Section 1 - Identification

(a)	**Product Identifier:**	Diphenhydramine Hydrochloride Injection, USP
(b)	**Product Code:**	83634-781-01 and 83634-781-41
	Common/Trade Name:	Benadryl (Preservative-free), Diphenhydramine
	Chemical Name:	2-(Diphenylmethoxy)-N,N-dimethylethylamine hydrochloride
	Chemical Family:	Antihistamine
(c)	**Product Use:**	Pharmaceutical, Injectable
	Product Type:	Regulated Prescription Drug
	Container Information:	Vial
(d)	**Distributor:**	Avenacy 10 N. Martingale Road, Suite 225, Schaumburg, IL 60173, 847-773-4901
(e)	**Emergency Telephone:**	855-283-6229

Section 2 - Hazards Identification

(a)	**GHS Classification of substance or mixture:**	Specific target organ systemic toxicity (repeated exposure): Category 2

(b) Signal Word, Hazard statement(s), Symbol(s), and/ or Precautionary statement(s):	**(c) Description of Hazards:**
GHS Signal Word:	Warning
GHS Hazard Statement:	H373 - May cause damage to organs through prolonged or repeated exposure: liver.
GHS Symbols:	
GHS Precautionary Statements:	P260: Do not breathe dust/fume/gas/mist/vapors/spray P314: Get medical attention/advice if you feel unwell P501: Dispose of contents/container in accordance with all local and national regulations
Other Hazards	An Occupational Exposure Value has been established for one or more of the ingredients (see Section 8).

Note: This document has been prepared in accordance with standards for workplace safety, which require the inclusion of all known hazards of the product or its ingredients regardless of the potential risk. The precautionary statements and warnings included may not apply in all cases. Your needs may vary depending upon the potential for exposure in your workplace.

Section 3 – Composition / Information on Ingredients

(a) Chemical Name	(b) Common Name / Synonym	% Composition or other measure	(c) CAS No.	(d) Impurities / Stabilizing Additives
2-(Diphenylmethoxy)-N,N-dimethylethylamine hydrochloride	Diphenhydramine Hydrochloride	50 mg/mL	147-24-0	N/A
Hydrochloric Acid	Hydrochloric Acid	q.s. for pH adjustment	7647-01-0	N/A
Sodium Hydroxide	Sodium Hydroxide	q.s. for pH adjustment	1310-73-2	N/A
Water for Injection	Water for Injection	q.s. to 1 mL	7732-18-5	N/A

Section 4 – First Aid Measures

Eye Exposure: Immediately flush eyes with water for at least 15 minutes. If irritation occurs or persists, get medical attention.

Skin Exposure: Remove contaminated clothing and shoes. Wash skin with soap and water. If skin irritation persists, get medical attention.

Ingestion: Get medical attention. Do not induce vomiting unless directed by medical personnel. Never give anything by mouth to an unconscious person.

Inhalation: Remove to fresh air. If not breathing, give artificial respiration. If discomfort persists, get medical attention.

Section 5 – Fire-fighting Measures

(a) Extinguishing Media: Use carbon dioxide, dry chemical, or water spray.
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(b) Hazardous Combustion Products: May emit toxic fumes of nitrogen oxides and hydrogen chloride.

(c)	**Special Protective Equipment / Precautions:**	**Advice for Fire-Fighters:** Wear approved positive pressure, self-contained breathing apparatus and full protective turn out gear. Evacuate area and fight fire from a safe distance.
(d)	**Fire / Explosion Hazards:**	Fine particles (such as dust or mist) may fuel fires/explosions.

Section 6 - Accidental Release Measures

Health and Safety Precautions:	Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.
Measures for Cleaning / Collecting:	Contain the source of spill if it is safe to do so. Collect spill with absorbent material. Clean spill area thoroughly.
Measures for Environmental Protections:	Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release.
Additional Considerations for Large Spills:	Non-essential personnel should be evacuated from the affected area. Report emergency situations immediately. Clean up operations should only be undertaken by trained personnel.

Section 7 - Handling and Storage

General Handling:	Avoid breathing vapor or mist. Avoid contact with eyes, skin and clothing. When handling, use appropriate personal protective equipment (see Section 8). Wash thoroughly after handling. Releases to the environment should be avoided. Review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure or environmental releases. Potential points of process emissions of this material to the atmosphere should be controlled with dust collectors, HEPA filtration systems or other equivalent controls.
Storage Conditions:	Store at 20° to 25°C (68° to 77°F); excursions permitted between 15° and 30°C (59° and 86°F). [See USP Controlled Room Temperature.]

