SAFETY DATA SHEET

Raltegravir Adult Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Raltegravir Adult Formulation

Manufacturer or supplier's details
Company : MSD
Address : 26 Talavera Road, Talavera Corp Centre, Macquarie Park
           New South Wales, 2113 Australia
Telephone : (61)-02-8988-8000
Emergency telephone number : (61)-02-8988-8000
E-mail address : EHSDATASTEWARD@msd.com
Telefax : 908-735-1496

Recommended use of the chemical and restrictions on use
Recommended use : Pharmaceutical

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification
Serious eye damage/eye irritation : Category 1
Reproductive toxicity : Category 2
Specific target organ toxicity - single exposure : Category 3

GHS label elements
Hazard pictograms : 
Signal word : Danger
Hazard statements : H318 Causes serious eye damage.
                   H335 May cause respiratory irritation.
                   H361d Suspected of damaging the unborn child.
Precautionary statements : Prevention:
                           P201 Obtain special instructions before use.
                           P202 Do not handle until all safety precautions have been read
                           and understood.
                           P261 Avoid breathing dust.
                           P271 Use only outdoors or in a well-ventilated area.
                           P280 Wear eye protection/ face protection.
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**SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS**

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Raltegravir</td>
<td>871038-72-1</td>
<td>&gt;= 30 - &lt; 60</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 10 - &lt; 30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>&lt; 10</td>
</tr>
</tbody>
</table>

**SECTION 4. FIRST AID MEASURES**

General advice: In the case of accident or if you feel unwell, seek medical advice immediately. When symptoms persist or in all cases of doubt seek medical advice.

If inhaled: If inhaled, remove to fresh air. Get medical attention.

In case of skin contact: In case of contact, immediately flush skin with soap and plenty of water. Remove contaminated clothing and shoes. Get medical attention. Wash clothing before reuse. Thoroughly clean shoes before reuse.

In case of eye contact: In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. If easy to do, remove contact lens, if worn. Get medical attention immediately.

If swallowed: If swallowed, DO NOT induce vomiting.
Get medical attention. Rinse mouth thoroughly with water.

Most important symptoms and effects, both acute and delayed:

- Causes serious eye damage.
- May cause respiratory irritation.
- Suspected of damaging the unborn child.
- Contact with dust can cause mechanical irritation or drying of the skin.

Protection of first-aiders:

First Aid responders should pay attention to self-protection, and use the recommended personal protective equipment when the potential for exposure exists (see section 8).

Notes to physician:

- Treat symptomatically and supportively.

SECTION 5. FIREFIGHTING MEASURES

Suitable extinguishing media:

- Water spray
- Alcohol-resistant foam
- Carbon dioxide (CO2)
- Dry chemical

Unsuitable extinguishing media:

- None known.

Specific hazards during firefighting:

- Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard.
- Exposure to combustion products may be a hazard to health.

Hazardous combustion products:

- Carbon oxides
- Metal oxides
- Oxides of phosphorus
- Nitrogen oxides (NOx)
- Fluorine compounds

Specific extinguishing methods:

- Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.
- Use water spray to cool unopened containers.
- Remove undamaged containers from fire area if it is safe to do so.
- Evacuate area.

Special protective equipment for firefighters:

- In the event of fire, wear self-contained breathing apparatus.
- Use personal protective equipment.

SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures:

- Use personal protective equipment.
- Follow safe handling advice and personal protective equipment recommendations.

Environmental precautions:

- Discharge into the environment must be avoided.
- Prevent further leakage or spillage if safe to do so.
- Retain and dispose of contaminated wash water.
- Local authorities should be advised if significant spills cannot be contained.

Methods and materials for containment and cleaning up:

- Sweep up or vacuum up spillage and collect in suitable container for disposal.
- Avoid dispersal of dust in the air (i.e., clearing dust surfaces...
with compressed air). Dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration. Local or national regulations may apply to releases and disposal of this material, as well as those materials and items employed in the cleanup of releases. You will need to determine which regulations are applicable. Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.

SECTION 7. HANDLING AND STORAGE

Technical measures: Static electricity may accumulate and ignite suspended dust causing an explosion. Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.

