# 1. IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND THE COMPANY/UNDERTAKING

**Product Identifier**
- **Material Name:** Estradiol Cypionate Injection, USP
- **Trade Name:** Depo®-Estradiol Sterile Solution
- **Chemical Family:** Mixture

**Relevant Identified Uses of the Substance or Mixture and Uses Advised Against**
- **Intended Use:** Pharmaceutical product for the treatment of menopause and/or female hypogonadism

## Details of the Supplier of the Safety Data Sheet

<table>
<thead>
<tr>
<th>Company</th>
<th>Address</th>
<th>Phone Number</th>
<th>Email</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer Inc</td>
<td>235 East 42nd Street, New York, New York 10017</td>
<td>1-800-879-3477</td>
<td><a href="mailto:pfizer-MSDS@pfizer.com">pfizer-MSDS@pfizer.com</a></td>
</tr>
<tr>
<td>Pfizer Pharmaceuticals Group</td>
<td>Ramsgate Road, Sandwich, Kent CT13 9NJ</td>
<td>+00 44 (0)1304 616161</td>
<td></td>
</tr>
</tbody>
</table>

**Emergency telephone number:**
- CHEMTREC (24 hours): 1-800-424-9300
- International CHEMTREC (24 hours): +1-703-527-3887

# 2. HAZARDS IDENTIFICATION

**Classification of the Substance or Mixture**
- **GHS - Classification**
  - Reproductive Toxicity: Category 1A
  - Carcinogenicity: Category 1A

**EU Classification:**
- EU Indication of danger: Carcinogenic: Category 1
- Toxic to reproduction: Category 1

**EU Risk Phrases:**
- R45 - May cause cancer.
- R60 - May impair fertility.
- R61 - May cause harm to the unborn child.

**Label Elements**
- **Signal Word:** Danger
- **Hazard Statements:**
  - H350 - May cause cancer
  - H360FD - May damage fertility. May damage the unborn child.
- **Precautionary Statements:**
  - P201 - Obtain special instructions before use
  - P202 - Do not handle until all safety precautions have been read and understood
  - P281 - Use personal protective equipment as required
  - P308 + P313 - IF exposed or concerned: Get medical attention/advice
  - P405 - Store locked up
  - P501 - Dispose of contents/container in accordance with all local and national regulations
SAFETY DATA SHEET

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Other Hazards
Australian Hazard Classification (NOHSC):

Note:
This document has been prepared in accordance with standards for workplace safety, which requires the inclusion of all known hazards of the product or its ingredients regardless of the potential risk. The precautionary statements and warning included may not apply in all cases. Your needs may vary depending upon the potential for exposure in your workplace.

3. COMPOSITION / INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>EU Classification</th>
<th>GHS Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorobutanol</td>
<td>57-15-8</td>
<td>Not Listed</td>
<td>Xn;R22</td>
<td>Acute Tox 4 (H302)</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Estradiol Cypionate</td>
<td>313-06-4</td>
<td>206-237-8</td>
<td>Carc. Cat.1; R45</td>
<td>Repr. Cat.1; R60/61 N; R50/53</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>N; R50/53</td>
<td>Carc. 1A (H350)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Aquatic Acute 1 (H400)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Aquatic Chronic 1 (H410)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.5</td>
</tr>
</tbody>
</table>

Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety. In accordance with 29 CFR 1910.1200, the exact percentage composition of this mixture has been withheld as a trade secret.

Additional Information:
* Proprietary
Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.

For the full text of the R phrases and CLP/GHS abbreviations mentioned in this Section, see Section 16

4. FIRST AID MEASURES

Description of First Aid Measures
Eye Contact: Rinse immediately with plenty of water, also under the eyelids, for at least 15 minutes. If irritation occurs or persists, get medical attention.

Skin Contact: Remove clothing and wash affected skin with soap and water. If irritation occurs or persists, get medical attention.
Ingestion: Never give anything by mouth to an unconscious person. Wash out mouth with water. Do not induce vomiting unless directed by medical personnel. Seek medical attention immediately.

