DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

**TRANSMITTED BY FACSIMILE**

Ger Vijfvinkel
President
Dutch Ophthalmic USA
One Little River Road
P.O. Box 968
Kingston, NH 03848

**Re: NDA # 21-670**
**VisionBlue® (trypan blue ophthalmic solution)**
**MACMIS ID # 13490**

# WARNING LETTER

Dear Mr. Vijfvinkel:

The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed a professional journal advertisement (ad) for VisionBlue® (trypan blue ophthalmic solution) submitted by Dutch Ophthalmic Research Center International (DORC) under cover of Form FDA 2253 and a website (http://www.dorc.nl) for VisionBlue also disseminated by DORC. The ad and website are false or misleading in that they present numerous efficacy claims for VisionBlue, but fail to communicate any risks associated with its use. Thus, the ad and website misbrand the drug in violation of Sections 502(a),(f), and (n) and 201(n) of the Federal Food, Drug, and Cosmetic Act (Act), 21 U.S.C. §§ 352(a),(f), and (n) and 321(n) and FDA's implementing regulations 21 CFR 201.100(d); 202.1(e)(1), (e)(3)(iii), (e)(5). Furthermore, DORC failed to submit a copy of the website pages accompanied by a completed transmittal Form FDA 2253 as required by 21 CFR 314.81(b)(3)(i). Your ad and website raise public health and safety concerns through their complete omission of risk information for VisionBlue by suggesting VisionBlue is safer than has been demonstrated.

**Background**

According to the Description section of the approved product labeling (PI), "VisionBlue® (trypan blue ophthalmic solution) 0.06% is a sterile solution of trypan blue (an acid di-azo group dye). VisionBlue® is a selective tissue staining agent for use as a medical aid in ophthalmic surgery." The Indications and Usage section of the PI states:

> "VisionBlue® is indicated for use as an aid in ophthalmic surgery by staining the anterior capsule of the lens."

The Contraindications section of the PI states:

> "VisionBlue® is contraindicated when a non-hydrated (dry state), hydrophilic acrylic intraocular lens (IOL) is planned to be inserted into the eye because the dye may be absorbed by the IOL and stain the IOL."

The Precautions section of the PI states:

> "General: It is recommended that after injection all excess VisionBlue® be immediately removed from the eye by thorough irrigation of the anterior chamber."

VisionBlue is also associated with other risks, as described in the Adverse Reactions section of the PI including discoloration of high water content hydrogen intraocular lenses and inadvertent staining of the posterior lens capsule and vitreous face (staining of the posterior lens capsule or vitreous face is generally self-limited, lasting up to one week).

**Omission of Risk Information**

Promotional materials are false or misleading if they fail to reveal material facts with respect to consequences that may result from the use of the drug as recommended or suggested by the materials. The ad and website are misleading because they present numerous efficacy claims for VisionBlue, but fail to communicate any risks associated with its use.

The ad includes claims such as, "FDA Approved Capsule Staining to Visualize the Capsulorhexis" and "Staining of the anterior lens capsule with VisionBlue® facilitates the visualization of the capsulorhexis, by creating a contrast between the blue stained capsule and the non-stained underlying lens mass."

In addition, the ad presents several efficacy claims under the header, "Clear Advantages of VisionBlue®" such as:

- "VisionBlue® can be injected directly onto the anterior lens capsule"
- "VisionBlue® greatly enhances the contrast between the anterior and posterior lens capsule and the adjacent tissue structures"

Similarly, the website includes the following claims: "VisionBlue® capsule staining therefore facilitates the performance of a capsulorhexis in the absence of a red fundus reflex, and reduces the risk of capsulorhexis-related complications by better visualization of radial capsule tears. VisionBlue® can be injected directly onto the anterior lens capsule and stains the capsule instantly. The capsule staining procedure is therefore quick and easy to perform."

The website presents several efficacy claims under the header, "Clear Advantages of VisionBlue®" such as:

- "VisionBlue® can be injected directly onto the anterior lens capsule and stains the capsule instantly;" and
- "VisionBlue® greatly enhances the contrast between the anterior and posterior lens capsule and the adjacent tissue structures."

The website also includes efficacy claims under the header, "VisionBlue® capsule staining to visualize the capsulorhexis in cataract surgery":

- "Greatly enhanced visualization of the capsulorhexis in eyes with mature cataracts or narrow pupil, in which the anterior lens capsule is often hardly visible to the surgeon during surgery;"
- "Persistent and clear outline of the peripheral rim of the capsulorhexis by the contrast between the stained rim and the adjacent lens mass;" and
- "Reduces risk of capsulorhexis-related complications by better visualization of radial capsule tears."

Notwithstanding these efficacy claims, neither the ad nor the website presents any risk information for VisionBlue. Furthermore, the ad fails to include a true statement of information in brief summary relating to side effects, contraindications, and effectiveness of VisionBlue as required by the Act and FDA regulations. 21 U.S.C. § 352(n); 21 CFR 202.1(e)(1). This complete omission of risk information from both the website and the ad poses a potential risk to the public health by suggesting that VisionBlue is safer than has been demonstrated.

**Failure to Submit Under Form FDA 2253**

FDA regulations require companies to submit any labeling or advertising devised for promotion of the drug product at the time of initial dissemination of the labeling and at the time of initial publication of the advertisement for a prescription drug product. Each submission is required to be accompanied by a completed transmittal Form FDA 2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) and is required to include a copy of the product's current professional labeling. You did not submit a copy of the website referred to in this letter to DDMAC under cover of Form FDA 2253 as required by 21 CFR 314.81(b)(3)(i).

**Conclusion and Requested Action**

For the reasons discussed above, the ad and website misbrand VisionBlue in violation of the Act and FDA's implementing regulations. 21 U.S.C. §§ 352(a),(f), and (n); 321(n); 21 CFR 201.100(d); 202.1(e)(1),(e)(3)(iii),(e)(5). Furthermore, the website was not submitted under cover of Form FDA 2253, as required by 21 CFR 314.81(b)(3)(i).

DDMAC requests that DORC immediately cease the dissemination of violative promotional materials for VisionBlue such as those described above. Please submit a written response to this letter on or before July 13, 2005, stating whether you intend to comply with this request, listing all violative promotional materials for VisionBlue such as those described above, and explaining your plan for discontinuing use of such materials. Because the violations described above are serious, we request, further, that your submission include a comprehensive plan of action to disseminate truthful, non-misleading, and complete corrective messages about the issues discussed in this letter to the audience(s) that received the violative promotional materials. Please direct your response to me at the Food and Drug Administration, Division of Drug Marketing, Advertising, and Communications, HFD-42, Room 8B-45, 5600 Fishers Lane, Rockville, MD 20857, facsimile at 301-594-6771. In all future correspondence regarding this matter, please refer to MACMIS ID # 13490 in addition to the NDA number. We remind you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for VisionBlue comply with each applicable requirement of the Act and FDA implementing regulations.

Failure to correct the violations discussed above may result in FDA regulatory action, including seizure or injunction, without further notice.

Sincerely,

*{See appended electronic signature page}*

Thomas Abrams, RPh, MBA
Division Director
Division of Drug Marketing, Advertising, and Communications

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**

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/s/

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Barbara Chong
6/28/05 10:37:40 AM
Signed for Thomas Abrams