Local/Total ventilation: If sufficient ventilation is unavailable, use with local exhaust ventilation.

Advice on safe handling: Do not breathe dust. Do not swallow. Do not get in eyes. Avoid prolonged or repeated contact with skin. Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment. Keep container tightly closed. Already sensitised individuals should consult their physician regarding working with respiratory irritants or sensitisers. Minimize dust generation and accumulation. Keep container closed when not in use. Keep away from heat and sources of ignition. Take precautionary measures against static discharges. Take care to prevent spills, waste and minimize release to the environment.

Hygiene measures: If exposure to chemical is likely during typical use, provide eye flushing systems and safety showers close to the working place. When using do not eat, drink or smoke. Wash contaminated clothing before re-use.

Conditions for safe storage: Keep in properly labelled containers. Store locked up. Keep tightly closed. Keep in a cool, well-ventilated place. Store in accordance with the particular national regulations.

Materials to avoid: Do not store with the following product types: Strong oxidizing agents

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Components with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of Control parameters / Permissible</th>
<th>Basis</th>
</tr>
</thead>
</table>


Engineering measures:
- Minimize workplace exposure concentrations.
- Apply measures to prevent dust explosions.
- Ensure that dust-handling systems (such as exhaust ducts, dust collectors, vessels, and processing equipment) are designed in a manner to prevent the escape of dust into the work area (i.e., there is no leakage from the equipment).
- If sufficient ventilation is unavailable, use with local exhaust ventilation.

Personal protective equipment
Respiratory protection:
- If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.
- Filter type: Particulates type

Hand protection
- Material: Chemical-resistant gloves

Remarks:
- Choose gloves to protect hands against chemicals depending on the concentration and quantity of the hazardous substance and specific to place of work. Breakthrough time is not determined for the product. Change gloves often! For special applications, we recommend clarifying the resistance to chemicals of the aforementioned protective gloves with the glove manufacturer. Wash hands before breaks and at the end of workday.

Eye protection:
- Wear the following personal protective equipment:
  - Chemical resistant goggles must be worn.
  - If splashes are likely to occur, wear:
    - Face-shield

Skin and body protection:
- Select appropriate protective clothing based on chemical resistance data and an assessment of the local exposure potential.
- Skin contact must be avoided by using impervious protective clothing (gloves, aprons, boots, etc.).
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Version 4.10  Revision Date: 09/13/2019  SDS Number: 13213-00015  Date of last issue: 24.04.2019
Date of first issue: 16.09.2014

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
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<tbody>
<tr>
<td>Appearance</td>
<td>powder</td>
</tr>
<tr>
<td>Colour</td>
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</tr>
<tr>
<td>Odour</td>
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</tr>
<tr>
<td>Odour Threshold</td>
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<tr>
<td>pH</td>
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</tr>
<tr>
<td>Melting point/freezing point</td>
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<td>Initial boiling point and boiling range</td>
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</tr>
<tr>
<td>Flash point</td>
<td>No data available</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Flammability (solid, gas)</td>
<td>May form explosive dust-air mixture during processing, handling or other means.</td>
</tr>
<tr>
<td>Flammability (liquids)</td>
<td>No data available</td>
</tr>
<tr>
<td>Self-ignition</td>
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</tr>
<tr>
<td>Upper explosion limit / Upper flammability limit</td>
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</tr>
<tr>
<td>Lower explosion limit / Lower flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Vapour pressure</td>
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</tr>
<tr>
<td>Relative vapour density</td>
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<tr>
<td>Density</td>
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<tr>
<td>Solubility(ies)</td>
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<tr>
<td>Water solubility</td>
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<td>Partition coefficient: n-octanol/water</td>
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<tr>
<td>Auto-ignition temperature</td>
<td>No data available</td>
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<tr>
<td>Decomposition temperature</td>
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<tr>
<td>Viscosity</td>
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<td>Viscosity, dynamic</td>
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</tr>
<tr>
<td>Viscosity, kinematic</td>
<td>No data available</td>
</tr>
<tr>
<td>Flow time</td>
<td>No data available</td>
</tr>
</tbody>
</table>
Explosive properties: Not explosive

Oxidizing properties: The substance or mixture is not classified as oxidizing.

