Safety Data Sheet

Bristol-Myers Squibb Company

1. IDENTIFICATION		
Product Information		
Product name	Opdivo® (nivolumab)10 - 20 mg/ml	
Version	7.1, 11.09.2017	
Jurisdiction	This Safety Data Sheet was prepared in accordance with the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) for the United States of America (USA) (CFR 1910.1200), European Union (EU) (EC 1272/2008) and United Nations (UN). The following countries utilize the UN GHS classification process: Mexico, Brazil, China, New Zealand, Canada, Japan, and Korea.	
Active substance	Nivolumab	
Synonyms	Opdivo® (nivolumab) injection, 40mg/4mL(10mg/mL); Opdivo® (nivolumab) injection, 100mg/10mL(10mg/mL); BMS-936558-01 Drug Substance, 20mg/ml; OPDIVO (nivolumab) injection; BMS-936558-01; MDX-1106; BMS-936558-01 Solution, 10 - 20 mg/ml; Opdivo 240mg; NIVOLUMAB INJECTION, 240 MG/VIAL	
Other information	Project Name: 071Z1, 061G4, 01102	
Intended Uses	This material is a finished drug product for patient use. It is used in the treatment of cancer.	
Company/Undertaking Identification		
Address	USA **Bristol-Myers Squibb Company** P.O. Box 191 New Brunswick, New Jersey 08903 United States of America 1-800-332-2056	Ireland **Bristol-Myers Squibb Company** Swords Laboratories, Watery Lane Swords, Ireland MG-GBS-MSDS-Request@bms.com 353-1813-9456
Emergency Phone No.	USA (also Canada, Puerto Rico and the Virgin Island): 1-800-424-9300 Other Countries: See "Section 16" for country-specific emergency phone numbers from CHEMTREC.	Ireland: 353-1813-9456

2. HAZARDS IDENTIFICATION	
Classification and Labelling Common to All Jurisdictions	
Classification	Not Rated
Precautionary Statements	Wash hands thoroughly after handling. Handle as a potentially hazardous material. Avoid ingestion, inhalation, skin and eye contact.
Other information	May enhance the potential for hypersensitivity and dermal sensitization response to other compounds. This effect is due to the mechanism of action. 5.6% of the mixture consists of ingredients(s) of unknown hazards to the aquatic environment.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Components	Concentration	CAS No.	EU only		Other Registration No.
			EC No./REACH Registration No.	H-code(s)	
Hazardous components					
Nivolumab	1 - 2 %	946414-94-4	--	--	--
Other ingredients					
Non-Hazardous Ingredients	> 95 %	Not available	--	--	--
See section 16 for H-code text.					

4. FIRST AID MEASURES

Eye contact	Rinse immediately with plenty of water for at least 15 minutes. Keep eye wide open while rinsing. Obtain medical attention.
Skin contact	Take off contaminated clothing and shoes immediately. Wash off immediately with plenty of water for at least 15 minutes. Obtain medical attention. Discard contaminated clothing or wash before re-use.
Inhalation	Move to fresh air. Oxygen or artificial respiration if needed. Obtain medical attention.
Ingestion	Do NOT induce vomiting. Consult a physician if necessary. Never give anything by mouth to an unconscious person.
Notes to Physician	Medical conditions aggravated include: autoimmune disorders. Refer to Section 11.
Medical Surveillance	The need for a pre-placement, follow-up physical examination and history for employees with potential exposure to this compound is to be evaluated by a physician that is thoroughly knowledgeable about both the toxicity of this compound and the extent of work place exposure. Baseline testing would include: a complete blood count with differential, a blood test for liver function. This exam should be overseen by a physician thoroughly knowledgeable about both the toxicity of this compound and the extent of work place exposure. Based on opportunity for exposure and duration of exposure a periodic follow-up examination may be considered. It is recommended that the content be similar to the pre-placement exam. 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.