Section 8 - Exposure Controls / Personal Protection

(a) Exposure Limits

Compound	Issuer	Type	Exposure Limit
Diphenhydramine Hydrochloride	OEL	TWA-8hr	150 µg/m^3

Hydrochloric Acid

ACGIH Ceiling Threshold Limit	2 ppm
Australia PEAK	5 ppm
	7.5 mg/m^3
Austria OEL – MAKs	5 ppm
	8 mg/m^3
Belgium OEL – TWA	5 ppm
	8 mg/m^3
Bulgaria OEL – TWA	5 ppm
	8 mg/m^3
Cyprus OEL – TWA	5 ppm
	8 mg/m^3
Czech Republic OEL – TWA	8 mg/m^3
Estonia OEL – TWA	5 ppm
	8 mg/m^3
Germany – TRGS 900 – TWAs	2 ppm
	3 mg/m^3
Germany (DFG) – MAK	2 ppm
	3 mg/m^3
Greece OEL – TWA	5 ppm
	7 mg/m^3
Hungary OEL – TWA	8 mg/m^3
Ireland OEL – TWAs	5 ppm
	8 mg/m^3
Italy OEL – TWA	5 ppm
	8 mg/m^3
Japan OEL – Ceilings	2 ppm
	3 mg/m^3
Latvia OEL – TWA	5 ppm
	8 mg/m^3
Lithuania OEL – TWA	5 ppm
	8 mg/m^3
Luxembourg OEL – TWA	5 ppm
	8 mg/m^3
Malta OEL – TWA	5 ppm
	8 mg/m^3
Netherlands OEL – TWA	8 mg/m^3
Poland OEL – TWA	5 mg/m^3
Portugal OEL – TWA	5 ppm
	8 mg/m^3
Romania OEL – TWA	5 ppm
	8 mg/m^3
Slovakia OEL – TWA	5 ppm
	8 mg/m^3
Slovenia OEL – TWA	5 ppm
	8 mg/m^3
Spain OEL – TWA	5 ppm

	7.6 mg/m^3
Switzerland OEL – TWAs	2 ppm
	3 mg/m^3
Vietnam OEL – TWA	5 mg/m^3

Sodium Hydroxide

ACGIH Ceiling Threshold Limit	2 mg/m^3
Australia PEAK	2 mg/m^3
Austria OEL – MAKs	2 mg/m^3
Bulgaria OEL – TWA	2 mg/m^3
Czech Republic OEL – TWA	1 mg/m^3
Estonia OEL – TWA	1 mg/m^3
France OEL – TWA	2 mg/m^3
Greece OEL – TWA	2 mg/m^3
Hungary OEL – TWA	2 mg/m^3
Japan OEL – Ceilings	2 mg/m^3
Latvia OEL – TWA	0.5 mg/m^3
OSHA Final PELS – TWAs	2 mg/m^3
Poland OEL – TWA	0.5 mg/m^3
Slovakia OEL – TWA	2 mg/m^3
Slovenia OEL – TWA	2 mg/m^3
Sweden OEL – TWAs	1 mg/m^3
Switzerland OEL – TWAs	2 mg/m^3

(b) Engineering Controls

Engineering controls should be used as the primary means to control exposure. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.

(c) Individual Protection Measures

Personal Protective Equipment:	Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE). Contact your safety and health professional or safety equipment supplier for assistance in selecting the correct protective clothing/equipment based on an assessment of the workplace conditions, other chemicals used or present in the workplace and specific operational processes.
Hand Protection:	Impervious gloves (e.g. Nitrile, etc.) are recommended if skin contact with drug product is possible and for bulk processing operations. (Protective gloves must meet the standards in accordance with EN374, ASTM F1001 or international equivalent.)
Eye Protection:	Wear safety glasses or goggles if eye contact is possible. (Eye protection must meet the standards in accordance with EN166, ANSI Z87.1 or international equivalent.)

