SECTION 1. IDENTIFICATION

Product name: Nomegestrol / Estradiol Formulation

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 29 CFR 1910.1200
Combustible dust

Carcinogenicity: Category 1A
Reproductive toxicity: Category 1A
Specific target organ toxicity - repeated exposure: Category 1 (Liver, Bone, Blood, Endocrine system)

GHS label elements
Hazard pictograms: 

Signal Word: Danger
Hazard Statements: If small particles are generated during further processing, handling or by other means, may form combustible dust concentrations in air.
H350 May cause cancer.
H360FD May damage fertility. May damage the unborn child.
H372 Causes damage to organs (Liver, Bone, Blood, Endocrine system) through prolonged or repeated exposure.

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.
P264 Wash skin thoroughly after handling.
P270 Do not eat, drink or smoke when using this product.
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.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chemical name</td>
</tr>
<tr>
<td></td>
<td>Cellulose</td>
</tr>
<tr>
<td></td>
<td>Estradiol</td>
</tr>
<tr>
<td></td>
<td>17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate</td>
</tr>
<tr>
<td></td>
<td>Talc</td>
</tr>
<tr>
<td></td>
<td>Titanium dioxide</td>
</tr>
</tbody>
</table>

Actual concentration 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 cause cancer.
May damage fertility. May damage the unborn child.
Causes damage to organs through prolonged or repeated exposure.
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 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
- Nitrogen oxides (NOx)

**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 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 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>Cellulose</td>
<td>9004-34-6</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Respirable)</td>
<td>5 mg/m³</td>
<td>NIOSH REL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (total)</td>
<td>10 mg/m³</td>
<td>NIOSH REL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (total dust)</td>
<td>15 mg/m³</td>
<td>OSHA Z-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (respirable fraction)</td>
<td>5 mg/m³</td>
<td>OSHA Z-1</td>
</tr>
<tr>
<td>Estradiol</td>
<td>50-28-2</td>
<td>TWA</td>
<td>0.05 µg/m³ (OEB 5)</td>
<td>Internal</td>
</tr>
</tbody>
</table>
Further information: Skin

<table>
<thead>
<tr>
<th>Substance</th>
<th>Wipe limit</th>
<th>TWA</th>
<th>Wipe limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate</td>
<td>0.5 µg/100 cm²</td>
<td>0.2 µg/m³</td>
<td>2 µg/100 cm²</td>
</tr>
<tr>
<td>Talc</td>
<td></td>
<td></td>
<td>OSHA Z-3</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td></td>
<td></td>
<td>NIOSH REL</td>
</tr>
</tbody>
</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. Dust formation may be relevant in the processing of this product. In addition to substance-specific OELs, general limitations of concentrations of particulates in the air at workplaces have to be considered in workplace risk assessment. Relevant limits include: OSHA PEL for Particulates Not Otherwise Regulated of 15 mg/m³ - total dust, 5 mg/m³ - respirable fraction; and ACGIH TWA for Particles (insoluble or poorly soluble) Not Otherwise Specified of 3 mg/m³ - respirable particles, 10 mg/m³ - inhalable particles.

Personal protective equipment:
Respiratory protection: General and local exhaust ventilation is recommended to maintain vapor exposures below recommended limits. Where concentrations are above recommended limits or are unknown, appropriate respiratory protection should be worn. Follow OSHA respirator regulations (29 CFR 1910.134) and use NIOSH/MSHA approved respirators. Protection provided by air purifying respirators against exposure to any hazardous chemical is limited. Use a positive pressure air supplied respirator if there is any potential for uncontrolled release, exposure levels are unknown, or any other circumstance where air purifying respirators may not provide adequate protection.

Hand protection
Material: Chemical-resistant gloves
Remarks

Choose gloves to protect hands against chemicals depending on the concentration 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:
Safety goggles

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).

