Schering-Plough Animal Health
Division of Schering-Plough Ltd.
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Middlesex, England UB9 6LS

SAFETY DATA SHEET

Schering-Plough urges each user or recipient of this MSDS to read the entire data sheet to become aware of the hazards associated with this material.

SECTION 1. IDENTIFICATION OF SUBSTANCE AND COMPANY INFORMATION

SDS NAME: **Nuflor Injectable Solution**

SYNONYM(S): Nuflor Swine Injectable
Nulfor Cattle Injectable

MSDS NUMBER: SP000757

EMERGENCY NUMBER(S): Schering-Plough Security Control Center (908) 820-6921 (24 hours)

(0 11 44) 1895 62 6000 (Schering-Plough Animal Health- Harefield)

SCHERING-PLOUGH MSDS HELPLINE: (908) 629-3657 (Worldwide)
Monday to Friday, 9am to 5pm (US Eastern Time)

SECTION 2. COMPOSITION AND INFORMATION ON INGREDIENTS

PRODUCT USE: Veterinary product

CHEMICAL FORMULA: Mixture.

The formulation for this product is proprietary information. Only hazardous ingredients in concentrations of 1% or greater and/or carcinogenic ingredients in concentrations of 0.1% or greater are listed in the Chemical Composition table. Active ingredients in any concentration are listed. For additional information about carcinogenic ingredients see Section 3.

CHEMICAL COMPOSITION

CHEMICAL NAME	CAS NUMBER	EU NUMBER	EU CLASSIFICATION	PERCENT
Florfenicol	73231-34-2			30
Polyethylene Glycol	25322-68-3			30-40
N-Methyl-2-Pyrrolidone	872-50-4	2128281	R36/38 Xi	20-30
Propylene Glycol	57-55-6	2003380		10-20

ADDITIONAL INFORMATION: This MSDS is written to provide health and safety information for individuals who will be handling the final product formulation during research and manufacture. For health and safety information for individual ingredients used during manufacturing, refer to the appropriate MSDS for each ingredient. Refer to the package insert or product label for handling guidance for the consumer.

See section 15 for EU hazard classification symbols and risk and safety phrases.

SECTION 3. HAZARDS IDENTIFICATION

EMERGENCY OVERVIEW

Light gold color
Viscous solution
Odor unknown

Irritating to eyes.
May be irritating to skin.
May cause allergic reactions in susceptible individuals.

May cause effects to:
- gastrointestinal tract
- male reproductive system
- fetus

May cause impaired fertility.
May cause birth defects.

Toxic to aquatic organisms.
May cause long-term adverse effects in the aquatic environment.

POTENTIAL HEALTH EFFECTS:

The following summary is based upon available information about the individual ingredients of the mixture, or of the expected properties of the mixture.

This product is not for use in humans. Clinical effects in humans have not been determined.

Florfenicol, the active ingredient in this product, is a broad spectrum antibiotioc used veterinary products. Florfenicol may cause allergic reactions in susceptible individuals. Based on animal studies, florfenicol may cause slight eye irritation, constipation, changes in blood cell counts, changes in stool, or liver effects. It may also cause developmental effects or effects to male reproductive organs.

Acute exposure to polyethelyene glycol may cause slight eye or skin irritation, abnormal taste, gas, nausea, vomiting, diarrhea, irregular heartbeat, low blood pressure, or fluid in the lungs. Repeated exposure of polyethylene glycol to damaged skin has been reported to cause kidney failure and necrosis.

N-methyl-2-pyrrolidone (NMP) is a moderate to severe eye irritant in humans. Prolonged occupational exposure to low concentrations has caused chronic eye irritation and headache. Prolonged or repeated skin contact may cause dermatitis with blistering, edema, and erythema.