Skin Protection:	Impervious protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations. (Protective clothing must meet the standards in accordance with EN13982, ANSI 103 or international equivalent.)
Respiratory Protection:	Under normal conditions of use, if the applicable Occupational Exposure Limit (OEL) is exceeded, wear an appropriate respirator with a protection factor sufficient to control exposures to below the OEL (e.g. particulate respirator with a half mask, P3 filter). (Respirators must meet the standards in accordance with EN140, EN143, ASTM F2704-10 or international equivalent.)

Section 9 - Physical and Chemical Properties

(a)	**Appearance**	clear, colorless, sterile solution
(b)	**Odor**	Odorless
(c)	**Odor Threshold**	Not available
(d)	**pH**	4.0 to 6.5
(e)	**Melting Point:**	Not available
(f)	**Initial Boiling Point:**	100°C
(g)	**Flash Point (Liquid) (°C)**	>61
(h)	**Evaporation Rate:**	Not available
(i)	**Flammability**	Not available
(j)	**Upper Lower Flammability or Explosion Limits**	Not available
(k)	**Vapor Pressure (kPa):**	2.3 (20°C)
(l)	**Vapor Density:**	Not available
(m)	**Relative Density**	1.05
(n)	**Solubility(ies)**	Freely soluble in water Highly soluble in alcohol
(o)	**Partition Coefficient: n-octanol/water**	Not available
(p)	**Auto-ignition Temperature**	Not available
(q)	**Decomposition Temperature**	Not available
(r)	**Viscosity**	Not available

Section 10 - Stability and Reactivity

(a)	**Reactivity**	Not determined
(b)	**Chemical Stability**	Stable under standard use and storage conditions.
(c)	**Possibility of Hazardous Reactions**	Not determined

(d)	**Conditions to Avoid**	Avoid direct sunlight, conditions that might generate heat, and sources of ignition.
(e)	**Incompatible Materials**	As a precautionary measure, keep away from strong oxidizers.
(f)	**Hazardous Decomposition Products**	Thermal decomposition products may include carbon monoxide, carbon dioxide, oxides of nitrogen and hydrogen chloride.

Section 11 - Toxicological Information

(a)	**Likely Routes of Exposure**	Skin, eyes, mouth
(b)	**Symptoms related to the physical, chemical and toxicological characteristics**	May cause skin irritation. Not an eye irritant. Not a skin sensitizer (based on animal data). May be harmful if swallowed. May cause central nervous system effects. Individuals sensitive to this chemical or other materials in its chemical class may develop allergic reactions.
(c)	**Delayed and immediate effects and chronic effects from short and long term exposure**	The most common adverse effects seen with the therapeutic use of diphenhydramine HCl include drowsiness, sleepiness, dizziness, sedation, and gastrointestinal disturbance. Higher doses may cause CNS stimulation and/or depression, and impairment of motor and cognitive skills.

(d) Acute Toxicity:

Component	Type	Route	Species	Dosage
Diphenhydramine Hydrochloride	LD_{50}	Oral	Rat	500 mg/kg
Diphenhydramine Hydrochloride	LD_{50}	Oral	Mouse	114 mg/kg
Diphenhydramine Hydrochloride	LD_{50}	Oral	Guinea Pig	284 mg/kg
Diphenhydramine Hydrochloride	LD_{min}	Oral	Human	10.1 mg/kg
Hydrochloric Acid	LD_{50}	Oral	Rat	238 to 277 mg/kg

Irritation/Sensitization:

Component	Study Type	Species	Severity

Diphenhydramine Hydrochloride	Eye Irritation	Rabbit	Non-Irritating
Diphenhydramine Hydrochloride	Skin Sensitization - Beuhler	Guinea Pig	Negative
Diphenhydramine Hydrochloride	Skin Sensitization - LLNA	Mouse	Negative

Skin Irritation/Sensitization has been reported in clinical use.

Repeated Dose Toxicity:

Component	Duration	Route	Species	Dosage	End Point	Target Organ
Diphenhydramine Hydrochloride	13 week(s)	Oral	Rat	310 mg/kg/day	LOAEL	Liver
Diphenhydramine Hydrochloride	2 year(s)	Oral	Rat	15 mg/kg/day	NOAEL	Liver
Diphenhydramine Hydrochloride	2 year(s)	Oral	Mouse	21 mg/kg/day	NOAEL	Liver

Chronic Effects/Carcinogenicity: Liver toxicity was seen in a two-year oral study in rats treated with diphenhydramine. A No-Observed-Adverse- Effect-Level (NOAEL) of 15 mg/kg/day was obtained for female animals. There was equivocal evidence of carcinogenic activity in male and female rats. No evidence of carcinogenic activity was observed in male or female mice.

