Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME
Coumestrol

STATEMENT OF HAZARDOUS NATURE

NFPA

SUPPLIER
Santa Cruz Biotechnology, Inc.
2145 Delaware Avenue
Santa Cruz, California 95060
800.457.3801 or 831.457.3800

EMERGENCY
ChemWatch
Within the US & Canada: 877-715-9305
Outside the US & Canada: +800 2436 2255
(1-800-CHEMCALL) or call +613 9573 3112

SYNONYMS
C15-H8-O5, "6H-benzofuro[3, 2-c](1)benzopyran-6-one, 3, 9-dihydroxy-", "3-benzofurancarboxylic acid, 2-(2, 4-dihydroxyphenyl)-6-hydroxy-, "delta lactone", cumoestrol, coumestrol, cumostrol, "3, 9-dihydroxy-6H-benzofuro[3, 2-c](1)benzopyran-6-one", "2-(2, 4-dihydroxyphenyl)-6-hydroxy-3-benzofurancarboxylic acid delta", lactone, "7", 6-dihydroxycoumarino(3', 4', 3, 2)coumarone", "coumestane phytoestrogen/ phytooestrogen"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

<table>
<thead>
<tr>
<th>Hazard</th>
<th>Min</th>
<th>Max</th>
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<tr>
<td>Flammability</td>
<td>1</td>
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<tr>
<td>Toxicity</td>
<td>2</td>
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<tr>
<td>Body Contact</td>
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<tr>
<td>Reactivity</td>
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<tr>
<td>Chronic</td>
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1 of 10
CANADIAN WHMIS SYMBOLS

EMERGENCY OVERVIEW
RISK
Harmful if swallowed.
Irritating to eyes, respiratory system and skin.

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED
- Accidental ingestion of the material may be harmful; animal experiments indicate that ingestion of less than 150 gram may be fatal or may produce serious damage to the health of the individual.
- Limited evidence exists that the substance may cause irreversible but non-lethal mutagenic effects following a single exposure.

EYE
- This material can cause eye irritation and damage in some persons.

SKIN
- This material can cause inflammation of the skin on contact in some persons.
- The material may accentuate any pre-existing dermatitis condition.
- Open cuts, abraded or irritated skin should not be exposed to this material.
- Entry into the blood-stream, through, for example, cuts, abrasions or lesions, may produce systemic injury with harmful effects.
Examine the skin prior to the use of the material and ensure that any external damage is suitably protected.

INHALED
- The material can cause respiratory irritation in some persons.
The body’s response to such irritation can cause further lung damage.
- Persons with impaired respiratory function, airway diseases and conditions such as emphysema or chronic bronchitis, may incur further disability if excessive concentrations of particulate are inhaled.
- Limited evidence exists that the substance may cause irreversible but non-lethal mutagenic effects following a single exposure.

CHRONIC HEALTH EFFECTS
- Long-term exposure to respiratory irritants may result in disease of the airways involving difficult breathing and related systemic problems.
Limited evidence suggests that repeated or long-term occupational exposure may produce cumulative health effects involving organs or biochemical systems.
Exposure to the material may cause concerns for human fertility, on the basis that similar materials provide some evidence of impaired fertility in the absence of toxic effects, or evidence of impaired fertility occurring at around the same dose levels as other toxic effects, but which are not a secondary non-specific consequence of other toxic effects.

Exposure to the material may cause concerns for humans owing to possible developmental toxic effects, on the basis that similar materials tested in appropriate animal studies provide some suspicion of developmental toxicity in the absence of signs of marked maternal toxicity, or at around the same dose levels as other toxic effects but which are not a secondary non-specific consequence of other toxic effects.

Exposure to the material may result in a possible risk of irreversible effects. The material may produce mutagenic effects in man. This concern is raised, generally, on the basis of appropriate studies with similar materials using mammalian somatic cells in vivo. Such findings are often supported by positive results from in vitro mutagenicity studies.

Human and animal exposures to the phytoestrogens (for example the isoflavones, some flavonoids, saponin, coumestans and lignans) can be high because these compounds are found in many foods. Interest in the dietary phytoestrogens derives from their apparent protective effects against cancer, cardiovascular disease and...
osteoporosis. High levels, over extended periods, may produce toxic effects. However, toxicological studies revealed that when administered in isolated or enriched form or at high doses isoflavones impair the function of the thyroid gland. It cannot be ruled out that this oestrogen-like effect also encourages the onset of breast cancer. Since women are more at risk of developing cancer in any case after menopause, the intake of food supplements with a high isoflavone content may present unexpected risks for this group of consumers.

