

Exposure Response Plan for Laboratory Handling of Tetrodotoxin

Background Information

Tetrodotoxin (TTX) is an extremely potent, low-molecular weight neurotoxin found in a variety of marine and terrestrial organisms, most notably pufferfish (Tetraodontiformes), and also in certain amphibians, octopus, and shellfish species. [CDC](#). TTX exerts its toxic effect by **binding to and blocking voltage-gated sodium channels**, preventing nerve impulse conduction and leading to progressive neuromuscular dysfunction and paralysis. [PubChem](#) TTX is widely used in biomedical research as a highly specific sodium channel blocker, but it remains a high-risk toxin because very small quantities can cause severe or fatal outcomes if mishandled. [PubChem](#)

Regulatory status (Select Toxin)

In the United States, tetrodotoxin is regulated as an HHS Select Toxin, with a permissible (exempt) aggregate amount of 500 mg per principal investigator under the federal Select Agent regulations (42 CFR Part 73); possession above permissible amounts can trigger additional regulatory requirements. [eCFR73](#)

Clinical significance (why it's dangerous)

TTX poisoning typically begins with **paresthesias/numbness (often around the lips/mouth)** and can progress to **weakness, ascending paralysis, and respiratory failure**. [CDC+marine toxins](#). There is **no known antidote**; management is primarily **supportive**, including airway and respiratory support when needed. [NCBI](#)

This response plan provides procedures for safe laboratory handling, spill containment, potential exposure response, and medical follow-up related to TTX to ensure compliance with institutional safety requirements and federal toxin controls. [eCFR73](#)

Host Range

TTX is associated with a broad range of organisms. Documented natural sources include pufferfish, and some amphibians, octopus, and shellfish species (and is discussed in the scientific literature as a marine neurotoxin with broad distribution). [CDC](#)

Modes of Transmission (Laboratory Context)

TTX is a toxin, not an infectious agent: it does not replicate in host tissues and is not transmitted person-to-person. Laboratory-associated intoxication occurs only through direct exposure to purified toxin, contaminated materials, or contaminated animal/tissue matrices. Potential routes of exposure in the lab include:

- **Inhalation:** aerosol or particulate generation (e.g., spills, dried residues, vortexing/centrifugation without sealed containment, improper handling of powders).
- **Percutaneous (injection/inoculation):** needlesticks, sharps injuries, cuts from contaminated glass/plastic.
- **Ingestion:** hand-to-mouth transfer from contaminated gloves/hands/surfaces.
- **Mucous membrane contact:** splashes/droplets to eyes, nose, or mouth.
- **Skin contact/absorption:** contact with contaminated solutions or residues (risk is higher with compromised skin).

Laboratory Hazards

The primary laboratory hazards associated with TTX involve exposure via inhalation, ingestion, mucous membrane contact, skin contact/absorption, or percutaneous injury, which can lead to rapid-onset neurologic effects and progressive paralysis, including respiratory compromise. [CDC](#)

Working with Animals Exposed to Tetrodotoxin – All laboratory Personnel must review the TTX standard operating procedures before beginning any of the work.

Biosafety Level

- Animal studies involving Tetrodotoxin must be conducted under Animal Biosafety Level 2 (ABSL-2) or enhanced ABSL-2 (ABSL-2+) conditions, depending on toxin concentration and procedure risk (e.g., injection, necropsy, aerosol potential).
- Procedures that may generate aerosols (e.g., toxin dilution, injection, necropsy) should be performed within a certified Class II biosafety cabinet (BSC).

Animal Handling and PPE

- Only trained and authorized personnel may handle animals treated with tetrodotoxin (TTX).
- Required PPE includes: lab coat or disposable gown, double nitrile gloves, (change outer gloves frequently) eye/face protection, and respiratory protection (N95 or equivalent) only if aerosol or powder exposure potential exists and per institutional respiratory protection program.
- Use appropriate restraint devices or bite-resistant gloves when handling animals that may exhibit neurologic impairment (e.g., weakness, paralysis, altered responsiveness).
- All TTX preparation and administration must be performed inside an approved primary containment device (e.g., certified chemical fume hood or BSC, as designated by EH&S), using safety-engineered sharps whenever possible.

- Sharps must be minimized and disposed of immediately in approved sharps containers.

