

## CHAPTER 11: AQUACULTURE DRUGS

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### UNDERSTAND THE POTENTIAL HAZARD

This chapter concerns the potential food safety hazard of animal drug residues in aquaculture products.

The primary purpose of aquaculture is to produce animals and plants for human consumption. Aquaculture is defined as farming of both animals and plants (including crustaceans, finfish, mollusks, amphibians, reptiles, seaweeds, and algae) in a natural or controlled environment. The term farming implies some form of intervention in the breeding and rearing process to increase and expand production, such as regular stocking, feeding, protection from predators, improvement of water quality, and enhancement of animal health conditions including prophylactic and treatment activities. Aquaculture can occur in freshwater, coastal, and marine environments, including inland ponds, tanks, reservoirs, rivers, lakes, estuaries, bays, fjords, and the open sea.

Note: Aquaculture plants (seaweed and algae) are not covered by the Seafood HACCP regulation.

There are numerous diseases currently associated with aquaculture species, and new ones are consistently emerging. In addition, outbreaks of diseases can be significantly accentuated in aquaculture operations due to the animals' proximity to each other, high population densities, frequently changing environmental conditions, and other stressors.

The most common reasons for the use of animal drugs in aquaculture are:

- to treat, control or prevent disease,
- to control parasites,
- to affect reproduction and growth,

- to provide tranquilization/sedation (e.g., for weighing, harvest), and
- for skeletal marking of fish fry (larvae) and fingerlings.

The food safety hazard associated with the use of animal drugs occurs during activities listed above, which can be performed at any stage of aquaculture operation. The use of unapproved drugs or misuse of approved drugs in farm-raised fish may result in residues in edible tissue and poses a potential risk to human health upon long-term exposure. These substances may be toxic, allergenic, mutagenic, or carcinogenic, may contribute to the development of antimicrobial resistance in pathogens that affect humans and animals, or may be a combination of these adverse effects.

Residue is defined by FDA Center for Veterinary Medicine (CVM) as any compound or metabolite of a compound that is present in edible tissues from food animals because of the use of a compound in or on animals. Residues can be from the compound itself, its metabolites, or any other substances formed in or on food as a result of the compound's use. The metabolism of some drugs varies according to species, and the toxic character of a compound in one animal species is not necessarily the same as that in others.

### • Animal Drugs for Use in Aquaculture

According to the Federal Food, Drug, and Cosmetic Act, a drug is defined as "an article intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals and an article (other than food) intended to affect the structure or any function of the body of man or other animals" (FD&C Act Sec.201.(g)(1)(B) & (C)).

As required by the Federal Food, Drug, and Cosmetic Act, an animal drug must be approved by FDA before a drug sponsor can legally sell the drug. During this pre-market review, the agency evaluates information submitted by the sponsor to make sure the drug is safe and effective for its intended use and that the drug is properly manufactured and adequately labeled and packaged. The drug's labeling should ensure the information remains truthful, complete, and not misleading. A drug for use in food animals, whether it is for direct medication or use in or on medicated feed, can be legally marketed and used in the US if it has been approved through:

- New Animal Drug Application (NADA), or
- Abbreviated New Animal Drug Application (ANADA), or
- Conditional New Animal Drug Application (CNADA).

An alternative to the new animal drug approval process is the Index of Legally Marketed Unapproved New Animal Drugs for Minor Species ([the Index](#)). The Index provides legal marketing status for certain drugs that have had their safety and effectiveness affirmed through another FDA review process (FD&C Act, Section 572). Drugs listed on the Index are only available for new animal drugs intended for use in:

- nonfood-producing minor species for which there is the certainty that the animal or edible products from the animal will not be consumed by humans or food-producing animals, and
- a hatchery, tank, pond, or other similar contained man-made structure in an early, nonfood life stage of a food-producing minor species, where safety for humans is demonstrated (e.g. larva, fry, fingerlings) (21 CFR 516.111).

In addition, under certain conditions authorized by FDA, unapproved new animal drugs may be used by experts, qualified by scientific training and experience, to investigate their safety and effectiveness if requirements of an Investigational New Animal Drug (INAD) exemption stated in 21 CFR 511 are met.

Each approval pathway mentioned above has different requirements, but they all lead to legal marketing status of the drug for which safety has been fully evaluated. For more information refer to New Animal Drug Application Guidance documents at <https://www.fda.gov/animal->

[veterinary/guidance-industry/new-animal-drug-application-guidances](#).

All drugs should be used judiciously, particularly drugs considered as "medically important" antimicrobials. Antimicrobials are essential for protecting human and animal health and should not be used in food-producing animals for production uses, such as to enhance growth or improve feed efficiency. They are deemed "medically important" because the antimicrobial or a member of that class of antimicrobials is also used to treat human disease, and such treatment might not be effective if the pathogenic bacteria become resistant to the drugs' therapeutic effect. The antimicrobial-resistant bacteria can be spread to humans through the food supply. Refer to CVM website for more information <https://www.fda.gov/animal-veterinary/antimicrobial-resistance/judicious-use-antimicrobials>

Relatively few drugs have been approved for aquaculture in the US. This factor may lead to the inappropriate use of unapproved drugs, general purpose chemicals, or approved drugs in a manner that deviates from the labeled instructions.

When a drug is approved by the FDA Center for Veterinary Medicine (CVM), the conditions of the approval are listed on the label or in the labeling (21 CFR 514.1). These conditions specify the species or group of species (e.g., freshwater-reared salmonids) for which the drug is approved for use; indications (disease or other circumstances) for use; dosage regimen; route of administration; and other limitations, including withdrawal period. The labeled withdrawal period must be followed to ensure that no harmful drug residues are present in the edible tissue of the animal when harvested for human consumption and offered for sale. Tolerances for some drug residues in the edible tissue have been established (21 CFR 556). In addition to the regulation(s), specific tolerance levels may also be found in Appendix 5 of this guidance document.

Effective January 1, 2017, all medically important antimicrobials intended for use in or on animal feed or in water for food-producing animal species require either a Veterinary Feed Directive (VFD) (21 CFR 558.6) or a prescription (Rx) (21 CFR 520). The use of a VFD or Rx drug is permitted only under the professional supervision of a licensed veterinarian. To be lawful, a VFD must be issued by a licensed veterinarian operating in compliance with all applicable licensing and practice requirements, including issuing the VFD in the context of a valid

Veterinarian-Client-Patient Relationship (VCPR) as defined in 21 CFR 530.3(i).

The increasing threat of antimicrobial resistance to both human and animal health compelled the FDA to remove production uses of medically important antibiotics and implement a requirement for veterinary oversight of their uses. Over-the-counter (OTC) antibiotics have been transitioned to VFD or Rx marketing status. A licensed veterinarian should be trained to understand not only when these medications are needed, but also what is the appropriate drug, dose, duration, and administration method for therapy. This requirement is aimed to help preserve a supply of effective antibiotics for situations of true need to protect animal and human health, and, in turn, food safety.

### ○ Extra-label Drug Use (ELDU)

The Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA) allows veterinarians to prescribe **approved** new animal or human drugs for uses other than those on the approved label. This is called “extra-label drug use” (ELDU) **The FDA defines extra-label drug use as “Actual use or intended use of a drug in an animal in a manner that is not in accordance with the approved labeling. This includes, but is not limited to, use in species not listed in the labeling, use for indications (disease and other conditions) not listed in the labeling, use at dosage levels, frequencies, or routes of administration other than those stated in the labeling, and deviation from labeled withdrawal period based on these different uses.” (21 CFR 530.3).** However, a veterinarian must not pursue the use of certain FDA-prohibited drugs in food-producing animals listed in 21CFR 530.3.

Furthermore, AMDUCA does not permit veterinarians to prescribe the extra-label use of medicated feeds. ELDU is limited to situations when there are no approved treatment options available, and the health of an animal is threatened or when suffering or death may result from failure to treat the affected animals. If a veterinarian determines that extra-label use of medicated feed is necessary and the only option, this use has to be consistent with all considerations described in Compliance Policy Guide Sec. 615.115 “[Extralabel Use of Medicated Feeds for Minor Species.](#)” The reader is strongly encouraged to be familiar with all considerations.

Only a licensed veterinarian may legally prescribe a drug under ELDU conditions.

An extra-label prescription must be for therapeutic purposes only and must not be used for production enhancement. As defined in 21CFR 530.3(h), a veterinarian is a person licensed by a U.S. state or territory, to practice veterinary medicine.

**NOTE:** Farmers in foreign countries should consult their country’s competent authority for information on prescription requirements, disease treatment options, and technical support. The OIE Aquatic Animal Health Code defines a veterinarian as a person with appropriate education, registered or licensed by the relevant regulatory authority of a country to practice veterinary medicine/science in that country.

The extra-label use restrictions are fully explained in 21 CFR Part 530, FDA CVM Program Policy and Procedures Manual 1240.4210, and CPG 615.115.

### ○ Unapproved Animal Drugs

FDA has serious concerns about unapproved animal drugs (any drug not approved or conditionally approved in the United States). These drugs have not been reviewed by FDA and may not meet the agency’s strict standards for safety and effectiveness. Unapproved animal drugs also may not be properly manufactured or properly labeled. They can potentially put the health of animals and people at risk, and their use is strictly prohibited. Any amount of residues in domestic or imported aquaculture products from an unapproved new animal drug would cause the product to be adulterated (FD&C Act 402(a)(2)(C)(ii)).

Imported aquaculture product would be denied entry into the United States if residue of an unapproved new animal drug is identified, even if the levels of residues are considered safe by a country where the new animal drug is lawfully used. The only exception is if there is an Import Tolerance in place for this compound in that particular tissue. The Federal Food, Drug, and Cosmetic Act (FD&C Act), as amended by the Animal Drug Availability Act of 1996 (ADAA), provides a basis for legally marketing food of animal origin that is imported into the United States and contains residues of animal drugs that are not approved or conditionally approved in the United States (unapproved new animal drugs). The ADAA granted the FDA the authority to establish or revoke tolerances for residues of such unapproved new animal drugs

present in imported, animal-derived food products. Refer to CVM's current list of [import tolerances](#) established for unapproved new animal drugs in imported food.

Information on the laws, regulations, guidance, and policies pertaining to drugs and the new animal drug approval process can be found on FDA's internet website, <https://www.fda.gov/animal-veterinary>.

To ensure unapproved drugs do not get into aquaculture products directly or inadvertently, farmers and the other facilities along the supply chain should implement a food safety and disease prevention and verification program based on the principles of Good Aquaculture Practices (GAqPs), current Good Manufacturing Practices (CGMPs) and Hazard Analysis and Critical Control Point (HACCP), where applicable.

However, according to the US FDA Seafood HACCP Regulation (21 CFR 123), it is the responsibility of the seafood processor to have an adequate strategy in place that effectively controls the aquaculture drug hazard.

- **APPROVED ANIMAL DRUGS FOR AQUACULTURE**

Animal Drugs for aquacultured food fish must meet human food safety standards assessed during the approval process. When a fish producer (farmer) or hatchery manager uses an approved drug for food fish as directed on the label, the treated fish are safe to eat.

The FDA-approved animal drugs for use in aquaculture, with information on their approved sponsor/supplier, species for which the approval has been granted, required withdrawal periods, and other conditions are listed below. Additional details on provisions of use (e.g., administration route, dosage level) can be obtained from the Code of Federal Regulations (CFR) as cited below; the labeling for the drug; and the FDA CVM Website, (the Animal Drugs @ FDA database: <https://animaldrugsatfda.fda.gov/>).

FDA's determination that these veterinary products are approved aquaculture drugs does not exempt facilities from complying with other federal, state, tribal, territorial, and local environmental requirements. For example, in the United States, facilities using these substances would still be required to comply with the National Pollutant Discharge Elimination System requirements.

