MATERIAL SAFETY DATA SHEET

1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION AND THE COMPANY/UNDERTAKING

Pfizer Inc
Pfizer Pharmaceuticals Group
235 East 42nd Street
New York, New York 10017
1-212-573-2222

Pfizer Ltd
Ramsgate Road
Sandwich, Kent
CT13 9NJ
United Kingdom
+00 44 (0)1304 616161

Emergency telephone number:
CHEMTREC (24 hours): 1-800-424-9300

Emergency telephone number:
ChemSafe (24 hours): +44 (0)208 762 8322

Material Name: Loestrin® 21 - 1/20 and 1.5/30 Tablets (Norethindrone Acetate and Ethinyl Estradiol Tablets, USP)

Trade Name: Loestrin®
Chemical Family: Mixture
Intended Use: Pharmaceutical product used as oral contraceptive

2. COMPOSITION/INFORMATION ON INGREDIENTS

Hazardous

Ingredient	CAS Number	EU EINECS List	%
Norethindrone Acetate	51-98-9	200-132-0	1.3-2.0
Ethinyl Estradiol	57-63-6	200-342-2	< 1.0
Alcohol SDA 3A	NOT ASSIGNED	Not listed	*
D & C yellow No. 10	8004-92-0	Not listed	*
Starch	9005-25-8	232-679-6	*
Magnesium stearate	557-04-0	209-150-3	*
Talc (non-asbestiform)	14807-96-6	238-877-9	*

Ingredient	CAS Number	EU EINECS List	%
Acacia	9000-01-5	232-519-5	*
Confectioner's sugar	MIXTURE	Not listed	*
FD&C Yellow No. 6; (Sunset yellow)	2783-94-0	220-491-7	*
Purified water	7732-18-5	231-791-2	*
Lactose NF, monohydrate	64044-51-5	Not listed	*
FD & C Blue No. 1	3844-45-9	223-339-8	*

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

3. HAZARDS IDENTIFICATION

Appearance: White tablets - 1/20 Green tablets - 1.5/30
Signal Word: WARNING

Statement of Hazard: Carcinogen
May cause reproductive system effects
May cause harm to the unborn child.

Additional Hazard Information:

Short Term: Dust may be absorbed through the skin and cause systemic effects. May be harmful if swallowed. (based on components) . Accidental ingestion may cause effects similar to those seen in clinical use.

Long Term: Occupational exposure to components of this mixture has resulted in menstrual irregularities in women and breast changes (enlargement, mammary secretions), loss of libido, and changes in sex hormone levels in men.

Known Clinical Effects: The use of oral contraceptives is associated with increased risks of myocardial infarction, thromboembolism, stroke, hepatic neoplasia, and gallbladder disease. The most common adverse effects seen during clinical use of oral contraceptives are menstrual irregularities.

EU Indication of danger:
Carcinogenic: Category 1
Toxic to reproduction: Category 1

EU Hazard Symbols:

EU Risk Phrases:

R45 - May cause cancer.
R60 - May impair fertility.
R61 - May cause harm to the unborn child.

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

4. FIRST AID MEASURES

Eye Contact: Immediately flush eyes with water 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: Get medical attention. Do not induce vomiting unless directed by medical personnel. Never give anything by mouth to an unconscious person.

Inhalation: Remove to fresh air. If not breathing, give artificial respiration. Get medical attention.

5. FIRE FIGHTING MEASURES

Extinguishing Media: Use carbon dioxide, dry chemical, or water spray.

Hazardous Combustion Products: No data available

Fire Fighting Procedures: Wear approved positive pressure, self-contained breathing apparatus and full protective turn out gear.

Fire / Explosion Hazards: Not applicable

6. ACCIDENTAL RELEASE MEASURES

Health and Safety Precautions: Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.

Measures for Cleaning / Collecting: Contain the source of spill if it is safe to do so. Collect spilled material by a method that controls dust generation. A damp cloth or a filtered vacuum should be used to clean spills of dry solids. Clean spill area thoroughly.

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

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

General Handling: If tablets or capsules are crushed and/or broken, avoid breathing dust and avoid contact with eyes, skin, and clothing. Minimize dust generation and accumulation. Use only in a well-ventilated area.

Storage Conditions: Store in a cool, dry, well-ventilated area.