Although phytooestrogens exist as the inactive glycoside in food products, bacterial beta-glycosidases, in the colon, hydrolyse the glycosides to the active aglycones. A common feature of the phytooestrogens is their striking similarity to 17beta-oestradiol and the synthetic oestrogen, diethylstilboestrol. There is evidence that phytooestrogens may mediate oestrogen-like effects by direct interaction with the oestrogen receptor of cells. Although the hormonal activity of phytooestrogens is two to five orders of magnitude below that of oestradiol, their high concentration in certain plants and their slower metabolic disposition, can lead to tissue levels exceeding those of endogenous oestrogens by a factor of a thousand or more.

There is also evidence that phytooestrogens may influence animal and human health by acting as antioxidants and hydrogen peroxide scavengers or by interfering with eicosanoid and cytokine production and cell signalling. Anogenital distance, puberty onset, oestrus cycling, growth, sex-organ weight and hormonal profile are indicators of oestrogen- or anti-oestrogen like activity. Of interest is the finding that low doses of the dietary isoflavone, genistein, taken by pregnant rats produced shorter anogenital distances in the offspring; high doses did not produce this effect. Exposure to a 5% flaxseed diet (high in lignans) during pregnancy and lactation, resulted in the delayed puberty onset in rats (anti-oestrogenic effect). By contrast, a 10% flaxseed diet produced an earlier onset of puberty (an oestrogenic effect), but longer oestrus cycles due to prolonged dioestrus (an antioestrogenic effect).

There have been many reports of phytooestrogens disrupting reproductive activity in sheep. Infertility in sheep (so-called "clover disease") has been traced to isoflavone concentrations in clover (up to 5% dry weight). Temporary infertility is attributed to increased embryo mortality and a reduction or cessation in ovulation. Permanent infertility, in sheep, is purported to occur after 3 years of exposure to dietary oestrogenic compounds; this infertility is due to permanent changes in the architecture of the cervix and also changes in the viscoelasticity of the cervical mucous which prevents the transport of sperm through the cervix. In addition to these effects, phytooestrogens exert effects on oestrogen-sensitive tissues such as the mammary gland and female reproductive organs of the ewe. Cattle have also been shown to be sensitive to the oestrogen-like effects of dietary phytooestrogens. Specific observations include swelling of the vulva, discharge of cervical mucous, uterus enlargements and cystic ovaries. Irregular oestrus cycles, including periods of anoestrus, and decreased rates of conception have also been reported. The impact on reproductive activity, by phytooestrogens on humans, is unknown.

The recent practice of feeding infants soy-based formula raises issues related to the long-term health effects of exposure during development. It has been recognised, for example, that the practice may be associated with goiter (thyroid enlargement associated with thyroid hormone deficiency) in humans and animals. Soy phytooestrogens inhibit thyroid hormone synthesis at concentrations which occur in infant formula. If sufficient inhibition of iodide uptake by the goiter occurs, formation of thyroid hormones is depressed. These hormones are essential to the regulation of oxygen consumption and metabolism throughout the body. Clinical manifestations of this so-called "hypothyroidism (or athyrea)" include low metabolic rate, a tendency to gain weight, somnolence, and myxoedema (a relatively hard oedema of the subcutaneous tissue), dryness and loss of hair, low body temperature, hoarseness, muscle weakness, a slow return of the muscle after tendon jerk, and slow mentation. When hypothyroidism occurs in women, early in pregnancy, the foetus is at risk of impaired physical and mental development, the severity of the impairment depending on the degree of hypothyroidism. Long term exposure to high dust concentrations may cause changes in lung function i.e. pneumoconiosis; caused by particles less than 0.5 micron penetrating and remaining in the lung.