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.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance

: powder

Color

: white

Odor

: odorless

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

: No data available

Evaporation rate

: No data available

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

: No data available
Relative vapor density : No data available
Relative density : No data available
Density : 1 g/cm³
Solubility(ies)
   Water solubility : No data available
Partition coefficient: n-octanol/water : No data available
Autoignition temperature : No data available
Decomposition temperature : No data available
Viscosity
   Viscosity, dynamic : No data available
   Viscosity, kinematic : No data available
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 reac-
tions : 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.
Product:
Acute oral toxicity : Acute toxicity estimate: > 5,000 mg/kg
Method: Calculation method

Components:
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

Estradiol:
Acute oral toxicity : LD50 (Rat): > 2,000 mg/kg
Acute toxicity (other routes of administration) : LD50 (Rat): > 300 mg/kg
Application Route: Subcutaneous

17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate:
Acute oral toxicity : LD50 (Rat): > 2,000 mg/kg
LD50 (Mouse): > 2,000 mg/kg
Acute toxicity (other routes of administration) : LD50 (Rat): > 2,000 mg/kg
Application Route: Intraperitoneal

Talc:
Acute oral toxicity : LD50 (Rat): > 5,000 mg/kg
Remarks: Based on data from similar materials

Titanium dioxide:
Acute oral toxicity : LD50 (Rat): > 5,000 mg/kg
Acute inhalation toxicity : LC50 (Rat): > 6.82 mg/l
Exposure time: 4 h
Test atmosphere: dust/mist
Assessment: The substance or mixture has no acute inhalation toxicity

Skin corrosion/irritation
Not classified based on available information.

Components:
Talc:
Species : Rabbit
Result : No skin irritation
Titanium dioxide:
Species : Rabbit
Result : No skin irritation

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

**Components:**

**Estradiol:**
Result : No eye irritation

**Talc:**
Species : Rabbit
Result : No eye irritation

**Titanium dioxide:**
Species : Rabbit
Result : No eye irritation

**Respiratory or skin sensitization**

**Skin sensitization**
Not classified based on available information.

**Respiratory sensitization**
Not classified based on available information.

**Components:**

**Estradiol:**
Routes of exposure : Skin contact
Species : Guinea pig
Assessment : Does not cause skin sensitization.
Result : negative

**Talc:**
Routes of exposure : Skin contact
Species : Humans
Result : negative

**Titanium dioxide:**
Test Type : Local lymph node assay (LLNA)
Routes of exposure : Skin contact
Species : Mouse
Result : negative

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

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

Estradiol:
Genotoxicity in vitro:
- Test Type: DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)
  Test system: mammalian cells
  Result: positive
- Test Type: Chromosome aberration test in vitro
  Test system: mammalian cells
  Result: positive
- Test Type: Chromosomal aberration
  Test system: mammalian cells
  Result: positive

Genotoxicity in vivo:
- Test Type: Chromosomal aberration
  Species: Rat
  Cell type: Bone marrow
  Result: negative
- Test Type: Chromosomal aberration
  Species: Mouse
  Cell type: Bone marrow
  Result: negative

17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate:
Genotoxicity in vitro:
- Test Type: Ames test
  Result: negative
- Test Type: Chromosome aberration test in vitro
  Result: negative
- Test Type: DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)
  Result: negative
- Test Type: In vitro mammalian cell gene mutation test
  Result: negative

Genotoxicity in vivo:
- Test Type: In vivo micronucleus test
Species: Rat
Application Route: Oral
Result: negative

Test Type: In vivo micronucleus test
Species: Mouse
Application Route: Oral
Result: negative

**Talc:**

Genotoxicity in vitro: Test Type: DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)
Result: negative

Genotoxicity in vivo: Test Type: Chromosome aberration test in vitro
Species: Rat
Application Route: Ingestion
Result: negative

**Titanium dioxide:**

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

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

**Carcinogenicity**
May cause cancer.

**Components:**

**Cellulose:**

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

**Estradiol:**

Species: Mouse
Application Route: Ingestion
Exposure time: 24 Months
LOAEL: 100 µg/kg
Result: positive
Target Organs: female reproductive organs

Species: Rat
Application Route: Subcutaneous
Exposure time: 13 weeks
LOAEL: 20 mg/kg body weight
Result: positive
Target Organs: Endocrine system
Carcinogenicity - Assessment: Positive evidence from human epidemiological studies