Inhalation: Remove to fresh air and keep patient at rest. Seek medical attention immediately.

Most Important Symptoms and Effects, Both Acute and Delayed
Symptoms and Effects of Exposure: No data available
Medical Conditions Aggravated by Exposure: None known

Indication of the Immediate Medical Attention and Special Treatment Needed
Notes to Physician: None

5. FIRE FIGHTING MEASURES

Extinguishing Media: Extinguish fires with CO2, extinguishing powder, foam, or water.

Special Hazards Arising from the Substance or Mixture
Hazardous Combustion Products: Carbon dioxide, carbon monoxide

Fire / Explosion Hazards: Fine particles (such as dust and mists) may fuel fires/explosions.

Advice for Fire-Fighters
During all fire fighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.

6. ACCIDENTAL RELEASE MEASURES

Personal Precautions, Protective Equipment and Emergency Procedures
Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.

Environmental Precautions
Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release.

Methods and Material for Containment and Cleaning Up
Measures for Cleaning / Collecting: Contain the source of spill if it is safe to do so. Collect spill with absorbent material. Clean spill area thoroughly.

Additional Consideration for Large Spills: Non-essential personnel should be evacuated from affected area. Report emergency situations immediately. Clean up operations should only be undertaken by trained personnel.

7. HANDLING AND STORAGE

Precautions for Safe Handling
Avoid contact with eyes, skin and clothing. Wash thoroughly after handling. Releases to the environment should be avoided. Review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure or environmental releases. Potential points of process emissions of this material to the atmosphere should be controlled with dust collectors, HEPA filtration systems or other equivalent controls.

Conditions for Safe Storage, Including any Incompatibilities
Storage Conditions: Store as directed by product packaging. Keep out of reach of children.
Specific end use(s): Pharmaceutical drug product
8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Control Parameters

Estradiol Cypionate
Pfizer OEL TWA-8 Hr: 0.2 µg/m³, Skin


Exposure Controls

Engineering Controls: Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.

Personal Protective Equipment: Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE).

Hands: Wear 2 layers of impervious disposable gloves to prevent skin contact.
Eyes: Wear safety glasses as minimum protection.
Skin: Wear impervious disposable protective clothing to prevent skin contact.
Respiratory protection: If the applicable Occupational Exposure Limit (OEL) is exceeded, wear an appropriate respirator with a protection factor sufficient to control exposures to below the OEL.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical State: Liquid
Color: Light yellow - Pale yellow
Odor: No data available.
Molecular Formula: Mixture

Solvent Solubility: No data available
Water Solubility: No data available
Solubility: Insoluble: Water
pH: No data available.
Melting/Freezing Point (°C): No data available
Boiling Point (°C): No data available
Partition Coefficient: (Method, pH, Endpoint, Value)

Estradiol
No data available
Estradiol Cypionate
No data available
Chlorobutanol
No data available
Cottonseed Oil
No data available

Decomposition Temperature (°C): No data available.
Evaporation Rate (Gram/s): No data available
Vapor Pressure (kPa): No data available
Vapor Density (g/ml): No data available
Relative Density: No data available
Viscosity: No data available

Flammability:

Autoignition Temperature (Solid) (°C): No data available
Flammability (Solids): No data available
Flash Point (Liquid) (°C): No data available
Upper Explosive Limits (Liquid) (% by Vol.): No data available
Lower Explosive Limits (Liquid) (% by Vol.): No data available
SAFETY DATA SHEET

Material Name: Estradiol Cypionate Injection, USP
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10. STABILITY AND REACTIVITY

Reactivity: No data available
Chemical Stability: Stable under normal conditions of use.
Possibility of Hazardous Reactions
Oxidizing Properties: No data available
Conditions to Avoid: Fine particles (such as dust and mists) may fuel fires/explosions.
Incompatible Materials: As a precautionary measure, keep away from strong oxidizers
Hazardous Decomposition Products: No data available