- **Route of Administration: Immersion (Refer to Appendix 11 for additional information such as indicated use, contraindication, tolerance levels, and extra-label use for the following aquaculture drugs)**

- Chloramine-T powder
- Formalin
- Hydrogen peroxide
- Oxytetracycline hydrochloride
- Tricaine methanesulfonate (MS-222)

- **Route of Administration: Injectable (Refer to Appendix 11 for additional information such as indicated use, contraindication, tolerance levels, and extra-label use for the following aquaculture drug)**

- Chorionic gonadotropin

- **Route of Administration: Medicated Articles/Feeds (Refer to Appendix 11 for additional information such as indicated use, contraindication, tolerance levels, and extra-label use for the following aquaculture drugs)**

- Florfenicol
- Oxytetracycline dihydrate
- Sulfamerazine
- Ormetoprim/Sulfadimethoxine combination

- **UNAPPROVED ANIMAL DRUGS FOR AQUACULTURE**

Animal drugs not evaluated and approved by CVM are not recognized as safe under any condition of intended use. It is reasonable to expect that the application of unapproved aquaculture drugs may result in unsafe levels of residues and render the food adulterated.

- **FDA high enforcement priority unapproved aquaculture drugs**

FDA CVM has identified a number of drugs and families of drugs historically **used in fish without the FDA approval** that are of high enforcement priority. Those drugs may have an impact on the safety of fish products for consumers because they are:

- known or suspected carcinogens;
- known or suspected mutagens;
- known or suspected serious toxicants; and/or
- antimicrobials that might be a factor in the emergence of antimicrobial resistance (AMR)

to drugs used in human medicine as well as in veterinary medicine.

The following compounds are **examples of unapproved drugs** that have been recognized as of human health concern (this list is not inclusive):

- Chloramphenicol;
- Nitrofurans;
- Fluoroquinolones;
- Quinolones (Oxolinic Acid, Flumequine, Nalidixic Acid);
- Malachite Green and metabolite;
- Gentian (Crystal) violet and metabolite;
- Isoeugenol;
- Avermectins;
- Sulfonamides;
- Trimethoprim;
- Steroids and Hormones.

#### ○ **Drugs prohibited from extra-label use**

The following drugs and families of drugs are prohibited for extra-label use in food-producing animals including fish, i.e., actual use or intended use of a drug in an animal in a manner that is not consistent with the FDA approved provisions of use and approved labeling (21 CFR 530.41(a)):

- Chloramphenicol;
- Clenbuterol;
- Diethylstilbestrol (DES);
- Dimetridazole, Iprnidazole, and other Nitroimidazoles;
- Furazolidone, and Nitrofurazone;
- Fluoroquinolones;
- Glycopeptides.

None of these drugs and family of drugs has been approved for use in fish.

#### ○ **FDA low regulatory priority unapproved aquaculture drugs**

Due to the broad definition of drug in the FD&C Act, many compounds that satisfy the conditions of the definition are considered drugs. CVM has identified several unapproved drugs used in aquaculture that are considered low-risk products when used in fish for human consumption. These drugs are also called "low regulatory priority."

The agency will exercise regulatory discretion in cases of the use of low regulatory priority compounds in fish if the following conditions are met:

- the substances are used for the stated indications;
- the substances are used at the stated levels;
- the substances are used according to good management practices;
- the product is of an appropriate grade for use in food animals; and
- use of these products is not likely to result in an adverse effect on the environment.

The agency's enforcement position on the use of these compounds **should not be considered** as FDA approval or an affirmation of their safety and effectiveness. The agency reserves the right to take a different position on the use of any, or all, of these substances at some time in the future.

In addition, the FDA's determination that these compounds are new animal drugs of low regulatory priority does not exempt facilities from complying with other federal, state, tribal, territorial, and local environmental requirements. For example, in the United States, facilities using these compounds would still be required to comply with the National Pollutant Discharge Elimination System requirements.

The following list identifies unapproved new animal drugs of low regulatory priority and provides their indicated use and usage levels (CVM's Policy and Procedures Manual Attachment: "Enforcement Priorities for Drug use in Aquaculture" Guide 1240.4200 <https://www.fda.gov/media/70193/download> ) Refer to Appendix 12 for indicated use for each of the following:

- Acetic acid
- Calcium chloride
- Calcium oxide
- Carbon dioxide gas
- Fuller's earth
- Garlic (whole form)
- Ice
- Magnesium sulfate
- Onion (whole form)
- Papain
- Potassium chloride
- Povidone iodine
- Sodium bicarbonate
- Sodium chloride
- Sodium sulfite
- Thiamine hydrochloride
- Urea and tannic acid

○ **FDA Import Tolerances for residues of unapproved new animal drugs present in imported seafood**

The following tolerances have been established for residues of new animal drugs that have not been approved in the US in imported seafood in order to allow the product be lawfully sold in the US:

**FDA Import Tolerances for Residues of Unapproved New Animal Drugs in Imported Seafood**

Requester	Drug	Species	Import Tolerance for Drug Residues in Edible Tissue	Year Established
Zoetis Inc.	Hexaflumuron	Salmonids	0.5 ppm for hexaflumuron in muscle with adhering skin	2021
Intervet Inc	Emamectin	Salmonids	100ppb for emamectin B1a in muscle with adhering skin	2019
ACD Pharmaceuticals	Benzocaine	Atlantic salmon and rainbow trout	50ppb benzocaine in muscle with adhering skin	2018
Novartic Animal Health USA, Inc.	Lufenuron	Salmonids	1.35pm lufenuron in muscle/adhering skin	2016
FVG Ltd.	Azamethiphos	Salmonids	0.02ppm azamethiphos in muscle/adhering skin	2016
Skretting Agricultural Research Center	Teflubenzuron	Atlantic salmon	0.5ppm teflubenzuron in muscle/adhering skin	2014

The most current list of Import Tolerances is available at <https://www.fda.gov/animal-veterinary/import-exports/import-tolerances>.

Additional information on aquaculture-related topics can be obtained from FDA/CVM at: <http://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/Aquaculture/default.htm>.

**DETERMINE WHETHER THE POTENTIAL HAZARD IS SIGNIFICANT**

The following guidance will assist you in determining whether animal drugs used in aquaculture operations are a significant food safety hazard at a processing step:

**1. Is it reasonably likely that unsafe levels of residues of aquaculture drugs will be introduced at this processing step?**

**NOTE:** A “residue” means any compound present in edible tissues that results from the use of a drug, and includes the drug, its metabolites, and any other substance formed in or on food because of the drug’s use (21 CFR 530.3)

- Under ordinary circumstances, if you are a primary (first) processor, it **would be** reasonably likely that unsafe levels of residues of aquaculture drugs could enter the process at the receiving of raw material step of any type of aquaculture species, including:

- Finfish;
- Crustaceans;
- Other aquatic food animals, such as frogs, snails, alligators.
- Under ordinary circumstances, it **would be** reasonably likely that unsafe levels of residues of aquaculture drugs could be introduced during aquatic holding (e.g., live lobster, crab in tanks) or transport of live fish.
- Under ordinary circumstances, it **would not be** reasonably likely to expect that aquaculture drugs could enter the process during the receiving of wild-caught fish **unless** they are kept live in holding tanks.

If you are receiving fish (other than live fish) from another processor, you might not need to identify aquaculture drugs as a significant hazard. The primary (first) processor should have appropriate measures in place to adequately control this hazard. However, the prudent secondary processor might request records from the supplying primary processor demonstrating that the product has been processed in compliance with the HACCP

regulation, and the hazard of aquaculture drugs has been addressed by the primary processor. Documentation may include but is not limited to, test results for drug residues reasonably likely to be present, HACCP monitoring records reflecting monitoring of aquaculture drug hazard approach, reports from the primary processor visits to the raw material supplier(s), etc. It is recommended that the secondary processor keep all relevant records in files.

## 2. Can unsafe levels of residues of aquaculture drugs that are reasonably likely to occur be eliminated or reduced to an acceptable level at this processing step?

The presence of animal drug residues in aquacultured products is associated with their use during the various stages of production, i.e. at the hatchery, on the farm and/or during holding and/or transport of live fish. This significant hazard occurs prior to the receipt of the raw material and should be considered by a primary processor at any processing step, but at the receiving of raw material step in particular. It is recommended that the primary processor has an understanding of aquaculture in general and more specifically about the operations associated with the products they process, what potential animal drugs may be used on farms and what control activities suppliers of raw material (farmer, middleman, collector) may have taken, in order to employ the appropriate preventive measure early in the process to eliminate the hazard of animal drug residues or to reduce the likelihood of its occurrence.

### • Preventive measures

- Preventive measures for the hazard of aquaculture drugs used in aquaculture operations are ordinarily employed at either the processor receiving step or at the farm before harvest (commonly called the “pre-harvest step”). They can include the following activities and should be coupled with an appropriate verification strategy:
  - Before receiving any raw material, the processor or an informed representative conducts a visit at the farm, holding, or transport facility to evaluate the existing conditions and practices that can contribute to a potential risk of the aquaculture drug hazard. This will include:

- a review of any program or strategy the farm implements (e.g., Good Aquaculture Practices (GAqPs)/ Best Management Practices (BMPs), or
- a record and document review of the farm activities and procedures to control or minimize the risk of aquatic animal’ diseases, including monitoring and maintaining of good water quality, managing animal feeding and feed storage, maintaining records of use and storage of animal drugs, medicated feed and other compounds (e.g., probiotics, vitamins, water conditioners).

This review should be conducted to ensure that all products used on the farm are in conformance with FDA regulations, guidance, and labeling instructions.

- Reviewing, at the time of receipt of each lot of the raw material, the appropriate farm(s) or other supplier’s drug usage records. This should include a list of all drugs used on the farm(s) and withdrawal times for each drug used (i.e. the date when the drug was started and stopped being used or administered), and when the raw material was harvested or collected from the site. All drugs should be used in conformance with applicable FDA regulations, guidance and labeling instructions.
- Reviewing, at the time of receipt of each lot of the raw material, a signed certification or declaration from the farmer or other supplier (middleman, broker, collector) that clearly states that no unapproved animal drugs were used during production, holding or transport of the lot of raw material delivered to the processor. If approved animal drugs were used, the certification or declaration should list all drugs used on the farm(s) and state that all drugs were approved by the FDA and were used in conformance with applicable FDA regulations, guidance, and labeling instructions.
- Conducting, at the time of receipt of each lot of the raw material, residue testing for approved drugs used on the farm and unapproved drugs that the processor may have knowledge to be potentially administered and are considered a high enforcement priority for species received;
- Reviewing, at the time of receipt of the raw material, evidence that the raw material

supplier/ farm operates under a competent third-party farm certification program. The evidence can be lot by-lot or continuing a third-party certificate, or a copy of documentation indicating that the farm is listed on an accessible, secure and valid web site administered by the third-party. The program can be administered and verified by a government competent authority or a private third-party entity.

The third-party farm certification program should include:

- Adequate controls for the aquaculture drug hazard and specifically address controls and preventive measures in place to reduce the risk of disease outbreaks and the use of animal drugs on the farm.
- The application of a biosecurity program designed to mitigate the risk factors for disease emergence and good aquaculture management practices that prevent and minimize the impact of diseases on animal health.
- A system in place that adequately documents animal drug use in compliance with FDA regulation, guidance, and labeling instructions.

While the third-party is administering preventative measures to control the aquaculture drug hazard, it remains the responsibility of the processor to evaluate the adequacy of the third-party control program. The processor should evaluate the adequacy of the third-party program implemented on the farm through a verification audit or inspection once a grow-out cycle, or at least once a year.