Storage Temperature: Store below 30°C

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Norethindrone Acetate
Pfizer OEL TWA-8 Hr: 0.8 ug/m^3, Skin

Ethinyl Estradiol
Pfizer OEL TWA-8 Hr: 40 ng/m^3, Skin

Starch
OSHA - Final PELS - TWAs: = 15 mg/m^3 TWA total
= 5 mg/m^3 TWA
ACGIH Threshold Limit Value (TWA) = 10 mg/m^3 TWA
Australia TWA = 10 mg/m^3 TWA

Magnesium stearate
ACGIH Threshold Limit Value (TWA) = 10 mg/m^3 TWA except stearates of toxic metals
Australia TWA = 10 mg/m^3 TWA

Talc (non-asbestiform)
OSHA - Final PELs - Table Z-3 Mineral D: = 20 mppcf TWA
ACGIH Threshold Limit Value (TWA) = 2 mg/m^3 TWA
Australia TWA = 2.5 mg/m^3 TWA containing no asbestos fibers
The exposure limit(s) listed for solid components are only relevant if dust may be generated.

Analytical Method: Analytical method available for Ethinyl Estradiol and Norethindrone Acetate. Contact Pfizer Inc for further information.

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:

Hands:	Not required for the normal use of this product. Wear protective gloves when working with large quantities.
Eyes:	Not required under normal conditions of use. Wear safety glasses or goggles if eye contact is possible.
Skin:	Not required for the normal use of this product. Wear protective clothing when working with large quantities.
Respiratory protection:	Not required for the normal use of this product. 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:	Tablet	**Color:**	White - 1/20 Green - 1.5/30
Molecular Formula:	Mixture	**Molecular Weight:**	Mixture

10. STABILITY AND REACTIVITY

Stability: Stable under normal conditions of use.
Conditions to Avoid: None known
Incompatible Materials: None known

Hazardous Decomposition Products: None known

11. TOXICOLOGICAL INFORMATION

General Information: The information included in this section describes the potential hazards of the individual ingredients, except where noted.

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

Magnesium stearate
Rat Oral LD50 > 2000 mg/kg
Rat Inhalation LC50 > 2000 mg/m^3

FD&C Yellow No. 6; (Sunset yellow)
Rat Oral LD50 > 10,000 mg/kg
Mouse Oral LD50 > 6,000 mg/kg

Starch
Mouse IP LD50 6600 mg/kg

Talc (non-asbestiform)
Rat Oral LD50 > 1600 mg/kg

D & C yellow No. 10
Rat Oral LD50 2000 mg/kg

Ethinyl Estradiol
Mouse Oral LD50 1737 mg/kg
Rat Oral LD50 1200 mg/kg

Norethindrone Acetate
Rat Oral LD50 > 5010 mg/kg
Mouse Oral LD50 > 5010 mg/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)

Acacia
Eye Irritation Rabbit Severe

Eye Irritation / Sensitization No data available
Skin Irritation / Sensitization No data available
Chronic Effects/Carcinogenicity The combination of ethinyl estradiol and norethindrone acetate was tested for carcinogenicity in mice, rats, and monkeys. Mice exhibited pituitary tumors. Rats developed mammary and benign liver-cell tumors along with endometrial carcinomas, hyperplastic nodules of the liver, and hepatocellular carcinomas. Monkeys treated for 10 years did not develop malignant tumors. There is significant evidence that combined oral contraceptives cause benign and malignant liver tumors in humans.

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

Ethinyl Estradiol
Embryo / Fetal Development Mouse No route specified 0.02 mg/kg/day LOEL Embryotoxicity, Not teratogenic

Norethindrone Acetate
Embryo / Fetal Development Rat No route specified 1 mg/kg/day LOEL Teratogenic
Embryo / Fetal Development Mouse No route specified 0.5 mg/kg/day LOEL Teratogenic
Embryo / Fetal Development Rat No route specified 3.5 mg/kg/day NOAEL Not Teratogenic

Reproductive Effects This product is an oral contraceptive and as such, may adversely effect fertility. Reproductive toxicity has been reported in male animals exposed to estradiol. Effects included a decrease in testicular size and a reduction in testosterone levels. Norethindrone acetate has been shown to effectively inhibit ovulation in rats.

Teratogenicity Rhesus monkeys given norethindrone acetate and ethinyl estradiol in combination exhibited embryo lethality and virilization of female offspring. There are conflicting reports concerning the ability of oral contraceptives to cause genital anomalies in exposed human fetuses.

