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

# Guidance for Industry

*This version of the guidance replaces the version made available April 2007. This guidance is for immediate implementation.*

For further information regarding this document, contact AskCVM@fda.hhs.gov.

FDA is issuing this guidance for immediate implementation in accordance with 21 CFR 10.115(g)(4). Submit comments on this guidance at any time. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the FDA-2020-D-1442.

Additional copies of this guidance document may be requested from the Policy and Regulations Staff, Center for Veterinary Medicine, Food and Drug Administration, 5001 College Park College Park 20740, and may be viewed on the Internet at https://www.fda.gov/animal-veterinary, https://www.fda.gov/regulatory-information/search-fda-guidance-documents, or http://www.regulations.gov.

**U.S. Department of Health and Human Services**
**Food and Drug Administration**
**Center for Veterinary Medicine (CVM)**
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*Contains Nonbinding Recommendations*

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*This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.*

## *I.* 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 a sedative or anesthetic for use in fish. This guidance document provides information regarding CVM's position for the use of clove oil and its isoeugenol and methyleugenol components as an anesthetic for fish.

This guidance is intended to remind fish health professionals that neither clove oil nor its methyleugenol or isoeugenol components are the subject of an approved new animal drug application or on a list of indexed animal drug products and, because of safety concerns, should not be used as a sedative or anesthetic in fish.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended but not required.

## II. Background

Clove oil is composed of a mixture of different compounds. Some of the components of clove oil include eugenol, isoeugenol, and methyleugenol. Although clove oil is generally 85% to 95% eugenol, the remaining components may vary. Neither clove oil nor its isoeugenol or methyleugenol components are the subject of an FDA-approved new animal drug application or listing on the Index of Legally Marketed Unapproved Drugs for Minor Species ("index listed").[1]

The only new animal drugs approved for use as a sedative or anesthetic in fish, as of the date of publication of this guidance document, are SYNCAINE® (MS-222, also known as tricaine methanesulfonate or TMS) and AQUI-S® E10% (eugenol). The conditions of use for these drugs can be viewed at https://animaldrugsatfda.fda.gov/. Additionally, as of the date of publication of this guidance document, there are two sedatives/anesthetics for use in non-food fish that are index listed:

[1] Under section 201(v) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) all drugs for fish and other minor species are new animal drugs unless subject to a final regulation concluding that certain exclusion criteria have been met and thus must be approved, conditionally approved, or index listed under sections 512, 571, and 572, respectively of the FD&C Act to be legally marketed.

Aquacalm™ (metomidate hydrochloride) and Alfaxan® Multidose IDX (alfaxalone). Conditions for use of these products can be found at https://www.fda.gov/animal-veterinary/minor-useminor-species/index-legally-marketed-unapproved-new-animal-drugs-minor-species.

## III. 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 showed equivocal carcinogenicity in rodents (mice), methyleugenol is carcinogenic to rodents (rats and mice), and isoeugenol is carcinogenic to rodents (mice). The status of toxicology studies conducted on these compounds can be found on the NTP website at https://ntp.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 methyleugenol or isoeugenol components in fish may adversely affect human food safety and animal food safety. This concern especially applies to use in fish intended for human or animal food and 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 methyleugenol or isoeugenol components have not been fully 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.

For more information on the regulation of fish anesthetics, contact CVM at AskCVM@fda.hhs.gov.

| Guidance History[*] | Date | Description |
|---|---|---|
| Level 1 Final Guidance | 6/11/2002 | |
| Level 2 Guidance | 6/07 | Consistent with Level 2 guidance procedures (21 CFR 10.115(g)(4)), an NOA was not issued for this guidance. Find the document at: Regulations.gov |
| Level 2 Guidance | 8/26 | Consistent with Level 2 guidance procedures (21 CFR 10.115(g)(4)), an NOA was not issued for this guidance.<br><br>Guidance revised to reflect recently approved animal drug and recent changes to CVM address and available contact information. |

*This table was implemented, beginning 8/2026 and previous guidance history may not be captured in totality.