Propylene glycol is considered to be relatively non-toxic. It is a mild irritant to the eyes and has been reported to irritate the skin. It may cause skin sensitization resulting in allergic contact dermatitis in susceptible individuals. Inhalation exposure to saturated and supersaturated atmospheres of propylene glycol for prolonged periods of time produced no adverse effects. Propylene glycol may cause nervous system depression, acidosis, stupor, and seizures after chronic ingestion.

LISTED CARCINOGENS

No carcinogens or potential carcinogens listed by IARC or EU Directive 90/394 (Annex I) in this mixture.

SECTION 4. FIRST AID MEASURES

INHALATION: Remove to fresh air. If any trouble breathing, get immediate medical attention. Administer artificial respiration if breathing has ceased. If irritation or symptoms occur or persist, consult a physician.

SKIN CONTACT: In case of skin contact, while wearing protective gloves, carefully remove any contaminated clothing, including shoes, and wash skin thoroughly with soap and water. If irritation or symptoms occur or persist, consult a physician.

EYE CONTACT: In case of eye contact, immediately rinse eyes thoroughly with plenty of water. If wearing contact lenses, remove only after initial rinse, and continue rinsing eyes for at least 15 minutes. If irritation occurs or persists, consult a physician.

INGESTION: Rinse mouth and drink a glass of water. Do not induce vomiting. If symptoms persist, consult a physician.

NOTE TO PHYSICIAN: This product contains florfenicol, a broad spectrum antibiotic which may cause allergic reactions in susceptible individuals.

SECTION 5. FIRE FIGHTING MEASURES

FLAMMABILITY DATA:

FLASH POINT: Not determined (liquids) or not applicable (solids)

SPECIAL FIRE FIGHTING PROCEDURES:
Wear full protective clothing and self-contained breathing apparatus (SCBA).

SUITABLE EXTINGUISHING MEDIA:
Carbon dioxide (CO2), extinguishing powder or water spray.

See Section 9 for Physical and Chemical Properties.

SECTION 6. ACCIDENTAL RELEASE MEASURES

PERSONAL PRECAUTIONS:
Wear appropriate personal protective equipment as specified in Section 8. Keep personnel away from the clean-up area.

SPILL RESPONSE / CLEANUP:
All spills should be handled according to site requirements and based on precautions cited in the MSDS. In the case of liquids, use proper absorbent materials. For laboratories and small-scale operations, incidental spills within a hood or enclosure should be cleaned by using a HEPA filtered vacuum or wet cleaning methods as appropriate. For large dry or liquid spills or those spills outside enclosure or hood, appropriate emergency response personnel should be notified. In manufacturing and large-scale operations, HEPA vacuuming prior to wet mopping or cleaning is required.

ENVIRONMENTAL PRECAUTIONS:
This product may be toxic to fish and/or aquatic organisms. Do not allow product to reach ground water, water course, sewage or drainage systems.

See Sections 9 and 10 for additional physical, chemical, and hazard information.

SECTION 7. HANDLING AND STORAGE

HANDLING:
Avoid skin and eye contact. Ensure adequate ventilation. Keep containers tightly closed when not in use.

STORAGE:
Store in a cool, dry, well ventilated area.

See Section 8 for exposure controls and additional safe handling information.

SECTION 8. EXPOSURE CONTROLS AND PERSONAL PROTECTION

The following guidance applies to the handling of the active ingredient(s) in this formulation.

S-P OCCUPATIONAL EXPOSURE GUIDELINE (OEG):
Schering-Plough Corporation has established an Occupational Exposure Guideline (OEG) of 180 mcg/m^3 (8-hr TWA) for Florfenicol. Consult your site safety professional for additional guidance.

EXPOSURE CONTROLS:
The health hazard risks of handling this material are dependent on many factors, including physical form, duration and frequency of process or task, and effectiveness of engineering controls. Site-specific risk assessments should be conducted to determine the feasibility and the appropriateness of all exposure control measures. Exposure controls for normal operating or routine procedures follow a tiered strategy. Engineering controls are the preferred means of long-term or permanent exposure control. If engineering controls are not feasible, substitution of approved materials or appropriate use of personal protective equipment (PPE) may be considered as alternative control measures. However, PPE should not be used as a method of permanent or long-term exposure control. Exposure controls for non-routine operations must be evaluated and addressed as part of the site-specific risk assessment.

