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

July 21, 2004

[ ]
Schering-Plough HealthCare Products, Inc.
Three Connell Drive
Berkeley Heights, NJ 07922-0603

Re: Request for Designation
Over-the-Counter Wart Removal System
Our file: RFD 2004.033
Dated: July 1, 2004
Received and Filed: July 1, 2004

Dear [ ]

The Food and Drug Administration (FDA) has completed its review of the request for designation (RFD) for the over-the-counter (OTC) Wart Removal System that you submitted on behalf of Schering-Plough HealthCare Products, Inc. (Schering-Plough) on July 1, 2004. The Office of Combination Products (OCP) filed the RFD on July 1, 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 intended for the removal of common warts and plantar warts on the bottom of the foot. The product is comprised of Schering-Plough's currently marketed over-the-counter (OTC) portable cryosurgical system, as well as an additional component of 17% salicylic acid, which is currently separately available OTC as a stand-alone wart removal product.[1] According to the RFD, the company wants to co-package the salicylic acid with the cryotherapy system to augment the efficacy of the system. The RFD explains that cryotherapy works by freezing wart/skin tissue. Upon contact with a cryogen, water within the affected skin cell is frozen to form crystals. As a result, the cell membrane is ruptured due to the expansion of the water crystals that are formed. Cryotherapy also results in damage to the cellular protein, mitochondria, and endoplasmic reticulum. The RFD further explains that, once cryotherapy is used, the layer of skin cells which has been frozen and is ruptured must be removed, whether through aggressive treatment or through natural exfoliation. Once the "dead skin" is removed, a new layer of wart/skin is exposed that can be frozen. The RFD states that studies have shown that salicylic acid can be used between freezing treatments to quicken the skin turnover rate, acting as an exfoliating agent by reducing the intracellular adhesion between skin cells. According to the RFD, cryotherapy alone typically requires one to three freezing treatments to remove common warts and up to four treatments for plantar warts. By

[1] The device is currently marketed OTC as Dr. Scholl's® Freeze Away Wart Remover, and is approved under 510(k) application, K031697. Currently, the 17% salicylic acid solution is separately marketed OTC as Dr. Scholl's® Clear Away Liquid Wart Remover. Wart remover drug products are marketed pursuant to a final monograph found at 21 CFR 358, Subpart B.

contrast, the RFD states, [redacted]

Schering-Plough recommends that the OTC Wart Removal System be assigned to CDRH for premarket review and regulation. The company asserts that the product's PMOA is that of a device (cryotherapy treatment), which is intended to freeze and rupture the skin cells, while the drug component (salicylic acid) plays a secondary role in exfoliating the "dead skin" between cryotherapy treatments.

Product Classification: Combination Product

We have determined that, because the product is comprised of both device (cryotherapy treatment system) and drug (17% salicylic acid) components, it is a combination product within the meaning of section 503(g) of the Federal Food, Drug, and Cosmetic Act (Act) and Title 21 of the Code of Federal Regulations (CFR) section 3.2(e)(2). In accordance with section 503(g)(1) 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 in CDRH and the Center for Drug Evaluation and Research (CDER).

This product has two modes of action. One action of the combination product is the action of the cryotherapy system to freeze and rupture the skin cells comprising the wart. Another action of the product is the salicylic acid's action to exfoliate "dead" skin cells between cryogenic therapy treatments. We have determined that your product's primary mode of action is attributable to the device component's role in the freezing and rupture of the skin cells comprising the wart, while the drug component plays a secondary role in exfoliating "dead" skin cells in between cryotherapy treatments. Accordingly, we are assigning the product to CDRH for premarket review and regulation under the medical device provisions of the Act.

We have also made preliminary determinations about other regulatory requirements that will apply to your combination product. These are subject to further review by the agency. 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 salicylic acid 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 as necessary. We encourage you to discuss with CDRH these and other regulatory requirements applicable to your combination product.

CDRH's Division of General, Restorative, and Neurological Devices (DGRND) will have lead responsibility for the combination product's premarket review and regulation. For further information about review requirements, please contact Della Hammond, General Surgery Devices Branch, DGRND, at 301-594-3090 ext. 162. 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

Leigh Hayes
Product Assignment Officer

cc: Della Hammond