DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

OCT 14 1998

WARNING LETTER

The Center for Research on Population & Security
322 Azalea Drive
Chapel Hill, NC 27514

Re: 99-HFD-312-01

Dear Dr.

This letter is in reference to the importation, processing, marketing, and possible exportation of quinacrine pellets and quinacrine inserters (each inserter contains seven quinacrine pellets). Labeling with your product states that the quinacrine is intended for "NONSURGICAL FEMALE STERILIZATION."

The Food and Drug Administration (FDA) has concluded that quinacrine pellets for non-surgical female sterilization is an unapproved new drug and a misbranded drug in violation of the Federal Food, Drug, and Cosmetic Act (Act), and an unsafe use of this drug product. The FDA is very concerned about the safety risks associated with the use of this drug for non-surgical female sterilization, and its effects on women and the fetus if a woman is, or becomes pregnant. This safety concern is shared by the World Health Organization (WHO), which has issued statements that quinacrine for non-surgical female sterilization should not occur until completion of toxicology, genotoxicity and possibly carcinogenicity testing. Reportedly, several countries including India and Chile, have banned this method of non-surgical sterilization. We are not aware of any country that has approved this product for non-surgical female sterilization.

Toxicology, genotoxicity, and carcinogenicity studies are normally part of appropriately designed, well controlled, clinical trials conducted under an Investigational New Drug

Application (IND) filed with the FDA. The Agency's safety concerns and IND requirements prior to marketing of this drug for non-surgical female sterilization were previously conveyed to you during your May 8, 1998 meeting with the FDA's Center for Drug Evaluation and Research (CDER) Division of Reproductive and Urologic Drug Products.

The possible safety risks associated with this drug's use include but are not limited to:

- possible increased risk for reproductive tract cancers
- development of abnormal uterine lesions
- ectopic pregnancy
- prolonged amenorrhea
- procedure failure (variable efficacy rates)
- fetal exposure

The FDA has reviewed your firm's product labeling, training materials, videos, instruction manuals, patient pamphlets, and Internet site for this product which demonstrate that your product is intended "to affect the structure or any function of the body," as described in section 201(g) of the Act. Consequently, your product, quinacrine pellets for non-surgical sterilization, is a drug.

The FDA is unaware of any scientific evidence from adequate and well-controlled studies that this drug is generally recognized as safe and effective for this intended use. Accordingly, this product is a "new drug" under section 201(p) of the Act and may not be marketed in the United States because it is not the subject of an approved application as described in section 505(b) of the Act.

Further, this drug is misbranded pursuant to section 502(f)(1) of the Act in that its labeling fails to bear adequate directions for the uses for which it is being offered.

Because this product is an unapproved new drug and misbranded under the Act, import of the product into the United States is prohibited by section 301(a),(d) of the Act.

In addition, based on the information available to FDA, the Act prohibits the export of this product from the United States to a foreign country. Although section 802 of the Act permits the export of certain unapproved new drugs from the United States, this product does not appear to comply with the requirements of that section. The principal provision authorizing the exportation of unapproved new drugs is section 802(b)(1)(A) of

the Act, and provides that a drug "may be exported to any country, if the drug...complies with the laws of that country and has valid marketing authorization by the appropriate authority" in Australia, Canada, Israel, New Zealand, Switzerland, South Africa, or any member nation in the European Union on the European Economic Area." A drug product exported pursuant to section 802 must meet several other requirements, including not being in conflict with the laws of the country to which it is to be exported (section 802(f)(3)), and not presenting an imminent hazard to the public health of the country to which it is to be exported (section 802(f)(4)). The information available to the FDA, however, indicates that the product at issue does not meet even the threshold requirement for export in that it is not approved for use in non-surgical female sterilization in any country listed in section 802(b)(1)(A). Export of this drug product, therefore, would violate the Act.

The violations described above do not necessarily constitute an exhaustive list. It is your responsibility to ensure that the drug products you distribute meet all the requirements of the Act and its implementing regulations. We request that you take prompt action to correct these violations and report to us within 15 days any and all actions you intend to take for correction as well as any actions to prevent any further violation. Failure to promptly correct these violations may result in regulatory action without further notice. Such actions may include seizure, injunction, and/or criminal prosecution.

You stated to us that the United States Pharmacopeia (U.S.P.) Convention has taken the position that quinacrine for sterilization has been sufficiently tested and its safety and efficacy adequately demonstrated, and listed this method as an accepted use of this drug for American women. The U.S.P. is a standard-setting organization in the areas of strength, quality, purity, and method of analysis. The fact that an ingredient is listed in any of the U.S.P. publications, including the U.S.P. DI does not mean that your product or another product is necessarily recognized as safe and effective for its intended uses. Further, the U.S.P. DI documents are not "full disclosure" documents that include all the information required by law and regulation.

On September 24, 1998 during a telephone conference call between yourself, this office, and our Raleigh, North Carolina field office, you were asked to identify the location of your remaining product inventory reportedly consisting of approximately

quinacrine pellets and quinacrine filled inserters. At that time and thus far, you have chosen not to provide us with the location of your products. The FDA is concerned about the health of women and children in the United States and other countries, and that this product may be exported to another country or distributed for use in the United States. We request that you immediately halt all distribution of any and all quinacrine under your control, identify its location, and voluntarily destroy it under FDA supervision.

Your reply to this letter should be addressed to William G. Nychis, Compliance Officer, U.S. Food & Drug Administration, OTC Compliance Team (HFD-312), at the address noted above. You may contact him directly by telephone (301-827-7362) if necessary.

Sincerely,

Bradford W. Williams
Director
Division of Labeling and
Nonprescription Drug Compliance
Center for Drug Evaluation and Research