- Preventive measures for the control of aquaculture drugs used during the holding of aquatic animals (e.g., lobster pounds) and live transport can include controlled application of animal drugs in a manner consistent with:
  - Established withdrawal periods;
  - Labeled instructions for use;
  - Conditions for extra-label use of FDA-approved drugs under a licensed veterinarian's supervision and in accordance with FDA regulations and guidance;
  - Conditions specified in the FDA list of low regulatory priority unapproved aquaculture drugs;

- Conditions of an INAD exemption meeting the criteria under 21 CFR.

- Verification

Each HACCP plan is required to have a verification step for all CCPs identified by the processor. Under ordinary circumstances, it is reasonably likely to expect the verification step for the aquaculture drug hazard to include an appropriate aquaculture drug testing strategy. The strategy should include collecting and testing raw material from each farm and/or supplier (whether testing is done at the production site, at receiving, in-process, or the end product). The number of samples and frequency of testing, type of drugs selected for testing, and analytical methods used will depend on the product processed. However, the overall strategy should be sufficient to demonstrate that the critical limit established is effective and working properly to control the aquaculture drug hazard. The verification activities may be carried out by competent individuals within a company, a qualified laboratory, third-party experts, or a regulatory agency. This strategy can vary according to a variety of factors and may need to be revised and adjusted.

The following can be considered when developing or re-evaluating an appropriate, representative aquaculture drug verification testing strategy;

- What approved animal drugs are typically used in your area and on the species of fish you process?
- What unapproved animal drugs or chemical compounds may potentially be used in your area on species of fish you process? Government, academia, third-party, or industry experts may be helpful in obtaining this information.
- Does the farm establish their own aquaculture drug testing program? Determine who collects and analyzes the samples, what type of drugs are tested for, and what analytical methods are used.
- Is the supplying farm registered or approved by a government regulatory agency or listed by a third-party certification body? If so, do they collect and analyze samples for drug residues during farm visits or inspections and share results?
- What is the compliance history of drug use and testing from a given farm, has product ever been tested positive for an unapproved drug or

do you have a long history of compliance and negative test results from this farm?

- What is your relationship with the farm; do you own it, is it part of the same company and raw material is regularly tested?
- Has the farm ever had a disease outbreak? If so, how recent and did they use any animal drugs for treatment?
- Does the farm ever use animal drugs; if no, do they have documentation to verify this information?
- Have you or your representative ever seen any animal drugs stored on the farm?

#### ○ **Animal Drug Residues, Processing and Intended Use of the Final Seafood Product**

Drug residue levels in aquaculture products are not normally expected to be significantly affected during common food processing activities (e.g., washing, sorting, grading, packing, fileting, breadng, cooking, brining, and freezing) or preparation techniques (e.g., cooking, baking, grilling or microwaving). Therefore, it is unlikely that any typical processing or intended use of the final product will eliminate or reduce to an acceptable level the aquaculture drug hazard.

### **IDENTIFY CRITICAL CONTROL POINTS**

The following guidance will assist you in determining whether a processing step is a critical control point (CCP) for the hazard of aquaculture drugs.

**Is the hazard the result of the use of aquaculture drugs during the raising of fish (i.e., aquaculture) or during aquatic holding (e.g., lobster pounds) or transport of live fish?**

#### • **RAISING FISH IN AN AQUACULTURE OPERATION**

If the hazard is the result of the use of drugs during the raising of fish in an aquaculture operation, do you have a relationship, association or agreement with the farmer that enables you to visit the farm before receipt of the fish?

**A. If you have such a relationship or agreement with the farmer**, then you might identify a pre-harvest step as the CCP for the hazard of aquaculture drugs. The preventive measure for this type of control can include:

##### a. **PROCESSOR'S ON-FARM VISITS**

Conducting an on-farm visit to review

farming conditions, including the farm's aquaculture drug use program.

A person representing the processor that is trained in aquaculture food safety should conduct a general inspection of each supplying farm at least once per grow-out cycle or more as needed. A report should be made for each visit carried out at each individual farm.

The report should include:

- date of the visit,
- name of person visiting the farm,
- observations (some observation suggestions are provided below), and
- areas that need improvement or correction.

The reports should be kept as part of the processor's HACCP records. The processor should have a procedure in place to document any follow-up enhancement or corrective steps taken by the farmer.

During a farm visit, the processor or representative should evaluate the farm's overall food safety and disease prevention program or strategy and history of animal drug use. Preventing diseases is an important element of controlling the aquaculture drug hazard, considering that the predominant reason for the use of unapproved or misuse of approved animal drugs is to treat (or attempt to treat) the diseased animals. The focus should be on ensuring that only FDA approved animal drugs and chemicals are used on the farm, that the drugs were administered correctly, in accordance with labeling instructions and/or according to a licensed veterinarian, and that the farm has the appropriate records to document their use (e.g., type of drug, indication for use (disease), dosage, a path the drug was administered, period of use, the withdrawal times).

The disease prevention strategy should include an effective biosecurity program and implementing good aquaculture practices that minimize the need for therapeutic agents such as antibiotics and other disease control veterinary medicinal products and chemical compounds.

A food safety and disease prevention program can be developed and administered voluntarily by the farm or can be required by a government competent authority regulation (e.g., mandatory Good Aquaculture Practices, Best Management Practices, farm registration/certification programs), or be a part of a third-party certification program. All of these programs should be designed to reduce the risk of disease and ensure that the product the processor receives does not contain unsafe levels of approved drugs or unapproved drug residues.

The processor may want to develop and use a checklist to document observations made while conducting a farm visit. The following are some specific components the processor should consider:

- Determine what drugs and/or medicated feed the farm uses;
- Determine if any compounds other than drugs were used for improving fish health and enhancing production (e.g., probiotics, vitamins, water conditioners);
- Examine records of any drugs and/or medicated feed used for each rearing unit (e.g., pond, cage) and the documented appropriate administration and withdrawal period information (e.g., when the drug was started and stopped, and how much time passed between the last drug treatment and fish harvest);
- Verify that the farmer has a copy of prescription or Veterinary Feed Directive (VFD) issued by a licensed veterinarian for drugs and/or medicated feed used on the farm;
- Examine records of feed source and feeding monitoring;
- Evaluate storage of drugs and/or medicated feed and regular feed;
- Evaluate storage of probiotics, vitamins, water conditioners;
- Evaluate storage of toxic chemicals including fuels, lubricants, pesticides, and other agriculture chemicals.
- Evaluate the farm's biosecurity program. The program should identify biosecurity vulnerabilities on the farm and set up internal and external barriers to control acknowledged risks that help to

prevent disease outbreaks and minimize the risk of introducing, spreading, or transmitting diseases, including viruses.

Biosecurity measures taken on the farms should be outlined in standard operating procedures (SOPs). SOPs should be implemented, followed constantly, reviewed periodically, and amended whenever necessary. For example, the program may comprise:

- implementing stock source program, e.g., use only specific or listed pathogen-free post-larva or fry,
- proper treatment of source water,
- restriction on physical access to the farm site, e.g., fence around the farming site,
- control of entry and movement of peoples and vehicles,
- prevention of wild and domestic animals' access,
- sanitary measures for people entering the farm, i.e., properly located and installed foot and hand dips, protective clothing,
- sanitary measures for vehicles entering the farm,
- using only properly clean and sanitized tools and equipment,
- pest control management.
- Evaluate the farm's disease or best management practice program:
  - list of the potential diseases associated with the species and the farming area,
  - monitoring for early signs or symptoms of disease,
  - procedure in case of disease outbreak (e.g., name and contact information for assistance, quarantine process of the infected animals and area, disposal of dead animals, disinfection of the infected area, water, and other appropriate areas before reuse or discharge into the environment).
- Review the farm's records of monitoring of water quality parameters such as dissolved oxygen, pH, ammonia, etc. that aid the animals' health;
- Evaluate the general sanitation on the farm, including properly located and installed toilets for workers, disposal of trash or rubbish, etc.;

- Determine storage of equipment (e.g., harvest nets, aerators), machinery fuels or oils;
- Determine if the water and ice used at harvest comes from potable water and containers are cleaned and disinfected;
- Observe harvest practices, if possible;
- Review the farm production lot identification system e.g., a unique code per farm location, harvested pond, harvest date, transport and delivery, etc.;
- Review training provided to the farm employees.

The farm visit should be coupled with appropriate verification to ensure that the strategy implemented at the farm is operative and effective, and the aquaculture drug hazard is adequately controlled. This strategy should also include testing for aquaculture drug residues reasonably likely to be present.

#### **Example 1:**

**This control approach is a control strategy referred to in this document as "Control Strategy Example 1 - On-Farm Visits."**

A primary processor of aquacultured tilapia that regularly purchases from the same grower should visit the grower before the fish are harvested and review farming conditions, including drug usage practices and records. In addition, the processor could also choose to receive a supplier's certificate that states all drugs used were approved by the FDA and that all drugs were used in conformance with applicable FDA regulations, guidance, and labeling instructions.

The processor should combine this control approach and monitoring procedure with an appropriate aquaculture drug verification testing strategy that is sufficient to demonstrate that the critical limit is effective and working properly to control the aquaculture drug hazard and should set the CCP at the pre-harvest step.

**B. If you do not have such a relationship or agreement with the farmer,** then you should identify the receiving step as the CCP for the hazard of aquaculture drugs. At the receiving step, you could exercise one of the following preventive measures:

#### a. SUPPLIER'S CERTIFICATION OR LETTER OF GUARANTEE

Reviewing, at time of receipt, the supplier's (farmer or middleman/ collector) lot-by-lot certification or letter of guarantee indicating all drugs and chemicals were approved and used properly.

This control measure should be coupled with a proper verification including an appropriate aquaculture drug verification testing strategy that is sufficient to demonstrate that the critical limit is effective and working properly to control the hazard.

#### **Example 2:**

**This control approach is a control strategy referred to in this document as "Control Strategy Example 2 - Supplier's (Farm or Middleman) Certification or Letter of Guarantee."**

1. A primary processor of aquaculture shrimp that purchases shrimp raw material directly from a contract farm should receive lot-by-lot certificates/ letters of guarantee from the farmer. The certificate/letter should state that all drugs used were approved by the FDA and were used in conformance with applicable FDA regulations, guidance, and labeled instructions. The processor should combine this control strategy and monitoring procedure with an appropriate aquaculture drug verification testing strategy that is sufficient to demonstrate that the critical limit is effective and working properly to control the aquaculture drug hazard and should set the CCP at receiving.
2. A primary processor of aquaculture shrimp that purchases shrimp raw material from a number of farms through a middleman or collector should request to 1) receive a lot-by-lot certificate/letter of guarantee from each farm the raw

material was collected from that states that all drugs used were approved by the FDA and were used in conformance with applicable FDA regulations, guidance and labeled instructions, 2) request that the middleman or collector provides a list of farms he bought shrimp from with affiliated lot numbers. This would allow him to trace the product back to a farm and pond level. The processor should combine this control strategy and monitoring procedure with an appropriate aquaculture drug verification testing strategy that is sufficient to demonstrate that the critical limit is effective and working properly to control the hazard and should set the CCP at receiving.

b. PROCESSOR'S PRE-QUALIFIED SUPPLIER PROGRAM

Managing a Pre-qualified Supplier Program and List and reviewing, at the time of receipt, that the farm is on the Pre-qualified Supplier List and presence of supplier certificate or letter of guarantee.

Refer to conducting an on-farm visit for examples of criteria that should be included in the pre-qualified program (pages 9-11). This control measure should be coupled with a proper verification, including an appropriate aquaculture drug verification testing strategy that is sufficient to demonstrate that the critical limit is effective and working properly to control the hazard.

**Example 3:**

**This control approach is a control strategy referred to in this document as "Control Strategy Example 3 – Processor's Pre-qualified Supplier Program"**

A primary processor of aquaculture shrimp regularly purchases shrimp raw material from a number of farms that have been pre-qualified according to the processors established criteria. The processor maintains a list of the names of all farms that have been pre-qualified.