Animal Monitoring and Clinical Signs

Animals receiving TTX may develop dose-dependent neurologic signs consistent with sodium-channel blockade, including:

- Decreased activity or lethargy
- Limb weakness or ataxia
- Reduced righting reflex
- Respiratory depression or labored breathing
- Progressive paralysis at higher doses
- Animals must be monitored at least daily, or more frequently as specified in the approved IACUC protocol.

Signs and Symptoms of Tetrodotoxin (TTX) Exposure

Tetrodotoxin is a potent neurotoxin that blocks voltage-gated sodium channels, preventing normal nerve impulse conduction. Symptoms are typically rapid in onset and dose-dependent, with progression from sensory disturbances to neuromuscular paralysis.

Early Signs and Symptoms

(often minutes to a few hours after exposure, depending on route and dose)

- Tingling, numbness, or paresthesia of the lips, tongue, face, or extremities
- Metallic or bitter taste in the mouth
- Dizziness or lightheadedness
- Headache
- Nausea, vomiting, abdominal pain
- Mild weakness or fatigue

Progressive / Moderate Symptoms

- Increasing muscle weakness
- Ataxia or difficulty walking
- Slurred speech (dysarthria)
- Difficulty swallowing (dysphagia)
- Hypersalivation
- Shortness of breath or shallow breathing

Severe / Life-Threatening Symptoms

- Ascending flaccid paralysis
- Respiratory muscle paralysis leading to respiratory failure

- Bradycardia or hypotension
- Loss of deep tendon reflexes
- Cyanosis
- Cardiac arrhythmias (in severe poisoning)

Key Clinical Features (Important for training)

- Mental status is usually preserved until late stages
- No fever (unless secondary complications occur)
- No known antidote
- Death, when it occurs, is typically due to respiratory failure

Onset by Exposure Route (Typical)

- Ingestion: 10 minutes to several hours (most common and fastest)
- Inhalation / mucous membrane / injection: minutes to hours
- Dermal contact: usually slower, increased risk with compromised skin

Medical Urgency

Any suspected exposure to TTX or onset of neurologic symptoms should be treated as a medical emergency:

- Call 911 for severe symptoms or breathing difficulty
- Seek immediate emergency evaluation even if symptoms appear mild
- Provide responders with information that TTX is a sodium-channel–blocking neurotoxin
- Early supportive care and respiratory support are critical for survival

Medical Precautions/Treatments

Prophylaxis

There is no antibiotic, chemoprophylaxis, or post-exposure preventive treatment available for tetrodotoxin (TTX) exposure. TTX is a non-infectious, low–molecular weight neurotoxin that does not replicate in the body; therefore, antibiotics are ineffective for prevention or treatment.

In laboratory and vivarium settings, prevention relies entirely on:

- Strict adherence to engineering controls (e.g., fume hood or approved primary containment),
- Appropriate personal protective equipment (PPE),
- Standard operating procedures (SOPs) designed to prevent inhalation, ingestion, mucous membrane contact, dermal exposure, or percutaneous injury.

Vaccines

There is no vaccine available for tetrodotoxin. Immunization is not possible and is not recommended for individuals working with TTX.

Pregnancy, Lactation, and Reproductive Health Considerations (TTX)

Tetrodotoxin (TTX) is a potent neurotoxin that blocks voltage-gated sodium channels and can cause rapid neuromuscular paralysis and respiratory failure. While human pregnancy-specific data are limited, TTX readily affects excitable tissues, and fetal and neonatal nervous systems are particularly vulnerable to sodium-channel–blocking agents. Because of the severity of toxicity, absence of an antidote, and limited safety data in pregnancy, the following precautions apply.

Required Precautions

- Pregnant, potentially pregnant, or lactating individuals should not handle tetrodotoxin or perform procedures involving TTX solutions, powders, contaminated animals, tissues, bedding, or waste without prior medical evaluation and clearance.
- Exposure risk applies to all routes (inhalation, ingestion, mucous membrane contact, dermal absorption, or percutaneous injury).
- These precautions apply regardless of dose, due to the high potency of TTX.

Medical Review and Accommodations

Pregnancy-related considerations and any work restrictions or accommodations are addressed through confidential medical evaluation with Occupational Health

ehsocchealth@ucr.edu

- Decisions regarding work modifications are handled individually and coordinated with HR and supervisory staff as appropriate, consistent with institutional accommodation policies.
- Pregnancy status is not assessed or disclosed through signage or laboratory screening.

