SAFETY DATA SHEET

Cimetidine Formulation

SECTION 1. IDENTIFICATION

Product name : Cimetidine Formulation
Other means of identification : No data available

Manufacturer or supplier's details
Company name of supplier : Merck & Co., Inc
Address : 2000 Galloping Hill Road
          Kenilworth - New Jersey - U.S.A. 07033
Telephone : 908-740-4000
Telefax : 908-735-1496
Emergency telephone : 1-908-423-6000
E-mail address : EHSDATASTEWARD@merck.com

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

SECTION 2. HAZARDS IDENTIFICATION

GHS classification in accordance with the Hazardous Products Regulations
Reproductive toxicity : Category 1B
Specific target organ toxicity - repeated exposure (Oral) : Category 2 (Liver, Kidney, Testis)

GHS label elements
Hazard pictograms :

Signal Word : Danger
Hazard Statements : H360D May damage the unborn child.
                  H373 May cause damage to organs (Liver, Kidney, Testis) through prolonged or repeated exposure if swallowed.

Precautionary Statements :
Prevention:
  P201 Obtain special instructions before use.
  P202 Do not handle until all safety precautions have been read and understood.
  P260 Do not breathe dust.
  P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.

Response:
  P308 + P313 IF exposed or concerned: Get medical advice/ attention.

Storage:
  P405 Store locked up.
Disposal:
P501 Dispose of contents/container to an approved waste disposal plant.

Other hazards
Dust contact with the eyes can lead to mechanical irritation.
Contact with dust can cause mechanical irritation or drying of the skin.
May form explosive dust-air mixture during processing, handling or other means.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>cimetidine</td>
<td>51481-61-9</td>
<td>&gt;= 30 - &lt; 60</td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 10 - &lt; 30</td>
</tr>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>&gt;= 1 - &lt; 5</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>&gt;= 1 - &lt; 5</td>
</tr>
</tbody>
</table>

Actual concentration or concentration range is withheld as a trade secret.

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 : If in eyes, rinse well with water. Get medical attention if irritation develops and persists.

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 : May damage the unborn child. May cause damage to organs through prolonged or repeated exposure if swallowed. Contact with dust can cause mechanical irritation or drying of the skin. Dust contact with the eyes can lead to mechanical irritation.

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. FIRE-FIGHTING MEASURES
Suitable extinguishing media

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

Unsuitable extinguishing media

- None known.

Specific hazards during fire fighting

- 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
- Nitrogen oxides (NOx)
- Sulfur oxides
- Metal oxides

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 fire-fighters

- 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 spillages 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 get on skin or clothing. Do not breathe dust. Do not swallow. Avoid contact with eyes. Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment. Keep container tightly closed. 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.

Conditions for safe storage: Keep in properly labeled containers. Store locked up. Keep tightly closed. Store in accordance with the particular national regulations.

Materials to avoid: Do not store with the following product types: Strong oxidizing agents Organic peroxides Explosives Gases

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>cimetidine</td>
<td>51481-61-9</td>
<td>TWA</td>
<td>1000 µg/m³ (OEL)</td>
<td></td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>CA AB OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Total dust)</td>
<td>10 mg/m³</td>
<td>CA BC OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (respirable dust fraction)</td>
<td>3 mg/m³</td>
<td>CA BC OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWAEOV (total dust)</td>
<td>10 mg/m³</td>
<td>CA QC OEL</td>
</tr>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>CA AB OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Total dust)</td>
<td>10 mg/m³</td>
<td>CA BC OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (respirable dust)</td>
<td>3 mg/m³</td>
<td>CA BC OEL</td>
</tr>
</tbody>
</table>
Cimetidine Formulation

Engineering measures: Use feasible engineering controls to minimize exposure to compound. All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.

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

Eye protection: Wear safety glasses with side shields or goggles. If the work environment or activity involves dusty conditions, mists or aerosols, wear the appropriate goggles. Wear a faceshield or other full face protection if there is a potential for direct contact to the face with dusts, mists, or aerosols.

Skin and body protection: Work uniform or laboratory coat.

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.

The effective operation of a facility should include review of engineering controls, proper personal protective equipment, appropriate degowning and decontamination procedures, industrial hygiene monitoring, medical surveillance and the use of administrative controls.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: powder

Color: No data available

Odor: No data available

Odor Threshold: No data available
pH : No data available

Melting point/freezing point : No data available

Initial boiling point and boiling range : No data available

Flash point : Not applicable

Evaporation rate : Not applicable

Flammability (solid, gas) : May form explosive dust-air mixture during processing, handling or other means.

Flammability (liquids) : No data available

Upper explosion limit / Upper flammability limit : No data available

Lower explosion limit / Lower flammability limit : No data available

Vapor pressure : Not applicable

Relative vapor density : Not applicable

Relative density : No data available

Density : No data available

Solubility(ies)
   Water solubility : No data available

Partition coefficient: n-octanol/water

Autoignition temperature : No data available

Decomposition temperature : No data available

Viscosity
   Viscosity, kinematic : Not applicable

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. Can react with strong oxidizing agents.

Conditions to avoid: Heat, flames and sparks. Avoid dust formation.
Incompatible materials: Oxidizing agents
Hazardous decomposition products: No hazardous decomposition products are known.

SECTION 11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure
Inhalation
Skin contact
Ingestion
Eye contact

Acute toxicity
Not classified based on available information.

Components:
cimetidine:
Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
LD50 (Mouse): 2,550 mg/kg
LD50 (Hamster): > 4,000 mg/kg

Acute toxicity (other routes of administration):
LD50 (Rat): 106 mg/kg
Application Route: Intravenous
LD50 (Rabbit): 164 mg/kg
Application Route: Intravenous
LD50 (Rat): 860 mg/kg
Application Route: Subcutaneous
LD50 (Mouse): 437 mg/kg
Application Route: Subcutaneous
Symptoms: Convulsions

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

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

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

Serious eye damage/eye irritation
Not classified based on available information.