Subchronic Effects: In a 13-week oral study, dose-related liver toxicity was seen in rats at doses of >13 mg/kg/day in males and > 15 mg/kg/day in females. The NOAEL in this study was ~6.5 mg/kg/day (males) and 7 mg/kg/day (females) There were no compound-related histological effects observed in mice.

Reproductive and Developmental Toxicity:

Component	Study Type	Route	Species	Dosage	End Point	Effect(s)
Diphenhydramine Hydrochloride	Embryo / Fetal Development	Oral	Rat	100 mg/kg/day	NOAEL	Not teratogenic, maternal toxicity, fetotoxicity
Diphenhydramine Hydrochloride	Embryo / Fetal Development	Oral	Mouse	80 mg/kg/day	NOAEL	Not teratogenic, maternal toxicity, fetotoxicity
Diphenhydramine Hydrochloride	Embryo / Fetal Development	Oral	Rat	50 mg/kg/day	NOAEL	Not teratogenic, maternal toxicity, fetotoxicity

Reproductive Effects: No evidence of impaired fertility was seen in studies performed in rats and rabbits at doses up to 5 times the human dose of diphenhydramine hydrochloride.

Teratogenicity: No evidence of harm to the fetus was seen in studies performed in rats and rabbits at doses up to 5 times the human dose of diphenhydramine hydrochloride.

Genetic Toxicity:

Component	Study Type	Cell Type/Organism	Result
Diphenhydramine Hydrochloride	Bacterial Mutagenicity (Ames)	*Salmonella*	Negative
Diphenhydramine Hydrochloride	*In Vitro* Mammalian Cell Mutagenicity	Mouse Lymphoma	Negative
Diphenhydramine Hydrochloride	*In Vitro* Chromosome Aberration	Chinese Hamster Ovary (CHO) cells	Positive without activation Negative with activation
Diphenhydramine Hydrochloride	*In Vitro* Sister Chromatid Exchange	Chinese Hamster Ovary (CHO) cells	Negative
Diphenhydramine Hydrochloride	*In Vitro* Unscheduled DNA Synthesis	Rat Hepatocyte	Negative
Hydrochloric Acid	Bacterial Mutagenicity (Ames)	*Salmonella*	Negative
Hydrochloric Acid	*In Vivo* Micronucleus	Rat	Negative

Carcinogenicity:

Component	Duration	Route	Species	Dosage	End Point	Result
Diphenhydramine Hydrochloride	2 year(s)	Oral	Rat	15 mg/kg/day	NOAEL	Not carcinogenic
Diphenhydramine Hydrochloride	2 year(s)	Oral	Mouse	46 mg/kg/day	NOAEL	Not carcinogenic

Carcinogenic Status: None of the components of this formulation are listed as a carcinogen by IARC, NTP or OSHA.

(e) Hazardous Chemical Listings

Diphenhydramine hydrochloride:

NTP: Not Listed **IARC**: Not Listed **OSHA**: Not Listed

Hydrochloric Acid:

NTP: Not Listed **IARC**: Group 3 (Non-Classifiable) **OSHA**: Not Listed

Section 12 - Ecological Information

The environmental characteristics of this material have not been fully evaluated. Releases to the environment should be avoided.

(a)	**Ecotoxicity**	N/A
(b)	**Persistence and degradability**	N/A
(c)	**Bioaccumulative potential**	N/A
(d)	**Mobility in soil**	N/A
(e)	**Other Adverse Effects**	N/A

Section 13 - Disposal Considerations

Waste Disposal: Dispose of waste in accordance with all applicable laws and regulations. Member State specific and Community specific provisions must be considered. Considering the relevant known environmental and human health hazards of the material, review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure and environmental release. It is recommended that waste minimization be practiced. The best available technology should be utilized to prevent environmental releases. This may include destructive techniques for waste and waste water.

Section 14 - Transport Information

Not regulated for transport under USDOT, EUADR, IATA, or IMDG regulations.

Section 15 - Regulatory Information

Below is selected regulatory information chosen primarily for possible Avenacy usage. This section is not a complete analysis or reference to all applicable regulatory information. Please consider all applicable laws and regulations for your country/state.

