Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

SAFETY DATA SHEET

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

SECTION 1. IDENTIFICATION OF SUBSTANCE AND CONTACT INFORMATION

SDS NAME: **Celestone Chronodose Injection (6 mg/mL)**

SYNONYM(S):
Celesdepot
Celestan Biphase Ampullen
Celestan Depot
Celestene Chronodose
Celeston Chronodose Injectable
Celeston Chronodose Injectabile
Celeston Injekt
Celestona Bifas 6 mg/mL Injektionsvatska
Celestone Chronodose Injectable
Celestone Chronodose Injection
Celestone Cronodose
Celestone Cronodose Inyectable
Celestone Soluspan Injectable
Celestone Soluspan Injection
Celestone Soluspan Inyectable
Cidoten Rapilento

MSDS NUMBER: SP000225

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

EU Transportation Emergencies - Carechem24:
+44 (0)208 762 8322 (24 hours/7 days/week)

SCHERING-PLOUGH SDS HELPLINE: +1 (908) 473-3371 (Worldwide)
Monday to Friday, 9am to 5pm (US Eastern Time)

SCHERING-PLOUGH SDS EMAIL: spmsds@spcorp.com

SECTION 2. HAZARDS IDENTIFICATION

EU CLASSIFICATION(S): R20, R61

EMERGENCY OVERVIEW

Colorless
Liquid
Odor unknown
May be harmful by inhalation, skin absorption or if swallowed.
May cause sensitization by skin contact.
May cause developmental effects.
May cause reproductive effects.
Causes effects to:
skin
endocrine system
May cause effects to:
muscoloskeletal system
nervous system
gastrointestinal tract
immune system
liver
kidney
reproductive system
fetus

POTENTIAL HEALTH EFFECTS:

The health hazard information presented below is for the active ingredient in this product.

Betamethasone is an anti-inflammatory corticosteroid used in the treatment of various disease states. As a class, corticosteroids are known to cause systemic effects such as reversible suppression of the hypothalamic-pituitary-adrenal (HPA) axis, increased blood sugar, sugar in the urine, impairment of glucose tolerance, and changes in general metabolism, bone metabolism, white blood cell counts, and some blood serum chemistry levels. The clinical relevance of these changes in healthy adults is unknown. Cushing's syndrome may occur from excessive exposure to corticosteroids. Use of aerosolized corticosteroid inhalers has caused nasal irritation or burning, occasional sneezing, runny or bloody nose. Rare instances of nasal ulceration, septum perforation and increased intraocular pressure have been reported following prolonged use of or overexposure to aerosolized corticosteroids. Prolonged use of systemic steroids is also known to be associated with the formation of cataracts and glaucoma. Corticosteroids may mask some signs of infection, and opportunistic infections may appear during their use due to effects on immune system. Persons with pre-existing skin conditions including dermatitis and acne, a history of asthma, or those taking or those with a history of taking systemic steroids are more susceptible to allergic reactions from exposure to steroids. Serious health effects including death have occured in asthmatic patients during transfer from systemic corticosteroid to topical corticosteroid clinical use.

The most common side effects in studies with betamethasone-containing topical preparations were local, including erythema, steroid-induced rosacea (redness, acne-like reaction on face), mild burning, itching, skin dryness and irritation. Betamethasone has been shown to decrease collagen synthesis in human skin following treatment with topical cream. Adverse reactions reported following injection of betamethasone include effects on fluid and electrolytes, musculoskeletal, gastrointestinal, dermatologic, neurological, endocrine, ophthalmic and metabolic parameters.

Corticosteroids are teratogenic in laboratory animals and may be considered teratogenic in non-human primates as well. Widespread clinical use of corticosteroids has resulted in very few reports of teratogenic activity in humans. There is no evidence of impaired fertility in humans treated with corticosteroids although hypo-adrenalism may occur in infants born to mothers receiving corticosteroids during pregnancy.

LISTED CARCINOGENS

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

SECTION 3. COMPOSITION AND INFORMATION ON INGREDIENTS

PRODUCT USE: Drug product

CHEMICAL FORMULA: Mixture.

The formulations for these products are proprietary information. These formulations have the same hazardous profile; however, the presence of hazardous ingredients may vary by formulation. 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 2.