5. FIRE-FIGHTING MEASURES

Flammable Properties	Not available
Extinguishing Media	Suitable extinguishing media: Dry chemical, Water spray, Foam Unsuitable extinguishing media: Do NOT use water jet.
Protection of Firefighters	Specific hazards: Not available Protective equipment: 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.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions	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.

6. ACCIDENTAL RELEASE MEASURES

Environmental precautions	Prevent release to drains and waterways. Prevent release to the environment.
Containment Methods	Contain spillage, and then collect with non-combustible absorbent material, (e.g. sand, earth, diatomaceous earth, vermiculite) and place in container for disposal according to local / national regulations (see section 13).
Cleanup Methods	Spill prevention procedures and a spill response procedure should be implemented. Absorb spillage using appropriate absorbent materials 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. Avoid generating aerosols in the event of containment loss.

7. HANDLING AND STORAGE

Handling Precautions	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.
Container Requirements	Store in sturdy containers appropriate to maintain the integrity of this material for its intended use. Store in spill containment pallet or other device to confine spills.
Storage Conditions	Store at 2 - 8°C. Protect against light. Do not freeze or shake. Keep away from heat, sparks and flames.
Specific use(s)	Refer to Section 1

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Exposure limit(s)	Company Guideline	ACGIH	Germany OEL	UK MEL
Nivolumab	200 µg/m3 TWA	--	--	--

Recommended Industrial Hygiene Monitoring Methods	A specific exposure sampling method is not available. Contact the Bristol-Myers Squibb AIHA accredited Industrial Hygiene Laboratory at (USA) 732-227-6338. 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.

EXPOSURE CONTROLS / PERSONAL PROTECTION FOR MATERIAL AS SUPPLIED

This formulation contains an active pharmaceutical ingredient (API) with the guideline limit noted above. To keep the API below the recommended guideline, the material as supplied should be controlled during handling to limit total airborne aerosol exposure to: 10,000 µg/m³ (For internal BMS use: Biological Control Category A ≥ 1 µg/m³).

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Engineering Controls and Ventilation	LABORATORIES: General laboratory dilution ventilation is acceptable for open handling of low energy small scale processes. Low energy processes (e.g. low velocity stirring, careful pouring, liquid chromatography, low energy pump transfers including fraction collection, tangential flow filtration concentration buffer exchange and pipette transfers with no blow out, etc.) should use protective shielding to limit aerosol spread. When handling larger quantities, during operations that may exceed the recommended exposure control limits or high energy processes (e.g. boiling, blending, ultra-sonication, uncapped vortexing, microfluidization, homogenizing, etc.) operations should be performed using standard laboratory controls such as a fume hood, biological safety cabinet (Class II, Type A2 with thimble connection, B1, or B2), glove box, approved vented enclosure and/or closed or contained systems. MANUFACTURING: Perform closed transfers when feasible. Avoid generation of aerosols. Control total aerosol levels to recommended control limits for material as supplied (based on concentration of API in material 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 laboratory coat. Wear disposable shoe covers as appropriate. 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.

9. PHYSICAL AND CHEMICAL PROPERTIES

General Information

Appearance

Physical State	liquid
Form	aqueous solution

9. PHYSICAL AND CHEMICAL PROPERTIES

Odour	
Odour	Not available
Odor Threshold	Not available
pH	6 (as aqueous solution)
Other information	
Bulk density	Not available
Evaporation rate	Not available
Molecular formula	Not applicable
Hydrolysis/Photolysis	Not available
Hygroscopicity	Not available
Molecular Weight	Not applicable
Log Octanol/Water Partition Coefficient [log Kow]	Not available
Surface Tension	Not available
pKa	Not available
Particle Size	Not available
Solubility, Water	Not available
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	Not available
Flammability	Not available
Flash point	Not available
Melting Point	Not available
Oxidizing Potential	Not available
Vapor Properties	
Vapor Density	Not available
Vapor Pressure	Not available
Saturated Vapor Concentration	Not available

10. STABILITY AND REACTIVITY

Stability	
Chemical Stability	Stable under recommended storage conditions.
Conditions to avoid	light
Materials to avoid	Not available

10. STABILITY AND REACTIVITY	
Hazardous decomposition products	Hazardous decomposition products formed under fire conditions.: carbon oxides (COx), nitrogen oxides (NOx)
Hazardous reactions	None known.

