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**1. PURPOSE**

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This Standard Operating Procedure (SOP) describes the guidelines for the use of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) in non-human primates, particularly marmosets.

**2. CONSIDERATIONS**

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1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) is a neurotoxin used to induce a model of Parkinson's disease in a variety of animal species. MPTP and its metabolites are known to produce irreversible and severe brain damage resulting in a parkinsonian syndrome with symptoms such as tremors, rigidity, slowness of movement and postural instability when injected, ingested, inhaled and/or absorbed.

Unsafe use of MPTP or MPTP-contaminated materials or specimens may result in neurological damage to its users.

MPTP and its toxic metabolites are excreted through the urine and feces of experimental animals. Exposure is through direct contact with the animal, the animal cage inner surfaces, and its bedding material

This SOP aims to ensure that the potential of exposure to MPTP is reduced as much as possible and that use of this agent poses no risk to research staff, animal care personnel, and other personnel working in the animal facility.

To minimize the risk of exposure, the Principal Investigator and/or delegate(s) must identify all points of hazard and put in place safe work practices for all steps involving contact with MPTP, as per procedures presented in this SOP and in consultation with the McGill Environmental Health and Safety (EHS) officer.

All hazardous agents must be listed in an approved Animal Use Protocol (AUP).

**3. RESPONSIBILITY**

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Principal investigator (PI) and their research staff, animal care staff, veterinary care staff.

**4. MATERIALS**

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**4.1. Personal protective equipment (PPE):**

- 4.1.1. NIOSH-approved, fit-tested, full face respirator or a self-contained breathing apparatus (SCBA)
- 4.1.2. N95 face mask
- 4.1.3. Tyvek® coverall with hood
- 4.1.4. Compatible chemical-resistant gloves (Nitrile)
- 4.1.5. Shoe covers
- 4.1.6. Disposable gown
- 4.1.7. Safety glasses, goggles or face shield

**4.2. Chemical fume hood or Type II B2 Biological Safety Cabinet****4.3. Absorbent pads****4.4. 1% bleach solution in water****4.5. A strong detergent****4.6. Biohazard disposal bags and boxes/containers****4.7. Deprenyl (selegiline), 5mg tablets**

## 5. PROCEDURES

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- 5.1. Prior Requirements:
  - 5.1.1. Use of MPTP must be described in the Facility Animal Care Committee (FACC) approved Animal Use Protocol (AUP). The MSDS must be attached to the AUP.
- 5.2. General precautions:
  - 5.2.1. Pregnant or breast-feeding women should not work with MPTP.
  - 5.2.2. Only investigators and/or staff members who are trained in MPTP and who are familiar with MPTP safety procedures and practices should prepare and administer MPTP, and monitor the animals during the high-risk period (i.e. 5 days post-MPTP injection).
  - 5.2.3. All containers of MPTP must be clearly labeled (ex.: MPTP - Neurotoxic) and stored as described in section 5.3 below.
  - 5.2.4. MPTP must be transported in unbreakable containers.
  - 5.2.5. Areas where MPTP is prepared and/or administered must be cleaned and decontaminated immediately following each procedure.
  - 5.2.6. Use only sterile solutions of MPTP for injection. Prepare by either filtration through a disposable 0.22 mm filter unit or by dissolving the compound in sterile saline or water. Do not autoclave MPTP solutions.
  - 5.2.7. Do not bend or recap needles. Safety needles should be used whenever possible.
  - 5.2.8. Thoroughly wash hands after handling or administering MPTP.
  - 5.2.9. Consider a preventive treatment of 5mg twice a day of deprenyl 3 to 5 days prior to and during MPTP experiments.
  - 5.2.10. In the event of accidental exposure, promptly complete a McGill University Accident, Incident & Occupational Disease Report form: <https://www.mcgill.ca/ehs/forms/forms/accident-and-incident-report>
- 5.3. Storage precautions:
  - 5.3.1. MPTP storage must be restricted to a designated area.
  - 5.3.2. Avoid large volumes or concentrated solutions.
  - 5.3.3. Vials of MPTP must be kept tightly closed until used and stored at room temperature within a secondary, unbreakable container.
  - 5.3.4. MPTP should be kept in a locked cabinet with a permanently affixed "MPTP – Neurotoxin" label. This cabinet must be secured to a non-removable surface in the dedicated area.
  - 5.3.5. Dispose of empty containers as described in section 6 below.
- 5.4. Handling and preparation of MPTP:
  - 5.4.1. Any handling of MPTP, including weighing of powder, preparation of dilutions and any procedure with the potential of producing aerosols, should be conducted in a certified chemical fume hood or in a Type II B2 Biological Safety Cabinet (BSC).
  - 5.4.2. The following personal protective equipment must be worn at all times when handling MPTP:
    - 5.4.2.1. N95 face mask
    - 5.4.2.2. 2 pairs of gloves
    - 5.4.2.3. Disposable gown
    - 5.4.2.4. Safety glasses, goggles or face shield
  - 5.4.3. PPE should be discarded as hazardous waste, see section 6 below.
  - 5.4.4. Work areas should be protected from spills by placing an absorbent pad with an impervious backing (absorbent material facing up) dampened with 1% bleach solution. Dispose of absorbent pad as a hazardous material.
  - 5.4.5. When working with powders, use of glass containers for weighing will reduce handling problems that result from the electrostatic properties of plastic.