CHEMICAL COMPOSITION

INGREDIENT	CAS NUMBER	EU NUMBER	EU CLASSIFICATION	PERCENT
Betamethasone Sodium Phosphate	151-73-5	205-797-0	T+, Xi R26, R43, R61, R48/20/21/22	0.39
Betamethasone Acetate	987-24-6	213-578-6	T, Xi: R23, R43, R61, R48/20/21/22	0.3

ADDITIONAL INFORMATION: This MSDS is written to provide health and safety information for individuals who will be handling the final product formulation during research, manufacturing, and distribution. 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 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 unless under the direction of a qualified medical professional or Poison Control Center. If symptoms persist, consult a physician.

SECTION 5. FIRE FIGHTING MEASURES

FLAMMABILITY DATA:

Flash Point: >93.3 deg C (>200 deg F)

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.

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

SECTION 7. HANDLING AND STORAGE

HANDLING:
Keep containers adequately sealed during material transfer, transport, or when not in use.

Appropriate handling of this material is 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. See Section 8 (Exposure Controls) for additional guidance.

STORAGE:
Store out of direct light. 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 HEALTH HAZARD CATEGORY (HHC):
The Schering-Plough Health Hazard Category (HHC) for this material is HHC4. Materials in this category are considered extreme health hazards. Health Hazard Categories are intended to be a component of workplace risk assessment. Consult your site safety and industrial hygiene staff for guidance on handling and control strategies.

S-P OCCUPATIONAL EXPOSURE GUIDELINE (OEG):
Schering-Plough Corporation has established an Occupational Exposure Guideline of 5 mcg/m^3 (8-hr TWA) for betamethasone (base).

HHC/OEG NOTATION(S):
This material has a notation of "S" for its ability to cause systemic toxicity through skin absorption.

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, appropriate use of personal protective equipment (PPE) may be considered as alternative control measures. 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:	Respiratory protective equipment (RPE) may be required for certain laboratory and large-scale manufacturing tasks if potential airborne breathing zone concentrations of substances exceed the relevant exposure limit(s). Workplace risk assessment should be completed before specifying and implementing RPE usage. Potential exposure points and pathways, task duration and frequency, potential employee contact with the substance, and the ability of the substance to be rendered airborne during specific tasks should be evaluated. Initial and ongoing strategies of quantitative exposure measurement should be obtained as required by the workplace risk assessment. All RPE must conform to local and regional specifications for efficacy and performance. Consult your site or corporate health and safety professional for additional 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 based on hazard, potential for contact, or level of exposure. 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.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

FORM:	Liquid
COLOR:	Colorless
ODOR:	Odor unknown
pH:	6.8-7.2
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:
Oxidizers. Strong acids and bases. Open flames and high temperatures.

HAZARDOUS DECOMPOSITION PRODUCTS / REACTIONS:
Carbon oxides (COx).

SECTION 11. TOXICOLOGICAL INFORMATION

The information presented below is for the active ingredient(s) in this product.

ACUTE TOXICITY DATA

INHALATION:
Betamethasone Sodium Phosphate: Inhalation LC50 (rat): 0.07 to 0.73 mg/L
In an acute inhalation study in rats, betamethasone sodium phosphate caused labored breathing, eye closure, and reduced activity at 3.5 mg/l, eye closure and reduced activity at 0.73 mg/l, and reduced activity at 0.071 mg/l. Labored breathing, nasal discharge, ano-genital staining, and body weight loss leading to mortality (6/6 animals) was observed 6 to 9 days following exposure to 3.5 mg/l. Similar, but delayed, responses leading to mortality (6/6 animals) 9-11 days after 0.73 mg/l exposure was reported. Weight loss without clinical signs or mortality (0/6 animals) was reported during the first week of exposure to 0.071 mg/l followed by recovery of the animals.

In an acute inhalation toxicity study in rats, betamethasone acetate has an LC50 of 0.28 mg/L (maximum obtainable dose). Gross toxic effects observed included reduced activity and eye closure during exposure. Emaciation and nasal discharge, with some mortality, occurred during the second week after exposure. Recovery from these effects was not seen in this study.

SKIN:
Betamethasone sodium phosphate was essentially not-irritating to the skin of rabbits. The only irritation seen was very slight (barely perceptible) erythema in one animal at 72 hours.

Betamethasone produced erythema which was present five hours after dosing in a skin irritation study in rabbits but resolved by 96 hours after dosing. There were no adverse skin changes detected in dermal toxicity studies of betamethasone diproprionate cream (0.05% or 0.1%) in hairless mice, rats, rabbits or dogs.

EYE:
Betamethasone sodium phosphate produced very mild, reversible ocular irritation in rabbits. The only irritation seen was very slight conjunctival redness in one of four animals and a small area of corneal ulceration in another animal, at 24 hours. All animals were free of irritation by Day 7.