RECOMMENDED PERSONAL PROTECTIVE EQUIPMENT (PPE):

Respiratory Protection:	In laboratories and small-scale operations, appropriate respiratory protection is required in situations where exposure may exceed any available recommended exposure limit. Consult your site safety staff for guidance. In manufacturing and large-scale operations, the use of powered air purifying respirators (PAPRs) or positive-pressure air supplied respirators with full-face coverage may be required, dependent on level of exposure. Consult your site safety staff for guidance.
Skin Protection:	Gloves that provide an appropriate barrier to the skin are recommended if there is potential for contact with this material. Consult your site safety staff for guidance.
Eye Protection:	Safety glasses with side shields. Use of goggles or full face protection may be required if there is potential for contact with this material. Consult your site safety staff for guidance.
Body Protection:	In small-scale or laboratory operations, lab coats or equivalent protection is required. Disposable Tyvek or other dust impermeable suit should be considered based on procedure or level of exposure. Use of additional PPE such as shoe coverings, gauntlets, hood, or head covering may be necessary. Consult your site safety staff for guidance. In large-scale or manufacturing operations, disposable Tyvek or other dust impermeable suit is recommended and based on level of exposure. Use of additional PPE such as shoe coverings, gauntlets, hood, or head covering may be necessary. Consult your site safety staff for guidance.

EXPOSURE LIMIT VALUES

See Schering-Plough occupational exposure guideline (OEG) listed above.

Refer to regional exposure limit lists for chemical specific guidance.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

FORM:	Viscous solution
COLOR:	Light gold color
ODOR:	Odor unknown
SOLUBILITY:	
Water:	Not determined

See Section 5 for flammability/explosivity information.

SECTION 10. STABILITY AND REACTIVITY

STABILITY/ REACTIVITY:
Stable under normal conditions.

CONDITIONS AND MATERIALS TO AVOID:
None known.

SECTION 11. TOXICOLOGICAL INFORMATION

The information presented below pertains to the following individual ingredients, and not to the mixture.

ACUTE TOXICITY DATA

INHALATION:
Rats exposed to florfenicol for 4 hours showed dry rales, anogenital staining, secretory discharge, soft stool, and decreased body weights. These effects were seen immediately or up to one-week post exposure. Some effects did not resolve by study termination. The inhalation LC50 (4 hr) was >0.28 mg/L in rats.

No mortalities were reported in rats following a 4-hour exposure to polyethylene glycol generated at 170 deg C.

Propylene glycol caused no adverse effects in monkeys or rats following exposure to saturated atmospheres for prolonged periods of time.

SKIN:
Florfenicol was not irritating to rabbit skin (PII = 0)

Polyethylene glycols (200-9000): Dermal LD50: >20 g/kg (unspecified species).
Polyethylene glycol was not irritating to the skin of rabbits and guinea pigs.
Polyethylene glycol was not irritating in a human patch test.

N-methyl-2-pyrrolidone (NMP): Dermal LD50 (rabbit): 8000 mg/kg
NMP was a moderate skin irritant to humans after a 24 hour exposure. It was not irritating after a 8 hour exposure. NMP was not a skin irritant to guinea pigs.

Propylene glycol: Dermal LD50: 20.8 g/kg (rabbit)
Propylene glycol was irritating in a human patch test. Propylene glycol was not irritating to the skin of rabbits, guinea pigs and swine.

EYE:
Florfenicol was slightly irritating to the eyes of rabbits.

Polyethylene glycols did not produce appreciable eye irritation in rabbits.

N-methyl-2-pyrrolidone was a moderate to severe eye irritant to humans and rabbits.

