Safety Data Sheet

Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound)

SECTION 1 IDENTIFICATION

Product identifier	Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound)
Recommended use	Injectable. This material is a finished drug product for patient use. It is used in the treatment of cancer. It is a protein nanoparticle formulation.
Contact Information	
Company name	TWi Pharmaceuticals USA, Inc.
Address	115 West Century Road, Suite 135 Paramus, NJ 07652
Telephone	1-201-762-1410 0
Fax	1-201-225-0051
E-mail address	QA.Service@twipharma.com drugsafety.twi@Labcorp.com
Emergency phone number	1-844-518-2989

SECTION 2 HAZARD IDENTIFICATION

Hazard Class / Category

Health hazards	Germ Cell Mutagenicity - Category 2
	Toxic To Reproduction - Reproductive Toxicity - Category 1B
	Toxic To Reproduction - Developmental Toxicity - Category 1B
	Specific Target Organ Systemic Toxicity (Repeated Exposure) - Category 1
Environment hazards	Hazardous To The Aquatic Environment - Chronic Hazard - Category 2

Hazard Symbol

Hazard Warning Danger

Hazard Statements

Suspected of causing genetic defects.
May damage fertility (male/female fertility).
May damage the unborn child (developmental toxicity).
Causes damage to organs (hematopoietic system, cardiovascular system, nervous system, gastrointestinal tract, liver, kidney, skin, reproductive organs) through prolonged or repeated exposure.

Toxic to aquatic life with long lasting effects.

Precautionary Statements

Obtain special instructions before use.
Do not handle until all safety precautions have been read and understood.
Use personal protective equipment as required.
Do not breathe dust.
Wash thoroughly after handling.
Do not eat, drink or smoke when using this product.
Avoid release to the environment.
Collect spillage.

SECTION 3 COMPOSITION/INFORMATION ON INGREDIENTS

Components	Concentration	CAS No.
Hazardous components Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound)	100%	Not available

SECTION 4 FIRST-AID MEASURES

Eye contact

Rinse immediately with plenty of water for at least 15 minutes. Keep eye wide open while rinsing. If exposed or concerned: Get medical attention/advice.

Skin contact

Take off contaminated clothing and shoes immediately. Wash off immediately with plenty of water for at least 15 minutes. Discard contaminated clothing or wash before re-use. If exposed or concerned: Get medical attention/advice.

Inhalation

Move to fresh air. Oxygen or artificial respiration if needed. If exposed or concerned: Get medical attention/advice.

Ingestion

Do NOT induce vomiting. Never give anything by mouth to an unconscious person. If exposed or concerned: Get medical attention/advice.

Notes to Physician

Medical conditions aggravated include: bone marrow suppression, cardiac irregularities, liver disease. This product has been reported to interact with the following medications: drugs that inhibit cytochrome P-450, drugs that induce cytochrome P-450. Material not fully tested. Refer to Section 11.

Medical Surveillance

Employees who are pregnant, are breast-feeding, or who are concerned with other reproductive issues should be encouraged to consult with the occupational health physician monitoring worker's health.

SECTION 5 FIRE-FIGHTING MEASURES

Extinguishing Media	Suitable extinguishing media: Dry chemical, Water spray, Foam
Unsuitable Extinguishing Media	Do NOT use water jet.
Special Fire-Fighting Equipment for Fire-Fighters	Use personal protective equipment. In the event of fire, wear self-contained breathing apparatus.
Hazardous Combustion Products	Carbon oxides (COx), nitrogen oxides (NOx)
Other information	Decontaminate protective clothing and equipment before reuse.

SECTION 6 ACCIDENTAL RELEASE MEASURES

Personal Precautions and Protection	Refer to protective measures listed in Sections 7 and 8. Use personal protective equipment. Examples include tightly fitting safety goggles, disposable lab coat of low permeability with cuffs, double gloves and shoe covers. Wear respiratory protection. Depending on the nature of the spill (quantity and extent of spill) additional protective clothing and equipment such as a self-contained breathing apparatus may be needed.
Environmental Precautions	Prevent release to drains and waterways. Prevent release to the environment.
Containment Methods	Wet down any dust to prevent generation of aerosols, if appropriate. Cover with suitable material.
Clean Up Procedures	Spill prevention procedures and a spill response procedure should be implemented. Contain and collect spillage and place in container for disposal according to local regulations (see Section 13). Clean spill area with a deactivating solution (if available) followed by detergent and water after spill pick-up. Handle waste materials, including gloves, protective clothing, contaminated spill cleanup material, etc., as appropriate for chemically and pharmacologically similar materials.

