DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Office of the Ombudsman
5600 Fishers Lane
Room 14B-03, HF-7
Rockville, MD 20857

Food and Drug Administration
Rockville MD 20857

October 7, 2002

Ronald A. Sherman, MD, Msc
36 Urey Court
Irvine, California 92612

Re: Request for Designation
Blow Fly Larvae
Our file: RFD 2002.031

Dear Dr. Sherman:

The Food and Drug Administration (FDA) has completed its review of your request for designation (RFD) covering blow fly larvae (maggots). The RFD was filed by this office on August 8, 2002.

According to the RFD, blow fly larvae will be used to treat [ ] foot wounds, pressure ulcers, venous stasis ulcers, and burns that have failed to respond to two or more courses of standard therapy. Medical maggots are placed on a wound and left in place for 24-72 hours. A new cycle of larvae may be place immediately after removal of the preceding cycle, though one or two days between cycles is generally recommended.

The RFD states that there are three simultaneous benefits to treating wounds with maggots: debridement, disinfection, and tissue growth. According to the RFD, debridement is largely a result of extracorporeal digestion. The maggots secrete proteolytic digestive enzymes, which dissolve necrotic tissue. The RFD states that maggot-induced [ ] is complex, and the details are not well understood. It may be that [ ] is a result of simple [ ] According to the RFD, it has also been shown that larvae and blow flies produce a [ ]s. Finally, according to the RFD, maggots [ ]

The larvae covered by the RFD are descendants of a [ ] Females are induced to deposit eggs [ ]; eggs are collected and disinfected in [ ]. The duration of the disinfection soak is determined by quality control cultures, testing each batch of eggs for growth of aerobic and anaerobic microorganisms. Disinfected eggs are placed into medical specimen containers, where they will hatch on a gauze pad soaked in a liquid diet [ ]

The RFD states that in the past, FDA officials suggested that the Center for Devices and Radiological Health (CDRH) would be the most appropriate center to review and regulate medical maggots.

We have considered the information contained in the RFD, and discussed the issues raised with staff in CDRH and the Center for Biologics Evaluation and Research (CBER). We conclude that medical maggots do not meet the definition of a medical device in that they appear to achieve their primary intended purpose through chemical action in or on the body of man:[1] dissolution of necrotic tissue by the maggots' proteoloytic digestive enzymes, and [ ]. Accordingly, we conclude that medical maggots are a biological product, as defined by the Public Health Service Act.[2]

We note further that many of the review issues will revolve around the process for manufacturing medical maggots – in particular, keeping the product free from adventitious agents. Because maggots must be alive in order to be effective, it will not be possible to use routine terminal sterilization protocols to ensure sterility. Consequently, it will be necessary to control all source materials during manufacture and use, which is best accomplished under the biologics regulatory scheme.

Accordingly, we conclude that medical maggots will be reviewed and regulated by CBER under the biologic licensing provisions of the Public Health Service Act. 42 U.S.C. § 351 et seq., 21 CFR Part 600. See also investigational new drug application regulations at 21 CFR Part 312. CBER's Office of Cellular, Tissues, and Gene Therapies will be the reviewing office. For further information, please contact:

Joyce Frey-Vasconcells
Acting Deputy Office Director
Office of Cellular, Tissues, and Gene Therapies, HFM-591,
1401 Rockville Pike
Rockville, MD 20852
301-827-5102

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[1] The term "device" ...means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article ...which does not achieve its primary intended purposes through chemical action within or on the body of man.... 21 U.S.C. § 201(g), section 321(g) of the Federal Food, Drug, and Cosmetic Act.

[2] No person shall sell, barter, or exchange ... any virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product ... applicable to the prevention, treatment or cure of diseases or injuries of man.... 42 U.S.C. § 351(a), section 262(a) of the Public Health Service Act.

You may request reconsideration of this classification and jurisdictional decision. Please contact Suzanne O'Shea, of this office, at 301-827-3390 for guidance on the procedures for requesting reconsideration or if you have other questions about this matter.

Sincerely yours,

Steven H. Unger
Ombudsman

cc: Joyce Frey-Vasconcells (HFM-591)

File

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Office of the Ombudsman
5600 Fishers Lane
Room 4B-44, HF-7
Rockville, MD 20857

Food and Drug Administration
Rockville MD 20857

April 18, 2003

Ronald A. Sherman, MD
36 Urey Court
Irvine, California 92612

Re: Request for Reconsideration
Blow Fly Larvae
Our file: RFD # 2002.031

Dear Dr. Sherman:

The Food and Drug Administration has completed its review of your Request for Reconsideration for blow fly larvae (maggots), which was received by this office on March 18, 2003. Your request seeks reconsideration of our October 7, 2002, decision that blow fly larvae are a biological product. We have reviewed the request, which contains a more complete description of how the product works than the original Request for Designation (RFD). We now conclude that blow fly larvae are a device within the meaning of section 201(h) of the Federal Food, Drug, and Cosmetic Act. A complete discussion follows.

According to the information submitted in the RFD and the Request for Reconsideration, blow fly larvae, or medical maggots, are a wound healing therapy that has been used for over 70 years to debride a variety of non-healing skin and soft tissue wounds, including [ ]

[ ]

The Request for Reconsideration recommends that maggot therapy be considered a combination product because the mechanism of action of the maggots is both the physical rasping of the maggots on the wound and the release of proteolytic enzymes. The request for reconsideration further recommends that the maggots be regulated by the Center for Devices and Radiological Health (CDRH).

In our initial designation decision we concluded that maggots did not meet the definition of a device[1] because they achieved their primary intended purpose through the chemical dissolution of necrotic tissue by the proteoloytic digestive enzymes [ ]

[ ]

[1] The term "device"... means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article ..., which does not achieve its primary intended purpose through chemical action within or on the body of man... 21 U.S.C. § 201 (h) of the Federal, Food, Drug, and Cosmetic Act.

The Request for Reconsideration, however, describes [ ] debridement by maggots' enzymes alone, without the physical contact and interaction of the maggots with the wound surface, (that is, when the maggots are contained in a bag that prevents direct contact with the wound) is less effective than when the maggots have direct contact with the wound. Review of the information submitted suggests that maggots' secretion of the proteoloytic enzymes without the accompanying physical rasping and tearing action on the necrotic tissue is not effective therapy. This may indicate that the primary mechanism of action is the rasping and tearing of the necrotic tissue. The proteolytic enzymes appear to aid in debridement secondarily to the maggots' physical rasping action.

We have reconsidered the information provided in the RFD, reviewed the more detailed product description provided in the Request for Reconsideration, and discussed the issues raised with staff in both centers. Based on our review we reverse our previous decision and conclude that medical maggots exert their primary intended use by a physical, not chemical, action and thus meet the definition of a device. (Moreover, they are applied to the wound by means of a medical dressing, also a device.) Therefore, they are neither a biological nor combination product, but are a device used together with another device. Accordingly, the maggots will be regulated by CDRH, under the device provisions of the Federal Food, Drug, and Cosmetic Act.

For further information regarding regulatory requirements, please contact:

Charles Durfor, Ph.D.
Plastics and Reconstructive Surgery Devices Branch
Center for Devices and Radiological Health
9200 Corporate Blvd, HFZ-410,
Rockville, MD 20850.

He may be reached by telephone at 301-594-3090.

If you have any questions concerning this matter please contact me at 301-827-3390.

Sincerely yours,

Suzanne O'Shea
Product Jurisdiction Officer

cc: Charles Durfor