<table>
<thead>
<tr>
<th>NAME</th>
<th>CAS RN</th>
<th>%</th>
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<tbody>
<tr>
<td>coumestrol</td>
<td>479-13-0</td>
<td>&gt;98</td>
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</tbody>
</table>
Section 4 - FIRST AID MEASURES

SWALLOWED
- IF SWALLOWED, REFER FOR MEDICAL ATTENTION, WHERE POSSIBLE, WITHOUT DELAY.
- Where Medical attention is not immediately available or where the patient is more than 15 minutes from a hospital or unless instructed otherwise

EYE
If this product comes in contact with the eyes
- Wash out immediately with fresh running water.
- Ensure complete irrigation of the eye by keeping eyelids apart and away from eye and moving the eyelids by occasionally lifting the upper and lower lids.

SKIN
If skin contact occurs
- Immediately remove all contaminated clothing, including footwear
- Flush skin and hair with running water (and soap if available).

INHALED
- If fumes or combustion products are inhaled remove from contaminated area.
- Lay patient down. Keep warm and rested.

NOTES TO PHYSICIAN
- for poisons (where specific treatment regime is absent)

--- BASIC TREATMENT ---
- Establish a patent airway with suction where necessary.
- Watch for signs of respiratory insufficiency and assist ventilation as necessary.
- Treat symptomatically.

Section 5 - FIRE FIGHTING MEASURES

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>Vapour Pressure (mmHG)</td>
<td>Negligible</td>
</tr>
<tr>
<td>Upper Explosive Limit (%)</td>
<td>Not available.</td>
</tr>
<tr>
<td>Specific Gravity (water=1)</td>
<td>Not available</td>
</tr>
<tr>
<td>Lower Explosive Limit (%)</td>
<td>Not available</td>
</tr>
</tbody>
</table>

EXTINGUISHING MEDIA
- Foam.
- Dry chemical powder.

FIRE FIGHTING
- Alert Emergency Responders and tell them location and nature of hazard.
- Wear breathing apparatus plus protective gloves.

GENERAL FIRE HAZARDS/HAZARDOUS COMBUSTIBLE PRODUCTS
- Combustible solid which burns but propagates flame with difficulty.
- Avoid generating dust, particularly clouds of dust in a confined or unventilated space as dusts may form an explosive mixture with air, and any source of ignition, i.e. flame or spark, will cause fire or explosion. Dust clouds generated by the fine grinding of the solid are a particular hazard; accumulations of fine dust may burn rapidly and fiercely if ignited.
- Combustion products include carbon monoxide (CO), carbon dioxide (CO2), other pyrolysis products typical of burning organic material.
- May emit poisonous fumes.
- May emit corrosive fumes.

FIRE INCOMPATIBILITY
- Avoid contamination with oxidizing agents i.e. nitrates, oxidizing acids, chlorine bleaches, pool chlorine etc. as ignition may result.
Section 6 - ACCIDENTAL RELEASE MEASURES

MINOR SPILLS
- Remove all ignition sources.
- Clean up all spills immediately.
- Avoid contact with skin and eyes.
- Control personal contact by using protective equipment.
- Use dry clean up procedures and avoid generating dust.
- Place in a suitable, labelled container for waste disposal.

MAJOR SPILLS
Moderate hazard.
- CAUTION Advise personnel in area.
- Alert Emergency Responders and tell them location and nature of hazard.

Section 7 - HANDLING AND STORAGE

PROCEDURE FOR HANDLING
- Avoid all personal contact, including inhalation.
- Wear protective clothing when risk of exposure occurs.

Empty containers may contain residual dust which has the potential to accumulate following settling. Such dusts may explode in the presence of an appropriate ignition source.
- Do NOT cut, drill, grind or weld such containers.
- In addition ensure such activity is not performed near full, partially empty or empty containers without appropriate workplace safety authorisation or permit.

RECOMMENDED STORAGE METHODS
- Polyethylene or polypropylene container.
- Check all containers are clearly labelled and free from leaks.