SECTION 7 HANDLING AND STORAGE

Handling	Avoid exposure - obtain special instructions before use. Avoid inhalation of vapour or mist. Keep away from heat and sources of ignition. Prevent release to drains and waterways.
Storage	Store in sturdy containers appropriate to maintain the integrity of this material for its intended use. Store at controlled room temperature (20-25°C). Do not store near incompatible substances. Excursions permitted to 15°- 30°C. Keep away from direct sunlight. Protect against light. Store in the dark. Keep in a dry place. Keep away from heat, sparks and flames. Store locked up.

SECTION 8 EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure limit(s)	Company Guideline	ACGIH	Germany OEL	UK MEL
Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound)	2 µg/m^3 8 hour-TWA	-	-	-

Recommended Industrial Hygiene Monitoring Methods	General - The health hazard risk of handling this material is dependent on many factors, including physical form, % API in material being handled, duration and frequency of process task, and effectiveness of controls. If it is necessary to handle this compound outside of engineering controls, an exposure risk assessment should be conducted and procedures documented by a qualified EHS professional.
Engineering Controls and Ventilation	**LABORATORIES**: When handling quantities up to 1 grams Total Weight (lyophilized materials), a standard laboratory with general laboratory dilution ventilation (e.g. 6-12 air changes per hour) is appropriate. Refer to HVAC standard DS-4301 for exact requirements. When handling quantities >1 gram - 100 grams Total Weight (lyophilized materials), work in a standard laboratory when manipulating materials, fume hood; biological safety cabinet (Class II Type A2 with thimble connection, B1, or B2); approved vented enclosure and closed processes for high energy biologic processes. When handling quantities >100 grams Total Weight (lyophilized materials), work in Development Laboratory or Biologic Pilot Plant Area using biological safety cabinet (Class II Type A2 with thimble connection, B1, or B2), glove box, or approved vented enclosure required. Closed processes for high energy biologic processes. Appropriate containment isolation technology. For low energy operations, use protective shielding (shields, absorbent lined trays or work surfaces) to limit spread of splash or splatter. Local exhaust ventilation is required. For high energy operations must be performed in closed or contained systems. Eliminate the use of all sharps, if possible. A documented risk assessment is required to support sharp usage. For all quantities noted - For low energy operations, use protective shielding (shields, absorbent lined trays or work surfaces) to limit spread of splash or splatter. Local exhaust ventilation is required. High-energy operations must be performed in closed or contained systems. Eliminate the use of all sharps, if possible. A documented risk assessment is required to support sharp usage. **MANUFACTURING**: Perform closed transfers when feasible. Avoid generation of dust. Control total dust levels to recommended control limits for material as supplied (based on concentration of API in aterial being handled). Establish a spill/leak procedure as outlined in Section 6 to address equipment failures/leaks. Exposures are typically controlled by GMP design specifications under normal operations. **CLINICAL**: When preparing drug in a clinical setting, use good clinical practice for drug preparation. If the potential for personal exposure exists, use an approved vented enclosure such as a fume hood or biological safety cabinet if available. Please refer to the general guidance at the beginning of this section.
Respiratory protection	Use and selection of respiratory protection is based upon an exposure risk assessment and potential for aerosol generation. When engineering controls are not sufficient to control exposure, wear an approved respiratory protection device that is adequate to

	control exposure based on measured or estimated airborne, and the rating for the device. Follow local regulatory requirements.
Eye protection	Wear safety glasses with side-shields. Face shields or chemical safety goggles may be required if contact potential exists or if corrosive materials are present. Note: Choice of eye protection may be influenced by the type of respirator which is selected.
Hand protection	When handling solutions wear impermeable gloves (e.g. latex or nitrile). Persons who are allergic to natural rubber latex should select gloves made from one of the other materials.
Skin and body protection	**LABORATORIES**: Wear a laboratory coat (EN 340). **MANUFACTURING**: Wear laboratory coat or full coverall of low permeability. Wear wrist gauntlets/sleeves and shoe covers as appropriate. **CLINICAL**: When preparing drug in clinical setting wear lab coat.
Hygiene	Wash hands and face before breaks and immediately after handling the product.
Environmental exposure controls	Prevent release to drains and waterways.

