MATERIAL SAFETY DATA SHEET

SECTION 1: CHEMICAL SUBSTANCE

PRODUCT NAME: Ipratropium Bromide Inhalation Solution, 0.02%

CHEMICAL NAME: 8-azoniabicyclo[3.2.1]-octane, 3-(3-hydroxy-1-oxo-2-phenylpropoxy)-8-methyl-8-(1-methylethyl)-, bromide, monohydrate (endo, syn)-,(±)-

GENERIC NAME: Ipratropium Bromide Monohydrate

MOLECULAR FORMULA: C_{20}H_{30}BrNO_3\cdot H_2O

MOLECULAR WEIGHT: 430.4

CAS NUMBER: 22254-24-6

PRODUCT USE: Bronchodilator

SYNONYMS: Sch 1000, Itrop, Ipratropiumbromide (German)

SECTION 2: COMPONENTS PER UNIT DOSE

<table>
<thead>
<tr>
<th>MATERIAL</th>
<th>EXPOSURE LIMITS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active Ingredient:</td>
<td></td>
</tr>
<tr>
<td>Ipratropium Bromide Monohydrate</td>
<td>2 \mu g/m^3**</td>
</tr>
<tr>
<td>Excipients:</td>
<td></td>
</tr>
<tr>
<td>Sodium Chloride</td>
<td>No TLV established*</td>
</tr>
<tr>
<td>Purified Water, USP</td>
<td>No TLV established*</td>
</tr>
<tr>
<td></td>
<td>*As per 1997 ACGIH</td>
</tr>
</tbody>
</table>

** This is a preliminary exposure control level. Where governmentally imposed occupational exposure limits which are lower than the PECL are in effect, such limits should take precedence.
SECTION 3: HAZARD IDENTIFICATION

EMERGENCY OVERVIEW

For Product:

Clear, colorless liquid.
Warning! May cause allergic reactions such as skin rashes, hives, bronchospasm, or swelling of the lips, tongue and throat. Contact with eyes causes pain, temporary blurring of vision or glaucoma. Will not burn. If involved in a fire, material emits toxic fumes. Use extinguishing media suitable for the material that is burning.

For Active Ingredient:

White to off-white crystalline powder.
May cause eye irritation - May be harmful if absorbed through the skin
May be harmful if swallowed

ROUTES OF ENTRY: Inhalation, Ingestion, Skin and Eye contact.

TARGET ORGANS: Liver, GI tract, adrenals, male reproductive organs and eyes.

For Product:

CONTRAINDICATIONS: Although rare, this product can cause immediate hypersensitivity in patients. Therefore, this product should not be used by patients who have had a previous allergic reaction to ipratropium bromide or to atropine and its derivatives.

ADVERSE REACTIONS TO PRODUCT: Headache, swelling of lips and tongue, upper respiratory tract infection, epistaxis (nosebleed), rhinitis (nasal discharge/irritation), nasal dryness, blood tinged nasal mucous, pharyngitis (sore throat), nausea, blurred vision, and increased sensitivity to light.

WARNING:

Direct eye contact with product may cause temporary blurring of vision, precipitation or worsening of narrow-angle glaucoma or eye pain. If these symptoms occur, contact your physician.

Immediate hypersensitivity (allergic) reactions may occur after use such as urticaria (hives), angioedema (giant hives), bronchospasm (spasms of the lung's bronchial tubes), oropharyngeal edema (swelling of the lips, tongue and throat) and rash.

For Active Ingredient:

ACUTE EXPOSURE: Eye, skin and/or respiratory irritation.

SIGNS AND SYMPTOMS OF EXPOSURE: Headache, swelling of lips and tongue, epistaxis (nosebleed), rhinitis (nasal discharge/irritation), nasal dryness, blood tinged nasal mucous, pharyngitis (sore throat), nausea, blurred vision, and increased sensitivity to light.
CHRONIC EXPOSURE: Possible hypersensitization (development of abnormal sensitivity).

MEDICAL CONDITIONS POTENTIALLY AGGRAVATED BY EXPOSURE: Dust allergies, pre-existing hypersensitivity (allergic reaction) to any of the product’s components, narrow angle glaucoma, prostatic hypertrophy, bladder neck obstruction, hepatic (liver) or renal (kidney) dysfunction.