Molecular weight: No data available

Particle size: No data available

SECTION 10. STABILITY AND REACTIVITY

Reactivity: Not classified as a reactivity hazard.

Chemical stability: Stable under normal conditions.

Possibility of hazardous reactions: May form explosive dust-air mixture during processing, handling or other means.

Conditions to avoid: Heat, flames and sparks.

Incompatible materials: Avoid dust formation.

Hazardsous decomposition products: Oxidizing agents

SECTION 11. TOXICOLOGICAL INFORMATION

Exposure routes: Inhalation

Skin contact

Ingestion

Eye contact

Acute toxicity:
Not classified based on available information.

Components:

Raltegravir:
Acute oral toxicity: LD50 (Mouse, male and female): > 2,000 mg/kg

Cellulose:
Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg

Acute inhalation toxicity: LC50 (Rat): > 5.8 mg/l

Exposure time: 4 h

Test atmosphere: dust/mist

Acute dermal toxicity: LD50 (Rabbit): > 2,000 mg/kg

Magnesium stearate:
Acute oral toxicity: LD50 (Rat): > 2,000 mg/kg

Method: OECD Test Guideline 423

Assessment: The substance or mixture has no acute oral toxicity

Remarks: Based on data from similar materials
Acute dermal toxicity: LD50 (Rabbit): > 2,000 mg/kg
Remarks: Based on data from similar materials.

Skin corrosion/irritation:
Not classified based on available information.

Components:

**Raltegravir:**
Species: Rabbit
Result: No skin irritation

**Magnesium stearate:**
Species: Rabbit
Result: No skin irritation
Remarks: Based on data from similar materials

Serious eye damage/eye irritation:
Causes serious eye damage.

Components:

**Raltegravir:**
Species: Bovine cornea
Result: Severe irritation

**Magnesium stearate:**
Species: Rabbit
Result: No eye irritation
Remarks: Based on data from similar materials

Respiratory or skin sensitisation:

Skin sensitisation:
Not classified based on available information.

Respiratory sensitisation:
Not classified based on available information.

Components:

**Raltegravir:**
Test Type: Local lymph node assay (LLNA)
Species: Mouse
Result: negative

**Magnesium stearate:**
Test Type: Maximisation Test
Exposure routes: Skin contact
Species: Guinea pig
Method: OECD Test Guideline 406
Result: negative
Remarks : Based on data from similar materials

**Chronic toxicity**

**Germ cell mutagenicity**
Not classified based on available information.

**Components:**

**Raltegravir:**

| Genotoxicity in vitro | Test Type: reverse mutation assay |
| Result: negative |

| Test Type: Alkaline elution assay |
| Test system: rat hepatocytes |
| Result: negative |

| Test Type: Chromosomal aberration |
| Method: OECD Test Guideline 473 |
| Result: negative |

| Genotoxicity in vivo | Test Type: In vivo micronucleus test |
| Species: Mouse |
| Result: negative |

| Test Type: Chromosomal aberration |
| Method: OECD Test Guideline 475 |
| Result: negative |

**Cellulose:**

| Genotoxicity in vitro | Test Type: Bacterial reverse mutation assay (AMES) |
| Result: negative |

| Test Type: In vitro mammalian cell gene mutation test |
| Result: negative |

| Genotoxicity in vivo | Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay) |
| Species: Mouse |
| Application Route: Ingestion |
| Result: negative |

**Magnesium stearate:**

| Genotoxicity in vitro | Test Type: In vitro mammalian cell gene mutation test |
| Result: negative |
| Remarks: Based on data from similar materials |

| Test Type: Chromosome aberration test in vitro |
| Method: OECD Test Guideline 473 |
| Result: negative |
| Remarks: Based on data from similar materials |

| Test Type: Bacterial reverse mutation assay (AMES) |
Carcinogenicity
Not classified based on available information.

Components:

Raltegravir:
Species: Mouse, male and female
Exposure time: 104 weeks
Result: negative

Cellulose:
Species: Rat
Application Route: Ingestion
Exposure time: 72 weeks
Result: negative

Reproductive toxicity
Suspected of damaging the unborn child.

