



**RISK ASSESSMENT BY AGENT: 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)**

CHARACTERISTICS	
<b>Type</b>	Biological neurotoxin
<b>Risk Group</b>	Risk group 2
<b>Natural Source</b>	A byproduct of the synthesis of 1-methyl-4-phenyl-4-propionoxypiperidine (MPPP). This meperidine analog had been synthesized in 1947 by Ziering and Lee.
<b>Laboratory Source</b>	Solid lyophilized powder in sealed bottle (with needle puncture top).
<b>Characteristics</b>	MPTP is a neurotoxin that selectively targets dopaminergic neurons leading to inhibition of complex I activity of mitochondria.

HAZARDS	
<b>Route of entry</b>	Hazard statement(s): Toxic if swallowed. Causes damage to organs (Nervous system). Precautionary statement(s) Do not breathe dust/ fume/ gas/ mist/ vapors/ spray. Wash skin thoroughly after handling. Do not eat, drink or smoke when using this product. IF SWALLOWED: Immediately call a POISON CENTER/ doctor. Rinse mouth. IF exposed or concerned: Call a POISON CENTER/ doctor.
<b>Signs and Symptoms</b>	Acute damage to the nervous system: bradykinesia, rigidity, postural/resting tremor, flexed posture, gait disturbances, loss of postural reflexes, loss of facial expression, drooling, speech disturbances, micrographia and seborrhea.
<b>Toxicity Dose Data</b>	Rat: LD <sub>50</sub> = <b>72 mg/kg (i.p.)</b> Mouse: LD <sub>50</sub> = <b>53.8 mg/kg (s.c.)</b> Mouse LD <sub>50</sub> = <b>150 mg/kg (oral)</b> Lowest toxic dose/duration, mouse: <b>150 mg/kg/5D-1 (i.p.)</b> Lowest published dose, rodent embryos: <b>40 mg/kg (i.p.); 25 mg/kg (s.c.); 35 mg/kg (i.m.)</b> No data available for humans.
<b>Metabolism Data</b>	There is minimal risk to animal caretakers as the amount of unmetabolized MPTP/MPP <sup>+</sup> excreted by the injected mice (i.c.v., microgram doses) is likely to be extremely low.

EXPOSURE CONTROLS / PERSONAL PROTECTION	
<b>Containment</b>	BSL-2, fume hood.
<b>PPE</b>	Lab coat, nitrile gloves (CE-approved) and safety goggles.
<b>Animal +PPE</b>	Yellow gown and surgical mask.
<b>Biohazardous Waste Management</b>	<b>Solid Waste:</b> Place in a bag and container provided by EHS and place in biohazardous waste boxes for off-site treatment. <b>Liquid:</b> Treat waste with bleach (1:10) for 15-30 minutes in a screw-cap container. Wrap in a bag, place in a biohazardous waste box for off-site disposal/treatment. <b>Animal Carcasses:</b> Place into biohazardous bags labelled in the freezer (non-food, necropsy room freezer) for off-site treatment. <b>Sharps:</b> Place all sharps, vials, Eppendorf tubes and pipette tips in a puncture proof sharps container.
<b>Lab Work Practices</b>	Do not work with toxin in a solid state. Do not open the container of MPTP (all reagents should be injected into the container to reconstitute the solution). ABSOLUTELY NO RECAPPING OF NEEDLES. Needles are immediately disposed of in the appropriate sharps container. Handle the MPTP bottle in a fume hood with appropriate PPE over a disposable work surface. To reconstitute the drug, the bottle/container is moved to a fumehood, and the bottle is never opened. Instead, the drug comes with a puncture top, allowing for reconstituion with DMSO, PEG and saline using a syringe without exposing the contents of the container to the air. Solutions of MPTP will be labeled with "MPTP Danger Acutely Toxic." Collect all disposable materials in a wide-mouth container (provided by EHS). Use a 10% bleach solution for cleaning (15 mins for a clean surface, 30+ minutes for spill; followed by a water rinse to decontaminate areas). Wash hands immediately after all handling of MPTP items. The MPTP vial is never exposed to the air, only extracted with the use of sterile Hamilton syringes/needles for stereotaxic surgery. Air is to be discharged from a filled syringes into absorbent padding to prevent splashing, then saturated with 10% bleach solution after use, then dispose of as chemical waste.