ORAL:
Betamethasone Sodium Phosphate: Oral LD50: 1607 mg/kg (mouse)

In an acute oral toxicity study in rats, betamethasone acetate has an oral LD50 of > 5000 mg/kg. Gross toxic effects observed in this study included urinary staining and no apparent food consumption.

SENSITIZATION:
A betamethasone dipropionate (0.05%) ointment formulation was determined to be a potentially weak sensitizer in guinea pigs. Local irritation at the intradermal injection sites was observed during the induction phase.

REPEAT DOSE TOXICITY DATA

SUBCHRONIC / CHRONIC TOXICITY:
Rabbits are the most sensitive species tested with regards to repeated topical skin application. Serious effects including death, hypothalamic-pituitary-adrenal (HPA) axis suppression, skeletal muscle wasting, immune organ atrophy, and abdominal distention in more than 50% of animals tested were observed following application for 10 to 30 days with 0.05% betamethasone propionate cream, lotion or ointment formulations. However, rats and mice demonstrated only minimal systemic effects, principally thymic involution, when either 0.05% or 0.1% cream was applied to skin six days a week for up to eight weeks.

In a 14-day oral toxicity study testing the 0.1% topical cream formulation in rats and mice, drug-related clinical signs including diarrhea, hypothermia and rough coat, were observed within three hours to six days after dosing. Hypoactivity and ptosis were also seen in rats. In a 28-day oral toxicity study in dogs treated with 0.05 to 1 mg/kg/day of betamethasone dipropionate, drug-related effects observed included reversible changes in hematological, biochemical and physiological data (increased fluid intake and urinary output, decreased hematocrit and hemoglobin values, alterations in white blood cell counts, increases in liver enzymes, thymic involution and adrenal atrophy) which were attributed to the known pharmacological activity of corticosteroid drugs.

REPRODUCTIVE / DEVELOPMENTAL TOXICITY:
Corticosteroids are known teratogens in rodent species with some teratogenic effects having been observed in non-human primates. They are generally teratogenic in laboratory animals when administered systemically at low dosages.

Subcutaneous administration of up to 0.42 mg of a mixture of betamethasone/sodium phosphate and betamethasone/acetate suspension, on days 12 and 13 of gestation in pregnant rats, caused decreases in maternal and fetal weight gain, occurence of cleft palate and omphalocele (umbilical hernia), and impaired growth of fetal heart, liver, adrenals, kidneys, and skeletal muscle. Dose-related increases in fetal resorptions in rabbits and mice following single intramuscular doses up to 1 and 33 mg/kg, respectively were observed. Additionally, betamethasone diproprionate has been shown to produce umbilical hernias, cephalocele (cranial protrusion) and cleft palate in rabbits when given intramuscular doses of 0.05 mg/kg/day during gestation. Suppression of adrenocorticotropic hormone (ACTH), following intramuscular administration of betamethasone in monkeys during gestation resulted in decreases in fetal adrenal weight, cortical cell size, appearance of apoptosis and cellular disorganization.

MUTAGENICITY / GENOTOXICITY:
Betamethasone was negative in a bacterial mutagenicity study (Ames) and mammalian cell mutagenicity assay (CHO/HGPRT) and positive in the in vitro human lymphocyte chromosome abberation assay. Equivocal results were seen in the in vivo mouse bone marrow micronucleus assay.

CARCINOGENICITY:
This material or product has not been evaluated for carcinogenicity.

SECTION 12. ECOLOGICAL INFORMATION

ECOTOXICITY DATA

There are no ecotoxicity data available for these products or their components.

ENVIRONMENTAL DATA

There are no environmental data available for these products or their components.

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 recommended exposure limit(s).

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

SECTION 14. TRANSPORT INFORMATION

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

SECTION 15. REGULATORY INFORMATION

The following classification is based on available data and is in accordance with European Union criteria.

EUROPEAN UNION REGULATIONS:

Indication of Danger: T - Toxic.

Risk Phrases:
R20 - Harmful by inhalation.
R61 - May cause harm to the unborn child.

Safety Phrases:
S45 - In case of accident or if you feel unwell, seek medical advice immediately (show label where possible).
S53 - Avoid exposure - obtain special instructions before use.
S 2 - Keep out of reach of children.
S46 - If swallowed, seek medical advice immediately and show this container or label.
S 1 - Keep locked-up.

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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