Components:

Raltegravir:
Effects on fertility:
Species: Rat, male and female
Application Route: Oral
General Toxicity: Parent: NOAEL: 600 mg/kg body weight
Result: negative

Effects on foetal development:
Species: Rat
Application Route: Oral
General Toxicity Maternal: NOAEL: >= 600 mg/kg body weight
Teratogenicity: LOAEL F1: 300 mg/kg body weight
Symptoms: Skeletal malformations
Result: positive
Species: Rabbit
General Toxicity Maternal: NOAEL: >= 1,000 mg/kg body weight
Teratogenicity: NOAEL: >= 1,000 mg/kg body weight
Result: negative

Reproductive toxicity - Assessment
Some evidence of adverse effects on development, based on animal experiments.

Cellulose:
Effects on fertility:
Test Type: One-generation reproduction toxicity study
Species: Rat
Application Route: Ingestion
Result: negative
Effects on foetal development:
Test Type: Fertility/early embryonic development
Species: Rat
Application Route: Ingestion
Result: negative

Magnesium stearate:
Effects on fertility:
Test Type: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test
Species: Rat
Application Route: Ingestion
Method: OECD Test Guideline 422
Result: negative
Remarks: Based on data from similar materials

Effects on foetal development:
Test Type: Embryo-foetal development
Species: Rat
Application Route: Ingestion
Result: negative
Remarks: Based on data from similar materials

STOT - single exposure
May cause respiratory irritation.

Components:

Raltegravir:
Exposure routes: Inhalation
Target Organs: Respiratory Tract
Assessment: May cause respiratory irritation.

STOT - repeated exposure
Not classified based on available information.

Repeated dose toxicity

Components:

Raltegravir:
Species: Dog
NOAEL: 90 mg/kg
Application Route: Oral
Exposure time: 371 d
Symptoms: Vomiting

Species: Rat
NOAEL: 30 mg/kg
LOAEL: 120 mg/kg
Application Route: Oral
Exposure time: 189 d
Target Organs: Stomach

Species: Mouse
NOAEL: 50 mg/kg
LOAEL: 500 mg/kg
Application Route : Oral
Exposure time : 14 Weeks
Target Organs : Stomach

Species : Rat
NOAEL : 50 mg/kg
LOAEL : 200 mg/kg
Application Route : Oral
Exposure time : 8 Weeks
Target Organs : Stomach

Cellulose:
Species : Rat
NOAEL : >= 9,000 mg/kg
Application Route : Ingestion
Exposure time : 90 Days

Magnesium stearate:
Species : Rat
NOAEL : > 100 mg/kg
Application Route : Ingestion
Exposure time : 90 Days
Remarks : Based on data from similar materials

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Components:

Raltegravir:
Ingestion : Symptoms: Nausea, Diarrhoea, Headache, Fever, Rash, Skin irritation

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

Raltegravir:
Toxicity to fish : LC50 (Pimephales promelas (fathead minnow)): > 100 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203

LC50 (Cyprinodon variegatus (sheepshead minnow)): > 100 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203

Toxicity to daphnia and other aquatic invertebrates : EC50 (Daphnia magna (Water flea)): > 100 mg/l
Exposure time: 48 h
### Toxicity to algae/aquatic plants
- **EC50**: Pseudokirchneriella subcapitata (green algae): 66 mg/l
- **Exposure time**: 96 h
- Method: OECD Test Guideline 202

- **NOEC**: Pseudokirchneriella subcapitata (green algae): 3.8 mg/l
- **Exposure time**: 96 h
- Method: OECD Test Guideline 202

### Toxicity to fish (Chronic toxicity)
- **NOEC**: Pimephales promelas (fathead minnow): 9.3 mg/l
- **Exposure time**: 33 d
- Method: OECD Test Guideline 210

### Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)
- **NOEC**: Daphnia magna (Water flea): 9.5 mg/l
- **Exposure time**: 21 d
- Method: OECD Test Guideline 211