- 5.4.6. When preparing solutions, it is recommended to wipe the exterior of containers often with 1% bleach solution.
- 5.4.7. Vials from which MPTP is drawn should have a septum or be covered with parafilm to eliminate potential aerosols and spills and to avoid drops on the needle end.
- 5.5. Administration of MPTP:
  - 5.5.1. The following PPE must be worn for MPTP administration:
    - 5.5.1.1. NIOSH-approved, fit-tested, full face respirator or a self-contained breathing apparatus (SCBA)
    - 5.5.1.2. Eye protection, i.e., face shield or goggles, depending on the model of respirator used
    - 5.5.1.3. Tyvek® coverall with hood
    - 5.5.1.4. 2 pairs of gloves
    - 5.5.1.5. Shoe covers
  - 5.5.2. Sedate or lightly anesthetize animals prior to MPTP injection. Refer to SOP 115 – NHP Anesthesia.
  - 5.5.3. Change outer pair of gloves after each injection and at the end of the injection schedule.
  - 5.5.4. Inspect injection sites for leakage or spilled solution and wipe with a small pad dampened with 1% bleach solution.
  - 5.5.5. When discarding syringes, do not clip, recap or remove needles from syringes. Before discarding, fill the syringe with 1% bleach solution and then place the syringe with attached needle in a sharps container to be disposed of as hazardous waste.
  - 5.5.6. At the end of the injection schedule, the remaining MPTP solution must be destroyed with an equivalent volume of 1% bleach solution.
  - 5.5.7. Dispose of empty containers as described in section 6 below.
- 5.6. Animal Handling and Husbandry:
  - 5.6.1. Research staff must inform the animal facility supervisor and veterinary care staff at least 2 week before administering MPTP to animals. This will ensure adequate preparation and availability of necessary equipment provided by the animal facility (e.g., disposal container, PPE, absorbent pads).
  - 5.6.2. Clearly indicate the hazard on the room door and place a warning sign. The room must remain locked at all times.
  - 5.6.3. The following PPE must be worn during the high risk period:
    - 5.6.3.6. NIOSH-approved, fit-tested, full face respirator or a self-contained breathing apparatus (SCBA)
    - 5.6.3.7. Eye protection, i.e., face shield or goggles, depending on the model of respirator used
    - 5.6.3.8. Tyvek® coverall with hood
    - 5.6.3.9. 2 pairs of gloves
    - 5.6.3.10. Shoe covers
  - 5.6.4. The entire floor of the procedure room or working area in the animal room should be covered with plastic-backed absorbent sheets.
  - 5.6.5. All cages housing animals that have been treated with MPTP must be clearly labeled with the following information:
    - 5.6.5.1. Name of agent
    - 5.6.5.2. Date of administration
  - 5.6.6. Interior surfaces of the cage, the surfaces that the animals and/or their excreta could physically touch, including food and drinking bottle, are to be considered contaminated for 5 days post-injection.
  - 5.6.7. Animals injected with MPTP should remain in the same cage for at least 5 days post-injection.
  - 5.6.8. Line cage bottoms and trays with plastic-backed absorbent pads.

