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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION
AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

CARTASOL YELLOW K-3GL

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Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

Cartasol Yellow K-3GL

1. IMPORTER

Sandoz Australia Pty Ltd, 675-685 Warrigal Road, Chadstone, Victoria 3148.

2. IDENTITY OF CHEMICAL

Trade Name: Cartasol Yellow K-3GL Conc.

Laboratory Names: Cartasol Gelb K3GL, RWA 3430Z, Cartasol Gelb K-RWA3430 (K-3GL), Cartasol Gelb K-3GL Lactat Conz, Cartasol Yellow K-3GL Lactat Conz, Cartasol Yellow K-3GL.

The applicant applied for exemption for the chemical name, molecular and structural formulae and molecular weight and spectral data. The chemical is not a hazardous chemical under the WSA definition and the application was allowed.

3. PHYSICAL AND CHEMICAL PROPERTIES

Cartasol Yellow K-3GL is a yellow powder with low volatility. Its physical and chemical properties include:

Melting Point: Not determined, decomposition at 128-138^{O}C.

Vapour Pressure: Not determined. It is not expected to be significant as the notified dye is a high molecular weight salt.

Water solubility: 226 g/L at 20^{O}C.

Flammability: non-flammable

Autoignition temperature: 320^{O}C.

Hydrolytic stability: The dye is hydrolytically stable under operational conditions (3.5 < pH < 9 and temperature < 60^{O}C).

Partition coefficient: (n-octanol/water) log P_{OW} = -1.32

Soil adsorption-desorption: Test not performed, but the dye is said to bind strongly to such materials as calcium carbonate, aluminium silicate and magnesium silicate during dyeing operations. In addition, a shortfall in the fish toxicity test (see below) compared with a distilled water control was interpreted by the notifier in terms of adsorption to silt/faeces. The notifier states under disposal that "the dye is readily adsorbed onto clay, soil, organic humus and similar land fill materials". Such behaviour is consistent with the dye's structure.

Dissociation constant: No data were provided, but ready dissociation in aqueous solution is indicated by the high water solubility and presence of quaternary ammonium centres.

4. PURITY OF THE CHEMICAL

Degree of purity: > 90%.

The applicant has applied for exemption from publication for detailed purity data, including the identity of impurities. These would not be classified as hazardous substances and the request was allowed.

5. INDUSTRIAL USES

Cartasol Yellow K-3GL is a dyestuff. The chemical will be imported into Australia in quantities of less than 1 tonne per year for the first 5 years. The dye will initially be imported

and used as 9% solution in paper dyeing processes. Subsequently, it may be used as a dyestuff in leather processes.

6. OCCUPATIONAL EXPOSURE

The number of workers who may be exposed has been estimated at 20 to 75. A maximum of 40 would be transporting and handling the chemical to and from the store. Present plans to import the chemical in solution as a liquid, and the expected low vapour pressure, preclude significant exposure by inhalation. Up to 35 workers would handle the liquid dyestuff or wet leather. Those handling dyed papers and leather, once dry, will not have any significant exposure to Cartasol Yellow K-3GL as the dye is bound to these materials firmly.

Workers transporting or moving the chemical within the plants should have no exposure under normal circumstances. In case of accidents occurring during transport and handling, exposure is expected to be at a minimum because of the low vapour pressure. Significant exposure would only occur if a spill results in skin contact.

Process workers engaged in repacking the dyestuff by running the liquid preparation from the 100 litre drums in which it is imported into 20 litre drums for local use and papermill and tannery workers involved in dosing the dyestuff liquid to machines, maintaining tank levels and ensuring that equipment is functional will have zero exposure by oral or inhalational routes under normal circumstances. Some skin contact may occur due to splashing or spillages.

Tannery workers handling the dyed leather while it is still wet may have dermal exposure if appropriate gloves are not used.

Precautions dictated by good housekeeping and general education and training given for the handling of dyestuffs are considered sufficient. Additional precautions are not recommended.

7. PUBLIC EXPOSURE

The potential for public exposure to this compound is expected to be low in normal circumstances due to its site of manufacture and its use pattern.

8. ENVIRONMENTAL EXPOSURE

Environmental Release

. Formulation, handling and disposal

The dye solution will be repacked, at the Sandoz Pigment Dispersion Plant in Moorabbin, from Schutz containers (800-1000 L) into 20-25 L containers for distribution. Hoses used for transfer will be flushed to sewer (100 g of dye per batch, or 0.6-0.8 kg per annum) and container residues (0.5 kg per batch, or 3-4 kg per annum) will be consigned with the container to landfill.

. Use

Being a reactive dye, Cartasol Yellow K3GL becomes chemically bound to substrate during use. The notifier indicates that the bulk of the dye (> 95%) will become bound during dyeing operations, with the remainder being discharged with wastewater to effluent treatment plants as a highly diluted solution.