The processor or his trained and competent agent conducts a visit at a farm and evaluates the level of compliance with the pre-qualification requirements before placing the supplier on the pre-qualified list.

The processor ensures that each farm has adequate controls in place to control the aquaculture drug hazard (refer to conducting on-farm visit for examples of criteria that could be considered in the pre-qualified program). **The processor should have a description of their pre-qualified established criteria on file. The processor should also maintain reports of their farm visit, verifying that the farm met the pre-qualified established criteria.**

The processor should check at the time of the raw material receipt: 1) if the supplier currently participates in the processor's pre-qualified program and is listed on the pre-qualified list, and 2) request a lot-by-lot or continuing certificate/letter of guarantee from each farm that states that the farm complies with the processor's pre-qualified program criteria and all drugs used were approved by the FDA and were used in conformance with applicable FDA regulations, guidance and labeled instructions.

The processor should combine this control strategy and monitoring procedure with an appropriate aquaculture drug verification testing strategy that is sufficient to demonstrate that the critical limit is effective and working properly to control the hazard and should set the CCP at receiving.

c. FARM'S RECORDS OF DRUG USE

Reviewing, at time of receipt of raw material, drug usage records on the farm.

This control measure should be coupled with an appropriate verification.

**Example 4:**

**This control approach is a control strategy referred to in this document as "Control Strategy Example 4 - Records of Drug Use."**

A primary processor of aquaculture shrimp that purchases raw material shrimp from a contract farm or multiple farms through various middlemen or collectors should receive drug usage records from all the farmers when the raw material is delivered. The records must allow the processor to determine that the farmer has only used aquaculture drugs approved by the FDA and were used in conformance with applicable FDA regulations, guidance, and labeled instructions.

Additionally, the processor should receive a lot-by-lot certificate stating that any INAD used was used in conformance with the food use authorization requirements. The processor should combine this control strategy and monitoring procedure with an appropriate aquaculture drug verification testing strategy that is sufficient to demonstrate that the critical limit is effective and working properly to control the hazard. The processor should set the CCP at receiving.

d. DRUG RESIDUE TESTING BY PROCESSOR

Conducting at time of receipt, drug testing on all lots for the presence of unapproved drugs considered as a high risk to human health and any approved drugs used on the farm.

It is recommended that testing is performed using quantitative analytical methods that measure residue concentration in the edible tissue. However, the testing can also be performed using the commercially available rapid screening test, e.g., ELISA, that would indicate the presence of a drug, family, or class of drugs. If the rapid screening test reveals that a drug residue is present, further testing with a quantitative method to confirm the result and follow-up with the supplier could be necessary.

**NOTE:** A limited number of rapid screening tests for aquaculture drugs are available. Tests may not be suitable to assay for all drugs that might be used in aquaculture species. Processors should be cautioned that tests that have not been validated may be unreliable. These tests may fail to detect a residue (false negative) or may give false positive results. Processors should ensure

that the tests that they intend to use are appropriate for the species and tissue to be tested, are obtained from a reputable supplier, and have been validated. Special attention should be paid to test kit storage conditions and expiration dates as they may affect their performance and reliability.

**Example 5:**

**This control approach is a control strategy referred to in this document as "Control Strategy Example 5 - Drug Residue Testing."**

A primary processor of aquaculture tilapia that purchases raw material tilapia through various brokers should screen all incoming lots of tilapia with a series of validated rapid tests that target the families of drugs that are reasonably likely to be used during grow-out (e.g., chloramphenicol, nitrofurans, fluoroquinolones, sulfonamides). The processor should set the CCP at receiving.

e. THIRD-PARTY FARM CERTIFICATION PROGRAM

Reviewing, at time of receipt, evidence (e.g., continuing or lot-by-lot third-party certificate, web-site listing) that the producer operates under a competent third-party farm certification program that covers biosecurity, disease prevention measures, and aquaculture drug use.

**Each supplier should be assigned a unique code/number for the purpose of identification.**

The third-party farm certification program can be administered by a government competent authority, a single individual, an organization, or other private entity that is acting separately and independently from the processor. Through the certification, the third-party would affirm that they have assessed, audited, inspected, or otherwise determined that an aquaculture farm has met their program requirements and controls the aquaculture drug hazard.

Processors who rely on the third-party farm certification of their raw material supplier should be knowledgeable of issues associated with aquaculture seafood and

the potential sources of contamination with animal drugs and other chemicals used on the farm for treatment or prevention of diseases. They should have expectations for the controls to be included in the third-party certification program criteria. It is the responsibility of the processor to determine the competency of the third-party and its program. The processor may seek technical assistance from an aquaculture food safety expert or consultant to determine the competency of a third-party and its certification program.

There are several factors that affect the health issues of fish and contribute to their diseases and illnesses. The major cause of the spread of diseases and pathogens into aquaculture systems has been mainly through the movement of animals, feed, broodstock, and seeds. The effective health management program needs to cover all levels of aquaculture activities from the production unit, such as ponds, tanks, cages, etc. as well as the entire farm and the area where the farm operates.

The strategy of a third-party program often includes two components: 1) fish health management practices to prevent diseases, and 2) assurance that in case of necessary drug treatments, only FDA approved animal drugs properly acquired (e.g., a veterinarian prescription), are administered, and that the farmer maintains adequate records of all drugs used.

Some third-party certification programs implement Good Aquaculture Practices (GAQPs), Best Management Program (BMP), or other similar programs to control the aquaculture drug hazard at farms. These preventative programs use a holistic approach to address the root cause or need for farmers to use antibiotics or chemicals by implementing practices that prevent or minimize the risk of diseases and keep the animals healthy until harvest. They also include a food safety component to ensure only approved drugs are used and support it with proper documentation.

While there are a variety of ways the third-party may choose to control the aquaculture drug hazard on the farm, it is important that they verify the program is effective

and working. The third-party program should evaluate and provide reasonable confidence that the farm operation is managed responsibly, farming practices meet the established criteria, and the food safety of the product is not compromised.

The credible third-party farm certification program should address three main areas: biosecurity, good animal health practices, and disease contingency plan. The following elements should be included.

1. A system for maintaining records that document:
  - The source of inputs such as feed, seed, animal drugs and antibiotics, additives, chemicals that are:
    - approved by the proper authorities
    - properly used
    - properly stored
    - properly labeled and identified.
  - Type, concentration, dosage, method of administration, and withdrawal times (if applicable) of chemicals, animal drugs, probiotics, water conditioners, and the reason for their use:
  - Monitoring of grow-out water quality
  - Monitoring of sanitary conditions on the farm
  - Transaction documentation
  - Training received and provided to workers.
2. Biosecurity controls for workers and visitors:
  - Perimeter fencing, netting, or other structures intended to keep animals or unauthorized personnel out of the farm
  - Monitoring access and movement on the farm
  - A cleaning and sanitizing program for employees, any equipment used on the farm, trucks or visitors entering the farm
  - Restricted access of farm and domestic or wild animals including pets to the grow-out area
  - Using pathogen-free or disease-resistant post larva, fry, or fingerlings to minimize the risk of introducing

diseases.

3. Training of workers:

- Health and hygienic practices
- Handling and/or administering veterinary medicines, probiotics, water treatment chemical compounds, disinfectants, and other substances.
- Recognize the early onset signs or symptoms of the potential diseases identified in the farm's disease contingency plan.

4. Traceability of stock and product.

The farm should be able to identify the hatchery or origin of all products they produce and the eventual buyer, purchaser, destination or outcome of their product.

5. Monitoring and management of water quality and growing area controls to prevent the spread or introduction of disease or contamination within and between aquaculture facilities and the natural environment.

6. Monitoring and maintaining records of the source of all water and ice used on the farm during and after harvest on the animals or on food contact surfaces, e.g., to clean totes, tubs, or other containers for transport of animals.

7. Waste and pollution management controls.

8. Fish health and welfare programs monitoring the health of seed, broodstock, and fish populations on the farm and the prevention of disease:

- Properly implement and manage controls of the sources of broodstock and seed for culture (larvae, post larvae, fry and, fingerling, etc.) to reduce the risk of carryover of potential human health hazards (e.g., residues of antimicrobials, parasites, etc.) into the growing stocks.
- Controls to assure that aquaculture activities are conducted in a manner to maintain the health and welfare

of farmed aquatic animals, e.g., minimize stress, and maintain a healthy culture environment at all phases of the production cycle.

- Controls of the usage, proper labeling/identification, and storage for veterinary medicinal products, probiotics, water treatment chemical compounds, disinfectants, and other substances to prevent contamination of growing areas or improper and/or unapproved use.
- Control of diseases with animal drugs and antimicrobials based on an accurate diagnosis.
- Use only approved drugs that are specific to control or treatment of disease. In some cases, drugs may only be prescribed and distributed by a licensed veterinarian.
- All animal drugs and chemicals or medicated feeds must be used according to the instructions of the manufacturer or veterinarian instruction with particular attention to withdrawal periods.
- Animal drugs should be used in accordance with practices that consider both domestic requirements and the requirements of the country(ies) of intended consumers. Banned, non-registered, and/or not permitted antimicrobial agents, medicinal products for veterinary use, and/or chemicals must not be used in aquaculture production, transportation, or product processing.

9. Written Disease Contingency Plan:

- Developed by the appropriate aquaculture expert(s) knowledgeable about the aquatic diseases associated with the species and the farming area or location.
- Identify the potential diseases in the plan.
- Training program for the farmworkers to recognize the early onset signs or symptoms of the potential diseases identified.
- Procedure in case of disease outbreak

- The name and contact information (including 24hr emergency) for assistance to:
  - diagnose the disease;
  - conduct the appropriate diagnostic or laboratory analysis;
  - prescribe and provide the appropriate treatment plan.
- Quarantine process of the infected animals and area, disposal of dead animals,
- Disinfection of the infected area, water, and other appropriate areas before reuse or discharge into the environment.

### ○ Third-Party Farm Reports

The third-party farm certifier should develop a report from each inspection or audit and make it available to the processor. The report should include:

- General observations related to farm compliance with the program criteria including drug controls (records of use, test results)
- Any deficiencies observed, and corrective actions needed
- Deadline for completion of the corrective actions
- Discussion and comments with the farm management.

### ➤ Third-Party Verification of Animal Drug Controls on the Farm

The third-party should implement a verification step for oversight of animal drugs administered at the farm to ensure the control strategy is properly implemented and effective. The verification should include both farm audits or inspections and analytical testing for approved animal drug residues used on the farm to ensure that no harmful residues are present. The prudent third-party certifier should also include testing for unapproved drugs of concern that may have an impact on the safety of fish products for consumers.

### ➤ Processor Evaluation of Third-Party

The processor should evaluate the third-party certification program periodically (e.g., once a year or once during the grow-out cycle) to determine if the necessary safety

points are addressed in the certification scheme and whether a certification scheme is implemented in accordance with described criteria. The processor should consider the assessment of inspection or audit reports and any analytical test results.

Reports of poor farm performance may necessitate more frequent audits or inspections, and any positive test for unapproved animal drugs may mean destroying product, investigation of the root cause, the need for corrective actions, or stopping the use of the third-party.

### Example 6:

**This control approach is a control strategy referred to in this document as “Control Strategy Example 6 – Third-party Farm Certification Program”**

A primary processor of aquaculture trout that regularly purchases the raw material from a third-party certified farm should obtain evidence (continuing or lot by-lot third-party certificate, web-site listing) that the farm operates under a qualified third-party farm certification program. The certificate or evidence should be valid for the dates of the grow-out period and in case of a continuing certification for one (1) year. The certification should attest that the program the farm operates under covers aquaculture food safety components, specifically proper drug use during the grow-out period for that specific species. The processor should set the CCP at receiving of the trout raw material.

