

Background Information on Prohibited Antimicrobial Agents in Seafood

Aquacultured Seafood Products on the Rise

Aquacultured (farm-raised) seafood has become the fastest growing sector of the world food economy and accounts for nearly half of all seafood production worldwide. About 80% of the seafood consumed in the U.S. is imported from approximately 62 countries and over 40% is aquacultured seafood. As the aquaculture industry continues to grow and compete with wild-caught seafood products, concerns regarding the use of prohibited animal drugs and unsafe chemicals and the misuse of animal drugs in aquaculture operations have increased substantially. (US Food and Drug Administration, 2007b.)

Prohibited Antimicrobial Agents in Aquacultured Products

The use and misuse of antibiotics in food increased around 2001, when testing in the European Union revealed the use of chloramphenicol (a prohibited antibiotic) in a number of food products, including seafood from several Asian countries. Thereafter, Canada and the United States similarly found chloramphenicol in some shipments of imported seafood and other food. (Collette, 2006) While the U.S. has tested farm-raised shrimp for chloramphenicol since 1994, once the violation records of the E.U. and Canada became known, the US Food and Drug Administration (FDA) developed more sensitive testing methodology and moved its levels of detection for chloramphenicol from 5.0 ppb to 1.0 ppb and finally its current detection level of 0.3 ppb. (Keyes, 2006) The FDA testing program for aquaculture drugs was revised and reissued in November 2005. The testing program includes antibiotics such as chloramphenicol, nitrofurans, fluoroquinolones, and quinolones, as well as nonantibiotic drugs like malachite green and ivermectin that are not approved for use in aquaculture fish. (Collette, 2006)

The use of prohibited antibiotics or chemicals in aquaculture raises significant public health concerns. The use of antibiotics or chemicals, such as malachite green, nitrofurans, fluoroquinolones, and gentian violet during various stages of aquaculture production can result in the presence of residues of the parent compound or its metabolites in the edible portion of the aquacultured seafood. Consuming aquacultured products with antibiotic residues from fluoroquinolones and chloramphenicol may contribute to an increase of antimicrobial resistance to this "critically important" class of antibiotics in human pathogens. Furthermore, prolonged

exposure to nitrofurans, malachite green, and gentian violet has been shown to have a carcinogenic affect with long-term exposure in lab animals. (US Food and Drug Administration 2005, US Food and Drug Administration 2007a; and US Food and Drug Administration 2007b). A brief discussion on the evidence that malachite green, gentian violet and nitrofurans cause cancer is available on the FDA web site (<http://www.cfsan.fda.gov/~frf/seadwpe.html#q12>).

Chloramphenicol is a broad-spectrum antibiotic that is not approved for use in food producing animals and has been prohibited from extra-label uses in food producing animals in the United States. In the US, use of chloramphenicol in humans is reserved for treatment of certain serious, potentially life-threatening infections. Antimicrobial doses correlate with a low incidence (1:30,000 to 1:50,000) of serious and potentially fatal blood disorders, such as idiosyncratic aplastic anemia. Since these adverse reactions are idiosyncratic and are not dose related, a safe level of exposure to chloramphenicol is unknown. Chloramphenicol is suspected to be a carcinogen and may potentially affect the reproductive system in humans. (US Food and Drug Administration, 2004)

Another public health concern for chloramphenicol exposure is its role as a precursor to aplastic anemia. Aplastic anemia occurs when bone marrow produces too few blood cells. The reduction in red blood cells causes hemoglobin levels to fall, while reduced numbers of white blood cells increase susceptibility to infection. A fall in the number of platelets affects clotting of the blood. (Fegan, 2002)

Malachite green (MG) has been used around the world in treating external fungal and parasitic infections on fish eggs, fish and shellfish. MG is an effective fungicide, especially as a general hatchery disinfectant. Leucomalachite green (LMG) is a metabolite of MG and is persistently found in fish tissues long after MG may no longer be detected. (Canadian Food Inspection Agency, 2006)

Prohibited Antimicrobial Agent Residues Found in Aquacultured Seafood Products Between 2001-2007.

SPECIES	RESIDUE
Crab	Chloramphenicol
Catfish, Basa, Tilapia and Other Pangasius	Malachite Green, Fluoroquinolones (includes Ciprofloxacin and Enrofloxacin), Gentian Violet
Whitespotted Clarias	Malachite Green
Walking Clarias Fish	Fluoroquinolones (includes Ciprofloxacin and Enrofloxacin)
Shrimp	Chloramphenicol, Malachite Green, Fluoroquinolones,

	nitrofurans, Gentian Violet
Dace	Malachite Green, Gentian Violet
Eel	Malachite Green, Gentian violet

Source: US Food and Drug Administration 2001 and 2007b.

FDA Violations

In the United States, use of malachite green, nitrofurans, fluoroquinolones, or gentian violet as drugs in aquacultured animals is illegal under Section 512 of the Federal Food, Drug, and Cosmetic Act (FFDCA). And presence of their residues in seafood adulterates the seafood under 402(a)(2)(C)(ii) of the FFDCA. (US Food and Drug Administration, 2007b.)

Also, malachite green, nitrofurans, fluoroquinolones and gentian violet are not generally recognized as safe under any conditions of intended use that may reasonably be expected to result in their becoming a component of food. Therefore, if these drugs are intended for any such use, they are unsafe food additives within the meaning of section 409 of the FDCA and would render the food adulterated under section 402(a)(2)(C)(i). (US Food and Drug Administration, 2007b.)

References

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<http://safeseafood.ucdavis.edu/background.htm>

Prohibited Antimicrobial Agents in Seafood

This site offers information on prohibited antimicrobial substances detected in seafood products during inspections conducted by the US Food and Drug Administration (FDA). Toxicity, increased antimicrobial resistance and cancer are primary FDA health and safety concerns for prohibiting the use of the following antimicrobial agents in food:

- Chloramphenicol
- Crystal Violet (Gentian Violet), Brilliant Green, Malachite Green and Leucomalachite Green
- Fluoroquinolones
- Nitrofurans

Links on this site lead to: background information on the health and safety issues, generic HACCP plans serving as guidelines for preventing the hazard in products, FDA analytical methods, and commercially developed rapid detection kits to assist in screening for the prohibited agents.

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<http://safeseafood.ucdavis.edu/index.html>