DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of Combination Products
15800 Crabbs Branch Way (HFG-3)
Suite 200
Rockville, MD 20855

Food and Drug Administration
Rockville MD 20857

May 13, 2004

[ ]
The Trylon Corporation
970 W. 190th Street, Suite 850
Torrance, CA 90502

Re: Request for Designation
ViziLite-Blue Oral Exam Kit
Our file: RFD 2004.014
Dated: March 16, 2004
Received and Filed: March 17, 2004

Dear Dr. [ ]

The Food and Drug Administration (FDA) has completed its review of the request for designation (RFD) for the ViziLite-Blue Oral Exam Kit that you submitted on March 16, 2004. The Office of Combination Products (OCP) filed the RFD on March 17, 2004. We have determined that the product is a combination product, and we have assigned it to the Center for Devices and Radiological Health (CDRH) as the lead agency center for premarket review and regulation based on our determination of the product's primary mode of action (PMOA).

Description of the Product

According to the RFD, the product is a visualization system that employs some of the same components and has the same mechanism of action as the previously cleared ViziLite Test Kit.[1] Similar to the ViziLite Test kit, the ViziLite-Blue Oral Exam Kit contains a hand-held disposable chemiluminescent light and a 1% Acetic Acid Rinse. What differentiates the ViziLite-Blue Oral Exam Kit from the previously cleared ViziLite Test Kit is the addition of the ViziLite-Blue Oral Lesion Identification and Marking System. This marking system contains one marking swab saturated with 1.3 ml of 0.5% Tolonium Chloride, a metachromatic dye also known as toluidine blue, and an additional swab of 1% Acetic Acid Rinse, to be used as a post-dye application cleansing swab.

According to the RFD, the product is indicated for use as an adjunct to conventional oral mucosal screening by incandescent light for the identification, evaluation, and monitoring of oral mucosal abnormalities in a population at increased risk for oral cancer. The RFD explains that a clinician applies one of the two acetic acid rinse swabs to the oral mucosa, and then shines the chemiluminescent light into a patient's mouth for the initial examination. Normal epithelium will absorb the ViziLite device's illumination and appear dark, while abnormal epithelium will reflect it and appear bright white. According to the 510(k) Summary submitted for K003995, under the ViziLite's chemiluminescent light, atypical or dysplastic mucosal abnormalities will appear as bright white, distinctly demarcated, sharply marginated areas that contrast the surrounding non-involved epithelium. With the product currently under consideration, if the chemiluminescent light reveals any white lesions, the clinician would stain these lesions for further identification and monitoring with the toluidine blue dye. The RFD suggests that the staining occurs when the toluidine blue is "dabbed" across the lesion already differentially identified with ViziLite.

[1] The Center for Devices and Radiological Health (CDRH) cleared the ViziLite Test Kit (a.k.a. ViziLite Comprehensive Exam Tray, K012070, and the OralLite Test Kit, K003995) pursuant to section 510(k) of the Federal, Food, Drug, and Cosmetic Act. The ViziLite Comprehensive Exam Tray and the OralLite Test Kit are indicated for use in combination with traditional oral examination by incandescent light by a health care provider to increase identification, evaluation, and monitoring of oral mucosal abnormalities in populations at increased risk for oral cancer.

The dye is transferred from the swab to the oral mucosa.[2] The dye remains in the mouth for 10-20 seconds before the second acetic acid rinse swab is applied to rinse the excess dye from the healthy epithelial cells and the rest of the mouth. The clinician then can sample and further study the stained lesions.

The Trylon Corporation (Trylon) asserts that the product is comprised of device components, and proposes that the agency assign the product to CDRH for premarket review and regulation. With regard to the toluidine blue component, the company explains that it is intended to serve a device function, which enhances the function of the chemiluminescent light. Trylon explains in the RFD that the dye is not proposed for use in the initial oral mucosal examination without prior lesion identification under incandescent light. Trylon claims that the dye is used simply to stain the previously identified lesions for further study.

Product Classification: Combination Product

The ViziLite test kit component of the ViziLite-Blue Oral Exam Kit has been cleared by CDRH as a device (K003995) for marketing as a stand-alone product.