Propylene glycol was slightly irritating to the eyes of rabbits.

ORAL:
Florfenicol: Oral LD50: >2000 mg/kg (rat, mouse).
Dogs (one animal/sex) were administered successive oral doses of florfenicol that ranged from 160 to 1280 mg/kg. No clinical effects occurred at doses up to 640 mg/kg. At 640 mg/kg, the only female died from inhalation of vomitus. Vomiting or soft stool occurred at 640 to 1280 mg/kg.

Polyethylene glycol 300: Oral LD50: 17 to 39 g/kg (rat, mouse, guinea pig, rabbit)

N-methyl-2-pyrrolidone: Oral LD50 (rat): 3900-4300 mg/kg

Propylene glycol: Oral LD50: 21 to 33.7 g/kg (rat), 10 to 20 g/kg (dog)
Propylene glycol caused dyspnea, cramps, loss of equilibrium, depression, analgesia, and death after prolonged moribund state in mice at doses ranging from 23.9 to 31.8 g/kg. In rabbits, 1 to 1.5 g/kg propylene glycol reduced intraocular pressure by raising the osmotic pressure of blood.

SENSITIZATION:
Florfenicol was not a skin sensitizer in guinea pigs.

Polyethylene glycols did not produce skin sensitization in guinea pigs.

N-methyl-2-pyrrolidone was not a skin sensitization in guinea pigs.

Propylene glycol did not cause sensitization in a human patch test.

REPEAT DOSE TOXICITY DATA

SUBCHRONIC / CHRONIC TOXICITY:
Florfenicol was administered orally to dogs, rats, and mice at dosages as high as 100 to 400 mg/kg/day for up to 13 weeks. Effects including decreased body weight, changes in liver weight or liver enzyme levels, changes in testicular weight, testicular atrophy, decreased white blood cell counts, and decreased hemoglobin levels were observed at high dosages. Cellular changes in the liver or lymph nodes of rats and mice, and histopathologic changes in the brain and spinal cord of dogs were also noted at these high dosages. Although some effects were reversible after a 4-week withdrawal from treatment, testicular effects in rats persisted. Intramuscular injections of 45 mg/kg of florfenicol in swine produced diarrhea, injection site lesions, decreased body weight, decreased food and water consumption, changes in serum electrolytes and proteins, decreased red blood cell and white blood cell counts, decreased spleen weight, and decreased kidney weight.

In 52-week oral toxicity studies in dogs and rats, high dosages of florfenicol (12 and 48 mg/kg/day, respectively) increased liver weight and produced cellular changes in the gall bladder of dogs. In rats, florfenicol at the high dosage reduced body weight gain, reduced testicular weight, induced changes in hematologic and clinical chemistry parameters, and increased the incidence of testicular tubular atrophy. In two-year chronic studies in mice and rats, florfenicol caused similar effects as those observed in other long-term studies including reduced body weight gain, reduced red blood cell count, reduced hemoglobin levels, and testicular effects such as small testes, tubular atrophy and aspermatogenesis in both the high dosage rats (48 mg/kg/day) and mice (200 mg/kg/day).

Polyethylene glycol 400 produced no adverse effects in dogs and rats fed 2% in the diet for one or two years, respectively. Repeated dermal exposure to polyethylene glycol 300 for an eight-week period had no effect on mice. Repeated inhalation exposure to 1008 mg/m^3 of a higher molecular weight polyethylene glycol increased lung weight, and also produced reversible increases in neutrophil counts in male rats.

Inhalation toxicity of N-methyl-2-pyrrolidone (NMP) was evaluated in male and female rats exposed to 0.1, 0.5, or 1.0 mg/L for four weeks. Mortality was seen in animals in the high-dosage group during the first nine days of exposure. Treatment-related effects noted in the high-dosage group included lethargy, irregular heartbeat, increased neutrophils, decreased lymphocytes, pulmonary edema and congestion, necrosis in hemopoietic cells, and atrophy or necrosis in lymphoid tissue. Surviving animals recovered following a two-week of recovery period.