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

Ethinyl Estradiol
Bacterial Mutagenicity (Ames) *Salmonella* Negative
Chromosome Aberration Human Lymphocytes Positive
Sister Chromatid Exchange Human Lymphocytes Positive
Chromosome Aberration Chinese Hamster Ovary (CHO) cells Positive
In Vivo Micronucleus Mouse Bone Marrow Positive

Norethindrone Acetate
Bacterial Mutagenicity (Ames) *Salmonella* Negative
In Vitro Chromosome Aberration Human Lymphocytes Positive
In Vitro Sister Chromatid Exchange Human Lymphocytes Negative
In Vivo Unscheduled DNA Synthesis Rat Hepatocyte Positive
In Vivo Direct DNA Damage Mouse Negative

Mutagenicity Genotoxicity testing results indicate that EE and NA do not directly interact with DNA but that they may produce non-specific chromosome damage.

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

Ethinyl Estradiol
80 Week(s) Mouse Oral, in feed 0.07 mg/kg/day LOEL Tumors, Pituitary gland
104 Week(s) Rat No route specified 0.07 mg/kg/day LOEL Malignant tumors, Liver
105 Week(s) Rat Oral, in feed 0.053 mg/kg/day NOEL Not carcinogenic

Norethindrone Acetate
2 Year(s) Male Rat Oral 3-4 mg/kg/day LOEL Malignant tumors, Liver
2 Year(s) Female Rat Oral 3-4 mg/kg/day LOEL Tumors, Female reproductive system
104 Week(s) Male Rat Intramuscular 10 mg/kg/day LOEL Malignant tumors, Mammary gland, Liver, Endocrine system
104 Week(s) Female Rat Intramuscular 10 mg/kg/day LOEL Malignant tumors, Liver, Mammary gland

Carcinogen Status: See below

FD & C Blue No. 1
IARC: Group 3

FD&C Yellow No. 6; (Sunset yellow)
IARC: Group 3

Talc (non-asbestiform)
IARC: Group 3

Ethinyl Estradiol
IARC: Group 1
NTP: Listed
OSHA: Present

Norethindrone Acetate
IARC: Group 2B
NTP: Listed
OSHA: Present

At increase risk from exposure: Cigarette smoking increases the risk of serious cardiovascular side effects from oral contraceptive use.

Additional Information: Small amounts of oral contraceptive steroids have been identified in the milk of nursing mothers, and a few adverse effects on the child have been reported. In addition, oral contraceptives given in the postpartum period may interfere with lactation by decreasing the quantity and quality of breast milk.

12. ECOLOGICAL INFORMATION

Environmental Overview: The environmental characteristics of this material have not been fully evaluated. Releases to the environment should be avoided.

13. DISPOSAL CONSIDERATIONS

Disposal Procedures: Dispose of waste in accordance with all applicable laws and regulations.

14. TRANSPORT INFORMATION

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

15. REGULATORY INFORMATION

EU Symbol: T

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.

EU Safety Phrases:

S22 - Do not breathe dust.
S36/37 - Wear suitable protective clothing and gloves.
S53 - Avoid exposure - obtain special instructions before use.

OSHA Label:
WARNING
Carcinogen
May cause reproductive system effects
May cause harm to the unborn child.

Canada - WHMIS: Classifications

WHMIS hazard class:
Class D, Division 2, Subdivision A

Norethindrone Acetate

California Proposition 65	developmental toxicity, initial date 10/1/91
Australia (AICS):	Present
EU EINECS List	200-132-0

Ethinyl Estradiol

California Proposition 65	carcinogen, initial date 1/1/88 developmental toxicity, initial date 4/1/90 (when mixed with Norethisterone)
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present

Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 4
EU EINECS List	200-342-2

Acacia

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS List	232-519-5

D & C yellow No. 10

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present

Starch

Inventory - United States TSCA - Sect. 8(b)	XU
Australia (AICS):	Present
EU EINECS List	232-679-6

FD&C Yellow No. 6; (Sunset yellow)

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS List	220-491-7

Purified water

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS List	231-791-2

Lactose NF, monohydrate

Australia (AICS):	Present

Magnesium stearate

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS List	209-150-3

Talc (non-asbestiform)

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS List	238-877-9

FD & C Blue No. 1

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS List	223-339-8

16. OTHER INFORMATION

Reasons for Revision: Updated Section 2 - Composition / Information on Ingredients. Updated Section 3 - Hazard Identification. Updated Section 4 - First Aid Measures. Updated Section 5 - Fire Fighting Measures. Updated Section 6 - Accidental Release Measures. Updated Section 8 - Exposure Controls / Personal Protection. Updated Section 10 - Stability and Reactivity. Updated Section 11 - Toxicology Information. Updated Section 13 - Disposal Considerations. Updated Section 15 - Regulatory Information.

Prepared by: Toxicology and Hazard Communication
Pfizer Global Environment, Health, and Safety

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End of Safety Data Sheet