STORAGE REQUIREMENTS
- Store in original containers.
- Keep containers securely sealed.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

<table>
<thead>
<tr>
<th>Source</th>
<th>Material</th>
<th>TWA ppm</th>
<th>TWA mg/m³</th>
<th>STEL ppm</th>
<th>STEL mg/m³</th>
<th>Peak ppm</th>
<th>Peak mg/m³</th>
<th>TWA F/CC</th>
<th>Notes</th>
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</thead>
<tbody>
<tr>
<td>Canada - Ontario Occupational Exposure Limits</td>
<td>coumestrol (Particles (Insoluble or Poorly Soluble) Not Otherwise)</td>
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<td>Canada - British Columbia Occupational Exposure Limits</td>
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<td>Location</td>
<td>Substance</td>
<td>Description</td>
<td>Limit</td>
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<td>US - Tennessee Occupational Exposure Limits - Limits For Air Contaminants</td>
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<td>(Particulates not otherwise regulated Respirable fraction)</td>
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<td>US - California Permissible Exposure Limits for Chemical Contaminants</td>
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<td>US - Oregon Permissible Exposure Limits (Z-1)</td>
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<td>(Particulates not otherwise regulated (PNOR) (f) Total Dust)</td>
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<tr>
<td>US - Michigan Exposure Limits for Air Contaminants</td>
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<td>(Particulates not otherwise regulated, Respirable dust)</td>
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<tr>
<td>US - Oregon Permissible Exposure Limits (Z-1)</td>
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<td>(Particulates not otherwise regulated (PNOR) (f) Respirable Fraction)</td>
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<tr>
<td>US - Wyoming Toxic and Hazardous Substances Table Z1 Limits for Air Contaminants</td>
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<td>(Particulates not otherwise regulated (PNOR)(f)- Respirable fraction)</td>
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<td>Canada - Prince Edward Island Occupational Exposure Limits</td>
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<td>(Particles (Insoluble or Poorly Soluble) [NOS] Inhalable particles)</td>
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**PERSONAL PROTECTION**
RESPIRATOR
- Particulate. (AS/NZS 1716 & 1715, EN 1432000 & 1492001, ANSI Z88 or national equivalent)

EYE
- Safety glasses with side shields.
- Chemical goggles.

HANDS/FEET
Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include
- frequency and duration of contact,
- chemical resistance of glove material,
- glove thickness and
dexterity
Select gloves tested to a relevant standard (e.g. Europe EN 374, US F739, AS/NZS 2161.1 or national equivalent).
- When prolonged or frequently repeated contact may occur, a glove with a protection class of 5 or higher (breakthrough time greater than 240 minutes according to EN 374, AS/NZS 2161.10.1 or national equivalent) is recommended.
- When only brief contact is expected, a glove with a protection class of 3 or higher (breakthrough time greater than 60 minutes according to EN 374, AS/NZS 2161.10.1 or national equivalent) is recommended.
- Contaminated gloves should be replaced.
Gloves must only be worn on clean hands. After using gloves, hands should be washed and dried thoroughly. Application of a non-perfumed moisturiser is recommended.
Experience indicates that the following polymers are suitable as glove materials for protection against undissolved, dry solids, where abrasive particles are not present.
- polychloroprene
- nitrile rubber
- butyl rubber
- fluorocautchouc
- polyvinyl chloride
Gloves should be examined for wear and/ or degradation constantly.

OTHER
- Overalls.
- P.V.C. apron.
- Barrier cream.
- Skin cleansing cream.
- Eye wash unit.

ENGINEERING CONTROLS
- Local exhaust ventilation is required where solids are handled as powders or crystals; even when particulates are relatively large, a certain proportion will be powdered by mutual friction.
- Exhaust ventilation should be designed to prevent accumulation and recirculation of particulates in the workplace.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES
Solid.
Does not mix with water.
<table>
<thead>
<tr>
<th>Property</th>
<th>State</th>
<th>Melting Range (°F)</th>
<th>Boiling Range (°F)</th>
<th>Flash Point (°F)</th>
<th>Decomposition Temp (°F)</th>
<th>Autoignition Temp (°F)</th>
<th>Upper Explosive Limit (%)</th>
<th>Lower Explosive Limit (%)</th>
<th>Volatile Component (%vol)</th>
<th>APPEARANCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>State</td>
<td>Divided solid</td>
<td>725</td>
<td>Not available</td>
<td>Not available</td>
<td>Not available</td>
<td>Not available</td>
<td>Not available</td>
<td>Not available</td>
<td>Negligible</td>
<td>Crystalline solid; does not mix well with water at acid and neutral pH. Sublimes at 325 deg. C.; sublimes in high vacuum at about 175 deg. C. Exhibits bright blue fluorescence in neutral or acid solution, greenish-yellow fluorescence in strong alkalies.</td>
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<td>Molecular Weight</td>
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<td>Specific Gravity (water=1)</td>
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<td>Evaporation Rate</td>
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</table>

**Section 10 - CHEMICAL STABILITY**

**CONDITIONS CONTRIBUTING TO INSTABILITY**
- Presence of incompatible materials.
- Product is considered stable.

**STORAGE INCOMPATIBILITY**
- Avoid reaction with oxidizing agents.

For incompatible materials - refer to Section 7 - Handling and Storage.