### • HOLDING

**If the hazard is by reason of aquatic holding** (e.g., lobster pounds), then you should identify the holding step as the CCP for aquaculture drugs. The preventive measure for this type of control is:

- Applying animal drugs in a manner consistent with:
  - Established withdrawal times;
  - Labeled instructions for use;
  - Conditions for extra-label use of FDA-approved drugs under a licensed veterinarian’s supervision and in accordance with FDA regulations and guidance;

- Conditions specified in the FDA “low regulatory priority” aquaculture drug list;
- Conditions of an INAD food use authorization granted by FDA.

### Example 7:

**This control approach is a control strategy referred to in this document as “Control Strategy Example 7 - Control During Holding.”**

A primary processor that uses oxytetracycline in the holding of live lobster in a lobster pound should use the drug as a medicated feed in accordance with labeled instructions and should document the withdrawal time of 30 days before selling. The processor should set the CCP at holding.

### • TRANSPORT

**A. If the hazard results from transportation of live fish**, then the processor should identify the receiving step as the CCP for aquaculture drugs. In this case, the processor should **refer to the guidance described in Control Strategy Examples 2 through 6.**

#### Example:

A primary processor that receives live tilapia from a broker on the broker’s truck should receive a lot-by-lot certificate from the broker. The certificates should state that all drugs were used in conformance with the applicable FDA regulations, guidance, and labeled instructions. The processor should combine this monitoring procedure with an appropriate aquaculture drug verification testing strategy and should set the CCP at receiving.

**B. If live transportation is on the processor’s own truck**, he should identify the transportation step as the CCP and **refer to Control Strategy Example 7 for guidance.**

#### Example:

A primary processor that receives live tilapia from the farmer on the processor’s own truck and uses drugs to control animal health during transportation (e.g., carbon dioxide as an anesthetizing agent at levels appropriate for the purpose) should control drug use during transportation and should set the CCP at transportation.

## DEVELOP A CONTROL STRATEGY

This section provides examples of seven control and verification strategies for aquaculture drug hazards. You may select a control strategy that is different from those which are suggested, provided that it complies with the requirements of the applicable US FDA food safety laws, regulations, and guidance.

While aquaculture drugs are predominately used at the hatchery, farm, during holding, or live transportation, it is the responsibility of the primary processor to have a strategy in place that effectively controls the aquaculture drug hazard.

Aquaculture, as an industry, varies widely around the world. This includes the species farmed; the production methods; the type of feed used; the availability and use of approved and unapproved drugs; the prevalence of diseases; and whether the processor can source raw material directly from farm or through middleman/collector or auction houses. In addition, the governmental regulatory structure, implementation, and oversight of food safety prevention programs at the production and processing level might differ from country to country.

Consequently, there are several factors the processor should consider when determining the appropriate control and verification strategy that would be suitable for the particular process and product. It is important to understand that the processor should have sufficient evidence and documentation to support the hazard control and verification strategy chosen to implement.

Some factors to consider may include:

- When developing the control strategy, the processor should take into consideration the source of raw material, particularly if it is procured from a middleman/collector, at an auction, or from a foreign primary processor.
- The processor should be able to trace back the raw material to a specific pond or cage, farm, farm cluster, and/or growing area.
- Regardless of the control strategy chosen, the processor should implement testing of the product for residues of animal drugs (and their metabolites) as a verification step. Information on the number of samples and frequency of testing, type of drugs to be tested, analytical methods, and the laboratory conducting testing should be sufficient to document that the critical limit identified in the HACCP plan is effective

and working properly. The processor should include all suppliers of the raw material in his testing strategy.

- If a rapid screening test kit (e.g., ELISA) is used for the product testing, the processor should ensure that the test kit is purchased from a reputable supplier, is intended for detection of a specific drug and/or metabolite(s), is properly stored, and is used before the expiration date. All test records should be kept for review.
- If testing is performed in the processor’s laboratory, periodically send the sample to a credible third-party laboratory to verify the adequacy of the testing methods and equipment.
- Processors and suppliers should review and keep records of aquaculture drug residue test results conducted by the country’s government regulatory authority.
- The processor should conduct a comprehensive follow-up investigation along with corrective actions when an unapproved drug residue is found in product during their own check or when an importer or foreign government notifies the processor that an unapproved drug residue was detected in the product. The result of the investigation should be recorded and retained in the files.
- The processor, government regulatory authority, or a credible third-party should verify through farm visits, farmer’s interviews, or other means that the farmer is, in fact, implementing any identified farm food safety control scheme or program they are participating in.
- Examples may include verifying that the farm is actually implementing a food safety program; the farmer or identified representative is actually signing the supplier’s certificate; a third-party, competent authority, or a farmers’ own food safety program is being implemented and is effective; and any third-party certificate is legitimate (i.e., not counterfeit) and current.
- Processors in countries that have and implement a robust, regulatory government food safety prevention and verification program on aquaculture farms should consider including this information when developing their HACCP aquaculture drug control strategy.
- Processors vertically integrated or commercially connected with a feed mill, hatchery, or farm(s) should consider

including this information when developing the HACCP aquaculture drug control strategy.

- Records should be kept to support and document all decisions leading to development of the HACCP plan.

The following are examples of control strategies included in this chapter:

<b>CONTROL STRATEGY</b>	<b>APPLY TO PRIMARY PROCESSOR</b>	<b>MAY APPLY TO SECONDARY PROCESSOR</b>
<b>On farm visit</b>	✓	
<b>Supplier’s certification/ letter of guarantee</b>	✓	✓
<b>Processor’s Pre-qualified Supplier Program</b>	✓	✓
<b>Records of drug use</b>	✓	✓
<b>Drug residue testing</b>	✓	✓
<b>Third-Party Farm Certification Program</b>	✓	✓
<b>Control During holding/ transport</b>	✓	✓

The primary (first) processor is required to have control measures in place to adequately control this hazard. However, the prudent secondary processor might request certification from the supplying primary processor, demonstrating that the product has been processed in compliance with the HACCP regulation, and the hazard of aquaculture drugs has been addressed by the primary processor. The secondary processor might also request additional information, e.g., records of test results for drug residues reasonably likely to be present, HACCP monitoring records of aquaculture drug hazard, a supplier certificate or letter of guarantee, a third-party certification or reports from the primary processor’s visit to the raw material supplier. It is recommended that the secondary processor keeps these records.

If the secondary processor uses imported aquaculture products for further processing, he should consider implementing one of the affirmative steps listed under 21CFR 123.12 “Special Requirements For Imported Products”

or use another means to verify that the original primary processor controlled the aquaculture drug hazard.

- **CONTROL STRATEGY EXAMPLE 1 – ON-FARM VISITS**

### Set Critical Limits

Conduct an on-farm visit to review general farm conditions and any farm management and biosecurity programs (e.g., Good Aquaculture Practices, Best Management Practices) in place to minimize the risk of diseases and to determine whether the animal drugs and other chemicals are used appropriately and in compliance with FDA regulation, guidance, and labeling. Aquaculture drugs are used on food-producing fish only if they have been:

- Approved by FDA or granted a conditional approval by FDA and used in accordance with all labeled conditions;

OR

- Approved by FDA and if used in an extra-label manner administered under a licensed veterinarian's supervision in accordance with FDA regulations and guidance;

OR

- Present on the most current FDA's list of low regulatory priority aquaculture drugs and used according to the provisions described on that list;

OR

- Used in compliance with FDA established Import Tolerance.

OR

- Used in food fish as an INAD subject to an investigational new animal drug exemption under 21 CFR Part 511, and used according to the requirements of that food use authorization;

AND

- Verified by the presence of a certificate from the producer indicating that
  - any investigational new animal drug used on the farm is subject to an investigational new animal drug exemption under 21 CFR Part 511, and fish intended for human

consumption are subject to a food use authorization,

AND

- the INAD is used in the fish according to the food use authorization requirements.

### Establish Monitoring Procedures

#### ➤ What Will Be Monitored?

- Written and signed report from on-site farm visit conducted within a grow-out cycle of the harvest and shipment of fish to the processor confirming that only FDA approved drugs in accordance with all label conditions have been used;

AND

- Certificate indicating proper INAD usage, if applicable.

#### ➤ How Will Monitoring Be Done?

- Review on-site farm visit report surveying the farm husbandry practices and procedures and showing a proper drug usage (refer to pages 9-11 for more information on on-site farm visits).

#### ➤ How Often Will Monitoring Be Done (Frequency)?

- At least once per grow-out cycle for each aquaculture farm site.

#### ➤ Who Will Do the Monitoring?

- Assigned employee who has training and understanding of aquaculture food safety and drug use controls for food-producing fish.

### Establish Corrective Action Procedures

#### Take the following corrective action to a product involved in a critical limit deviation:

- Reject the product if the on-site visit document is not present or not current

OR

- Isolate and hold until the on-site farm document is provided and /or the farm lot(s) in question

are sampled and tested for potential drug residues.

- Do not buy the product or have the product shipped from the production site to a feed or food processor.

AND

**Take the following corrective action to regain control over the operation after a critical limit deviation:**

- Discontinue use of the supplier/farm until evidence is obtained that the farm food safety and disease prevention strategy is in place and farming conditions have been improved and drug use and treatment practices have changed.

### Establish a Recordkeeping System

- On-site farm visit report evaluating farming conditions;

AND

- On-farm drug usage program and procedures;

AND

- Certificate of proper use under an INAD exemption meeting the criteria under 21 CFR 511, if applicable.

### Establish Verification Procedures

- Collect a representative number of samples of the raw material from each farm, in-process product, or finished product in order to verify that the farm is not using unapproved drugs or misusing approved drugs and analyze for those drug residues that are reasonably likely to be present. Specify drugs for which analysis will be conducted, the protocol for sample collection, and the analytical method to be used for each drug;

AND

- If testing is performed in the processor's laboratory, periodically send the sample to a credible third-party laboratory to verify the adequacy of the testing methods and equipment (e.g., by comparing results with those obtained using an Association of Official Analytical Collaboration ([AOAC](#)) International or equivalent method, or by analyzing proficiency samples;

AND

- Review monitoring, verification, and corrective action records within one (1) week of preparation to ensure they are complete and any critical limit deviations that occurred were appropriately addressed.

## TABLE 11-1

### Control Strategy Example 1 – ON-FARM VISITS

This table is an example (**for illustrative purposes only**) of a portion of a Hazard Analysis Critical Control Point (HACCP) plan using “Control Strategy Example 1 - On-Farm Visits.” This example illustrates how a primary processor of farm-raised tilapia can control aquaculture drugs. **An actual plan should specify under the Verification step: the aquaculture drugs for which analysis will be conducted, the protocol for sample collection, and the analytical method to be used for each drug. This information can be provided in a footnote or in a separate document.**

Aquaculture drugs may be only one of several significant hazards for this product. Refer to Tables 3-2 and 3-4 (Chapter 3) for other potential hazards (e.g., environmental chemical contaminants and pesticides).