CARCINOGENICITY: Not listed as carcinogen/potential carcinogen by NTP, IARC Monographs or OSHA.

SECTION 4: EMERGENCY FIRST AID PROCEDURES

Persons developing anaphylactic (life-threatening) reactions, such as difficulty in breathing or unconsciousness, must receive immediate medical attention.

INGESTION: Rinse mouth out with large amounts of water. Do not induce vomiting or give anything by mouth to an unconscious or convulsing person. Seek immediate medical attention.

INHALATION: Remove affected person to a well-ventilated area and get immediate medical attention. If breathing becomes difficult, give oxygen. If breathing stops, give artificial respiration.

SKIN CONTACT: Remove contaminated clothing. Flush affected area with copious amounts of soap and water. If irritation or rash develops, get medical attention.

EYE CONTACT: Remove contact lenses if necessary. Flush eyes with large amounts of running water for at least 15 minutes. Seek medical attention if blurred vision or sensitivity to light occurs.

NOTE TO PHYSICIAN: Acute systemic overdose by inhalation is unlikely since Ipratropium Bromide Inhalation Solution is not well absorbed after inhalation at up to four-fold the recommended dose, or after oral administration at up to forty-fold the recommended dose. Treat symptomatically.

SECTION 5: FIRE AND EXPLOSION HAZARD DATA

<table>
<thead>
<tr>
<th>Flash Point</th>
<th>Flammable Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/A</td>
<td>Upper N/A</td>
</tr>
<tr>
<td></td>
<td>Lower N/A</td>
</tr>
</tbody>
</table>

FIRE EXTINGUISHING MEDIA: Water spray, dry chemical, carbon dioxide or foam as appropriate for surrounding fire and materials.

SPECIAL FIRE FIGHTING PROCEDURES: As with all fires, evacuate personnel to safe area. Firefighters should use self-contained breathing equipment and protective clothing. Use water spray to keep fire-exposed containers cool and protect against all exposures.

UNUSUAL FIRE AND EXPLOSION HAZARDS

For Product: None known.

For Active Ingredient: Dust can be explosive.
SECTION 6: SPILL AND ACCIDENTAL RELEASE MEASURES

STEPS TO BE TAKEN IN THE EVENT OF A SPILL: Wear approved respirator and chemically compatible gloves if containers have been compromised. Vacuum or sweep up spillage. Avoid creating dust. Place spillage in appropriate container for waste disposal. Wash contaminated clothing before reuse. Ventilate area, wash down spill site, and control wash water.

SECTION 7: PRECAUTIONS FOR SAFE HANDLING AND USE

For Product:

HANDLING AND STORAGE PRECAUTIONS: Avoid contact with eyes, skin or clothing. Avoid breathing dust or vapors. Avoid freezing. Store in airtight container between 59°F (15°C) and 86°F (30°C). Protect from light. Store unused vials in the foil pouch. KEEP OUT OF REACH OF CHILDREN.

For Active Ingredient:

HANDLING AND STORAGE PRECAUTIONS: Avoid contact with eyes, skin or clothing. Avoid breathing dust or vapors. Avoid generating dust. Store in airtight container. Protect from light and extreme heat.

OTHER PRECAUTIONS: Wash thoroughly after handling material. Wear fresh clothing daily. Wash contaminated clothing before reuse.

SECTION 8: CONTROL MEASURES

ENGINEERING CONTROLS: Minimize dust generation. Use closed equipment where possible. Use spot ventilation to remove dust from the work area. If operations generate dusts, use explosion-proof ventilation equipment to control airborne levels. (See section 2 for exposure limits.) Use appropriate respiratory protection based on an industrial hygiene survey.

RESPIRATORY PROTECTION: The need for respiratory protection should be determined by an industrial hygiene survey. (See section 2 for exposure limits.) NIOSH/MSHA approved respirators for protection should be used if respirators are found to be necessary.

VENTILATION: General ventilation should be adequate to maintain exposure levels below recommended established exposure limits. If general ventilation is not sufficient, local exhaust is recommended.