SECTION 9 PHYSICAL AND CHEMICAL PROPERTIES

Appearance	
Physical state	Solid.
Form	White to off-white Lyophilized powder which is packaged in vials.
Odour	
Odour	Odorless
Ordor Threshold	Not available
Important healthy safety and environmental information	
pH	6 - 7.5 (reconstituted)
Other information	
Bulk density	Not available
Evaporation rate	Not available
Hydrolysis/Photolysis	Not available
Hygroscopicity	Not available
Molecular Weight	Not applicable

Log Octanol/Water Partition Coefficient [log Kow]	3.69. This result is from a study on a structurally-and/or pharmacologically-related substance.
Surface Tension	Not available
pKa	Not available
Particle Size	Not available
Solubility, Water	Insoluble
Specific Gravity/Relative density	Not available
Viscosity, dynamic	Not available
Viscosity, kinematic	Not available
% Volatile	Not available
Thermal/Stability properties	
Autoignition temperature	Not available
Boiling Point	Not available
Thermal decomposition	Not available
Explosive Limits, LEL	Not available
Explosive Limits, UEL	Not available
Explosiveness	Non-explosive based on chemical structure.
Flammability	Not available
Flash Point	Not available
Melting Point	216 °C approximately
Oxidizing Potential	Non-oxidizer based on chemical structure.
Vapor Properties	
Vapor Density	Not available
Vapor Pressure	Not available
Saturated Vapor Concentration	Not available

SECTION 10 STABILITY AND REACTIVITY

Chemical Stability	Stable under normal conditions.
Conditions to avoid	Light
Materials to avoid	Strong oxidizing agents, strong acids and strong bases.
Hazardous decomposition products	Hazardous decomposition products formed under fire conditions.: carbon oxides (COx), nitrogen oxides (NOx).
Hazardous reactions	None known.
Sensitivity to static discharge/Dust exp.	Although material has not been specifically tested, fine dust suspended in air in sufficient concentration and in the presence of an ignition source may pose a

potential explosion hazard. Provide appropriate bonding and grounding protection to control static charge. Powder handling equipment such as dust collectors, dryers, and mills may require additional protective measures (e.g. explosion venting, inerting, etc.).

SECTION 11 TOXICOLOGICAL INFORMATION

Routes of Entry	Ingestion, inhalation, Eye contact, Skin contact
Eye Irritation	Not available
Skin Irritation	Not available
Respiratory Irritation	Not available
Sensitization	Not available
Acute Toxicity Study	**Acute toxicity (other routes of administration)** LD50 (rat, intravenous): >120 mg/kg low exposure effects include (<= 300 mg/kg): mortality, microscopic changes were observed in the following organs: male reproductive organs. LD50 (mouse, intravenous): 447 mg/kg LD50 (dog, intravenous): >8.4 mg/kg low exposure effects include (<= 300 mg/kg): hypoactivity, gastrointestinal effects, oedema, microscopic changes were observed in the following organs: male reproductive organs. LD50 (Pig, intravenous): >6 mg/kg low exposure effects include (<= 300 mg/kg): decreased body weight, decreased appetite, vomiting, diarrhoea, decreased white blood cell count.
Repeated Dose Toxicity	3 - 4 Weeks intravenous (Once per 5-7 days) rat, monkey study with recovery period (4 Weeks) (males and females): LOAEL (4 week, rat) = 10 mg/kg; Low dose effects include (< = 100 mg/kg): decreased body weight, decreased food consumption, vomiting, abnormal posture, fecal changes, changes in red blood cell parameters, decreased white blood cell count, changes in urine chemistry, changes in clinical chemistry parameters, mortality, increased organ weights included:, spleen, decreased organ weights included:, thymus, pituitary gland, testes, liver, thyroid gland, parathyroid gland. Low dose microscopic effects include: lymphoid tissue, heart, male reproductive organs, liver, nervous system, skin, eyes. Effects still present after recovery include: microscopic changes were observed in the following organs: male reproductive organs, nervous system, eyes.
Genetic Toxicity	**Mutagenicity Assessment** This material was positive in genotoxicity assays in animals. (This result is from a study on a structurally-and/or pharmacologically-related substance.)
Carcinogenicity	Not available.
Reproductive Toxicity	12 Weeks intravenous (1/week) male reproductive toxicity (rat) (parent, males) NOAEL = 2 mg/kg Effects on offspring include: reduction in litter size. Paternal effects include: impaired spermatogenesis, mortality. Effects occurred in male fertility. **Assessment Reproductive Toxicity** Reproductive toxicant. See also “Repeated Dose Toxicity” for information on reproductive effects.