**Example Only See Text for Full Recommendations**

**TABLE 11-1**

**Control Strategy Example 1 – ON-FARM VISITS**

(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
Critical Control Point	Significant Hazard(s)	Critical Limits	Monitoring				Corrective Action(s)	Records	Verification
			What	How	Frequency	Who			
Pre-harvest	Aquaculture drugs	<ol style="list-style-type: none"> <li>1. Farm visit to review farming conditions including evaluation of the farm’s aquaculture drug use and disease prevention strategy</li> <li>2. Aquaculture drugs are used on fish only if the drugs have been:               <ol style="list-style-type: none"> <li>a. approved by FDA or granted conditional approval by FDA and used in accordance with all labeled conditions;</li> <li>b. approved by FDA and if used in an extra-label manner administered under a licensed veterinarian’s supervision in accordance with FDA regulations and guidance;</li> <li>c. present on the list of low regulatory priority aquaculture drugs and used in accordance with the provisions in the list; OR</li> <li>d. used in food fish as an INAD in accordance with the requirements of the food use. authorization; OR</li> <li>e. used in compliance with FDA established Import Tolerance.</li> </ol> </li> </ol>	<p>Written and signed report from on-site farm visit conducted within a grow-out cycle of the harvest and shipment of fish to the processor.</p> <p>AND</p> <p>Certificate indicating proper INAD usage, if applicable</p>	<p>Review on-site farm visit document showing proper drug usage</p> <p>Visual check for INAD certificate, if applicable</p>	At least once per grow-out cycle for each aquaculture farm	Assigned employee trained in aquaculture food safety	<p>Reject the product if the report not present or not current</p> <p>OR</p> <p>Isolate and hold until on-site visit report provided or the farm lot in question is sampled and tested for potential drug residues</p> <p>AND</p> <p>Do not have the product shipped from the production site for processing.</p> <p>AND</p> <p>Discontinue use of the supplier until evidence is obtained that drug treatment practices have changed</p>	<p>On-site visit report including on-farm drug usage program and procedures</p> <p>Certificate of INAD usage, if applicable</p>	<p>Collect a representative number of samples of the raw material from each farm or finished product and analyze for those drug residues that are reasonably likely to be present</p> <p>AND</p> <p>If testing is performed in the processor’s laboratory periodically send the sample to a credible third-party laboratory to verify the adequacy of the testing methods and equipment (e.g., by comparing results with those obtained using AOAC or equivalent methods)</p> <p>AND</p> <p>Review monitoring, verification, and corrective action records within 1 week of preparation</p>

- **CONTROL STRATEGY EXAMPLE 2 - SUPPLIER'S CERTIFICATION**

### Set Critical Limits

A written and signed certificate or letter of guarantee provided by the farmer or other supplier(s), e.g., middleman or collector for each lot of incoming raw material declaring that aquaculture drugs are used on fish only if they have been:

- Approved by FDA or granted a conditional approval by FDA and used in accordance with all labeled conditions;

OR

- Approved by FDA and if used in an extra-label manner administered under a licensed veterinarian's supervision in accordance with FDA regulations and guidance;

OR

- Present on the most current FDA's list of low regulatory priority aquaculture drugs and used according to the provisions described on that list;

OR

- Used in compliance with FDA established Import Tolerance.

OR

- Used in food fish as an INAD subject to an investigational new animal drug exemption under 21 CFR Part 511 and used according to the requirements of that food use authorization.

**NOTE:** If a raw material is outsourced from countries with known problems of use of unapproved drugs and other unsafe chemicals during the raising of fish, the prudent processor makes sure that the product meets food safety requirements and is in compliance with US FDA laws and regulations. The processor may consider implementation of affirmative steps listed under 21CFR 123.12 Special Requirements for Imported Products.

### Establish Monitoring Procedures

#### ➤ What Will Be Monitored?

- Presence of a certificate signed by the farmer or authorized farmer's

representative, or another supplier (e.g., middleman, collector) indicating proper drug usage.

- If applicable, presence of certificate from the producer indicating that any investigational new drug used in fish intended for human consumption is subject to an investigational new animal drug exemption under 21 CFR Part 511 and that the INAD is used according to the requirements of the food use authorization.

#### ➤ How Will Monitoring Be Done?

- Visual check for the presence of a certificate or letter of guarantee of proper drug use.

#### ➤ How Often Will Monitoring Be Done (Frequency)?

- Each lot received.

#### ➤ Who Will Do the Monitoring?

- Any person who has training and understanding of the principles of the controls.

### Establish Corrective Action Procedures

**Take the following corrective action to a product involved in a critical limit deviation:**

- Reject the lot;

OR

- Hold the lot until a certificate can be provided;

OR

- Hold and analyze the lot for those aquaculture drugs that are reasonably likely to be present.

**NOTE:** If testing is performed, the following specific information should be recorded: the protocol for sample collection, aquaculture drugs for which analyses were conducted, and the analytical method used for each drug.

AND

**Take the following corrective action to regain control over the operation after a critical limit deviation:**

- Discontinue use of the supplier until evidence is obtained that the supplier will comply with the certification controls.

**Establish a Recordkeeping System**

- Copy of certificates or letters of guarantee;  
AND
- Receiving record showing lots received and the presence or absence of a certificate or letter of guarantee of proper drug use.  
AND
- Certificate of proper use under an INAD exemption meeting the criteria under 21 CFR 511, if applicable.

**Establish Verification Procedures**

- Collect a representative number of samples of the raw material from each farm, in-process product, or finished product and analyze for those drug residues that are reasonably likely to be present. Specify drugs for which analysis will be conducted, the protocol for sample collection, and the analytical method to be used for each drug;  
AND
- If testing is performed in the processor's laboratory, periodically send the sample to a credible third-party laboratory to verify the adequacy of the testing methods and equipment (e.g., by comparing results with those obtained using an Association of Official Analytical Collaboration (AOAC) International (<https://www.aoac.org/about-aoac-international/>) or equivalent method, or by analyzing proficiency samples;  
AND
- If raw material collected and delivered by a middleman, request a list of farms he bought shrimp from with affiliated lot's numbers.  
AND

- Review monitoring, corrective action, and verification records within one (1) week of preparation to ensure they are complete and any critical limit deviations that occurred were appropriately addressed.

**TABLE 11-2**

**Control Strategy Example 2 – SUPPLIER’S CERTIFICATION OR LETTER OF GUARANTEE**

This table is an example (for illustrative purposes only) of a portion of a HACCP plan using “Control Strategy Example 2 - Supplier’s Certification.” This example illustrates how a primary processor of farm-raised shrimp can control aquaculture drugs. **An actual plan should specify under the Verification step: the aquaculture drugs for which analysis will be conducted, the protocol for sample collection, and the analytical method to be used for each drug. This information can be provided in a footnote or in a separate document.**

Aquaculture drugs may be only one of several significant hazards for this product. Refer to Tables 3-3 and 3-4 (Chapter 3) for other potential hazards (e.g., environmental chemical contaminants and pesticides).

**Example Only: See Text for Full Recommendations**

(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
Critical Control Point	Significant Hazard(s)	Critical Limits	Monitoring				Corrective Action(s)	Records	Verification
			What	How	Frequency	Who			
Receiving	Aquaculture Drugs	Certificate or letter of guarantee indicating proper drug usage for all lots of incoming pond- raised shrimp	Presence of a certificate or letter of guarantee indicating proper drug usage  Certificate indicating proper INAD usage, if applicable	Visual Check	Each Lot received	Receiving employee trained in aquaculture food safety	Reject the lot if certificate or letter of guarantee is absent  Discontinue use of the supplier until evidence is obtained that the supplier will comply with the certification controls	Producer’s drug usage certificate or letter of guarantee  Certificate of INAD usage, if applicable  Receiving record	Collect a representative number of samples of the raw material from each farm and analyze for those drug residues that are reasonably likely to be present  If testing is performed in the processor’s laboratory, periodically send the sample to a credible third-party laboratory to verify the adequacy of the testing methods and equipment (e.g., by comparing results with those obtained using AOAC or equivalent methods)  If raw material collected and delivered by a middleman, request a list of farms he bought shrimp from with affiliated lot numbers.  Review monitoring, verification, and corrective action records within 1 week of preparation

- **CONTROL STRATEGY 3 -PROCESSOR'S PRE-QUALIFIED SUPPLIER PROGRAM**

**Set Critical Limits**

All supplying farms participate in the processor's described and documented pre-qualified supplier program and are on the supplier/vendor list at the time of raw material delivery;

AND

A written and signed certificate or letter of guarantee provided by the farmer (continuing or lot-by-lot) declaring compliance with the processor's pre-qualification requirements and confirming that aquaculture drugs are used on fish only if they have been:

- Approved by FDA or granted a conditional approval by FDA and used in accordance with all labeled conditions;

OR

- Approved by FDA and if used in an extra-label manner administered under a licensed veterinarian's supervision in accordance with FDA regulations and guidance;

OR

- Present on the most current FDA's list of low regulatory priority aquaculture drugs and used according to the provisions described on that list;

OR

- Used in compliance with an established Import Tolerance.

OR

- Used in food fish as an INAD subject to an investigational new animal drug exemption under 21 CFR Part 511 and used according to the requirements of that food use authorization.

**Establish Monitoring Procedures**

➤ **What Will Be Monitored?**

- Presence of farm(s) on the processor's pre-qualified list;

AND

- Presence of a certificate/letter of guarantee signed by the farmer or farmer's representative declaring that the lot was produced in compliance with the processor's program requirements.

➤ **How Will Monitoring Be Done?**

- Visual check that farm(s) are on the processor's supplier/vendor list;

AND

- Visual check for the presence of a certificate or letter of guarantee.

➤ **How Often Will Monitoring Be Done (Frequency)?**

- Each lot received.

➤ **Who Will Do the Monitoring?**

- Any person who has an understanding of the principles of the controls.

**Establish Corrective Action Procedures**

**Take the following corrective action for a product involved in a critical limit deviation:**

- Reject the lot if the farm is not on the processor's pre-qualified list

OR

- If the farm on the processor's pre-qualified list did not provide a certificate or letter of guarantee:
  - Reject the lot;

OR

- Hold the lot until a certificate can be provided;

OR

- Hold and analyze the lot for those aquaculture drugs that are reasonably likely to be present.

AND

**Take the following corrective action to regain control over the operation after a critical limit deviation:**

- Do not accept the raw material from the farm not on the processor's pre-qualified list
- AND
- Conduct on-farm evaluation to ensure that the supplier complies with the processor's pre-qualified program
- AND
- Discontinue use of the supplier until evidence is obtained that the supplier will comply with the processor's pre-qualified program requirements.

**Establish a Recordkeeping System**

- The processor's current list of pre-qualified farms
- AND
- Receiving records showing lot received and presence or absence of a certificate or letter of guarantee;
- AND
- The processor inspection report of pre-qualified farms
- AND
- Copy of testing results for aquaculture drugs that are reasonably likely to be present, if applicable.

**Establish Verification Procedures**

- Conduct on-site visits of farms participating in the processor's pre-qualification program to evaluate their compliance regularly (at minimum, once per grow-out period). Refer to conducting on-farm visit for examples of criteria that should be included in the pre-qualified program.
- AND
- Review the processor's pre-qualified list weekly to ensure it is up to date.
- AND

- Collect a representative number of samples of the raw material from each farm and analyze for those drug residues that are reasonably likely to be present:

**NOTE:** If testing is performed, the following specific information should be recorded: the protocol for sample collection; aquaculture drugs for which analysis were conducted, and the analytical method used for each drug.

AND

- If testing is performed in the processor's laboratory, periodically send the sample to a credible third-party laboratory to verify the adequacy of the testing methods and equipment (e.g., by comparing results with those obtained using an Association of Official Analytical Collaboration (AOAC) International (<https://www.aoac.org/about-aoac-international/>) or equivalent method, or by analyzing proficiency samples;
- AND
- Review monitoring, verification, and corrective action records within 1 week of preparation to ensure they are complete, and any critical limit deviations that occurred were appropriately addressed.

**TABLE 11-3**

**CONTROL STRATEGY EXAMPLE 3 - PROCESSOR’S PRE-QUALIFIED SUPPLIER PROGRAM**

This table is an example (for illustrative purposes only) of a portion of a Hazard Analysis Critical Control Point (HACCP) plan using “Control Strategy Example 3 – Processor’s Pre-Qualified Supplier Program.” This example illustrates how a primary processor of farm-raised shrimp can control aquaculture drugs. **An actual plan should specify under the Verification step: the aquaculture drugs for which analysis will be conducted, the protocol for sample collection, and the analytical method to be used for each drug. This information can be provided in a footnote or in a separate document.**

Aquaculture drugs may be only one of several significant hazards for this product. Refer to Tables 3-2 and 3-4 (Chapter 3) for other potential hazards (e.g., environmental chemical contaminants and pesticides).