<b>Animal Work Practices</b>	House animals in disposable cages, and do not change cages or bedding for 72 hours post-surgery. After this period, bag and dispose of cage and bedding as <u>chemical waste</u> . All cages will be labelled properly for proper cleaning/disposal for DVR staff. After this time, animals can be re-housed in standard rodent housing with enrichment. For surgeries, MPTP will be loaded directly into the Hamilton syringe in the stereotaxic apparatus using an infusion pump (needle is lowered using the arms of the apparatus so user never comes close to the needle) and then directly infused into specific brain regions along the nigrostriatal region. Needles will be cleaned for 15 minutes with a 10% bleach solution, rinsed with a water solution before continuing with the next surgery. After each surgery, all disposable material is collected, bagged and disposed of as chemical waste. Any sharps used during surgery will be placed in a sharps container provided by EHS. Again, NO recapping of needles are permitted. Further, needles must not be bent, sheared, broken, recapped, removed from disposable syringes, or otherwise manipulated before disposal.
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	swallowed: give water to drink (two glasses at most). Seek medical advice immediately. In exceptional cases only, if medical care is not available within one hour, induce vomiting (only in persons who are wide awake and fully conscious), administer activated charcoal (20 - 40 g in a 10% slurry) and consult a doctor as quickly as possible.
<b>Reporting</b>	Report all incidents to the DVR Director, IACUC and Employee Health immediately. Notify Biosafety: 305-243-3269.

STABILITY AND VIABILITY	
<b>Disinfectants</b>	10% Bleach
<b>Physical Inactivation</b>	DO NOT AUTOCLAVE ANY MPTP BOTTLES/SOLUTIONS. Only use bleach solutions for cleaning and water to rinse.

FIRST AID / MEDICAL	
<b>First Aid or Treatment</b>	Immediately ingest four (4) selegiline HCl 5 mg capsules. Initiate first aid at the worksite
<b>Prophylaxis</b>	PPE as advised.
<b>Immunization</b>	N/A

EMERGENCY PROCEDURES	
<b>Minor Spills</b>	Notify others working in the lab. Cover area of the spill with absorbent pads and apply bleach solution, working from the perimeter towards the center. Allow at least 15 minutes of contact time. Rinse well with water and cleanup and dispose of spill materials.
<b>Major Spills</b>	Evacuate the laboratory and call EHS Biosafety: 305-243-3269.
<b>Exposures</b>	<b>Ocular</b> In case of eye contact: rinse out with plenty of water (15 minutes at eye wash station minimum). Call in ophthalmologist. Remove contact lenses.
	<b>Full body</b> In case of skin contact: Take off immediately all contaminated clothing. Rinse skin with water/shower (15 minutes minimum). Call a physician immediately.
	<b>Other</b> If inhaled After inhalation: fresh air. Immediately call physician. If breathing stops: immediately apply artificial respiration, if necessary also oxygen. If

REFERENCES	
<b>BMBL: 6th Edition</b>	<a href="https://www.cdc.gov/labs/pdf/SF_19_308133-A_BMBL6_00-BOOK-WEB-final-3.pdf">https://www.cdc.gov/labs/pdf/SF_19_308133-A_BMBL6_00-BOOK-WEB-final-3.pdf</a>
<b>Canadian PSDS</b>	<a href="https://cdn.caymanchem.com/cdn/msds/16377m.pdf">https://cdn.caymanchem.com/cdn/msds/16377m.pdf</a> <a href="https://ehrs.upenn.edu/health-safety/lab-safety/chemical-hygiene-plan/fact-sheets/fact-sheet-mptp-safe-handling">https://ehrs.upenn.edu/health-safety/lab-safety/chemical-hygiene-plan/fact-sheets/fact-sheet-mptp-safe-handling</a>
<b>CDC</b>	<a href="https://www.cdc.gov/niosh/nioshtic-2/20034837.html">https://www.cdc.gov/niosh/nioshtic-2/20034837.html</a> <a href="https://www.cdc.gov/mmwr/preview/mmwrhtml/00000360.htm">https://www.cdc.gov/mmwr/preview/mmwrhtml/00000360.htm</a>