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A. Purpose

This SOP describes the personnel training, occupational medicine and safety precautions required for use with MPTP and MPTP-treated animals at the University of Southern California.

B. MPTP Information

MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) is a prodrug to the neurotoxin MPP⁺ commonly used to induce parkinsonism symptoms in experimental animal models of Parkinson's disease (PD) by destroying the dopamine-producing neurons of the substantia nigra. Exposure to MPTP can produce irreversible neurological damage indistinguishable from PD in humans and animals. The inappropriate handling of MPTP may result in exposure and irreversible neurological damage to research staff.

Excretion of un-metabolized MPTP can occur during the first day post injection and MPTP metabolites can be excreted up to five days post injection. Excretion is mainly in the urine. MPTP metabolites in the urine are not considered volatile and will be absorbed by the bedding.

Likely exposure routes for researchers are needle sticks, aerosolized droplets, skin exposure, or inhalation of aerosols from MPTP-contaminated bedding. Exposure potential is greatest during preparation, administration and when handling animal bedding during the first 72 hours after administration.

C. Acronyms

DAR	Department of Animal Resources
EH&S	Environmental Health and Safety
MPTP	1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine
MPP ⁺	1-methyl-4-phenylpyridium
PD	Parkinson's disease
PI	Principal Investigator
PPE	Personal Protective Equipment
SOP	Standard Operating Procedure

D. Prior to beginning work with MPTP

1. Training Requirements

All staff that will be using or handling MPTP must be trained by the PI in the proper procedures to safely work with MPTP and MPTP-treated animals. Refresher training is required annually. All initial and refresher training shall be documented with the name of the PI or trainer, date of training, attendees' signatures and list of topics covered (see Appendix 1)

Training will cover at a minimum the following topics:

- ☐ Hazards associated with the use of MPTP
- ☐ Procedures for preparing MPTP solutions including engineering controls such as a functioning fume hood and PPE requirements
- ☐ Procedures for the proper transport of MPTP solutions between labs
- ☐ Procedures for the proper administration of MPTP to animals including engineering controls and PPE requirements
- ☐ Procedures for the proper notification and signage of MPTP work in animal housing and procedure rooms
- ☐ Procedures for the proper disposal of contaminated bedding and animal carcasses within the first 72 hours post MPTP administration
- ☐ Procedures for the proper disposal of other MPTP waste that may be generated, i.e. remaining MPTP solution or contaminated PPE
- ☐ Procedures for proper work area decontamination
- ☐ Procedures for proper spill and emergency procedures

2. Occupational Medicine Requirements

All staff that will be using or handling MPTP must be enrolled with Occupational Medicine Program through EH&S. Staff must have a medical evaluation prior to the start of MPTP work and annually thereafter to ensure there are no contraindications for the use of Selegiline hydrochloride (post exposure prophylaxis for MPTP). The Selegiline is to be obtained prior to MPTP work begins and shall be immediately available for use in case of exposure. Selegiline shall be stored in a secondary container with the label "FOR MPTP USE ONLY" and must be checked periodically to ensure it has not expired.

Each staff member must have medical clearance and prescription prior to MPTP work (see Appendix 2).

E. Laboratory Set-up

1. MPTP Preparation

- ☐ MPTP as received from the manufacturer must be stored in a labeled, sealed leak- proof secondary container or other IBC-approved manner.
- ☐ MPTP solutions are to be stored in a freezer in similar manner with a sealed, leak proof, secondary container.
- ☐ The fume hood and the secondary container must both be labeled with the proper hazard label, i.e. neurotoxin (see Appendix 3).
- ☐ If solutions of MPTP must be prepared from powdered form, IBC-approval required.
- ☐ Disposable lab ware should be used with MPTP solutions. If non-disposable plasticware is used it must be triple rinsed with 1% bleach prior to washing. The effluent must be collected and disposed of as liquid chemical waste.

2. PPE Requirements

The following PPE is required while working with MPTP:

- ☐ Disposable closed front gown
- ☐ Double gloves
- ☐ Hair bonnet
- ☐ Safety goggles or face shield
- ☐ Shoe booties

PPE shall be removed prior to leaving MPTP designated space.

Frequent glove changes are recommended, as needed.

Damaged or contaminated PPE should be changed immediately and disposed as solid chemical waste.