Developmental Toxicity	Intravenous (daily) Study of Embryo-Fetal Development (rat) (parent, females) NOAEL = 0.5 mg/kg (embryo/fetus) NOAEL = 0.5 mg/kg Fetal effects include: decreased body weight, skeletal variation, malformations, mortality. Maternal effects include: decreased weight gain, decreased body weight, decreased food consumption, increased resorption incidence, mortality. **Developmental Toxicity Assessment** Compound produced effects on the fetus at doses similar to those which produced effects on the maternal animal. However, the effects noted in the fetus are consistent with those expected based on the mechanism of action of this substance.
Human experience	**Experiences with Human Exposure** Intravenous patient population (1/week-1/3 weeks) low exposure - acute effects include: decreased appetite, nausea, vomiting, diarrhea, constipation, dehydration, mouth effects, fatigue, chills, fever, cough, oedema, headache, dizziness, depression, insomnia, rash, skin effects, changes in electrolytes, hyperglycemia, increased liver enzymes, changes in clinical chemistry parameters, anemia, neutropenia, thrombocytopenia, increase in heart rate, congestive heart failure, changes in blood pressure, peripheral neuropathies, kidney effects, liver effects, eye effects, musculoskeletal pain, joint pain, infection.
Target Organs	Hematopoietic system, cardiovascular system, nervous system, gastrointestinal tract, liver, kidney, skin, reproductive organs.
Symptoms	Not available
Other Toxicity Information	Not available
Other Information	Some of the toxicological data presented is derived from a structurally or pharmacologically similar compound.

SECTION 12 ECOLOGICAL INFORMATION

Ecotoxicity Effects

Acute Toxicity to Fish

LC50 (Pimephales promelas (fathead minnow), 96 H): > 7.1 mg/l. (limit of solubility). This result is from a study on a structurally-and/or pharmacologically-related substance.

Acute Toxicity to Aquatic Invertebrates

EC50 (Daphnia magna (Water flea), 48 H): > 0.74 mg/l. (limit of solubility). This result is from a study on a structurally-and/or pharmacologically-related substance.

Toxicity to Aquatic Plants

EC50 (Pseudokirchneriella subcapitata (formerly Selenastrum capricornutum), Growth rate, 72H): >0.16 mg/l (limit of solubility). This result is from a study on a structurally-and/or pharmacologically-related substance.

EC50 (Pseudokirchneriella subcapitata (formerly Selenastrum capricornutum), Growth rate, 72 H): > 0.55 mg/l (limit of solubility)

Toxicity to Microorganisms

Respiration inhibition, EC50 (Activated Sludge): > 1,000 mg/l. This result is from a study on a structurally-and/or pharmacologically-related substance.

Chronic Toxicity to Fish

Early-life Stage LOEC (Pimephales promelas (fathead minnow), 33 Days): 0.1 mg/l. This result is from a study on a structurally-and/or pharmacologically-related substance.

Early-life Stage NOEC (Pimephales promelas (fathead minnow), 33 Days): 0.05 mg/lThis result is from a study on a structurally-and/or pharmacologically-related substance.

Chronic Toxicity to Aquatic Invertabrates

EC50 (Daphnia magna (Water flea), 21 Days): 0.058 mg/l (Reproduction Test). This result is from a study on a structurally-and/or pharmacologically-related substance.