**17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate:**

- **Species**: Rat
- **Application Route**: oral (feed)
- **Activity duration**: 52 Weeks
  - **Result**: negative

- **Species**: Mouse
- **Application Route**: oral (feed)
- **Activity duration**: 20 mg/kg body weight
- **Result**: positive

**Target Organs**: Mammary gland, Pituitary gland

Carcinogenicity - Assessment: Weight of evidence does not support classification as a carcinogen

**Talc:**

- **Species**: Mouse
- **Application Route**: inhalation (dust/mist/fume)
- **Exposure time**: 2 Years
- **Result**: negative

**Titanium dioxide:**

- **Species**: Rat
- **Application Route**: inhalation (dust/mist/fume)
- **Exposure time**: 2 Years
- **Method**: OECD Test Guideline 453
- **Result**: positive
- **Remarks**: The mechanism or mode of action may not be relevant in humans.

Carcinogenicity - Assessment: Limited evidence of carcinogenicity in inhalation studies with animals.

**IARC**

- Group 2B: Possibly carcinogenic to humans

**OSHA**

- No component of this product present at levels greater than or equal to 0.1% is on OSHA’s list of regulated carcinogens.

**NTP**

- Known to be human carcinogen

  **Estradiol**

  (Estrogens, Steroidal)

<table>
<thead>
<tr>
<th>Compound</th>
<th>CAS Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol</td>
<td>50-28-2</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
</tr>
</tbody>
</table>

**Reproductive toxicity**

- May damage fertility. May damage the unborn child.
### Components:

#### 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

#### Estradiol:

**Effects on fertility**
- Test Type: One-generation reproduction toxicity study
- Species: Rat
- Application Route: Ingestion
  - Fertility: LOAEL: 0.5 mg/kg body weight
  - Result: Effects on fertility.

  - Test Type: One-generation reproduction toxicity study
    - Species: Rat
    - Duration of Single Treatment: 90 d
    - Fertility: LOAEL: 0.69 mg/kg body weight
    - Result: Effects on fertility.

  - Test Type: Two-generation study
    - Species: Mouse
    - Application Route: Oral
    - Fertility: LOAEL: 0.1 mg/kg body weight
    - Result: Effects on fertility.

**Effects on fetal development**
- Test Type: Embryo-fetal development
  - Species: Mouse, female
  - Application Route: Subcutaneous
  - Teratogenicity: LOAEL: 4 mg/kg body weight
  - Symptoms: Malformations were observed.
  - Result: positive, Teratogenic effects.

  - Test Type: One-generation reproduction toxicity study
    - Species: Rat
    - Application Route: Subcutaneous
    - Teratogenicity: LOAEL: 2.5 µg/kg body weight
    - Symptoms: Reduced body weight
    - Result: positive, Embryotoxic effects and adverse effects on the offspring were detected.

  - Test Type: Embryo-fetal development
    - Species: Rat
    - Application Route: Subcutaneous
    - Developmental Toxicity: LOAEL: 0.2 mg/kg body weight
    - Symptoms: Early Resorptions / resorption rate, Reduced number of viable fetuses, Reduced body weight
    - Result: Embryotoxic effects and adverse effects on the
offspring were detected only at high maternally toxic doses

Reproductive toxicity - Assessment

17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate:

Effects on fetal development

Test Type: Development
Species: Rat
Application Route: Oral
Result: negative

Test Type: Embryo-fetal development
Species: Rabbit
Application Route: Oral
Result: negative, No teratogenic effects.

Reproductive toxicity - Assessment

Positive evidence of adverse effects on sexual function and fertility from human epidemiological studies.

Talc:

Effects on fetal development

Test Type: Embryo-fetal development
Species: Rat
Application Route: Ingestion
Result: negative

STOT-single exposure

Not classified based on available information.

STOT-repeated exposure

Causes damage to organs (Liver, Bone, Blood, Endocrine system) through prolonged or repeated exposure.