11. TOXICOLOGICAL INFORMATION

Information on Toxicological Effects
General Information: The information in this section describes the hazards of various forms of the active ingredient. Occupational studies have shown that males working with estrogen-like compounds have shown clinical signs of hyperestrogenism including enlarged breasts and milk secretion. Loss of libido, breast tenderness, and changes in sex hormone levels have also occurred. Occupational exposure in females has resulted in menstrual irregularities (breakthrough bleeding, menstrual flow changes, spotting and amenorrhea). Repeat-dose studies in animals have shown a potential to cause adverse effects on reproductive system the developing fetus.
Known Clinical Effects: Clinical use of this drug has caused nausea, vomiting, abdominal cramping, weight changes, fluid retention, changes in sexual desire (libido), breast development in males (gynecomastia), loss of hair, mental depression, menstrual irregularities, lack of menstrual periods (amenorrhea), changes in cervical erosion and secretion, breast enlargement, breast pain.

Acute Toxicity: (Species, Route, End Point, Dose)

Estradiol Cypionate
Mouse Subcutaneous LD 50 > 1000 mg/kg

Chlorobutanol
Rat Oral LD50 510 mg/kg

Cottonseed Oil
Rat Oral LD50 > 90 ml/kg

Acute Toxicity Comments: A greater than symbol (>) indicates that the toxicity endpoint being tested was not achievable at the highest dose used in the test.

Irritation / Sensitization: (Study Type, Species, Severity)

Chlorobutanol
Eye Irritation Rabbit Mild
Skin Irritation Rabbit Mild

Repeated Dose Toxicity: (Duration, Species, Route, Dose, End Point, Target Organ)

Estradiol
90 Day(s) Rat Oral 0.003 mg/kg/day NOAEL Blood, Female reproductive system, Male reproductive system, Endocrine system, Liver
11. TOXICOLOGICAL INFORMATION

Reproduction & Developmental Toxicity: (Study Type, Species, Route, Dose, End Point, Effect(s))

**Estradiol**
- Reproductive & Fertility-Females  | Rat  | Oral  | 0.003 mg/kg/day | LOAEL | Reproductive toxicity
- Embryo / Fetal Development  | Rat  | Intramuscular  | 30 mg/kg/day | LOAEL | Fetotoxicity

Genetic Toxicity: (Study Type, Cell Type/Organism, Result)

**Estradiol**
- Sister Chromatid Exchange  | Human Lymphocytes | Positive
- Micronucleus  | Human | Positive
- Chromosome Aberration  | Human | Negative
- *In Vivo* Direct DNA Damage  | Hamster | Positive
- *In Vivo* Micronucleus  | Rodent Bone Marrow | Negative

**Estradiol Cypionate**
- Direct DNA Interaction  | Negative
- *In Vitro* Micronucleus  | Human Lymphocytes | Negative
- *In Vitro* Micronucleus  | Mouse Lymphoma | Negative
- Mammalian Cell Mutagenicity  | Chinese Hamster Ovary (CHO) cells | Negative

Chlorobutanol

- *In Vitro* Bacterial Mutagenicity (Ames)  | *Salmonella* | Positive
- *In Vitro* Micronucleus  | Mouse Bone Marrow | Negative

Carcinogenicity: (Duration, Species, Route, Dose, End Point, Effect(s))

**Estradiol**
- 2 Year(s)  | Female Mouse | Oral  | 0.1 mg/kg | LOEL | Tumors, Mammary gland, Female reproductive system

Carcinogen Status:

See below

**Estradiol**

- IARC:  | Group 1 (Carcinogenic to Humans)
- NTP:  | Listed

12. ECOLOGICAL INFORMATION

Environmental Overview:

Environmental properties have not been investigated. Releases to the environment should be avoided.

