DYNAVAX

Safety Data Sheet

BRK-SDS-0009

Version: 02

Effective Date: 26 Jan 2017

1. PRODUCT AND COMPANY IDENTIFICATION

Product Name: **HEPLISAV Drug Product**

Product Description: HEPLISAV™ Drug Product contains Hepatitis B surface antigen (HBsAg; non-infectious, yeast-cell derived recombinant protein) and a single-stranded 22-base synthetic cytidine-phospho-guanosine phosphorothioate oligodeoxynucleotide (CpG-ODN) agonist of the Toll-like Receptor 9 (TLR9) in a sterile phosphate buffered saline solution.

Intended Use: HEPLISAV™ is indicated for immunization against infection caused by all known subtypes of hepatitis B virus in adults 18 years of age and older.

Manufacturer:
Dynavax Technologies Corporation
2929 Seventh Street, Suite 100
Berkeley, CA 94710-2753
(510)-848-5100 *(office hours 8:00 a.m. to 5:00 pm PST)*

2. HAZARD IDENTIFICATION

Classification of the Substance: Specific Target Organ Toxicity (Repeated or Prolonged Exposure), Category 1.

Label Elements:

Signal Word: Caution

Hazard Statement(s): May cause damage to the kidneys, liver, spleen, and hematopoietic system with prolonged or repeated exposure through parenteral route.

Precautionary Statement(s): None.

Symbols:

Hazard Not Otherwise Classified: None.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance:

Ingredient/Chemical Name	CAS Number	Concentration (% weight)
Hepatitis B surface antigen (HBsAg)	None	0.004%
CpG phosphorothioate oligodeoxynucleotide (CpG-ODN) 1018 with 22 bases	None	0.6%
Polysorbate 80	9005-65-6	0.01%
Phosphate buffered saline	None	Diluent (pH 6.5 to 7.5)

4. FIRST AID MEASURES

Eye Contact: Immediately irrigate with eyewash solution or clean water, holding the eyelids apart, for at least 15 minutes. Obtain medical attention.

Skin Contact: Take off all contaminated clothing immediately. After contact with skin, wash immediately with plenty of water. Obtain medical attention if ill effects occur.

Inhalation: Remove patient from exposure, keep warm and at rest. Obtain medical attention if ill effects occur.

Ingestion: Wash out mouth with water and give 200 to 300 mL of water to drink. Do NOT induce vomiting as a First-Aid measure. Obtain medical attention if ill effects occur.

Most Important Symptoms/Effects, Acute & Delayed: This material is for research and development purpose only. Refer to Section 11: Toxicological Information.

Indication of Immediate Medical Attention & Special Treatment Needed: Symptomatic treatment and supportive therapy as indicated. Emergency medical treatment advice varies within different countries. For further information consult the Local National Poisons Information Services.

5. FIRE-FIGHTING MEASURES

Suitable Extinguishing Media: Not combustible, see section 15.

Unsuitable Extinguishing Media: None known.

Special Hazards Arising From the Chemical: None known.

Special Protective Equipment and Precautions for Firefighters: A self-contained breathing apparatus and suitable protective clothing should be worn in fire conditions.

6. ACCIDENTAL RELEASE MEASURES

Personal Precautions: Ensure suitable personal protection during removal of spillages. See Section 8. Prevent entry into drains, sewers or watercourses.

Methods and Materials for Containment and Clean-up: Moisten spillages with water and collect spill with absorbent material. Transfer to a container for disposal. Wash the spillage area with water.

7. HANDLING AND STORAGE

Precautions for Safe Handling: Avoid contact with skin and eyes.

Conditions for Safe Storage, Including Any Incompatibilities: Store and ship refrigerated at 2 to 8°C. DO NOT FREEZE.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Occupational Exposure Limit Values: No OSHA PEL or ACGIH TLV assigned.

Appropriate Engineering Controls: Atmospheric levels should be controlled using the principles of good occupational hygiene practice as specified in a workplace risk assessment. Prevent entry into drains, sewers or watercourses.

Individual Protection Measures, Such as Personal Protective Equipment (PPE):

Hands: Impervious gloves to prevent skin contact and absorption.

Eye/Face: Wear chemical safety goggles or protective eye glasses.

Skin: Lab coat or other appropriate protective clothing.

Respiratory Protection: As necessary, use NIOSH/MSHA approved respiratory protection consistent with the workplace risk assessment. Consult a qualified safety and health professional for additional guidance, as needed.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: Clear, colorless liquid

Odor: Not available.

Odor Threshold: Not available.

pH: 6.5 to 7.5

Melting Point/Freezing Point: Not available.

Initial Boiling Point and Boiling Range: Not available.

Flash Point: Not available.

Evaporation Rate: Not Available.

Flammability (Solid, Gas): Not Available.

Upper/Lower Flammability or Explosive Limits: Not Available.

Vapor Pressure: Not available.

Vapor Density: Not Available.

Relative Density: Not Available.

Solubility: Freely soluble in aqueous phosphate buffered saline at a neutral pH.

Partition Coefficient: Not Available.

Auto-ignition Temperature: Not Available.

Decomposition Temperature: Not Available.

Viscosity: Not available.

10. STABILITY AND REACTIVITY

Reactivity: No reactivity hazards known under normal (ambient) conditions.

Chemical Stability: Stable under normal (ambient) storage and handling conditions.

Possibility of Hazardous Reactions: No dangerous reaction known under normal (ambient) conditions.

Conditions to Avoid: Avoid exposure to oxidizers.

Incompatible Materials: Oxidizers.

Hazardous Decomposition Products: None known.

