applicable laws is hereby claimed.

The Company is available to discuss this application at the Agency's convenience. Please contact the undersigned at the addresses given above.

Sincerely,

D Mitchell

David Mitchell, M.Sc.
Senior Manager, Regulatory Affairs

cc: Richard Felten, Senior Reviewer, ODE I, CDRH, FDA (complete copy of Volume 1)
Jonathan Kahan, US Representative, Hogan & Hartson (cover letter only)
Lori Gorski, Project Manager, Division of Antiinflammatory, Analgesic and Ophthalmic Drug Products, CDER (15 complete copies of Volume 1)

QLT Inc. 887 Great Northern Way
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August 21, 2000

NDA [illegible] AMENDMENT

Wiley Chambers, MD
Deputy Director
Division of Antiinflammatory, Analgesic and Ophthalmic Drug Products
9201 Corporate Boulevard
Building 2
Rockville, Maryland
USA 20850

Attn: Document Control Room

NDA 21-119/S-001
VISUDYNE™ (verteporfin for injection)
Amendment to a Pending Application

Dear Dr. Chambers:

Enclosed please find a single archival copy of 6 volumes of angiograms and photographs to support the efficacy supplement filed on August 14. Provided are baseline data for all 120 patients enroled in the pathologic myopia study (Study BPD OCR 003 – PM), 12-month data for all PM patients who had a 12-month visit, as well as baseline data for 25 of the 26 patients enroled in the ocular histoplasmosis study (Study BPD OCR 004).

Please contact me directly with any comments or questions you may have about this submission.

Yours sincerely,

David Mitchell, M.Sc.
Senior Manager, Regulatory Affairs

ORIGINAL

cc: Cover letter only:
Richard Felten, Senior Reviewer, ODE I, CDRH, FDA
Jonathan Kahan, US Representative, Hogan & Hartson
Lori Gorski, Project Manager, Division of Antiinflammatory, Analgesic and Ophthalmic Drug Products, CDER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville MD 20857

AUG 24 2000

NDA 21-119/S-001

PRIOR APPROVAL SUPPLEMENT

QLT Inc.
Attention: David Mitchell, Senior Manager Regulatory Affairs
c/o Jonathan S. Kahan
Hogan and Hartson
555 Thirteenth Street, NW
Washington, D.C. 20004-1109

Dear Mr. Mitchell:

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product:	Visudyne (verteporfin for injection), 15 mg
NDA Number:	21-119
Supplement Number:	S-001
Review Priority Classification:	Priority (P)
Date of Supplement:	August 14, 2000
Date of Receipt:	August 14, 2000

This supplement proposes a revision to the labeled indication for the product.

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on October 13, 2000, in accordance with 21 CFR 314.101(a).

Under 21 CFR 314.102(c) of the new drug regulations, you may request an informal conference with this Division (to be held approximately 90 days from the above receipt date) for a brief report on the status of the review but not on the application's ultimate approvability. Alternatively, you may choose to receive such a report by telephone.

Please cite the application number listed above at the top of the first page of any communications concerning this application. All communications concerning this supplemental application should be addressed as follows:

U.S. Postal Service:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Anti-Inflammatory, Analgesic
and Ophthalmic Drug Products, HFD-550
Attention: Division Document Room
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Anti-Inflammatory, Analgesic
and Ophthalmic Drug Products, HFD-550
Attention: Division Document Room
9201 Corporate Boulevard
Rockville, Maryland 20850-3202

If you have any questions, call Lori M. Gorski, Project Manager, at (301) 827-2090.

Sincerely,

/S/ 8/23/00

Leslie Vaccari
Chief, Project Management Staff
Division of Anti-Inflammatory, Analgesic and
Ophthalmic Drug Products, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research

QLT Inc. 887 Great Northern Way
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October 2, 2000

NDA SUPPL AMENDMENT

Wiley Chambers, MD
Deputy Director
Division of Antiinflammatory, Analgesic and Ophthalmic Drug Products
9201 Corporate Boulevard
Building 2
Rockville, Maryland
USA 20850
Attention: Document Control Room

BL
SE1-001

NDA 21-119/S-001
VISUDYNE™ (verteporfin for injection)
Amendment to a Pending Application
Labeling Amendment

Dear Dr. Chambers:

Enclosed please find three copies of an amendment to the draft package insert for NDA 21-119, Supplement S-001. An electronic copy of both the edited and clean insert is included.

Revisions to labeling (draft indication statement) for the two approved devices will be submitted directly to CDRH with a desk copy forwarded to Lori Gorski, Project Manager.

Please contact me directly with any comments or questions you may have about this submission.

