

Pertussis Toxin (PTX)

Pertussis toxin (PTX) is a potent exotoxin produced by Bordetella pertussis. PTX is a large molecular weight (105,000) protein consisting of six subunits.

General Safety considerations:

- There have not been any known fatal lab exposures to PTX. Although extremely potent, the toxin can be safely handled with minimal risk if all of the handling procedures outlined in the laboratory's Biosafety Protocol are stringently followed.
- Exposure routes: Inhalation, oral, and parenteral (through the skin).
- After exposure to PTX, the PI and supervisor MUST notify the UW-Madison Office of Biological Safety (OBS) and UW-Madison Occupational Medicine staff. A First Report of Exposure/Release MUST be submitted within 24 hours of any exposure to PTX.
- PTX is a virulence factor contributing to infection by *B. pertussis*, which causes Whooping Cough. In combination with other virulence factors, PTX can cause a variety of symptoms, including inflammation of the airway.
- PTX is generally acquired in powdered form. Dry forms of pertussis toxin are **always** handled in a chemical fume hood or ducted certified biological safety cabinet. **Be extremely careful** when handling any amount of pertussis toxin in dry form. Only order as much as you need to use in the immediate future. Resuspend the entire vial at once rather than weighing out aliquots.
- PTX is readily inactivated by autoclaving or treatment with 10% bleach solution (0.5% sodium hypochlorite) for at least 30 minutes.
- Avoid using PTX with Sharps if at all possible.

Special considerations

- It is highly recommended that all personnel handling PTX have a current immunization for pertussis toxin (Tdap, DTap, etc.).

Biosafety Protocol

At UW-Madison, research laboratories that utilize purified pertussis toxin in their research programs must list information about use of the toxin in their Bio-ARROW protocol. Following is information about adding Pertussis Toxin to specific sections of the Bio-ARROW protocol:

Select Agents

- PTX is not a Select Agent Toxin.

Recombinant Materials

- Experiments involving genes coding any portion of pertussis toxin must be reviewed and approved by the UW-Madison IBC.

Microbes

- Microbes treated with PTX are handled at BSL2 or (if applicable) BSL3.

Biological Toxins: Biological Toxins Details

- Select Agent: No
- Botulinum Toxin: No
- Biological Toxin Select Agent Inventory: Not applicable.
- Amount: Estimated maximum total amount of PTX you will have in your laboratory
- Form: Enter all forms handled (dry/lyophilized, aqueous, etc.) and note if the dry/lyophilized form is only handled for reconstituting.
- LD50: 10 ug/kg (estimated human; parenteral)
- Biosafety Level: BSL2
- Storage only: Select “yes” only if all of the PTX in the laboratory is currently in storage and is not in active use in your research program.

Cells, Organs, Tissues, or Biological Specimens

- Cells and tissues are treated with PTX in a biological safety cabinet at BSL2. Requests to handle any amount of PTX outside of containment must be reviewed by the Office of Biological Safety and approved by the IBC.
- Treated cells or tissues are subsequently handled at BSL2.

Vertebrate Animals

- ABSL2 housing is adequate for most animal studies involving PTX. OBS staff will work with labs to determine the required biosafety level for these animals and whether administration of PTX to animals must occur in a BSC
- Note that because PTX is a very large protein toxin, rodents treated parenterally (IV, IP, subcutaneous, IM) with PTX should not excrete PTX in their urine. Thus, bedding for injected rodents should not contain PTX. However, animals treated orally with PTX potentially may excrete the toxin in their feces, and thus it might be present in the bedding.

Containment

- Aerosol Generating Activities: Unless handling of very small amounts of PTX outside of containment is approved by the IBC, the toxin must be handled within a Biological Safety Cabinet (BSC).
- Aerosol Generating Activities: Cage changes for animals treated parenterally with pertussis toxin does not require a BSC unless needed for a separate reason (also infected with a pathogen, for instance).
- Aerosol Generating Activities: Cage changes for animals treated orally with PTX must occur in a BSC.