Mice and rats were fed NMP dosages ranging from 2,000 to 30,000 ppm and 500 to 10,000 ppm for 28 days in rats and mice, respectively. Decreased body weight gains as well as clinical chemical changes, indicating possible alterations in lipid, protein, and carbohydrate metabolism, occurred in male rats dosed with 18,000 ppm and in both sexes dosed with 30,000 ppm. In mice, swelling of the epithelium of the distal parts of the renal tubules was observed at dosages of 7,500 ppm or higher. The NOAELs for these studies were 6,000 ppm for male rats, 18,000 pppm for female rats, and 2,500 ppm for mice. In a reproductive study, rats exposed to 116 ppm of NMP for 100 exposure days had a detectable decrease in response to sound.

Propylene glycol caused no adverse effects in monkeys or rats exposed to saturated vapor concentrations for 12 to 18 months. Rats exposed to 25 or 50% (7.7 and 13.2 g/kg/day) propylene glycol in water died within 69 days in a 140 day study. In a separate study, a diet of 30% propylene glycol was not well tolerated in young rats, and dams could not bring their young to weaning; diets containing 40, 50, or 60% propylene glycol were lethal after a few days.

REPRODUCTIVE / DEVELOPMENTAL TOXICITY:
In a two-generation reproductive study, oral administration as high as 12 mg/kg/day of florfenicol reduced epididymal weights, decreased pup survival, and reduced lactation index in rats. Data suggest an association between low epididymal weight and the ability to sire a litter. The study NOAEL was 3 mg/kg/day.

There was no evidence of teratogenicity in rats administered florfenicol at dosages of 4, 12 or 40 mg/kg/day. Slight maternal toxicity, evidenced by decreased food and water consumption, was observed above 4 mg/kg/day. At 40 mg/kg/day, an increased incidence of delayed ossification and decreased fetal weight occurred. The NOAEL for maternal and fetal toxicity in rats was determined to be 4 mg florfenicol/kg/day. No evidence of major adverse effects were observed on the embryo/fetus in mice at dosages up to 60 mg/kg/day. However, in a dose-range finding study in mice, there was a slight increase in the incidence of fetuses exhibiting retarded skeletal ossification, LOEL: 40 mg/kg/day dosage. Based on these combined results, it was concluded that the NOAEL for fetal effects was between 3 and 40 mg florfenicol/kg/day in mice.

Polyethylene glycol 200 was developmentally toxic in mice, causing malformations and other fetotoxicity, but elicited no similar response in rats at even higher doses.

N-methyl-2-pyrrolidone (NMP) was not teratogenic to the offspring of rats exposed to 0.1 or 0.36 mg/L by inhalation from days 6 to 15 of gestation. No adverse reproductive effects were found in male or female rats exposed to airborne concentrations up to 116 ppm (6hr/day x 100 days) in a two-generation reproductive study. NMP was fetotoxic and teratogenic to the offspring of mice and rats following dermal, oral, or intraperitoneal exposure during gestation [NOEL: 1154 mg/kg/day (oral; mice); 237 mg/kg/day (oral and dermal; rats); LOEL: 166 mg/kg/day (IP; mice)]. Maternal toxicity was also observed in these studies.

Propylene glycol caused decreased food consumption, retarded growth, smaller litters, changes in breeding patterns, and inhibited weaning in rats that were fed 30% propylene glycol through six generations; however, this may have been due to nutritional insufficiency. Propylene glycol was not teratogenic in rabbits, monkeys or chickens.

MUTAGENICITY / GENOTOXICITY:
Florfenicol was negative in a bacterial mutagenicity study (Ames), a mammalian mutagenicity study (mouse lymphoma), a bone marrow micronucleus assay, an in vitro chromosomal aberration assay (CHO cells), a cytogenetics assay in bone marrow, and an unscheduled DNA synthesis assay in rat hepatocytes.