F. Administration to Animals

1. Injections of MPTP to mice

- ☐ Rodents are mechanically restrained prior to starting the MPTP administration
- ☐ Administration to rodents must take place in a certified fume hood
- ☐ Researchers administering the MPTP or working nearby must be wearing the appropriate PPE
- ☐ All work surfaces must be covered with absorbent plastic backed pads
- ☐ Safety engineered disposable needles must be used
- ☐ Syringes and needles are immediately placed into a sharps container after use
- ☐ All absorbent pads are removed once work is completed and placed in a chemical solid waste container
- ☐ PPE is removed and placed in a chemical solid waste container.
- ☐ Solid waste such as absorbent pads or PPE that contained or has been contaminated with MPTP is placed in a leak proof solid chemical waste container and labeled as "MPTP WASTE" (Appendix 4)

2. Animal Rooms, Cages, and Cage Signage

- ☐ *Dust-free bedding or disposable cages* must be used with animals treated with MPTP.
- ☐ Blue cage cards are displayed with MPTP and the date of injection as well as "DO NOT HANDLE;" blue cage cards are displayed for 7 days post injection as per DAR SOPs and the "DO NOT HANDLE" label will be displayed for 72 hours post injection.
- ☐ The chemical hazard sign for MPTP must be placed on the door to the housing room of animals injected with MPTP and removed after 72 hours when no hazard risk exists.

3. First Cage Change for Animals Treated with MPTP (Contaminated Bedding)

- ☐ Cages must NOT be changed for 72 hours post MPTP injection
- ☐ The first cage change after injection is to be done in a certified fume hood or Type II B2 BSC by research personnel
- ☐ Research personnel must be wearing the appropriate PPE
- ☐ All work surfaces must be covered with absorbent plastic backed pads
- ☐ Animals are placed into a clean cage
- ☐ The outside of the cages with bedding inside are sprayed with 1% bleach and allowed to dry.
- ☐ The dust-less bedding is disposed in a chemical solid waste container
- ☐ Absorbent pads and all solid materials are removed from the work area and disposed into a chemical

- solid waste container
- ☐ PPE is removed and placed in the chemical solid waste container.

4. Subsequent Cage Changes for Animals Treated with MPTP (Non-Contaminated Bedding)

- ☐ Cage changes after the first 72 hours may be performed as conventional cage changes

5. Disposal of Animal Carcasses

- ☐ Carcasses that have received MPTP within the last 72 hours must be disposed placed in a clear plastic bag, then placed in a freezer, for pick up by EH&S as chemical waste
- ☐ Three days post injection carcasses shall be disposed as conventional animals

G. Spill and Emergency Procedures

1. In the event of a *known* percutaneous or mucous membrane exposure to MPTP

- ☐ Immediately take the indicated dose of Selegiline as directed by prescribing physician
- ☐ Initiate first aid at the worksite:
 - ☐ Contaminated skin should be washed with soap and water for at least 15 minutes
 - ☐ Contaminated eyes and mucous membranes should be irrigated for at least 15 minutes
- ☐ Go directly to the nearest approved medical center: <https://ehs.usc.edu/usc-approved-medical-facilities/> (see Appendix 5)
- ☐ Notify EH&S and the PI as soon as safely possible

2. In the event of a *suspected* exposure to MPTP

- ☐ Immediately take indicated dose of Selegiline as directed by prescribing physician
- ☐ Go directly to the nearest approved medical center: <https://ehs.usc.edu/usc-approved-medical-facilities/>
- ☐ Notify EH&S and the PI as soon as possible

3. Spill procedures inside a fume hood

- ☐ Remove any contaminated PPE and place it in the solid chemical waste container
- ☐ Wash hands for 15 minutes and replace PPE
- ☐ Clean up the spill with 1% bleach made fresh and absorbent material, i.e. paper towels
- ☐ Remove plastic backed pads into the chemical waste container
- ☐ Clean all exposed environmental surfaces with 1% bleach
- ☐ Dispose of all contaminated waste and clean-up materials as hazardous chemical waste
- ☐ Replace work surface with plastic backed absorbent pads

4. Spill procedures outside a fume hood? (bedding or other spill)

- ☐ Remove any contaminated PPE and replace
- ☐ Restrict access to the area
- ☐ Cover the spill with absorbent material if liquid based, i.e. paper towels
- ☐ Pour 1% fresh bleach solution in spiral motion working from the outside to inside of spill area, allow the liquid to sit for 30 minutes

- ☐ Collect absorbent material and wipe excess liquid treating all contaminated material as hazardous chemical waste

