

Guidance for Industry

Concerns Related to the use of Clove Oil as an Anesthetic for Fish

(This version of the guidance replaces the version that was made available in June 11, 2002. This guidance document has been revised to clarify our position on the use of clove oil as an anesthetic for fish.)

This level 2 guidance document provides information regarding the use of clove oil and its components as an anesthetic for fish.

Comments and suggestions regarding this guidance document should be submitted to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852. Submit electronic comments to <http://www.fda.gov/dockets/ecomments>. All comments should be identified with the exact title of the document.

For questions regarding information about regulatory discretion, contact Ms. Fran Pell, Center for Veterinary Medicine (HFV-235), Food and Drug Administration, 7519 Standish Place, Rockville, MD 20855, 240-276-9211.

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Veterinary Medicine
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Concerns Related to the use Clove Oil as an Anesthetic for Fish

This document represents the Agency's current thinking on concerns related to the use of clove oil as an anesthetic for fish. It does not create or confer any rights for or on any person and does not operate to bind the Food and Drug Administration (FDA) or the public. An alternative approach may be used as long as it satisfies the requirements of the applicable statute and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

Introduction

The Food and Drug Administration's Center for Veterinary Medicine (FDA/CVM) has had many inquiries regarding the use of clove oil, and/or the active components of clove oil, as an anesthetic for use in fish. This guidance document provides information regarding CVM's position for the use of clove oil and its components as an anesthetic for fish.

Background

Current scientific information suggests that clove oil is actually a mixture of different compounds. Some of the ingredients of clove oil include eugenol, isoeugenol and methyleugenol. Although clove oil is generally 85 to 95% eugenol, the remaining components may vary. Isoeugenol is the compound considered by some aquaculturists to have the best anesthetic effect. However, neither clove oil nor any individual active ingredient of clove oil (including eugenol, isoeugenol, or methyleugenol) is the subject of an FDA approved new animal drug application.

Although clove oil and some of its components are generally recognized as safe (GRAS) for use in dental cement or as food additives, neither clove oil nor any of its components are GRAS for use as an anesthetic for fish.

The only new animal drug approved for use as an anesthetic in fish as of the date of publication of this guidance document, is MS-222 (Finquel[®] or Tricaine-S[®]), also known as tricaine methanesulfonate. This drug has a 21-day withdrawal time. The conditions of use for this drug can be viewed at <http://www.accessdata.fda.gov/scripts/animaldrugsatfda>.

Safety Concerns over the Use of Clove Oil and its Components in Fish

Historically, clove oil and isoeugenol have been used in foods and eugenol has been used in animal foods. However, concerns regarding this class of chemical compounds led to the nomination of eugenol, isoeugenol, and methyleugenol for investigation under the National Toxicology Program (NTP). The NTP conducts studies in nominated drugs and chemicals to determine their potential to cause cancer. Studies have been completed for eugenol, isoeugenol, and methyleugenol. NTP determined that eugenol is an equivocal carcinogen and methyleugenol is carcinogenic to rodents. While the in-life studies are

complete for isoeugenol, the NTP has not yet reached a conclusion regarding its carcinogenicity. The status of toxicology studies conducted on these compounds can be found on the NTP website at <http://ntp-server.niehs.nih.gov/>. A search for 'eugenol' brings up all the related test results.

Because some clove oil products may contain or include either methyleugenol or isoeugenol, or both, CVM is concerned that the use of clove oil or its components in fish may adversely affect human food safety and animal food safety. This concern especially applies to the use of Clove Oil or any of its components in fish intended for use in human or animal food, and from use in those fish that may be released into public waters where they would be available as food for other aquatic species, or could be caught and end up in the human food supply. In addition, because clove oil and its components have not been evaluated for target animal safety, CVM is also concerned that the use of any of these compounds may adversely affect fish, including endangered aquatic species.

This guidance is intended to remind producers that neither clove oil nor any of its components are the subject of an approved new animal drug application and, because of safety concerns, should not be used as an anesthetic in fish. For more information on drugs that are acceptable for use as an anesthetic for fish, contact Ms. Fran Pell, at (240) 276-9211.