Example Only: See Text for Full Recommendations

(1)	(2)	(3)	(4) (5) (6) (7)				(8)	(9)	(10)
Critical Control Point	Significant Hazard(s)	Critical Limits	Monitoring				Corrective Action(s)	Records	Verification
			What	How	Frequency	Who			
Receiving	Aquaculture drugs	All supplying farms participate in the processor’s pre-qualified supplier program and are on the supplier/vendor list.	Presence of the farm on the Pre-qualified Supplier List	Visual check	Each lot	Receiving employee trained in aquaculture food safety	Reject the product  Do not accept the raw material from non-prequalified supplier	The current list of prequalified suppliers	Conduct on-site visits of farms participating in the processor’s pre-qualification program to evaluate their compliance regularly (at minimum, once per grow-out period).  Review the processor’s pre-qualified list weekly to ensure it is up to date.  Collect a representative number of samples of the raw material from each farm and analyze for those drug residues that are reasonably likely to be present

(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
			Monitoring						
Critical Control Point	Significant Hazard(s)	Critical Limits	What	How	Frequency	Who	Corrective Action(s)	Records	Verification
Receiving	Aquaculture drugs	<p>A signed certificate or letter of guarantee (continuous or lot-by-lot) declaring compliance with the processor's pre-qualification requirements and confirming that aquaculture drugs are used on fish only if they have been:</p> <ul style="list-style-type: none"> <li>Approved by FDA or granted a conditional approval by FDA and used in accordance with all labeled conditions;</li> </ul> <p>OR</p> <ul style="list-style-type: none"> <li>Approved by FDA and if used in an extra-label manner administered under a licensed veterinarian's supervision in accordance with FDA regulations and guidance;</li> </ul> <p>OR</p> <ul style="list-style-type: none"> <li>Present on the most current FDA's list of low regulatory priority aquaculture drugs and used according to the provisions described on that list;</li> </ul> <p>OR</p> <ul style="list-style-type: none"> <li>Used in compliance with an established Import Tolerance.</li> </ul> <p>OR</p> <ul style="list-style-type: none"> <li>Used in food fish as an INAD according to the requirements of that food use authorization</li> </ul>	<p>Presence of a certificate or letter of guarantee</p> <p>Certificate indicating proper INAD usage, if applicable</p>	Visual check	Each lot	Receiving employee trained in aquaculture food safety	<p>If the farm on the processor's pre-qualified list: Reject the lot OR Hold the lot until a certificate can be provided; OR Hold and analyze the lot for those aquaculture drugs that are reasonably likely to be present. Conduct on-farm evaluation to ensure that the supplier complies with the processor's pre-qualified program AND Discontinue use of the supplier until evidence is obtained that the supplier will comply with the processor's pre-qualified program requirements.</p>	<p>Receiving records showing lot received and presence or absence of a certificate or letter of guarantee</p> <p>Copy of testing results for aquaculture drugs that are reasonably likely to be present, if applicable</p> <p>Certificate of INAD usage, if applicable</p>	<p>If testing is performed in the processor's laboratory periodically send the sample to a credible third-party laboratory to verify the adequacy of the testing methods and equipment (e.g., by comparing results with those obtained using AOAC or equivalent methods)</p> <p>Review monitoring, verification, and corrective action records within 1 week of preparation</p>

Chapter 11: Aquaculture Drugs

- **CONTROL STRATEGY EXAMPLE 4 - RECORDS OF DRUG USE**

### Set Critical Limits

Records of drug usage for each delivery from each farm that show aquaculture drugs were used only if the drugs have been:

- Approved by FDA or granted conditional approval by FDA and used in accordance with all labeled conditions;

OR

- Approved by FDA and if used in an extra-label manner administered under a licensed veterinarian's supervision in accordance with FDA regulations and guidance;

OR

- Present on the most current FDA's list of low regulatory priority aquaculture drugs and used according to the provisions described on that list;

OR

- Used in compliance with FDA established Import Tolerance.

AND

- A lot-by-lot certificate from the farmer indicating that any investigational new animal drug (INAD) used in fish intended for human consumption is subjected to an investigational new animal drug exemption under 21 CFR Part 511 and that the INAD is used according to the food use authorization requirements.

### Establish Monitoring Procedures

#### ➤ What Will Be Monitored?

- Records of on-farm drug use;
- AND
- Certificate indicating proper INAD usage.

#### ➤ How Will Monitoring Be Done?

- Visual check of drug use records and INAD certificate of proper use.

#### ➤ How Often Will Monitoring Be Done (Frequency)?

- Each lot received.

#### ➤ Who Will Do the Monitoring?

- Any person who has an understanding of the principles of the controls.

### Establish Corrective Action Procedures

#### Take the following corrective action for a product involved in a critical limit deviation:

- Reject the lot

AND

#### Take the following corrective action to regain control over the operation after a critical limit deviation:

- Discontinue use of the supplier until evidence is obtained that drug treatment practices have changed and/or the producer will comply with the certification controls.

### Establish a Recordkeeping System

- Records of drug usage on the farm;

AND

- Certificate of proper use under an INAD exemption meeting the criteria under (21CFR Part 511), if applicable.

### Establish Verification Procedures

- Collect a representative number of samples of the raw material from each farm, in-process product, or finished product, and analyze for those drug residues that are reasonably likely to be present. Specify drugs for which analysis will be conducted, the protocol for sample collection, and the analytical method to be used for each drug;

AND

- If testing is performed in the processor's laboratory, periodically send the sample to a credible third-party laboratory to verify the adequacy of the testing methods and equipment (e.g., by comparing results with those obtained using an Association of Official Analytical

Collaboration (AOAC) International (<https://www.aoac.org/about-aoac-international/>) or equivalent method, or by analyzing proficiency samples;

AND

- Review monitoring, verification, and corrective action records within 1 week of preparation to ensure they are complete and any critical limit deviations that occurred were appropriately addressed.

## TABLE 11-4

### Control Strategy Example 4 – RECORDS OF DRUG USE

This table is an example (**for illustrative purposes only**) of a portion of a HACCP plan using “Control Strategy Example 4 - Records of Drug Use.” This example illustrates how a farm-raised shrimp processor can control aquaculture drugs. **An actual plan should specify under the Verification step: the aquaculture drugs for which analysis will be conducted, the protocol for sample collection, and the analytical method to be used for each drug. This information can be provided in a footnote or in a separate document.**

Aquaculture drugs may be only one of several significant hazards for this product. Refer to Tables 3-3 and 3-4 (Chapter 3) for other potential hazards (e.g., chemical contaminants).

**Example Only: See Text for Full Recommendations**

**TABLE 11-4**

**Control Strategy Example 4 – RECORDS OF DRUG USE**

(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
Critical Control Point	Significant Hazard(s)	Critical Limits	Monitoring				Corrective Action(s)	Records	Verification
			What	How	Frequency	Who			
Receiving	Aquaculture drugs	<p>Drug usage records for each delivery that show that drugs were used on fish only if the drugs have been:</p> <ul style="list-style-type: none"> <li>• Approved by FDA or granted conditional approval by FDA and used in accordance with all labeled conditions;</li> <li>• Approved by FDA and if used in an extra-label manner administered under a licensed veterinarian’s supervision in accordance with FDA regulations and guidance;</li> <li>• Present on the most current FDA’s list of low regulatory priority aquaculture drugs and used according to the provisions described in the list</li> </ul> <p>Used in food fish in compliance with an established Import Tolerance.</p>	Records of on-farm drug usage from each farm	Visual check	Each lot received	Receiving trained employee in aquaculture food safety	<p>Reject the lot</p> <p>Discontinue use of the supplier until evidence is obtained that drug use and treatment practices have changed</p>	<p>Farmer’s drug usage records</p> <p>Receiving record</p>	<p>Collect a representative number of samples of the raw material from each farm and analyze for those drug residues that are reasonably likely to be present.</p> <p>If testing is performed in the processor’s laboratory, periodically send the sample to a credible third-party laboratory to verify the adequacy of the testing methods and equipment (e.g., by comparing results with those obtained using AOAC or equivalent methods).</p> <p>Review monitoring, verification, and corrective action records within 1 week of preparation</p>

(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
			Monitoring						
Critical Control Point	Significant Hazard(s)	Critical Limits	What	How	Frequency	Who	Corrective Action(s)	Records	Verification
Receiving	Aquaculture drugs	Lot-by-lot certificate from the producer indicating that any investigational new aquaculture drug (INAD) used in fish intended for human consumption is used according to the requirements of the food use authorization, if applicable	Certificate indicating proper INAD usage, if applicable	Visual check	Each lot received	Receiving trained employee in aquaculture food safety	Reject the lot  Discontinue use of the supplier until evidence is obtained that the supplier will comply with the certification requirements	Certificate of INAD usage  Receiving record	Collect a representative number of samples of the raw material from each farm and analyze for those drug residues that are reasonably likely to be present.  If testing is performed in the processor's laboratory, periodically send the sample to a credible third-party laboratory to verify the adequacy of the testing methods and equipment (e.g., by comparing results with those obtained using AOAC or equivalent methods).  Review monitoring, verification, and corrective action records within 1 week of preparation

- **CONTROL STRATEGY EXAMPLE 5 - DRUG RESIDUE TESTING**

### Set Critical Limits

- No fish may contain residues of an unapproved drug (other than for those with an established import tolerance, those used under an INAD according to the requirements of the food use authorization, or used in accordance with the criteria specified in the list of low regulatory priority aquaculture drugs);

AND

- No fish may contain residues of an approved drug that is above FDA established tolerance level for that drug.

### Establish Monitoring Procedures

#### ➤ What Will Be Monitored?

- Fish edible portion for those drug residues that are reasonably likely to occur.

#### ➤ How Will Monitoring Be Done?

- Obtain a representative number of samples from the lot of raw material supplied by each farm and test for drugs using validated analytical methods.

#### ➤ How Often Will Monitoring Be Done (Frequency)?

- Each lot received.

#### ➤ Who Will Do the Monitoring?

- Any person who is qualified by training or experience to perform the analyses.

### Establish Corrective Action Procedures

**Take the following corrective action to a product involved in a critical limit deviation:**

- Reject the lot.

AND

**Take the following corrective action to regain control over the operation after a critical limit deviation:**

- Discontinue use of the supplier until evidence is obtained that drug treatment practices have changed.

### Establish a Recordkeeping System

- Results of testing conducted to control the hazard (critical limit)

AND

- Results of verification testing

### Establish Verification Procedures

- If testing is performed in the processor's laboratory, periodically send the sample to a credible third-party laboratory to verify the adequacy of the testing methods and equipment (e.g., by comparing results with those obtained using an Association of Official Analytical Collaboration (AOAC) International (<https://www.aoac.org/about-aoac-international/>) or equivalent method, or by analyzing proficiency samples;

AND

- Review monitoring, corrective action and verification records within 1 week of preparation to ensure they are complete and any critical limit deviations that occurred were appropriately addressed.

**TABLE 11-5**

**Control Strategy Example 5 – DRUG RESIDUE TESTING**

This table is an example (for illustrative purposes only) of a portion of a HACCP plan using “Control Strategy Example 5 - Drug Residue Testing.” This example illustrates how a primary processor of farm- raised Tilapia can control aquaculture drugs.

An actual plan should specify in the:

1. **Critical Limits:** the aquaculture drugs that are reasonably likely to be present and the critical limits to be applied to each drug; and
  2. **Verification steps:** the aquaculture drugs for which analysis will be conducted, the protocol for sample collection, and the analytical method to be used for each drug.
- This information can be provided in a footnote or in a separate document.