NOEC (Daphnia magna (Water flea), 21 Days): 0.023 mg/l (Reproduction Test). This result is from a study on a structurally-and/or pharmacologically-related substance.

Mobility

Not available

Persistence and Degradability

Biodegradation

Biodegradation (28 Days): 42%; Inherently biodegradable- biodegrades in the environment. This result is from a study on a structurally-and/or pharmacologically-related substance.

Stability in water

Hydrolysis (pH 5): Half-life - 65.6 Days; Degree of hydrolysis- 28 Days; Low rate of hydrolysis in Water. This result is from a study on a structurally-and/or pharmacologically-related substance.

Hydrolysis (pH 7): Half-life - 18.6 Days; Degree of hydrolysis- 28 Days; Low rate of hydrolysis in water. This result is from a study on a structurally-and/or pharmacologically-related substance.

Hydrolysis (pH 9): Half-life - 13.9 Days; Degree of hydrolysis- 28 Days; Low rate of hydrolysis in water. This result is from a study on a structurally-and/or pharmacologically-related substance.

Sorption/Desorption

Koc (soil): 341-1,270 Stable in soil
(This result is from a study on a structurally-and/or pharmacologically-related substance.)

Koc (Sludge): 343-707 Stable in sludge
(This result is from a study on a structurally-and/or pharmacologically-related substance.)

Bioaccumulative Potential

Bioconcentration factor (BCF): 3 (Cyprinus carpio (Carp)) 28-day. This result is from a study on a structurally-and/or pharmacologically-related substance.

PBT and vPvB Assessment

Does not fulfill PBT or vPvB criteria. This result is from a study on a structurally-and/or pharmacologically-related substance.

SECTION 13 DISPOSAL CONSIDERATIONS

Disposal instructions

Disposal should be in accordance with applicable regional, national and local laws and regulations. Local regulations may be more stringent than regional or national requirements. This information presented only applies to the material as supplied.

Disposal by incineration is recommended.

SECTION 14 TRANSPORT INFORMATION

IATA/ICAO

Status	Regulated
UN number	UN3077
Proper shipping name	Environmentally hazardous substance, solid, n.o.s. (Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound))
Hazard class	9
Packing group	III
Labelling	9

US DOT

Status:	Regulated
UN number	UN3077
Proper shipping name	Environmentally hazardous substance, solid, n.o.s. (Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound))
Hazard class	9
Packing group	III
Labelling	9

IMDG

Status:	Regulated
UN number	UN3077
Proper shipping name	Environmentally hazardous substance, solid, n.o.s. (Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound))
Hazard class	9
Packing group	III
Labelling	9
EmS	F-A, S-F

ADR

Status:	Regulated
UN number	UN3077
Proper shipping name	Environmentally hazardous substance, solid, n.o.s. (Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound))
Hazard class	9
Packing group	III
Labelling	9

RID

Status:	Regulated
UN number	UN3077
Proper shipping name	Environmentally hazardous substance, solid, n.o.s. (Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound))
Hazard class	9
Packing group	III
Labeling	9

Transportation Classification for All Modes	Marine Pollutant

Other Information	Marine Pollutant

SECTION 15 REGULATORY INFORMATION

United States of America

313 Toxic Release inventory	No components listed on the SARA 313 inventory.	
TSCA Inventory	Not listed. Food, drug and cosmetic products are exempt from TSCA.	
California Prop. 65	Developmental toxicant	Paclitaxel
	Reproductive toxicant (male)	Paclitaxel
	Reproductive toxicant (female)	Paclitaxel
Regulatory Authorizations and Restrictions:	Authorized Generic Medicine. The NDA Number is 21660.	

SECTION 16 OTHER INFORMATION

No information found.

Issue date	November 9, 2021
Version #	01
Disclaimer	TWi Pharmaceuticals USA, Inc. cannot anticipate all conditions under which this information and its product, or the products of other manufacturers in combination with its product, may be used. It is the user's responsibility to ensure safe conditions for handling, storage and disposal of the product, and to assume liability for loss, injury, damage or expense due to improper use. The information in the sheet was written based on the best knowledge and experience currently available.