It is expected that initially one and subsequently up to three paper mills will incorporate the dye into writing and photocopying papers. This will involve transfer of the liquid to a large dilution tank followed by introduction of diluted dye to the paper making process at the "wet end" of the machine. During dyeing, up to 5% of the dye becomes bound to suspended cellulose fines and fillers which pass out with the waste water. This suspended material will be extracted during waste water treatment and consigned to landfill (with sludge). It is estimated that each mill will dispose of 1.8 kg with sludge to landfill from a monthly budget of 400 kg liquid dye (36 kg notified substance). The amount of unfixed dye remaining in solution in the waste water is said to be a minute fraction of that disposed of with sludge.

The company notes that possibly up to three tanneries may also use this dye, with a maximum use of not greater than 50 kg per year. Tanneries are expected to use 2.5 kg of the dye per batch of leather, of which no more than 0.1 kg will be disposed of with sludge. Sandoz estimates that a maximum of 1-2 kg will be disposed of to landfill from tanneries annually, but provides no further details.

Environmental Fate

The bulk of the dye will be bound to paper or leather and in this state is not expected to impact on the environment.

While the dye is water soluble, its cationic nature results in removal from solution through binding to suspended particles and dissolved organic matter. Residues which escape binding to the paper or leather substrates will be sent to landfill bound to fibre or mineral fillers as part of a sludge, where they can be expected to remain immobile.

The amount of dye which will remain unfixed and be discharged with waste water is said to be extremely small. Assuming as a worst case that residual dye (5% of applied) is discharged in solution with no binding to suspended fibre and mineral fillers as part of an effluent stream of 50 ML, the concentration in effluent would be around 10 ppb. Accumulation of residues in the aquatic environment is not expected as the dye has high solubility and returned a positive result for ready biodegradability (74% loss of dissolved organic carbon in 28 d according to OECD Test Guideline 301E).

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Table 1: Summary of acute toxicity studies.

Test	Species	Outcome	Ref
Oral	Rat	LD_{50}>5000 mg/kg (M&F)	(1)
Dermal	Rat	LD_{50}>2000 mg/kg (M&F)	(2)
Skin irritation	Rabbit	Non-irritant	(3)
Eye irritation	Rabbit	Slight irritant	(4)
Skin sensitisation	Guinea Pig	Non-sensitising	(5)

9.1.1 Oral Toxicity OECD Guideline No 401

A limit test was carried out in a group of five male and five female KFM-Han Wistar, (outbred SPF-quality) rats. Each animal received 5000 mg/kg Cartasol Yellow K-3GL in a 4% solution of CMC (carboxymethyl cellulose) sodium salt in water and was observed for a period of 15 days. No deaths occurred during the period of study and the only clinical signs observed were sedation and ruffled fur over the first 24 hour period. Necropsy revealed that one male and 2 females had dark, red, mottled lungs. The oral LD_{50} for the test compound was greater than 5000mg/kg.

9.1.2 Dermal Toxicity OECD Guideline No 402

Toxicity after dermal application was assessed in a group of five male and five female KFM-Han Wistar (outbred SPF- quality) rats. A dose of 2000 mg/kg was applied to the back of each animal 24 hours after shaving. The test article was applied evenly with a syringe and covered with an occlusive dressing. After this, the treated area was washed then dried and the skin examined for any adverse reactions. Animals continued to be observed for a fifteen day period after the application of the test article.

No deaths occurred during the study and the only adverse effect noted during observation was erythema between day 2 and day 6, and discolouration of the skin between day 2 and day 13. Some females showed sedation during the first day and scaly skin between days 6 and 13.

Necropsy and macroscopic examination revealed no pathological changes in the treated or the control group. The dermal LD_{50} was found in this test to be >2000 mg/kg.

9.1.3 Skin Irritation OECD Guideline No 404

Three New Zealand white rabbits, 2 male, 1 female were used to determine the skin irritant potential of Cartasol Yellow. Five hundred mg Cartasol Yellow, as the powder, was applied to the intact skin of the area which had been shaved 24 hours previously. After application the skin was covered with an occlusive dressing for a 4 hour period. At the end of this time, the dressing was removed and the area washed with lukewarm tap water. The skin reaction was assessed at 24, 48 and 72 hour

intervals after the removal of the dressing. Colouration of the skin by the dye was observed in all animals treated with the test compound. No signs of erythema were visible through the yellow tint nor were there any signs of oedema or corrosion. The chemical was considered to be non-irritant to the skin in this test.