Polyethylene glycol was negative in a bacterial mutagenicity study (Ames), results were inconclusive in a bacterial DNA repair study.

N-methyl-2-pyrrolidone (NMP) induced aneuploidy in Saccharomyces. NMP was negative in a bacterial (Salmonella) mutagenicity assay, an in vitro mouse micronucleus assay, and in an in vitro chromosomal aberration assay (CHO cells).

Propylene glycol was negative in a bacterial mutagenicity study (Ames).

CARCINOGENICITY:
This material has not been evaluated for carcinogenicity.

Florfenicol was not carcinogenic in a 2-year study in rats administered dosages up to 48 mg/kg/day for 5 days a week or in mice at dosages up to 200 mg/kg/day for 5 days per week.

N-methyl-2-pyrrolidone was not carcinogenic in rats exposed, by inhalation, to 0.04 to 0.4 mg/L for six hours/day for two years.

Propylene glycol was not carcinogenic when applied to the skin, or when given orally in mice and rats.

SECTION 12. ECOLOGICAL INFORMATION

The information presented below pertains to the following ingredient(s) and does not apply to the final product or its formulation(s).

ECOTOXICITY DATA

INGREDIENT ECOTOXICITY

Florfenicol: 96-hr LC50 (bluegill): >830 mg/L
Florfenicol: 96-hr LC50 (trout): >780 mg/L
Florfenicol: 48-hr EC50 (daphnid): >330 mg/L
Florfenicol: Algae maximum cell density: MIC = 1.5 mg/L
Florfenicol: Algae maximum growth rate: MIC >2.9 mg/L

Propylene glycol: 96-hr LC50 (sheepshead minnow): 23,800 mg/L
Propylene glycol: 48-hr EC50 (daphnid): >43,500 mg/L
Propylene glycol: 72-hr EC 50 (green algae): >19,000 mg/L

ENVIRONMENTAL DATA

OTHER INGREDIENT ENVIRONMENTAL DATA:

Florfenicol is not readily biodegradable but there is evidence of inherent biodegradability.

Propylene glycol is expected to be readily biodegradable.

SECTION 13. DISPOSAL CONSIDERATIONS

MATERIAL WASTE:
Disposal must be in accordance with applicable federal, state/provincial, and/or local regulations. Incineration is the preferred method of disposal, when appropriate. Operations that involve the crushing or shredding of waste materials or returned goods must be handled to meet the ECG or OEG.

PACKAGING AND CONTAINERS:
Disposal must be in accordance with applicable federal, state/provincial, and/or local regulations.

SPECIAL ENVIRONMENTAL HANDLING PROCEDURES:
Do not allow product to reach ground water, water courses, sewage or drainage system.

SECTION 14. TRANSPORT INFORMATION

This material is not subject to the transportation regulations of DOT, ICAO, IMO, and the ADR.

SECTION 15. REGULATORY INFORMATION

EUROPEAN UNION REGULATIONS:

Indication of Danger:

Xn - Harmful.
N - Dangerous For The Environment.



Risk Phrases:
R62 - Possible risk of impaired fertility.
R63 - Possible risk of harm to the unborn child.
R36/38 - Irritating to eyes and skin.
R51/53 - Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

Safety Phrases:
S36 - Wear suitable protective clothing.
S46 - If swallowed, seek medical advice immediately and show this container or label.
S61 - Avoid release to the environment. Refer to special instructions/Safety data sheets.
S24/25 - Avoid contact with skin and eyes.

SECTION 16. OTHER INFORMATION

Although reasonable care has been taken in the preparation of this document, we extend no warranties and make no representations as to the accuracy or completeness of the information contained therein, and assume no responsibility regarding the suitability of this information for the user's intended purposes or for the consequence of its use. Each individual should make a determination as to the suitability of the information for their particular purpose(s).

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