H. References

- Przedborski, S., Jackson-Lewis, V., Naini, A., Jakowec, M., Petzinger, G., Miller, R., and Arkam, M. (2001) The parkinsonian toxin 1-methy-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP): a technical review of its utility and safety. *Journal of Neurochemistry*, 76, 1265-1274.
- Jackson-Lewis, V. and Przedborski, S. (2007) Protocol for the MPTP mouse model of Parkinson's disease. *Nature Protocols*. 2(1), 141-151.
- Procedures for Working with MPTP (1-methy-4-phenyl-1,2,3,6-tetrahydropyridine) and MPTP Treated Animals. University of Washington 11/2013.
- Selegiline Drug Information from PubMed Health:
<https://www.ncbi.nlm.nih.gov/pubmedhealth/PMHT0012098/?report=details#warning>

Appendix 2

Selegiline Information from PubMed Health

Published: April 1, 2017

Selegiline (By mouth)

se-LE-ji-leen

Treats [Parkinson disease](#). This medicine is an MAOI.

Drug classes

Antiparkinsonian ([About this - PubMed Health](#))

Uses

Uses of This Medicine

- Selegiline is used in combination with levodopa or levodopa and carbidopa combination to treat Parkinson's disease (sometimes called shaking palsy or paralysis agitans). This medicine works to increase and extend the effects of levodopa, and may help to slow the progress of Parkinson's disease.
- This medicine is available only with your doctor's prescription.

How To Use

- Capsule, Tablet, Dissolving Tablet
- Utility of MOA-B inhibitors against toxin exposure has not been evaluated in humans. Protection in animal models is based on large doses (20 mg/kg) administered either prior to or immediately after MPTP lesioning (20-30 mg/kg doses)

Drugs and Foods to Avoid

- You must avoid many other medicines while you are using Selegiline. These medicines used together could cause serious health problems, including death. Ask your doctor before you use any other medicine. You may need to wait 1 to 5 weeks before you can use the other medicine.
- Do not use Selegiline if you are also using cyclobenzaprine, dextromethorphan, meperidine, methadone, propoxyphene, St John's wort, or tramadol. Do not use this medicine if you have used another MAO inhibitor within the past 14 days.
- Some other medicines that may interact with Selegiline include carbamazepine, nafcillin, phenobarbital, phenytoin, rifampin, cough and cold medicine (such as dextromethorphan, ephedrine), or medicine to treat depression or mental health problems. This is not a complete list.

When Not To Use

- This medicine is not right for everyone. Do not use it if you had an allergic reaction to Selegiline.

Warnings

- Tell your doctor if you are pregnant or breastfeeding, or if you have kidney problems, liver problems, dyskinesia, high blood pressure, or a history of mental health problems. Tell your doctor if you have phenylketonuria (PKU).

This medicine may cause the following problems:

- High or low blood pressure
- Serotonin syndrome (when used with other medicines)

- Dyskinesia (trouble controlling movements)
- Unusual changes in behavior, compulsive behavior, hallucinations
- Increased risk of skin cancer
- This medicine may make you drowsy. It may even cause you to fall asleep without warning while you are driving or doing other activities. Do not drive or do anything that could be dangerous until you know how this medicine affects you. Stand up slowly if you feel dizzy or lightheaded.
- Do not stop using this medicine suddenly. Your doctor will need to slowly decrease your dose before you stop it completely.
- Your doctor will check your progress and the effects of this medicine at regular visits. Keep all appointments.
- Keep all medicine out of the reach of children. Never share your medicine with anyone.

Possible side effects

Summary

Call your doctor right away if you notice any of these side effects:

- Allergic reaction: Itching or hives, swelling in your face or hands, swelling or tingling in your mouth or throat, chest tightness, trouble breathing
- Anxiety, restlessness, fever, sweating, nausea, vomiting, diarrhea, seeing or hearing things that are not there
- Chest pain, fast, slow, or uneven heartbeat, severe headache
- Confusion, unusual changes in mood or behavior, behaviors you cannot control
- Lightheadedness, dizziness, fainting
- Muscle spasms, twitching, uncontrolled movements (especially of the face, neck, or back)
- Unusual drowsiness or sleepiness
- If you notice these less serious side effects, talk with your doctor:
- Headache
- Mild nausea, upset stomach
- Pain when swallowing, swelling, redness, or sores in the mouth
- If you notice other side effects that you think are caused by this medicine, tell your doctor.
- Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.
- [More side effects of this drug](#)

Brand names include

- Eldepryl, Zelapar
- There may be other brand names for this medicine.