Components:

Estradiol:

Target Organs: Liver, Bone, Blood, Endocrine system
Assessment: Causes damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:

Cellulose:

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

Estradiol:

Species: Rat
LOAEL: >= 0.17 mg/kg
Application Route: Ingestion
SAFETY DATA SHEET

Nomegestrol / Estradiol Formulation

Exposure time : 90 d
Target Organs : Mammary gland, Ovary, Uterus (including cervix), Liver, Bone, Endocrine system, Blood, Testis

17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate:
Species : Mouse
NOAEL : 20 mg/kg
Application Route : Oral
Exposure time : 52 Weeks

Species : Rat
NOAEL : 20 mg/kg
Application Route : Oral
Exposure time : 52 Weeks

Titanium dioxide:
Species : Rat
NOAEL : 24,000 mg/kg
Application Route : Ingestion
Exposure time : 28 Days

Species : Rat
NOAEL : 10 mg/m³
Application Route : inhalation (dust/mist/fume)
Exposure time : 2 y

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Components:

Estradiol:
Inhalation : Symptoms: tingling, Nose bleeding
Skin contact : Symptoms: Skin irritation, Redness, pruritis
Ingestion : Symptoms: Headache, Gastrointestinal disturbance, Dizziness, Vomiting, Diarrhea, water retention, liver function change, changes in libido, breast tenderness, menstrual irregularities

17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate:
Ingestion : Symptoms: acne, amenorhea, Headache, Dizziness, Nausea, breast tenderness, changes in libido, insomnia, musculoskeletal pain, mood swings, muscle pain, muscle twitching

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

Cellulose:
### Toxicity to fish

**Nomegestrol / Estradiol Formulation**

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

- **Estradiol**: LC50 (Oryzias latipes (Japanese medaka)): 3.9 mg/l
  - Exposure time: 96 h

### Toxicity to daphnia and other aquatic invertebrates

- **Nomegestrol**: EC50 (Daphnia magna (Water flea)): 2.7 mg/l
  - Exposure time: 48 h

- **Estradiol**: NOEC (Pseudokirchneriella subcapitata (green algae)): 1.7 mg/l
  - Exposure time: 72 h
  - Method: OECD Test Guideline 201

- **Nomegestrol**: EC50 (Pseudokirchneriella subcapitata (green algae)): > 1.7 mg/l
  - Exposure time: 72 h
  - Method: OECD Test Guideline 201

### Toxicity to algae/aquatic plants

- **Nomegestrol**: NOEC (Oryzias latipes (Japanese medaka)): 0.000003 mg/l
  - Exposure time: 160 d
  - Method: OECD Test Guideline 210

- **Estradiol**: NOEC (Daphnia magna (Water flea)): 0.2 mg/l
  - Exposure time: 21 d

### Toxicity to microorganisms

- **Nomegestrol**: EC50: > 100 mg/l
  - Exposure time: 3 h
  - Test Type: Respiration inhibition
  - Method: OECD Test Guideline 209

- **Estradiol**: NOEC: 100 mg/l
  - Exposure time: 3 h
  - Test Type: Respiration inhibition
  - Method: OECD Test Guideline 209

### 17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate:

- **Nomegestrol**: EC50 (Pseudokirchneriella subcapitata (green algae)): > 3.07 mg/l
  - Exposure time: 72 h
  - Method: OECD Test Guideline 201

- **Estradiol**: NOEC (Pseudokirchneriella subcapitata (green algae)): 0.69 mg/l
  - Exposure time: 72 h
  - Method: OECD Test Guideline 201

### Toxicity to fish (Chronic toxicity)

- **Nomegestrol**: NOEC (Oryzias latipes (Japanese medaka)): 0.000003 mg/l
  - Exposure time: 160 d
  - Method: OECD Test Guideline 210

### Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)

- **Nomegestrol**: NOEC (Daphnia magna (Water flea)): 3.65 mg/l
  - Exposure time: 21 d

### Toxicity to algae/aquatic plants

- **Nomegestrol**: EC50 (Pseudokirchneriella subcapitata (green algae)): > 3.07 mg/l
  - Exposure time: 72 h
  - Method: OECD Test Guideline 201