- 5.6.9. Animal cages must be cleaned daily:
  - 5.6.9.1. Removed soiled pads lining the cage bottoms and place them in the hazardous waste container; replace used linings with fresh pads.
- 5.6.10. Counter tops in the procedure room or area should be decontaminated with 1% bleach solution.
- 5.6.11. Floor coverings should be carefully removed when necessary and disposed of as hazardous waste.
- 5.6.12. Routine animal care can be re-instituted five days post last MPTP injection and once the procedure room and housing area have been thoroughly cleaned.
- 5.6.13. All items contaminated or potentially contaminated with MPTP (e.g. cages, needles, gloves, absorbent pads) must be discarded as hazardous materials or decontaminated with 1% bleach and cleaned.
- 5.7. Small spills and leakage:
  - 5.7.1. Use absorbent pads to soak up all liquid spill material.
  - 5.7.2. Immediately spray the pads with 1% bleach solution, allow to soak for 10 minutes, then remove, and place these in hazardous waste disposal bags.
  - 5.7.3. The dry area is then soaked with 1% bleach solution, rinsed with water, then washed several times with detergent, rinsed with water, and dried with pads. Discard all materials in hazardous waste bags.
  - 5.7.4. To clean powder spills, cover with a disposable towel dampened with 1% bleach solution, then pick up all materials and put into a hazardous waste container. Soak the area with 1% bleach solution, rinse with water, then wash several times with detergent, rinse with water, and dry with pads. Discard all materials in hazardous waste bags.
  - 5.7.5. If clothes become contaminated with MPTP, immediately remove clothing and shower. Report directly to a medical service.
- 5.8. In case of accidental exposure:
  - 5.8.1. Potential routes of exposures include: inhalation, eye contact, skin absorption, ingestion and unintentional injection.
  - 5.8.2. Report the incident immediately to your supervisor. A McGill University Accident, Incident & Occupational Disease Report form must be completed: <https://www.mcgill.ca/ehs/forms/forms/accident-and-incident-report>
  - 5.8.3. Splash in eyes:
    - 5.8.3.1. Flush eyes with water or normal saline solution for 20 to 30 minutes.
  - 5.8.4. Skin exposure:
    - 5.8.4.1. Immediately flush affected skin with water while removing and isolating all contaminated clothing.
  - 5.8.5. Ingestion:
    - 5.8.5.1. Do not induce vomiting. Volatile chemicals have a high risk of being aspirated into the lungs during vomiting which increases the medical problems.
    - 5.8.5.1. If the victim is conscious and not convulsing, give 1 or 2 glasses of water to dilute the chemical and immediately call a hospital or poison control center.
    - 5.8.5.2. If the victim is convulsing or unconscious, do not give anything by mouth, ensure that the victim's airway is open and lay the victim on his/her side with the head lower than the body. Immediately seek emergency medical care.
  - 5.8.6. MAO-B inhibitors, such as deprenyl, prevent the conversion of MPTP to its toxic metabolite, thereby preventing neurotoxicity. Four 5mg deprenyl tablets may be administered immediately after accidental exposure.
  - 5.8.7. Consult a physician following accidental exposure.

5.9. Preparation of 1% bleach solution:

- 5.9.1. Wear personal protective equipment when preparing and using disinfectant solution.
- 5.9.2. Mix 1 part 5% chlorine bleach with 4 parts water.
- 5.9.3. Label all storage containers.

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**6. WASTE DISPOSAL**

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- 6.1. Animal carcasses must be double-bagged before disposal.
- 6.2. All disposal containers must be labeled "MPTP - Neurotoxin".
- 6.3. All items contaminated or potentially contaminated with MPTP (e.g., absorbent pads, PPE) must be discarded in double biohazard bags, biohazard boxes or rigid containers for incineration.
- 6.4. Any vials or containers with remaining MPTP solution must be destroyed with an equivalent volume of 1% bleach solution prior to disposal.
- 6.5. Containers are disposed of by incineration through the Waste Management department.

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**7. REFERENCES**

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- 7.1. Przedborski S, Jackson-Lewis V, Naini AB, Jakowec M, Petzinger G, Miller R, Akram M. "The parkinsonian toxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP): a technical review of its utility and safety". *Journal of Neurochemistry* 76, 1265-1274 (2001).
- 7.2. National Institutes of Health (NIH), Office of Research Services, Division of Occupational Health and Safety: Procedures for Working with MPTP or MPTP-Treated Animals:  
[http://www.ors.od.nih.gov/sr/dohs/Documents/Procedures\\_for\\_Working\\_with\\_MPTP\\_or\\_MPTP\\_Treated\\_Animals.pdf](http://www.ors.od.nih.gov/sr/dohs/Documents/Procedures_for_Working_with_MPTP_or_MPTP_Treated_Animals.pdf)

**SOP REVISION HISTORY**

DATE OF MODIFICATION	DETAILS
March 2016	Updated links to EHS forms