11. TOXICOLOGICAL INFORMATION			
Routes of Entry			
Eye Irritation	Not available		
Skin Irritation	Not available		
Respiratory Irritation	Not available		
Sensitization	Not available		
Acute Toxicity Study	**Acute toxicity (other routes of administration)** Nivolumab LD50 (monkey, intravenous): > 10 mg/kg low exposure effects include (<= 300 mg/kg): measurable drug-specific antibodies. No mortality occurred.		
Repeated Dose Toxicity	Nivolumab 1 - 3 months intravenous (1 - 2/ week) monkey study with recovery period (4 weeks) (males and females): NOEL (3 month, monkey) = 10 mg/kg; Low dose effects include (< = 100 mg/kg): changes in thyroid hormones, measurable drug-specific antibodies.		
Genetic Toxicity	Not available		
Carcinogenicity	Not available		
Carcinogenicity	**ACGIH**	**IARC**	**NTP**
Nivolumab	--	--	--
Reproductive Toxicity	Not available		
Developmental Toxicity	Nivolumab intravenous (2/week) Study of Pre- and Postnatal Development (monkey) (parent, females) NOAEL = 50 mg/kg (embryo/fetus) LOAEL = 10 mg/kg Fetal effects include: mortality. **Developmental Toxicity Assessment** Selective developmental toxicant		
Human experience	**Experiences with Human Exposure** Nivolumab Clinical trial(s) low exposure - acute effects include: fatigue, headache, diarrhoea, nausea, lung toxicity, vomiting, rash, redness and swelling of skin, itching, loss of appetite, cough, fever, dry mouth, dehydration, hepatitis, muscle pain, joint pain, back pain, abdominal pain, decreased body weight, infusion reaction, anemia, changes in blood chemistry		

11. TOXICOLOGICAL INFORMATION

	, decreased white blood cell count, changes in clinical chemistry parameters, changes in urine chemistry, changes in thyroid hormones, change in liver enzymes.
Target Organs	Nivolumab immune system, endocrine system, lungs, gastrointestinal tract, liver, skin
Symptoms	Nivolumab See "Human Experience".
Pharmacokinetics/ Toxicokinetics	Nivolumab Absorption: Proteins greater than 10 kilodaltons (kDa) are not expected to exhibit systemic bioavailability of greater than 1% by the inhalation route. This finding is based on limited inhalation studies with proteins of similar molecular weights. Distribution: Data available upon request. Metabolism: Data available upon request. Elimination: Half-life = 25 Day(s)
Other Toxicity Information	**Other Toxicity Tests** Nivolumab In vivo safety pharmacology test(s) : monkey = No cardiovascular or hemodynamic changes were observed.
Other Information:	The toxicological information provided in this SDS may not be applicable to occupational routes of exposure. Therefore, this substance is not classified according to GHS criteria. May enhance the potential for hypersensitivity and dermal sensitization response to other compounds. This effect is due to the mechanism of action. Nivolumab The toxicological information provided in this SDS may not be applicable to occupational routes of exposure. Therefore, this substance is not classified according to GHS criteria. May enhance the potential for hypersensitivity and dermal sensitization response to other compounds. This effect is due to the mechanism of action.

12. ECOLOGICAL INFORMATION

Ecotoxicity effects	Not available
Mobility	Not available
Persistence and degradability	Not available
PBT and vPvB assessment	Not available

13. DISPOSAL CONSIDERATIONS

Advice On Disposal And Packaging	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.
Other information	Disposal by incineration is recommended.

14. TRANSPORT INFORMATION

This material is not a dangerous good for the purpose of transportation in all modes.

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.

EU Regulation (EC) No 1272/2008)

DRUG PRODUCT

Classification	Medicinal products are exempt from classification and labeling requirements under EU Regulation (EC) No 1272/2008.
Regulatory Authorizations and Restrictions:	Not available

16. OTHER INFORMATION

Text of H-code(s) mentioned in Section 3.