**Section 11 - TOXICOLOGICAL INFORMATION**

coumestrol

**TOXICITY AND IRRITATION**

**COUMESTROL**

unless otherwise specified data extracted from RTECS - Register of Toxic Effects of Chemical Substances.

Asthma-like symptoms may continue for months or even years after exposure to the material ceases. This may be due to a non-allergic condition known as reactive airways dysfunction syndrome (RADS) which can occur following exposure to high levels of highly irritating compound. Key criteria for the diagnosis of RADS include the absence of preceding respiratory disease, in a non-atopic individual, with abrupt onset of persistent asthma-like symptoms within minutes to hours of a documented exposure to the irritant. A reversible airflow pattern, on spirometry, with the presence of moderate to severe bronchial hyperreactivity on methacholine challenge testing and the lack of minimal lymphocytic inflammation, without eosinophilia, have also been included in the criteria for diagnosis of RADS. RADS (or asthma) following an irritating inhalation is an infrequent disorder with rates related to the concentration of and duration of exposure to the irritating substance. Industrial bronchitis, on the other hand, is a disorder that occurs as result of exposure due to high concentrations of irritating substance (often particulate in nature) and is completely reversible after exposure ceases. The disorder is characterised by dyspnea, cough and mucus production.

No significant acute toxicological data identified in literature search.

**NOTE** Substance has been shown to be mutagenic in at least one assay, or belongs to a family of chemicals producing damage or change to cellular DNA. Endocrine changes, changes in serum composition, maternal effects, effects on fertility, effects on embryo/foetus recorded.

**Section 12 - ECOLOGICAL INFORMATION**

No data
Section 13 - DISPOSAL CONSIDERATIONS

Disposal Instructions
All waste must be handled in accordance with local, state and federal regulations.
- Puncture containers to prevent re-use and bury at an authorized landfill.
Legislation addressing waste disposal requirements may differ by country, state and/ or territory. Each user must refer to laws operating in their area. In some areas, certain wastes must be tracked.
A Hierarchy of Controls seems to be common - the user should investigate:

- Reduction
- Reuse
- Recycling
- Disposal (if all else fails)

This material may be recycled if unused, or if it has not been contaminated so as to make it unsuitable for its intended use. Shelf life considerations should also be applied in making decisions of this type. Note that properties of a material may change in use, and recycling or reuse may not always be appropriate.

DO NOT allow wash water from cleaning equipment to enter drains. Collect all wash water for treatment before disposal.
- Recycle wherever possible.
- Consult manufacturer for recycling options or consult Waste Management Authority for disposal if no suitable treatment or disposal facility can be identified.

Section 14 - TRANSPORTATION INFORMATION

NOT REGULATED FOR TRANSPORT OF DANGEROUS GOODS: DOT, IATA, IMDG

Section 15 - REGULATORY INFORMATION

coumestrol (CAS: 479-13-0) is found on the following regulatory lists;
“Canada Non-Domestic Substances List (NDSL)”, “US Toxic Substances Control Act (TSCA) - Chemical Substance Inventory”

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE
- Cumulative effects may result following exposure*.
- May possibly affect fertility*.
- May possibly be harmful to the foetus/ embryo*.
- Exposure may produce irreversible effects*.
* (limited evidence).

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Classification of the preparation and its individual components has drawn on official and authoritative sources as well as independent review by the Chemwatch Classification committee using available literature references. A list of reference resources used to assist the committee may be found at: www.chemwatch.net/references.

The (M)SDS is a Hazard Communication tool and should be used to assist in the Risk Assessment. Many factors determine whether the reported Hazards are Risks in the workplace or other settings. Risks may be determined by reference to Exposures Scenarios. Scale of use, frequency of use and current or available engineering controls must be considered.

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