Toxicity:

Aquatic Toxicity: (Species, Method, End Point, Duration, Result)

**Estradiol**
- *Daphnia magna* (Water Flea)  | N/A | LC50  | 48 Hours | 0.0039 mg/L
- *Oncorhynchus mykiss* (Rainbow Trout)  | N/A | LC50  | 96 Hours | > 0.05 mg/L
- *Desmodesmus subcapitata* (Green Alga)  | N/A | NOEC  | 72 Hours | 2.48 mg/L

Chronic Aquatic Toxicity: (Species, Method, Duration, Endpoint, Result, Adverse Endpoint)
13. DISPOSAL CONSIDERATIONS

Waste Treatment Methods: Dispose of waste in accordance with all applicable laws and regulations. Member State specific and Community specific provisions must be considered. Considering the relevant known environmental and human health hazards of the material, review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure and environmental release. It is recommended that waste minimization be practiced. The best available technology should be utilized to prevent environmental releases. This may include destructive techniques for waste and wastewater.

14. TRANSPORT INFORMATION

The following refers to all modes of transportation unless specified below.

Not regulated for transport under USDOT, EUADR, IATA, or IMDG regulations.

15. REGULATORY INFORMATION

Safety, Health and Environmental Regulations/Legislation Specific for the Substance or Mixture

Canada - WHMIS: Classifications
WHMIS hazard class:
Class D, Division 2, Subdivision A

Chlorobutanol
CERCLA/SARA 313 Emission reporting Not Listed
California Proposition 65 Not Listed
Inventory - United States TSCA - Sect. 8(b) Present
15. REGULATORY INFORMATION

Standard for the Uniform Scheduling for Drugs and Poisons: Schedule 2
EU EINECS/ELINCS List: Not Listed

Estradiol Cypionate
- CERCLA/SARA 313 Emission reporting: Not Listed
- California Proposition 65: Not Listed
- Inventory - United States TSCA - Sect. 8(b): Present
- Australia (AICS): Present
- EU EINECS/ELINCS List: 206-237-8

Cottonseed Oil
- CERCLA/SARA 313 Emission reporting: Not Listed
- California Proposition 65: Not Listed
- Inventory - United States TSCA - Sect. 8(b): Present
- Australia (AICS): Present
- EU EINECS/ELINCS List: 232-280-7

16. OTHER INFORMATION

Text of R phrases and GHS Classification abbreviations mentioned in Section 3

Acute toxicity, oral-Cat.4; H302 - Harmful if swallowed
Carcinogenicity-Cat.1A; H350 - May cause cancer
Reproductive toxicity-Cat.1A; H360FD - May damage fertility. May damage the unborn child.
Hazardous to the aquatic environment, acute toxicity-Cat.1; H400 - Very toxic to aquatic life
Hazardous to the aquatic environment, chronic toxicity-Cat.1; H410 - Very toxic to aquatic life with long lasting effects

Xn - Harmful
Carcinogenic: Category 1
Toxic to reproduction: Category 1
N - Dangerous for the environment

R22 - Harmful if swallowed.
R45 - May cause cancer.
R60 - May impair fertility.
R61 - May cause harm to the unborn child.
R50/53 - Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

Data Sources: Publicly available toxicity information.

Reasons for Revision:
- Updated Section 1 - Identification of the Substance/Preparation and the Company/Undertaking.
- Updated Section 3 - Composition / Information on Ingredients.
- Updated Section 2 - Hazard Identification.
- Updated Section 7 - Handling and Storage.
- Updated Section 8 - Exposure Controls / Personal Protection.
- Updated Section 11 - Toxicology Information.
- Updated Section 12 - Ecological Information.

Revision date: 31-May-2015

Pfizer Inc believes that the information contained in this Material Safety Data Sheet is accurate, and while it is provided in good faith, it is without warranty of any kind, expressed or implied. If data for a hazard are not included in this document there is no known information at this time.
End of Safety Data Sheet