Yours sincerely,

DUPLICATE

David Mitchell, M.Sc.
Senior Manager, Regulatory Affairs

cc: (letter only)
Jonathan Kahan, US Representative, Hogan & Hartson
Richard Felten, Senior Reviewer, ODEI, CDRH, FDA

QLT Inc. 887 Great Northern Way
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December 8, 2000

Wiley Chambers, MD
Deputy Director
Division of Antiinflammatory, Analgesic and Ophthalmic Drug Products
9201 Corporate Boulevard
Building 2
Rockville, Maryland
USA 20850

NDA SUPPL AMENDMENT
SU
SE1-001

Attention: Document Control Room

NDA 21-119/S-001
VISUDYNE™ (verteporfin for injection)
Information Amendment
4-Month Safety Update

Dear Dr. Chambers:

Enclosed find three copies of the 4-month safety update to the supplemental NDA submitted on August 14, 2000. Please contact me directly with any questions you may have regarding this submission.

Yours sincerely,

David Mitchell
Senior Manager, Regulatory Affairs

cc: Jonathan Kahan, U.S. Representative, Hogan & Hartson (cover letter only)
Richard Felten, Senior Reviewer, ODE I, CDRH, FDA (Volume 1)

QLT Inc. 887 Great Northern Way
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SE1-001 BK

January 29, 2001

Wiley Chambers, MD
Deputy Director
Division of Antiinflammatory, Analgesic and Ophthalmic Drug Products
9201 Corporate Boulevard
Building 2
Rockville, Maryland
USA 20850
Attention: Document Control Room

NDA 21-119/S-001
VISUDYNE™ (verteporfin for injection)
Amendment to a Pending Application
Clinical

Dear Dr. Chambers:

Per your telephone request of January 15, 2001, enclosed please find three copies of updated clinical information on the use of Visudyne™ as follows:

1. An update of the visual acuity (VA) data, including a short summary, summary tables, data listings and electronic datasets for:
   - 12-months of follow-up for OHS (ocular histoplasmosis syndrome) patients treated in Study BPD OCR 004 and
   - 24-months of follow-up for VIP-PM (pathologic myopia) and VIP-AMD (age-related macular degeneration) patients treated in Studies BPD OCR 003-PM and –AMD.

2. A summary of all available historical control VA data for OHS patients in the clinical literature, including a written summary and comparison to VA outcomes following Visudyne therapy in Study BPD OCR 004, plus copies of literature cited.

3. A summary of all gastrointestinal cancer adverse events from all verteporfin studies, both controlled and uncontrolled, as well as from post-marketing surveillance.

4. A completed 12-month clinical report, report appendices, electronic copy of the report and electronic datasets for Study BPD OCR 004.

Items 1 to 3 (noted above) are provided in Volume 1 and the study report (Item 4) is provided in Volumes 2 to 6. A single deskcopy of this entire submission has been forwarded directly to Lori Gorski, Project Manager. Enclosed in the desk copy is a single

DUPLICATE

copy of the electronic data for this submission, and this is comprised of two CD-ROMs: one for the SAS datasets for VA (Items 1, 2 and 4) and one for the Word documents (text for Items 1 to 4).

Please contact me directly with any concerns or questions you may have about this submission.

Yours sincerely,

David Mitchell
Senior Manager, Regulatory Affairs

cc: (letter only)
Jonathan Kahan, US Representative, Hogan & Hartson
Richard Felten, Senior Reviewer, ODEI, CDRH, FDA
Lori Gorski, Project Manager, DAAODP, CDER, FDA

NDA SUPPL AMENDMENT

QLT Inc. 887 Great Northern Way Vancouver, BC Canada V5T 4T5
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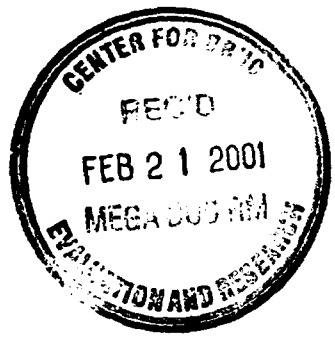

February 19, 2001

Wiley Chambers, MD
Deputy Director
Division of Antiinflammatory, Analgesic and Ophthalmic Drug Products
9201 Corporate Boulevard
Building 2
Rockville, Maryland
USA 20850

Attention: Document Control Room

NDA 21-119/S-001
VISUDYNE™ (verteporfin for injection)
Amendment to a Pending Application
Response to Approvable Letter

Dear Dr. Chambers:

Enclosed please find three copies of our response to the two outstanding deficiencies noted in the Approvable Letter dated February 2, 2001.

In response to Item 1, and in addition to the information submitted on January 29, 2001, we hereby enclose information in response to the request for a statistical comparison between historical control data and Visudyne treatment data, as well as a discussion of the impact caused by differences between the patient groups compared.

In response to Item 4, requesting the submission of a complete listing of adverse reactions as should have been presented in Table 47 (Page 146-149) of the Pathologic Myopia Study Report OCR 003 PM, please note that the information originally submitted in this report was complete. Although a part of the header information on the table stated "Table X of 5", this was a typographical error and should have read "Table X of 4."

We are advised that because a 4-month safety update (current to September 8), and visual acuity update (current to January 16) have been submitted recently (December 8, 2000 and January 29, 2000, respectively), the safety update noted in the Approvable Letter is not required at this time. Please note that at this time we have no draft promotional materials for the proposed indication.