Components:

Starch:
Species : Rabbit
Result : No eye irritation

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

Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

Components:

Starch:
Test Type : Maximization Test
Routes of exposure : Skin contact
Species : Guinea pig
Result : negative
Magnesium stearate:

Test Type: Maximization Test
Routes of exposure: Skin contact
Species: Guinea pig
Method: OECD Test Guideline 406
Result: negative
Remarks: Based on data from similar materials

Germ cell mutagenicity
Not classified based on available information.

Components:

cimetidine:
Genotoxicity in vitro:
- Test Type: Bacterial reverse mutation assay (AMES)
  Result: negative
- Test Type: Chromosomal aberration
  Result: negative
- Test Type: unscheduled DNA synthesis assay
  Test system: rat hepatocytes
  Result: negative
- Test Type: unscheduled DNA synthesis assay
  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

Starch:
Genotoxicity in vitro:
- Test Type: Bacterial reverse mutation assay (AMES)
  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
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Carcinogenicity
Not classified based on available information.

Components:
cimetidine:
Species: Rat
Application Route: Oral
Exposure time: 2 Years
Target Organs: Testis
Remarks: Benign tumor(s)

Carcinogenicity - Assessment: No evidence of carcinogenicity in animal studies.

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

Reproductive toxicity
May damage the unborn child.

Components:
cimetidine:
Effects on fertility: Test Type: Fertility/early embryonic development
Species: Rat
Application Route: Oral
Fertility: NOAEL: 950 mg/kg body weight
Result: No effect on reproduction capacity.

Effects on fetal development: Test Type: Development
Species: Rat
Application Route: Oral
Developmental Toxicity: LOAEL: 17 mg/kg body weight
Symptoms: male reproductive effects
Remarks: Adverse effects were observed in males only.

Reproductive toxicity - Assessment: May damage the unborn child.

Cellulose:
Effects on fertility: Test Type: One-generation reproduction toxicity study
Species: Rat
Application Route: Ingestion
Result: negative
Effects on fetal 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 fetal development: Test Type: Embryo-fetal development
Species: Rat
Application Route: Ingestion
Result: negative
Remarks: Based on data from similar materials

STOT-single exposure
Not classified based on available information.

STOT-repeated exposure
May cause damage to organs (Liver, Kidney, Testis) through prolonged or repeated exposure if swallowed.

Components:
cimetidine:
Routes of exposure: Oral
Target Organs: Liver, Kidney, Testis
Assessment: May cause damage to organs through prolonged or repeated exposure.

Repeated dose toxicity
Components:
cimetidine:
Species: Rat
LOAEL: 160 mg/kg
Application Route: Oral
Exposure time: 2 Months
Target Organs: Gastrointestinal tract
Remarks: May cause damage to organs.

Species: Rat
NOAEL: 200 mg/kg
Application Route: Oral
Exposure time: 12 Months
Symptoms: No adverse effects.
### Species: Rat
- **LOAEL**: 950 mg/kg
- **Application Route**: Oral
- **Exposure time**: 2 y
- **Target Organs**: Liver, Testis, Prostate
- **Remarks**: May cause damage to organs.

### Species: Dog
- **NOAEL**: 366 mg/kg
- **Application Route**: Oral
- **Exposure time**: 12 Months
- **Target Organs**: Liver, Kidney, Prostate
- **Remarks**: May cause damage to organs.

### Species: Dog
- **NOAEL**: 144 mg/kg
- **Application Route**: Oral
- **Exposure time**: 4 y
- **Symptoms**: No adverse effects.

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

### Starch:
- **Species**: Rat
- **NOAEL**: >= 2,000 mg/kg
- **Application Route**: Skin contact
- **Exposure time**: 28 Days
- **Method**: OECD Test Guideline 410

### 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:

- **cimetidine**
  - **Ingestion**: Symptoms: The most common side effects are: Headache, Dizziness, Nausea, skin rash, Itching, May cause, central nervous system effects, gynecomastia, impotence, kidney effects.
  - **Remarks**: May cause harm to breast-fed children.
Ecotoxicity

Components:

cimetidine:

Ecotoxicology Assessment
Acute aquatic toxicity: Toxic effects cannot be excluded
Chronic aquatic toxicity: Toxic effects cannot be excluded

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.

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:

Cellulose:
Biodegradability : Result: Readily biodegradable.

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

Bioaccumulative potential

Components:

cimetidine:
Partition coefficient: n-octanol/water : log Pow: 0.40

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.

Domestic regulation

TDG
SAFETY DATA SHEET

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Not regulated as a dangerous good

SECTION 15. REGULATORY INFORMATION

The ingredients of this product are reported in the following inventories:

- AICS: not determined
- DSL: not determined
- IECSC: not determined

SECTION 16. OTHER INFORMATION

Full text of other abbreviations

- ACGIH: USA. ACGIH Threshold Limit Values (TLV)
- CA BC OEL: Canada. British Columbia OEL
- CA QC OEL: Québec. Regulation respecting occupational health and safety, Schedule 1, Part 1: Permissible exposure values for airborne contaminants
- ACGIH / TWA: 8-hour, time-weighted average
- CA AB OEL / TWA: 8-hour Occupational exposure limit
- CA BC OEL / TWA: 8-hour time weighted average
- CA QC OEL / TWA EV: Time-weighted average exposure value

AICS - Australian Inventory of Chemical Substances; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50% of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; n.o.s. - Not Otherwise Specified; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transporta-
Sources of key data used to compile the Material Safety Data Sheet:

Revision Date: 03/23/2020

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.

CA / Z8