PERSONAL PROTECTIVE EQUIPMENT
Eye Protection: Safety goggles.
Hand Protection: Rubber gloves.
Protective Clothing: Laboratory coats.
Other: Eye wash.

**WORK/HYGIENIC PRACTICES:** Do not permit eating, drinking or smoking near this material.

### SECTION 9: PHYSICAL/CHEMICAL CHARACTERISTICS

**For Product:**

**APPEARANCE AND ODOR:** Clear colorless solution with little or no odor.

**For Active Ingredient:**

**APPEARANCE AND ODOR:** White to off-white crystalline powder, with little or no odor.

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boiling Point</td>
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<tr>
<td>Vapor Pressure (mmHg)</td>
<td>N/A</td>
</tr>
<tr>
<td>Vapor Density</td>
<td>N/A</td>
</tr>
<tr>
<td>Water Solubility</td>
<td>Soluble</td>
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<tr>
<td>Specific Gravity</td>
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</tr>
<tr>
<td>Melting Point</td>
<td>N/A</td>
</tr>
<tr>
<td>Evaporation Rate</td>
<td>N/A</td>
</tr>
<tr>
<td>pH</td>
<td>3.4</td>
</tr>
</tbody>
</table>

### SECTION 10: REACTIVITY DATA

**STABILITY:** Stable.

**CONDITIONS TO AVOID:** None known.

**INCOMPATIBLE MATERIALS:** Iodine.

**HAZARDOUS DECOMPOSITION OR BY-PRODUCTS:** When heated to decomposition or under fire conditions, material emits toxic fumes of bromide.

**HAZARDOUS POLYMERIZATION:** Will not occur.

### SECTION 11: TOXICOLOGICAL INFORMATION

**ACUTE TOXICITY:**

- 1700 – 4000 mg/kg oral – rat LD$_{50}$
- 1000 – 2000 mg/kg oral – mouse LD$_{50}$
- 400 – 1300 mg/kg inhalation – dog LD$_{50}$

**TERATOGENICITY:** PREGNANCY CATEGORY B: No evidence of risk in humans. Either animal studies show risk, but human findings do not or animal studies show no risk; however, adequate human studies have not been performed. Consult physician before using if you suspect you are pregnant, are pregnant or nursing.
CARCINOGENESIS/MUTAGENESIS: Two year oral carcinogenicity studies in rats and mice revealed no carcinogenic activities at doses up to 6mg/kg/day. This dose corresponds in rats and mice, respectively, to about 200 and 100 times the maximum recommended human daily dose (MRHD) on a mg/mg2 basis of Ipratropium Bromide Inhalation Solution.

Results of mutagenicity studies (Ames test, mouse dominant lethal test, mouse micronucleus test and chromosome aberration of bone marrow in Chinese hamsters) were negative.

IMPAIRMENT OF FERTILITY: Fertility of male or female rats at oral doses up to 50 mg/kg/day was unaffected by ipratropium bromide administration.

SECTION 12: ECOLOGICAL INFORMATION

None known.

SECTION 13: DISPOSAL CONSIDERATIONS

WASTE DISPOSAL CONSIDERATIONS: Dispose of in accordance with local, state and federal regulations. Recommended method is incineration or landfill.

SECTION 14: TRANSPORTATION INFORMATION

This product is not subject to the regulations for the safe transport of hazardous materials.

DOT Hazard Class: Not regulated.

SECTION 15: REGULATORY INFORMATION

This material is not listed on the US TSCA Inventory. Therefore, it can only be used for TSCA exempt purposes such as R&D or drug use.
SECTION 16: OTHER INFORMATION

Date Revised: 10/05/2004

We believe that the information contained within this MSDS is current as of the date issued. Since the use of this information and these opinions and the conditions of use of this material are not within the control of Nephron Pharmaceuticals Corporation, it is the user’s obligation to determine the conditions of safe use of this material. Nephron Pharmaceuticals Corporation urges the users of this product to study this MSDS and become aware of any hazards associated with this material. In the interests of safety, the information contained in this MSDS should be made available to your employees, agents and contractors who handle this material.

SEE CURRENT PACKAGE INSERT FOR FURTHER INFORMATION.