11. TOXICOLOGY INFORMATION

The toxicological properties of this material have been investigated in mice and rats and no significant toxicities were observed. For research and developmental purposes only.

Repeat-dose Toxicity: (Species, Regimen, Route, Dose, Target Organs, Endpoint)

- Mice; 3 doses (Weeks 0, 2, and 4); intramuscular; 0.5 mcg/dose HBsAg combined with 1, 5 or 50 mcg 1018/dose; spleen, liver and injection-sites; NOAEL not defined.
- Rats; 4 doses (Weeks 0, 2, 4 and 6); intramuscular; 4 mcg HBsAg + 600 mcg 1018/dose or 20 mcg HBsAg + 3000 mcg 1018/dose; spleen, liver, lymph nodes, bone marrow, and injection-sites; NOAEL 20 mcg HBsAg + 3000 mcg 1018.

Reproductive and Developmental Toxicity: (Species, Regimen, Route, Dose, Target Organs, Endpoint)

- Rats, 4 doses (prior to mating on day 1 and day 19 and on gestation day 6 and day 18); intramuscular; 2.5 mcg HBsAg + 1.5, 15, 300 or 3000 mcg 1018/dose; injection sites; liver, kidneys, adrenals, spleen, lymph nodes; NOAEL 2.5 mcg HBsAg+ 3000mcg 1018.

Effects of Repeat-dose in Humans:

The HEPLISAV formulation is a vaccine indicated for immunization against infection caused by all known subtypes of hepatitis B virus. HEPLISAV is a non-infectious subunit viral vaccine consisting of surface antigen of hepatitis B virus produced in yeast cells in combination with 1018 adjuvant. In studies involving adults 18 years of age or older, the most frequent effects in individuals receiving HEPLISAV included injection-site reactions (pain, redness and swelling), malaise, headache, and fatigue.

Likely Routes of Exposure:

Ingestion: Not available.

Inhalation: Not available.

Skin Contact: Not available.

Eye Contact: Not available.

Symptoms Related to the Physical, Chemical, and Toxicological Characteristics: Parenteral exposure could generate an immune response to the protein antigen (HBsAg) resulting in systemic and local responses (e.g., antibody seroconversion, and positive skin reaction). May contain yeast protein from the manufacturing process of HBsAg which could affect yeast-sensitive individuals; anaphylaxis has been reported with other commercial recombinant hepatitis B vaccines produced in yeast. May activate the immune system and cause skin rashes and flu-like symptoms such as fever.

Delayed and Immediate Effects and Chronic Effects from Short- and Long-Term Exposure:

Acute Toxicity: Not available.

Skin Corrosion/Irritation: Not available.

Serious Eye Damage/ Eye Irritation: Not available.

Local Effects: Non-adverse injection site reactions (erythema, edema) observed in rats given 4 intramuscular doses 4 mcg HBsAg + 600 mcg 1018/dose or 20 mcg HBsAg + 3000 mcg 1018/dose. Parenteral exposure to HBsAg + 1018 could generate an immune response locally (eg, positive skin reaction; eg, erythema and swelling in skin tissues).

Respiratory Sensitization: Not available.

Skin Sensitization: Not available.

Germ Cell Mutagenicity: Not available for HBsAg + 1018 vaccine formulation. The 1018 adjuvant alone was negative for mutagenic and clastogenic effects in vitro and in vivo assays (ie, bacterial reverse mutation, chromosome aberration and mouse erythrocyte micronucleus assay).

Carcinogenicity: Not available.

Reproductive Toxicity: There were no reproductive or developmental effects observed in female rats administered HBsAg + 1018.

Specific Target Organ Toxicity, Single Exposure: Not available.

Specific Target Organ Toxicity, Repeated Exposure: May cause damage to the kidneys, liver, spleen, and hematopoietic system with prolonged exposure through parenteral route.

Aspiration Hazard: Not available.

12. ECOLOGICAL INFORMATION

Ecotoxicity: Not available.

Persistence and Degradability: Not available.

Bio accumulative Potential: Not available.

Mobility in Soil: Not available.

Other adverse Effects: Not available.

13. DISPOSAL CONSIDERATIONS

Disposal should be in accordance with applicable U.S. Federal, State, and local laws and regulations. This information presented below only applies to the material as supplied. The identification based on characteristic(s) or listing may not apply if the material has been used or otherwise contaminated. It is the responsibility of the waste generator to determine the toxicity and physical properties of the material generated to determine the proper waste identification and disposal methods in compliance with applicable regulations.

14. TRANSPORT INFORMATION

U.S. DOT (ground): Not regulated as a hazardous material for transport.

ICAO/IATA (air): Not regulated as a hazardous material for transport.

15. REGULATORY INFORMATION

U.S. Federal Regulations: Not listed on the U.S. TSCA inventory. This product is a drug and is exempt from TSCA regulation when manufactured, processed or distributed in commerce for use as a drug.

SARA 301 Extremely Hazardous Substance: No

SARA 311/312 Hazardous Chemical: Chronic Health Hazard

U.S. State Regulations:

California Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65): This material is not known to contain any chemicals currently listed as carcinogens or reproductive toxins.

National Fire Protection Association (NFPA) Rating:

Health: 1

Fire: 0

Reactivity: 0

Special: None

16. OTHER INFORMATION

The information provided here is believed to be accurate and represents the best information currently available.

DOCUMENT APPROVALS

Electronic signatures on the final page of this document indicate the document has been reviewed and approved, and the document is acceptable for use.

REVISION HISTORY

Rev	Summary of Changes
02	Update format to meet current regulations. Added new information where available.
01	Initial issue