DUPLICATE

We now consider our response to the February 2, 2001 Approvable Letter to be complete.

Please contact me directly with any concerns or questions you may have about this submission.

Yours sincerely,

for David Mitchell
Senior Manager, Regulatory Affairs

cc: Jonathan Kahan, US Representative, Hogan & Hartson (letter only)
Richard Felten, Senior Reviewer, ODEI, CDRH, FDA (letter only)
Lori Gorski, Project Manager, DAAODP, CDER, FDA (complete desk copy)

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February 23, 2001

Wiley Chambers, MD
Deputy Director
Division of Antiinflammatory, Analgesic and Ophthalmic Drug Products
9201 Corporate Boulevard
Building 2
Rockville, Maryland
USA 20850

NC
S E1-001

Attention: Document Control Room

NDA 21-119/S-001
VISUDYNE™ (verteporfin for injection)
Amendment to a Pending Application
Response to Approvable Letter

Dear Dr. Chambers:

This letter is to clarify information submitted on February 19, 2001 in response to deficiencies noted in the approvable letter issued on February 2, 2001.

In the approvable letter we are requested to update the NDA by submitting all available safety information regarding Visudyne™. At this time there is no new information regarding safety which has not already been submitted in a 4-month safety update (current to September 8) on December 8, 2000, and visual acuity update (current to January 16) on January 29, 2000. New safety information will be submitted as it becomes available.

It is our understanding that all deficiencies have now been addressed by the two amendments submitted on January 29, 2001 and February 19, 2001.

Please contact me directly with any concerns or questions you may have about this submission.

Yours sincerely,

for David Mitchell
Senior Manager, Regulatory Affairs

cc: Jonathan Kahan, US Representative, Hogan & Hartson
Richard Felten, Senior Reviewer, ODEI, CDRH, FDA
Lori Gorski, Project Manager, DAAODP, CDER, FDA

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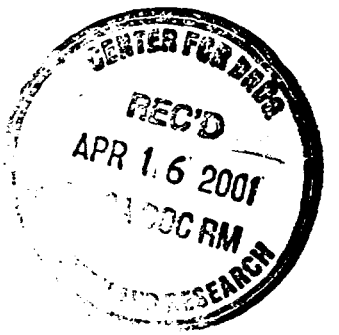

April 12, 2001

Wiley Chambers, MD
Deputy Director
Division of Antiinflammatory, Analgesic and Ophthalmic Drug Products
9201 Corporate Boulevard
Building 2
Rockville, Maryland
USA 20850

N.000(C)

NDA 21-119/S-001
VISUDYNE™ (verteporfin for injection)
Amendment
Environmental Assessment

Dear Dr Chambers:

Further to a telephone request from Lori Gorski on April 12, 2001, QLT is submitting an updated copy of the Claim for Categorical Exclusion from Environmental Assessment for Visudyne.

Please contact me directly with any questions or comments you may have about this submission.

Yours sincerely

Caroline Stokl

Caroline Stokl, Ph.D.,
Sr. Manager, Regulatory Affairs

cc: Jonathan Kahan, US representative, Hogan & Hartson
Lori Gorski, Project Manager, DAAODP, CDER, FDA

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August 20, 2001

Wiley Chambers, MD
Deputy Director
Division of Antiinflammatory, Analgesic and Ophthalmic Drug Products
9201 Corporate Boulevard
Building 2
Rockville, Maryland
USA 20850

Attention: Document Control Room

NDA 21-119/S-001
VISUDYNE™ (verteporfin for injection)
Information Amendment
Final Draft Labeling

Dear Dr. Chambers:

Enclosed please find three copies of the final draft labeling for VISUDYNE™ (verteporfin for injection) per the revisions agreed upon with FDA during a teleconference today.

If you have any questions or comments regarding this submission, please do not hesitate to contact me directly.

Yours sincerely,

David Mitchell
Associate Director, Regulatory Affairs

cc: (cover letter only)
Jonathan Kahan, U.S. Representative, Hogan & Hartson
Richard Felten, Senior Reviewer, ODE I, CDRH, FDA
(one complete copy)

QLT Inc. 887 Great Northern Way
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August 21, 2001

Wiley Chambers, MD
Deputy Director
Division of Antiinflammatory, Analgesic and Ophthalmic Drug Products
9201 Corporate Boulevard
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Rockville, Maryland
USA 20850

Attention: Document Control Room

NDA 21-119/S-001
VISUDYNE™ (verteporfin for injection)
Information Amendment
Request for Exclusivity

Dear Dr. Chambers:

We hereby request an additional three years exclusivity for verteporfin for injection in regards to our efficacy supplement S-001.

If you have any questions or comments regarding this submission, please do not hesitate to contact me at the number above.

Yours sincerely,

David Mitchell
Associate Director, Regulatory Affairs

cc: (cover letter only)
Jonathan Kahan, U.S. Representative, Hogan & Hartson
Richard Felten, Senior Reviewer, ODE I, CDRH, FDA
Lori Gorski, Project Manager, Division of Antiinflammatory, Analgesic and Ophthalmic Drug Products, CDER