PPE

- At minimum, lab coat, eye protection, and disposable gloves must be worn when handling PTX or PTX -treated materials.
- Depending on the research activities being performed with PTX, a fit-tested respirator (N95, etc.) may also be required.

Disinfection and Inactivation - Animal

- Because pertussis toxin is a large protein toxin, rodents treated parenterally (IV, IP, subcutaneous, IM) with pertussis toxin should not excrete the toxin in their urine. Thus, bedding for injected rodents should not contain pertussis toxin. However, animals treated orally with pertussis toxin potentially may excrete the toxin in their feces, and thus it might be present in the bedding. If bedding may contain Pertussis toxin, then bedding should be autoclaved prior to disposal.
- Carcasses of animals injected with pertussis toxin should not need to be autoclaved prior to pick-up for incineration unless they need to be autoclaved for a different reason (also infected with a Risk Group 3 pathogen, for instance).

Disinfection and Inactivation - General: Biotoxins

- PTX is inactivated by steam autoclaving or by treatment with 10% aqueous bleach solution for 30 minutes.
- Because of the potential aerosol risk, spills of PTX must include evacuation of the lab for at least 30 minutes to allow dissipation of aerosols.

Spill and Release Procedures:

- Please note that the Biosafety in Microbiological and Biomedical Laboratories (BMBL), current edition, recommends the following PPE are worn during a cleanup for a liquid toxin spill: mask, gloves, safety glasses or goggles and laboratory coat.

Signage

- A "Toxins in Use" sign is posted on the laboratory door when tetrodotoxin is being handled. The sign can be removed when no toxin is in use.
- Cage cards must specify that animals have been treated with PTX.

Occupational Health Considerations

- It is highly recommended that all personnel handling pertussis toxin have a current immunization for pertussis toxin (Tdap, DTap, etc.).

Emergency Response

- UW-Madison Occupational Medicine provides Medical Response plans for biological toxins and infectious agents through a link at <https://ehs.wisc.edu/workplace-safety/occupational-medicine-2/>.
- Emergency Response - General: In the event of exposure to PTX, immediately wash or flush the affected area with soap and water for 15 minutes. Use an eyewash for 15 minutes after a splash to the eye. After a needlestick, immediately remove gloves and

“bleed out” the wound under running water for 15 minutes. Consult UW-Madison Occupational Medicine or the UW Hospital Emergency Department ASAP after any exposure to any amount or type of pertussis toxin. Report exposures as soon as possible to the PI and/or laboratory supervisor. PI or supervisor must submit a First Report of Exposure/Release form as soon as possible, and within 24 hours.

Occupational Health Considerations

- It is highly recommended that all personnel handling PTX have a current immunization for pertussis toxin (Tdap, DTap, etc.).

Laboratory Training

- Individuals handling PTX or working in a laboratory where PTX is being handled must receive training about potential risks from exposure to the toxin as well as safe handling of the toxin as outlined in the biosafety protocol.
- A separate spill protocol specifically for PTX may be required.

Research Description

- Briefly describe what you will be doing with PTX, including the amount that may be utilized at any one time. Specify the form of PTX handled (typically aqueous).
- Specify the location(s) and biosafety level(s) for research involving PTX.
- Staff from the Office of Biological Safety (OBS) will review the potential exposure risks for research activities proposed with PTX and may require additional PPE or modified handling practices prior to the start of the research.

Contacts and Additional Information

The sources listed may provide additional information about safe use of pertussis toxin in research laboratories at UW-Madison:

- Office of Biological Safety (OBS); biosafety@fpm.wisc.edu, 608-263-2037
- Chemical Safety Department; chemsafety@fpm.wisc.edu, 608-265-5700
- Occupational Medicine; occmmed@uhs.wisc.edu, 608-265-5610
- First Report of Exposure or Release Form; <https://ehs.wisc.edu/first-report-of-biological-exposure-or-release-event/>
- Bio-ARROW KnowledgeBase; <https://kb.wisc.edu/arrow/ibc/page.php?id=43188>