- **Estradiol**: NOEC (Pseudokirchneriella subcapitata (green algae)): 0.69 mg/l
  - Exposure time: 72 h
  - Method: OECD Test Guideline 201

### Toxicity to microorganisms (Chronic toxicity)

- **Nomegestrol**: NOEC (Zebrafish): 0.0013 mg/l
  - Exposure time: 27 d

- **Estradiol**: NOEC (Daphnia magna (Water flea)): 3.65 mg/l
  - Exposure time: 21 d
### Toxicity to microorganisms

<table>
<thead>
<tr>
<th>Component</th>
<th>EC50 (Natural microorganism):</th>
<th>Exposure time:</th>
<th>Test Type:</th>
<th>Method: OECD Test Guideline 209</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nomegestrol / Estradiol</td>
<td>&gt; 2.8 mg/l</td>
<td>3 h</td>
<td>Respiration inhibition</td>
<td>209</td>
</tr>
<tr>
<td></td>
<td>NOEC (Natural microorganism):</td>
<td>2.8 mg/l</td>
<td>Respiration inhibition</td>
<td>209</td>
</tr>
</tbody>
</table>

### Talc:

- **Toxicity to fish**
  - LC50 (Brachydanio rerio (zebrafish)): > 100,000 mg/l
  - Exposure time: 24 h

### Titanium dioxide:

- **Toxicity to fish**
  - LC50 (Oncorhynchus mykiss (rainbow trout)): > 100 mg/l
  - Exposure time: 96 h
  - Method: OECD Test Guideline 203

### Persistence and degradability

#### Components:

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

- **Estradiol:**
  - Biodegradability: Result: rapidly degradable
  - Biodegradation: 84 %
  - Exposure time: 24 hrs

#### Bioaccumulative potential

- **Estradiol:**
  - Partition coefficient: n-octanol/water: log Pow: 4.01
17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate:

Bioaccumulation:
- Species: Zebrafish
- Bioconcentration factor (BCF): 44

Partition coefficient: n-octanol/water
- log Pow: 3.7

Mobility in soil

Components:

Estradiol:
- Distribution among environmental compartments: log Koc: 3.81

17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate:
- Distribution among environmental compartments: log Koc: 3.35
- Method: OECD Test Guideline 106

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
- UN number: UN 3077
- Proper shipping name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Estradiol, 17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate)
- Class: 9
- Packing group: III
- Labels: 9

IATA-DGR
- UN/ID No.: UN 3077
- Proper shipping name: Environmentally hazardous substance, solid, n.o.s. (Estradiol, 17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate)
- Class: 9
- Packing group: III
- Labels: Miscellaneous
- Packing instruction (cargo aircraft): 956
- Packing instruction (passen-
ger aircraft) Environmentally hazardous : yes

IMDG-Code
UN number : UN 3077
Proper shipping name : ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.
(Estradiol, 17-Hydroxy-6-methyl-19-nopregn-4,6-diene-3,20-dione 17-acetate)

Class : 9
Packing group : III
Labels : 9
EmS Code : F-A, S-F
Marine pollutant : yes

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code
Not applicable for product as supplied.

Domestic regulation

49 CFR
UN/ID/NA number : UN 3077
Proper shipping name : Environmentally hazardous substance, solid, n.o.s.
(Estradiol, 17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate)

Class : 9
Packing group : III
Labels : CLASS 9
ERG Code : 171
Marine pollutant : yes (Estradiol, 17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate)
Remarks : Above applies only to containers over 119 gallons or 450 liters., Shipment by ground under DOT is non-regulated; however it may be shipped per the applicable hazard classification to facilitate multi-modal transport involving ICAO (IATA) or IMO.

Special precautions for user
The transport classification(s) provided herein are for informational purposes only, and solely based upon the properties of the unpackaged material as it is described within this Safety Data Sheet. Transportation classifications may vary by mode of transportation, package sizes, and variations in regional or country regulations.