<https://www.ncbi.nlm.nih.gov/pubmedhealth/PMHT0012098/?report=details#warning>

Appendix 3

The following sign should be posted on the fume hood where MPTP preparation and work will be conducted:



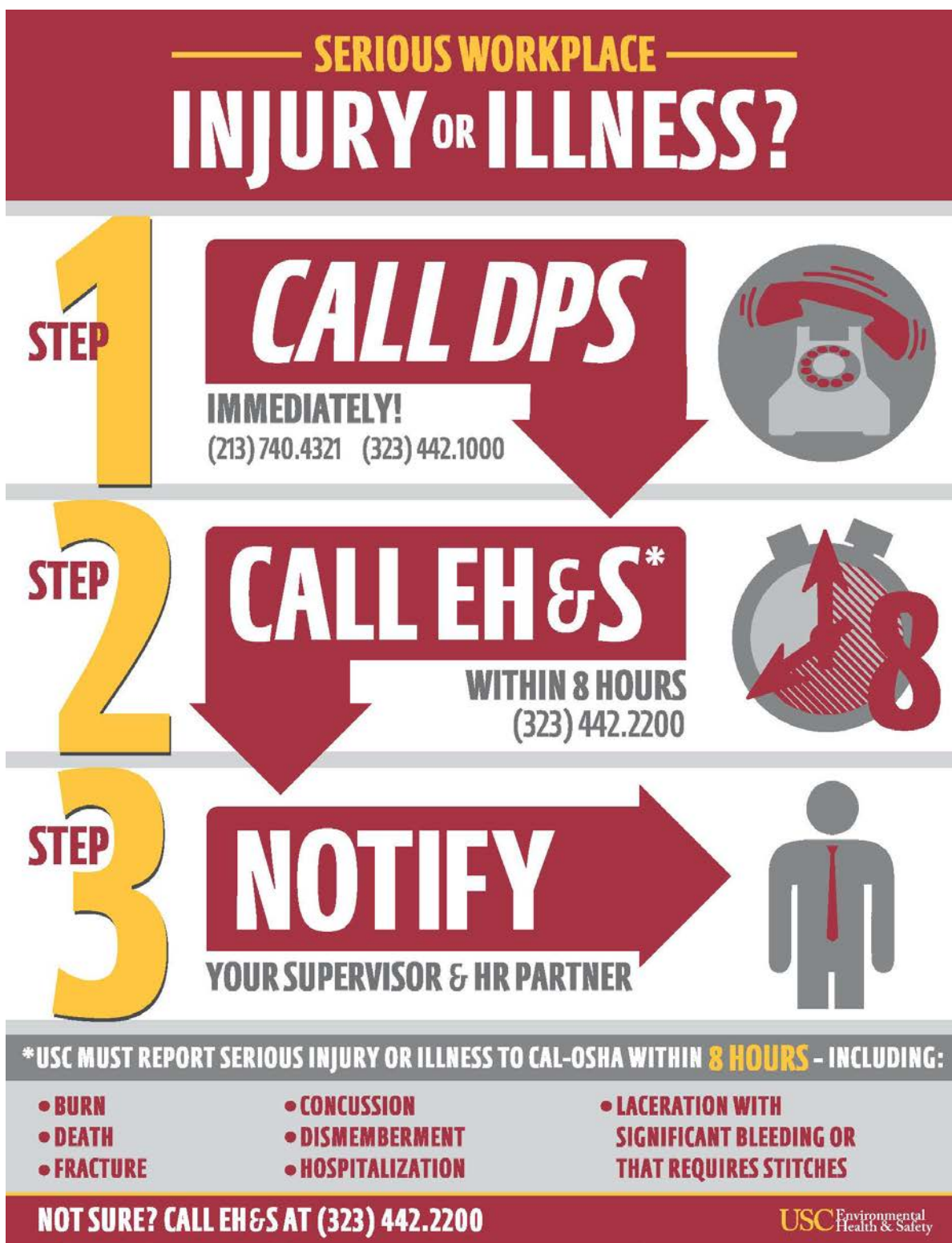
Appendix 4

Appropriate waste containers for MPTP solid waste include:

The following sign should be posted on all waste containers for MPTP waste:



Appendix 5



PDF version: <https://ehs.usc.edu/files/1-2-3-Serious-Injury-Reporting-flyer.pdf>