### Toxicity to microorganisms
- **EC50**: > 1,000 mg/l
- **Exposure time**: 3 h
- **Test Type**: Respiration inhibition
- Method: OECD Test Guideline 209

- **NOEC**: 1,000 mg/l
- **Exposure time**: 3 h
- **Test Type**: Respiration inhibition
- Method: OECD Test Guideline 209

**Cellulose:**
- **Toxicity to fish**: LC50 (Oryzias latipes (Japanese medaka)): > 100 mg/l
- **Exposure time**: 48 h
- **Remarks**: Based on data from similar materials

**Magnesium stearate:**
- **Toxicity to fish**: LC50 (Leuciscus idus (Golden orfe)): > 100 mg/l
- **Exposure time**: 48 h
- **Method**: DIN 38412
- **Remarks**: Based on data from similar materials

- **Toxicity to daphnia and other aquatic invertebrates**: EL50 (Daphnia magna (Water flea)): > 1 mg/l
- **Exposure time**: 47 h
- **Test substance**: Water Accommodated Fraction
- **Remarks**: Based on data from similar materials
  - No toxicity at the limit of solubility

- **Toxicity to algae/aquatic plants**: EL50 (Pseudokirchneriella subcapitata (green algae)): > 1 mg/l
- **Exposure time**: 72 h
- **Test substance**: Water Accommodated Fraction
- **Method**: OECD Test Guideline 201
- **Remarks**: Based on data from similar materials
  - No toxicity at the limit of solubility
## Toxicity to microorganisms

**NOELR** (Pseudokirchneriella subcapitata (green algae)): > 1 mg/l  
Exposure time: 72 h  
Test substance: Water Accommodated Fraction  
Method: OECD Test Guideline 201  
Remarks: Based on data from similar materials

**Toxicity to microorganisms**: EC10 (Pseudomonas putida): > 100 mg/l  
Exposure time: 16 h  
Test substance: Water Accommodated Fraction  
Remarks: Based on data from similar materials

## Persistence and degradability

### Components:

**Raltegravir**:
- Biodegradability: Result: rapidly degradable  
  Biodegradation: 50%  
  Exposure time: 9 d  
  Method: OECD Test Guideline 302B

**Stability in water**:
- Hydrolysis: < 10% (5 d)  
  Method: OECD Test Guideline 111

**Cellulose**:
- Biodegradability: Result: Readily biodegradable.

**Magnesium stearate**:
- Biodegradability: Result: Not biodegradable  
  Remarks: Based on data from similar materials

## Bioaccumulative potential

### Components:

**Raltegravir**:
- Partition coefficient: n-octanol/water: log Pow: -0.328

**Magnesium stearate**:
- Partition coefficient: n-octanol/water: log Pow: > 4

**Mobility in soil**:
No data available

**Other adverse effects**:
No data available
SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods
Waste from residues : Dispose of in accordance with local regulations.
Contaminated packaging : Empty containers should be taken to an approved waste handling site for recycling or disposal.
If not otherwise specified: Dispose of as unused product.

SECTION 14. TRANSPORT INFORMATION

International Regulations
UNRTDG
Not regulated as a dangerous good
IATA-DGR
Not regulated as a dangerous good
IMDG-Code
Not regulated as a dangerous good
Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code
Not applicable for product as supplied.

National Regulations
ADG
Not regulated as a dangerous good

SECTION 15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture

Prohibition/Licensing Requirements : There is no applicable prohibition or notification/licensing requirements, including for carcinogens under Commonwealth, State or Territory legislation.

SECTION 16. OTHER INFORMATION

Further information
Revision Date : 09/13/2019
Date format : dd.mm.yyyy

Full text of other abbreviations
ACGIH : USA. ACGIH Threshold Limit Values (TLV)
AU OEL : Australia. Workplace Exposure Standards for Airborne Con-
The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and shall not be considered a warranty or quality specification of any type. The information provided relates only to the specific material identified at the top of this SDS and may not be valid when the SDS material is used in combination with any other materials or in any process, unless specified in the text. Material users should review the information and recommendations in the specific context of their intended manner of handling, use, processing and storage, including an assessment of the appropriateness of the SDS material in the user’s end product, if applicable.

AU / EN