Not available

Recommended Restrictions for Use:

Not available

SDS preparation information

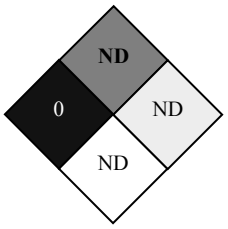
Prepared by	Global Environment, Health, Safety, and Sustainability 1-732-227-7380
Prepared on	17.08.2017 DD/MM/YYYY
	This Safety Data Sheet has been revised. This data sheet contains changes from the previous version in section(s): 2, 3, 4, 8, 11, 15, and 16.

Other information

HMIS	Health	0
	Flammability	Not Determined (ND)
	Reactivity	Not Determined (ND)
	Personal protective equipment	See Section 8.

NFPA

Health	0
Fire	ND
Reactivity	ND
Special	ND



Country- Specific Emergency Phone Numbers

CHEMTREC In-Country Dial Numbers	Local # Provided in Country	Toll Free in Country*	Greeting Language
CHEMTREC South Africa*		0-800-983-611	English
CHEMTREC Argentina (Buenos Aires)	+(54)-1159839431		Latin American Spanish
CHEMTREC Brazil (Rio De Janeiro)	+(55)-2139581449		Portuguese
CHEMTREC Chile (Santiago)	+(56)-25814934		Latin American Spanish
CHEMTREC Colombia *		01800-710-2151	Latin American Spanish
CHEMTREC Mexico*		01-800-681-9531	Latin American Spanish
CHEMTREC Peru (Lima)	+(51)-17071295		Latin American Spanish
CHEMTREC China*	4001-204937		Mandarin
CHEMTREC Hong Kong (Hong Kong)*		800-968-793	Cantonese
CHEMTREC India *		000-800-100-7141	Hindi
CHEMTREC Indonesia*		001-803-017-9114	Indonesian
CHEMTREC Japan (Tokyo)	+(81)-345209637		Japanese
CHEMTREC Malaysia *		1-800-815-308	Malay
CHEMTREC Philippines *		1-800-1-116-1020	Tagalog
CHEMTREC Singapore*		800-101-2201	Mandarin
CHEMTREC Singapore	+(65)-31581349		Mandarin
CHEMTREC South Korea*		00-308-13-2549	Korean
CHEMTREC Taiwan*		00801-14-8954	Mandarin
CHEMTREC Thailand *		001-800-13-203-9987	Thai
CHEMTREC Vietnam (Ho Chi Minh City)	+(84)-838012436		Vietnamese
CHEMTREC Australia (Sydney)	+(61)-290372994		English
CHEMTREC Belgium (Brussels)	+(32)-28083237		French and Flemish
CHEMTREC Czech Republic (Prague)	+(420)-228880039		Czech
CHEMTREC France	+(33)-975181407		French
CHEMTREC Germany *		0800-181-7059	German
CHEMTREC Hungary (Budapest)	+(36)-18088425		Hungarian
CHEMTREC Italy *		800-789-767	Italian
CHEMTREC Italy (Milan)	+(39)-0245557031		Italian
CHEMTREC Netherlands	+(31)-858880596		Dutch
CHEMTREC Poland (Warsaw)	+(48)-223988029		Polish
CHEMTREC Spain*		900-868538	European Spanish
CHEMTREC Sweden (Stockholm)	+(46)-852503403		Swedish
CHEMTREC Switzerland (Zurich)	+(41)-435016715		German
CHEMTREC UK (London)	+(44)-870-8200418		English
CHEMTREC Bahrain (Bahrain)	+(973)-16199372		Arabic
CHEMTREC Israel (Tel Aviv)	+(972)-37630639		Hebrew
*Phone numbers for countries marked with an asterisk must be dialed within the country			

The information contained in this SDS is believed to be accurate and represents the best information reasonably available at the time of preparation. However, we make no warranty, express or implied, with respect to such information. and we assume no liability from its use.