Rationale

- There is no known antidote or prophylaxis for TTX.
- Severe maternal toxicity can result in secondary fetal hypoxia due to respiratory compromise.
- Conservative controls are warranted under the precautionary principle when reproductive toxicity data are limited but hazard severity is high.

Immediate Response Following Exposure

If an exposure occurs, stop work immediately. If you are working with another person, ask them to assist you and follow the steps below.

Reporting Exposure Incidents

1. Stop working immediately and alert nearby personnel.
2. Secure the area to prevent others from entering until it can be assessed by the Biosafety Officer or EH&S representative.
3. Remove contaminated PPE carefully to avoid secondary contact.
 - Place all disposable materials (gloves, gowns, wipes) in a biohazard bag for decontamination or disposal.
4. Decontaminate exposed skin immediately by washing thoroughly with soap and copious amounts of water.
 - For mucous membrane exposure (eyes, mouth, nose), flush with running water or sterile saline for at least 15 minutes.
5. Report on the incident to the:
 1. **PI or laboratory supervisor**
 2. **Anyone may contact the UCI Medical Center Infectious Disease Fellow on call at 714-456-6011 for immediate counseling and guidance. UCR maintains an agreement with the UCI Center for Occupational and Environmental Health (COEH) Clinic, which serves as our Occupational Health provider and reviews UCR's Animal Occupational Health Program.**
 3. **UCR Biosafety Officer (BSO) and EHSRM at (951) 827-5528.**
 4. **Occupational Health ehsochealth@ucr.edu**

Undergraduate Student Employees report your injury to your supervisor (or go to [Employee Injuries](#)).

For life-threatening injuries, call 911 immediately.

For all other injury types, seek Medical Treatment at UCR's preferred Occupational Clinics. Visit the [Medical Treatment Facilities](#) webpage to learn more about where to seek medical treatment.

References

- Centers for Disease Control and Prevention. (n.d.). Tetrodotoxin poisoning associated with puffer fish consumption. <https://www.cdc.gov>
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- Isbister, G. K., & Kiernan, M. C. (2005). Neurotoxic marine poisoning. *The Lancet Neurology*, 4(4), 219–228.
- Noguchi, T., & Arakawa, O. (2008). Tetrodotoxin—Distribution and accumulation in aquatic organisms and cases of human intoxication. *Marine Drugs*, 6(2), 220–242. <https://www.mdpi.org/marinedrugs/papers/md6020220.pdf>
- U.S. Department of Health & Human Services. (2023). Select agent regulations: 42 CFR Part 73. *Electronic Code of Federal Regulations*. <https://www.ecfr.gov/current/title-42/chapter-I/subchapter-F/part-73>

Print this and carry it in your wallet in case of an emergency

	University of California, Riverside BIOLOGICAL TOXIN CARD	
<p>My job requires me to work with Tetrodotoxin and animals injected with Tetrodotoxin.</p>		
<p>If the person with this card exhibits any of the symptoms listed on the back, immediately contact the UCI Medical Center Infectious Disease Fellow on call at (714) 456-6011. For immediate medical counseling on what to do right away, proceed to the nearest Emergency Department and present this card. For more information or to report an incident call: UC Riverside, Occupational Health, at (951) 827-5528.</p>		
<p>TETRODOTOXIN Routes of exposure include inhalation of dust/aerosols, ingestion via hand-to-mouth transfer, dermal contact/absorption (especially through compromised skin), mucous membrane contact (eyes/nose/mouth), and accidental injection/inoculation (e.g., needlesticks/sharps or animal bites)</p>		
<p><u>POISONING ONSET:</u> Rapid onset (10 to 45 minutes) or delayed onset (3 to 6 hours but rarely longer). Death may occur as early as 20 minutes, or as late as 24 hours after exposure. <u>SYMPTOMS:</u> Tingling of the tongue and mouth. Vertigo or dizziness. Feelings of doom. Weakness. Nausea and vomiting. <u>TREATMENT:</u> No specific antitoxin is available. Supportive care. Anticipation of progressive ascending paralysis, the mainstay of treatment is respiratory support and supportive care until the tetrodotoxin is eliminated. Stomach evacuation by the emergency department if ingested.</p>		

*Identification: Provide your UCR Student ID, Employee ID, UCR NetID, UCR Email, or Date of Birth.