We have determined that the toluidine blue component of your product meets the definition of a drug in the Federal Food, Drug, and Cosmetic Act (Act), but does not meet the Act's definition of a device[3]. The toluidine blue component of your product is a drug within the meaning of section 201(g) of the Act because it is an article intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man; and/or an article intended to affect the structure or any function of the body. However, the toluidine blue does not meet the device definition because it has not been shown with scientific evidence to achieve its primary intended purpose without chemical or metabolic action within the body. According to your RFD, the swab saturated with toluidine blue dye is intended to stain the lesions. In achieving this purpose, the dye [redacted]. Based on the information in your RFD, FDA's understanding of the dye's mechanism of action, and the current published literature, we have determined that [redacted] through chemical action within or on the body, and therefore the dye does not meet the definition of a device. The classification of the toluidine blue component of your product as a drug is consistent with the jurisdictional classification of other dyes [redacted] We are not aware of any legally marketed devices with a similar mechanism of action.

We have determined that, because the product is comprised of both device and drug components, it is a combination product within the meaning of section 503(g) of the Act and Title 21 of the Code of Federal Regulations (CFR) section 3.2(e)(2). In accordance with section 503(g) of the Act and 21 CFR section 3.4, assignment of a lead Center to conduct the review of a combination product is based on the Agency's determination of the product's primary mode of action.

Assignment of Lead Center: CDRH

We have considered the information in the RFD and discussed the issues with staff from CDRH, the Center for Drug Evaluation and Research (CDER), and the Office of Chief Counsel. This product has two modes of action. One action of the product is the action of the device component to differentially illuminate and demarcate normal and unhealthy tissue. Another action of the product is the drug component's action to mark the lesions for further examination. We have determined that your combination product's primary mode of action is attributable to the device component's role in the differential illumination and demarcation of normal tissue and lesions, while the drug

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[2] The maximum dose of the dye that can be delivered from one swab is [redacted]

[3] Section 201(h) of the Act states that a device is intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease, or intended to affect the structure or function of the body of man. A device may not achieve its primary intended purposes through chemical action within or on the body of man nor can it be dependent upon being metabolized for the achievement of its primary intended purposes.

component plays a subordinate role in marking the lesions for further study. Accordingly, we are assigning the combination product to CDRH for premarket review and regulation under the medical device provisions of the Act.[4]

We have also made preliminary determinations about other regulatory requirements that will apply to your combination product. The combination product will be subject to manufacturing (21 CFR 820) and adverse event reporting requirements (21 CFR 803) applicable to medical devices. However, current good manufacturing practices for drugs will apply to the manufacture of the toluidine blue dye component in accordance with section 501(a)(2)(B) of the Act and, in addition to the device quality system requirements, may also apply to certain aspects of the manufacture of the combination product. Any clinical investigations of the combination product are subject to the investigational device exemption (IDE) requirements found in 21 CFR 812 and should be conducted in conformity with those regulations. CDRH will consult with CDER regarding the drug component of your product. We encourage you to discuss with CDRH these and other regulatory requirements applicable to your combination product.

CDRH's Division of Anesthesiology, General Hospital, Infection Control, and Dental Devices (DAGID), Dental Devices Branch, will have lead responsibility for the combination product's premarket review and regulation. For further information on how to proceed, please contact Dr. Susan Runner, Chief, Dental Devices Branch, at (301) 827-5283, ext. 117. Please include a copy of this letter with your initial submission to CDRH.

You may request reconsideration of the classification or assignment of your product within 15 days of receipt of this letter. If you wish to request reconsideration, or for any other questions about this letter, please contact me at (301) 827-9229. Finally, the Office of Combination Products is available to you as a resource for questions or issues that may arise throughout the development of your product. You may reach us at the above address or by email at combination@fda.gov.

Sincerely,

Leigh Hayes
Product Assignment Officer
Office of Combination Products

cc: Dr. Susan Runner

[4] Any change in dose or administration of the dye, or change in exposure time of the oral mucosa to the dye, may affect the primary mode of action of the product and would require a separate jurisdictional determination.