Aquaculture drugs may be only one of several significant hazards for this product. Refer to Tables 3-2 and 3-4 (Chapter 3) for other potential hazards (e.g., environmental chemical contaminants and pesticides).

Example Only: See Text for Full Recommendations

(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
			<b>Monitoring</b>						
<b>Critical Control Point</b>	<b>Significant Hazard(s)</b>	<b>Critical Limits</b>	<b>What</b>	<b>How</b>	<b>Frequency</b>	<b>Who</b>	<b>Corrective Action(s)</b>	<b>Records</b>	<b>Verification</b>
Receiving	Aquaculture drugs	<ol style="list-style-type: none"> <li>1. No fish may contain residues of unapproved drugs (other than those with an established import tolerance, those used under an INAD subject to an investigational new animal drug exemption under 21 CFR Part511 according to requirements of the food use authorization, or those included on the list of low regulatory priority aquaculture drugs)</li> <li>2. No fish may contain residues of an approved drug that is above FDA tolerance for that drug</li> </ol>	Fish edible portion for drug residues	Obtain samples and analyze for drugs using validated analytical methods	Each lot received	Quality assurance personnel	Reject the lot  Discontinue use of the supplier until evidence is obtained that drug treatment practices have changed	Analytical testing results to control hazard (critical limit) and verification	If testing is performed in the processor’s laboratory, periodically send the sample to a credible third-party laboratory to verify the adequacy of the testing methods and equipment (e.g., by comparing results with those obtained using AOAC or equivalent methods)  Review monitoring, verification, and corrective action records within 1 week of preparation

- **CONTROL STRATEGY EXAMPLE 6 – Third-party Farm Certification Program**

### Set Critical Limits.

Documentation indicating that the aquaculture farm operates under a third-party farm certification program. The program should include adequate controls for the aquaculture drug hazard, and measures implemented prevent this hazard from occurring (i.e., biosecurity and disease prevention plan). The third-party farm certification program with the food safety component can be administered and verified through a qualified government competent authority or a private third-party entity (A list of third-party certification bodies that have been accredited under the FDA's voluntary Accredited Third-Party Certification Program is available at the FDA Data Dashboard <https://www.fda.gov/food/importing-food-products-united-states/accredited-third-party-certification-program-public-registry-accredited-third-party-certification>).

The documentation confirming that a farm operates under a third-party certification program and implements adequate controls for the aquaculture drug hazard may include:

- a valid certificate that accompanies each lot of incoming aquacultured product, or
- a valid certificate issued for each farm by a third-party declaring that the farm currently operates continually under their program (the continuing certification), and
- a copy of documentation indicating that the farm is listed on an accessible secure and valid web site administered by the competent authority or third-party (real-time listing).

Each farm/supplier should be assigned a unique code/number for the identification purpose.

### NOTES:

1. Overall, a third-party farm program should provide reasonable assurances that the farm operation is managed responsibly, the farming practices meet the established criteria, and there is a high level of confidence in the safety of the product.

The focus of an effective aquaculture farm food safety program should be on ensuring that only approved animal drugs and chemicals are used on the farm and that they are administered or applied correctly and in compliance with US FDA regulations.

A disease prevention strategy should also be a part of the program. This includes requiring farms to have an effective biosecurity program and implementing good aquaculture practices that minimize the need for therapeutic agents, such as antibiotics and other disease control compounds that may not be approved for use in fish. Refer to pages 13-16 for more information and examples of criteria to be included in a third-party farm certification program.

2. While a farm may be under a third-party certification program, it remains the processor's responsibility to ensure and verify their products do not contain unapproved animal drug residues and/or residues of drugs approved by the FDA do not exceed tolerance levels established for those drugs by the FDA.

### Establish Monitoring Procedures.

#### ➤ What Will Be Monitored?

- Certificate/documentation indicating that the farm operates under a third-party farm certification program.

#### ➤ How Will Monitoring Be Done?

- Visual check for presence of a certificate/documentation.

#### ➤ How Often Will Monitoring Be Done (Frequency)?

- Each lot received must be checked for the presence of certificate or documentation that the farm operates under a third-party farm certification program. Documents may be issued on a lot-by-lot or continuing basis (i.e., at least once during each grow-out period).

#### ➤ Who Will Do the Monitoring?

- Any person who has training, knowledge and understanding of aquaculture food safety and fundamentals of the third-party farm certification program.

### Establish Corrective Action Procedure.

#### Take the following corrective action to a product involved in a critical limit deviation:

- Reject the lot;  
OR
- Hold the lot until the documentation/certificate can be provided;  
OR
- Hold and analyze the lot for those aquaculture drugs that are reasonably likely to be present.

**NOTE:** If testing is performed, the following specific information should be recorded: the protocol for sample collection; aquaculture drugs for which analyses were conducted, and the analytical method used for each drug.

AND

#### Take the following corrective action to regain control over the operation after a critical limit deviation:

- Discontinue use of the supplier until evidence is obtained that the supplier will comply with the certification controls.

### Establish a Recordkeeping System

- Third-party farm certificate or a copy of online farm listing;  
AND
- Receiving record showing lots received and presence or absence of a certificate/online farm listing.  
AND
- Testing results for aquaculture drugs that are reasonably likely to be present, showing the third-party program criteria are effective as applicable.  
AND
- A report of evaluation of the third-party farm certification program with emphasis on the food safety component of aquaculture drugs use.

### Establish Verification Procedures

- Evaluate the adequacy of the food safety component identified in the third-party farm certification program initially and at least once a year to determine if:
  - the program addresses the aquaculture drug food safety hazard and
  - the program is properly implemented and verified.

**NOTE:** See pages 13-16 for description of criteria that should be included in a third-party farm certification program.

AND

- Review results of farm inspection and verification audits conducted by the third-party food safety program and any testing for drug residues carried out on the farm at least annually;

AND

- Review monitoring, corrective action, and verification records within 1 week of preparation to ensure they are complete and any critical limit deviations that occurred were appropriately addressed.

**TABLE 11-6**

**CONTROL STRATEGY EXAMPLE 6 – THIRD-PARTY CERTIFICATION PROGRAM**

This table is an example (for illustrative purposes only) of a portion of a HACCP plan using “Control Strategy Example 6 – Third Part Farm Certification Program.” This example illustrates how an aquacultured trout processor can control aquaculture drugs.

Aquaculture drugs may be only one of several significant hazards for this product. Refer to Tables 3-2 and 3-4 (Chapter 3) for other potential hazards (e.g., environmental chemical contaminants).

Example Only: See Text for Full Recommendations

(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
Critical Control Point	Significant Hazard(s)	Critical Limits	Monitoring				Corrective Action(s)	Records	Verification
			What	How	Frequency	Who			
Receiving	Aquaculture drugs	Documentation/certificate that the farm operates under the qualified third-party farm certification program and adequately addresses aquaculture drug hazard.	Presence of a third-party certificate  OR Documentation showing the farm listing on the third-party website (e.g. a government administered program)	Visual check	Each lot	Receiving trained employee in aquaculture food safety and the third-party documentation requirements for this critical limit	Reject the lot  OR Hold the lot until the documentation/certificate can be provided  OR Hold and analyze the lot for those aquaculture drugs that are reasonably likely to be present.  AND Discontinue use the supplier until evidence is obtained that the supplier complies with the documentation requirements	Third-party farm certificate or a copy of online farm listing by the third-party entity  Receiving record  Testing results for aquaculture drugs that are reasonably likely to be present, if applicable  Report of the third-party program evaluation	Evaluate the adequacy of the third- party farm certification program food safety component and its implementation initially and at least once a year.  Review results of farm inspection and verification audits conducted by the third-party and test results carried out on the farm, at least annually  Review monitoring, verification, and corrective action records within 1 week of preparation

## • CONTROL STRATEGY EXAMPLE 7 - CONTROL DURING HOLDING

### Set Critical Limits

Aquaculture drugs are used on food fish only if they have been:

- Approved by FDA or granted a conditional approval by FDA and used in accordance with all labeled conditions;

OR

- Approved by FDA and used in an extra-label manner under a licensed veterinarian's supervision in accordance with FDA regulations and guidance;

OR

- Present on the most current FDA's list of low regulatory priority aquaculture drugs and used according to the provisions described in the list;

OR

- Used in food fish as an INAD subject to an investigational new animal drug exemption under 21 CFR Part 511, and used according to the requirements of the food use authorization;

OR

- Used in food fish in compliance with an established Import Tolerance for the drug.

### Establish Monitoring Procedures

#### ➤ What Will Be Monitored?

- Type of aquaculture drug used;
- AND
- Date and quantity of drug use;
- AND
- Any other conditions of drug usage that are relevant to:
    - Established withdrawal period;
    - Labeled instructions;
    - Extra-label use of an FDA-approved drug administered under a veterinarian's supervision in accordance with FDA regulations and guidance;

- Conditions specified in the FDA list of low regulatory priority aquaculture drugs;

OR

- Requirements of the INAD food use authorization, if applicable;

AND

- Date of distribution of the finished product.

#### ➤ How Will Monitoring Be Done?

- Visually, observe and record drug use and finished product distribution.

#### ➤ How Often Will Monitoring Be Done (Frequency)?

- Every time aquaculture drugs are used during holding or transportation;

AND

- Every time the finished product is distributed.

#### ➤ Who Will Do the Monitoring?

- Any person who has an understanding of principles of the controls.

### Establish Corrective Action Procedures

#### Take the following corrective action to a product involved in a critical limit deviation:

- Destroy the product if unapproved drug residues detected;

OR

- For approved/conditionally approved drug with an established tolerance level or import tolerance level:
  - hold the product until the mandatory withdrawal period has been met and until the drug residue level is below the established tolerance. These corrective actions should be verified by collecting and analyzing a representative number of samples of the product, using an appropriate analytical method.

AND

**Take the following corrective action to regain control over the operation after a critical limit deviation:**

- Modify drug use practices.

#### **Establish a Recordkeeping System**

- Drug use records;

AND

- Records indicating date of distribution of the finished product.

AND

- Results of verification testing for residues of drug used during holding or transport.

#### **Establish Verification Procedures**

- Test the product for residues of drug used during holding before distribution
- Review monitoring and corrective action records within 1 week of preparation to ensure they are complete, and any critical limit deviations that occurred were appropriately addressed.

**TABLE 11-7**

**Control Strategy Example 7 – CONTROL DURING HOLDING**

This table is an example (for illustrative purposes only) of a portion of a HACCP plan using “Control Strategy Example 7 - Control During Holding.” This example illustrates how a processor that holds live lobster in a lobster pound can control aquaculture drugs.

Aquaculture drugs may be only one of several significant hazards for this product. Refer to Tables 3-3 and 3-4 (Chapter 3) for other potential hazards (e.g., environmental chemical contaminants, pesticides and natural toxins).

**Example Only: See Text for Full Recommendations**

(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
Critical Control Point	Significant Hazard(s)	Critical Limits	Monitoring				Corrective Action(s)	Records	Verification
			What	How	Frequency	Who			
Holding	Aquaculture drugs	Lobster will be withheld from distribution for 30 days after treatment with oxytetracycline in accordance with the labeled directions for use  No other aquaculture drugs will be used	Type of aquaculture drug used, date and quantity and withdrawal time	Visual observation of drug use and records	Every time aquaculture drugs are used	Production trained employee	Destroy the lot when unapproved drugs are used  Hold the product  Collect a sample of the finished product and analyze for residues of drug used (oxytetracycline)  Release the product if the drug residue level is below the tolerance (2 ppm)  Hold the product if the drug residue level exceeds the tolerance and retest  Modify drug use practices	Drug use record	Test the product for residues of drug used during holding before distribution  Review monitoring and corrective action records within 1 week of preparation
			Date of finished product distribution	Visual check of product distribution and records	Every time finished product is shipped	Shipping supervisor		Shipping record	

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