SECTION 15. REGULATORY INFORMATION

EPCRA - Emergency Planning and Community Right-to-Know

CERCLA Reportable Quantity
This material does not contain any components with a CERCLA RQ.

SARA 304 Extremely Hazardous Substances Reportable Quantity
This material does not contain any components with a section 304 EHS RQ.

SARA 302 Extremely Hazardous Substances Threshold Planning Quantity
This material does not contain any components with a section 302 EHS TPQ.

SARA 311/312 Hazards : Combustible dust
Carcinogenicity
Reproductive toxicity
Specific target organ toxicity (single or repeated exposure)

**SARA 313**
This material does not contain any chemical components with known CAS numbers that exceed the threshold (De Minimis) reporting levels established by SARA Title III, Section 313.

**US State Regulations**

**Pennsylvania Right To Know**
- D-Glucose, 4-O-.beta.-D-galactopyranosyl-, monohydrate: 64044-51-5
- Cellulose: 9004-34-6
- Estradiol: 50-28-2
- Talc: 14807-96-6

**California Prop. 65**
WARNING: This product can expose you to chemicals including Estradiol, which is/are known to the State of California to cause cancer. For more information go to www.P65Warnings.ca.gov.

**California List of Hazardous Substances**
- Estradiol: 50-28-2
- Polyvinyl pyrrolidone: 9003-39-8
- Talc: 14807-96-6

**California Permissible Exposure Limits for Chemical Contaminants**
- Cellulose: 9004-34-6
- Talc: 14807-96-6

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

- **AICS**: not determined
- **DSL**: not determined
- **IECSC**: not determined
## SECTION 16. OTHER INFORMATION

### Further Information

<table>
<thead>
<tr>
<th>NFPA 704:</th>
<th>HMIS® IV:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health</td>
<td>HEALTH</td>
</tr>
<tr>
<td>Flammability</td>
<td>FLAMMABILITY</td>
</tr>
<tr>
<td>Instability</td>
<td>PHYSICAL HAZARD</td>
</tr>
<tr>
<td>Special hazard</td>
<td></td>
</tr>
</tbody>
</table>

**NFPA 704:**
- Health: 0
- Flammability: 1
- Instability: 0

**HMIS® IV:**
- HEALTH: 3
- FLAMMABILITY: 3
- PHYSICAL HAZARD: 0

HMIS® ratings are based on a 0-4 rating scale, with 0 representing minimal hazards or risks, and 4 representing significant hazards or risks. The "*" represents a chronic hazard, while the "/" represents the absence of a chronic hazard.

### Full text of other abbreviations

- ACGIH: USA. ACGIH Threshold Limit Values (TLV)
- NIOSH REL: USA. NIOSH Recommended Exposure Limits
- OSHA Z-1: USA. Occupational Exposure Limits (OSHA) - Table Z-1 Limits for Air Contaminants
- OSHA Z-3: USA. Occupational Exposure Limits (OSHA) - Table Z-3 Mineral Dusts
- ACGIH / TWA: 8-hour, time-weighted average
- NIOSH REL / TWA: Time-weighted average concentration for up to a 10-hour workday during a 40-hour workweek
- OSHA Z-1 / TWA: 8-hour time weighted average
- OSHA Z-3 / TWA: 8-hour time weighted average

AICS - Australian Inventory of Chemical Substances; ASTM - American Society for the Testing of Materials; bw - Body weight; CERCLA - Comprehensive Environmental Response, Compensation, and Liability Act; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DOT - Department of Transportation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; EHS - Extremely Hazardous Substance; 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; HMIS - Hazardous Materials Identification System; 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; MSHA - Mine Safety and Health Administration; n.o.s. - Not Otherwise Specified; NFPA - National Fire Protection Association; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable
SAFETY DATA SHEET

Nomegestrol / Estradiol Formulation

Effect Loading Rate; 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; RCRA - Resource Conservation and Recovery Act; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; RQ - Reportable Quantity; SADT - Self-Accelerating Decomposition Temperature; SARA - Superfund Amendments and Reauthorization Act; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative


Revision Date: 09/13/2019

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.

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