Diphenhydramine hydrochloride

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Australia (AICS)	Present
EU EINECS/ELINCS List	205-687-2

Hydrochloric Acid

CERCLA/SARA 313 Emission reporting	1.0 %
CERCLA/SARA Hazardous Substances and their Reportable Quantities	5000 lb 2270 kg
CERCLA/SARA - Section 302 Extremely Hazardous TPQs	500 lb
CERCLA/SARA - Section 302 Extremely Hazardous Substances EPCRA RQs	5000 lb
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS)	Present
Standard for the Uniform Scheduling for Drugs and Poisons	Schedule 5 Schedule 6
EU EINECS/ELINCS List	231-595-7

Sodium Hydroxide

CERCLA/SARA 313 Emission reporting	Not Listed
CERCLA/SARA Hazardous Substances and their Reportable Quantities	1000 lb 454 kg
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS)	Present
Standard for the Uniform Scheduling for Drugs and Poisons	Schedule 5 Schedule 6
EU EINECS/ELINCS List	215-185-5

Water for Injection

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS)	Present
REACH - Annex IV - Exemptions from the obligations of Register	Present
EU EINECS/ELINCS List	231-791-2

Section 16 - Other Information

As of the date of effectiveness, we are providing available information relevant to the handling of this material in the workplace. All information contained herein is offered with the good faith belief that it is accurate. THIS SAFETY DATA SHEET SHALL NOT BE DEEMED TO CREATE ANY WARRANTY OF ANY KIND (INCLUDING WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE). In the event of an adverse incident associated with this material, this safety data sheet is not intended to be a substitute for consultation with appropriately trained personnel. Nor is this safety data sheet intended to be a substitute for product literature which may accompany the finished product.

For additional information contact:

Avenacy
10 N. Martingale Road, Suite 225
Schaumburg, IL 60173
847-773-4901

Glossary: This glossary contains definitions of general terms used in SDSs. Not all of these Glossary Terms will apply to this SDS.

ACGIH	American Conference of Governmental Industrial Hygienists
AICS	Australian Inventory of Chemical Substances
AIHA	American Industrial Hygiene Association
ANSI	American National Standards Institute
CAS Number	Chemical Abstract Service Registry Number
CERCLA	Comprehensive Environmental Response Compensation and Liability Act (of

CHAN	Chemical Hazard Alert Notice
CHEMTREC	Chemical Transportation Emergency Center
DOT	Department of Transportation
DSL	Domestic Substances List
ECHA	European Chemicals Agency
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of Notified Chemical Substances
EPA	Environmental Protection Agency
GHS	Globally Harmonized System of Classification and Labelling of Chemicals
HEPA	High Efficiency Particulate Air (Filter)
HMIS	Hazardous Materials Identification System
IARC	International Agency for Research on Cancer
ICAO/IATA	International Civil Aviation Organization/International Air Transport
IMO	International Maritime Organization
KOW	Octanol/Water Partition Coefficient
LEL	Lower Explosive Limit
MSDS	Material Safety Data Sheet
MSHA	Mine Safety and Health Administration
NA	Not Applicable, except in Section 14 where NA = North America
NE	Not Established
NADA	New Animal Drug Application
NAIF	No Applicable Information Found
NCI	National Cancer Institute
NDSL	Non-Domestic Substances List
NFPA	National Fire Protection Association
NIOSH	National Institute for Occupational Safety and Health
NPDES	National Pollutant Discharge Elimination System
NOS	Not Otherwise Specified
NTP	National Toxicology Program
OSHA	Occupational Safety and Health Administration
OEL	Occupational Exposure Limit
PEL	Permissible Exposure Limit (OSHA)
RCRA	Resource Conservation and Recovery Act
RQ	Reportable Quantity
RTECS	Registry of Toxic Effects of Chemical Substances
SARA	Superfund Amendments and Reauthorization Act
SDS	Safety Data Sheet
STEL	Short Term Exposure Limit
TLV	Threshold Limit Value (ACGIH)
TPQ	Threshold Planning Quantity
TSCA	Toxic Substances Control Act
TWA	Time Weighted Average/8 Hours Unless Otherwise Noted
UEL	Upper Explosive Limit
UN	United Nations
USP	United States Pharmacopeia
WEEL	Workplace Environmental Exposure Level (AIHA)
WHMIS	Workplace Hazardous Materials Information System