9.1.4 Eye Irritation OECD Guideline No 405

Eye irritation was measured by instillation of 300 mg Cartasol Yellow K-3GL into the left eye of 3 New Zealand White rabbits. The right eye was untreated and acted as a control. Eyes were examined 1, 24, 48 and 72 hours after administration and irritation assessed according to the OECD Test Guideline. All animals showed a slight erythema of the conjunctiva 1 hour after application and, after 24 hours, 1 animal showed a mild erythema of the conjunctiva which had cleared at 48 hours. No other signs of eye irritation were observed. Under the conditions of this test the chemical was considered to be a slight eye irritant in rabbits.

9.1.5 Skin Sensitisation OECD guideline No 406

To test for the skin sensitising potential of Cartasol Yellow, a maximisation test was conducted. At the start of the induction phase, intradermal injections were made with the following solutions: i) Freund's complete adjuvant 50:50 with physiological saline, ii) the test article 0.1% in physiological saline, iii) the solutions used in i) and ii) 50:50.

One week after initial induction, a filter paper soaked in the test material (25%) was placed on the skin for 48 hours under an occlusive dressing. Vehicle control (saline) and positive control (DNCB) animals were also treated.

In the challenge phase, two weeks after the topical induction application, a filter paper soaked in test material (25%) was applied to the skin for 48 hours, and the test sites were assessed. A second challenge was performed two weeks after the first challenge, at a different skin site.

No positive skin response was noted in animals following the first or second challenge with the test material, and under the

conditions of this study, Cartasol Yellow K-3GL was not a skin sensitiser in guinea pigs. In the positive control (DNCB) group, only 60% of animals showed a positive response after challenge, and the response was unusually slight, so it may not have been possible to detect minor reactions to the test material using this experimental protocol.

9.2 Mutagenicity

9.2.1 Salmonella typhimurium reverse mutation assay OECD Guideline No 471

An experiment performed in 1986 (6), used 5 strains of *Salmonella typhimurium* (TA1535, TA1537, TA1538, TA98 and TA 100) in two independent experiments. Concentrations of Cartasol Yellow K-3GL ranged up to 5,000ug per plate. In strain TA1538, with metabolic activation, in the 5,000ug per plate dose level the revertant count approximately doubled, in experiment 1 and in experiment 2. By contrast, the positive controls 2 amino-anthracene (2-AA) and benzo[a]pyrene (B[a]P) did not cause great increases. 2-AA, in concentrations of 0.5ug per plate, showed an approximate 3.5 fold increase in the revertant count to 73 colonies per plate in experiment 1 and a four and a half fold increase in experiment 2, B[a]P at 5mg per plate showed an approximate four fold increase to 84 revertant colonies per plate in experiment 1 and an approximate four fold increase to a revertant count of 84 in experiment 2. The highest concentration showed marginal mutagenic activity with metabolic activation in strain TA 1538.

In a repeat study (7), Cartasol Yellow K-3GL was tested for mutagenicity in 5 strains of *Salmonella Typhimurium*, TA1535, TA1537, TA1538, TA98 and TA100. Two independent experiments were performed. In both, concentrations of Cartasol Yellow K-3GL ranging between 10 and 5000 ug/plate were used with and without metabolic activation. Negative and solvent control groups were used. Positive controls were used as follows:

Without metabolic activation	sodium azide (10 ug/plate); and 4 nitro-o-phenynene-diamine in DMSO (50 ug/plate).
With metabolic activation	2 amimo-anthracene in DMSO, 10 ug/plate.

No increase in the number of revertant colonies per plate were observed with the test compound, in any concentration up to 5000 ug/plate, with any of the five strains used with or without metabolic activation. The positive controls in this experiment increased revertant colony numbers. The results in the repeat testing indicate that Cartasol Yellow K-3GL is not genotoxic in *Salmonella typhimurium*.

9.2.2 Mouse Microneucleus Essay OECD Guideline No 474

Three groups of mice (6 male and 6 female/group) were administered a single oral dose of Cartasol Yellow K-3GL 5000 mg/kg, carboxymethyl cellulose (negative control) in distilled water, or cyclophosphamide 50mg/kg as positive control (8).

Bone marrow samples from 5 mice of each group were assessed at 24, 48 and 72 hours after dosing. The dose of 5,000mg/kg Cartasol Yellow K-3GL had been previously determined to be the maximum tolerated dose causing no mortality in 6 animals. Treated mice showed no increase in micronucleated polychromatic erythrocytes in either males or females treated with 5,000mg/kg Cartasol Yellow. Males showed a decreased ratio of polychromatic erythrocyte/normochromatic erythrocyte. This was not observed in the females. Positive control groups showed a significant increase in the number of micronucleated polychromatic erythrocytes 24 hours and 48 hours after dosing and a reduced PCE/NCE ratio. The results of this study suggest that administration of Cartasol Yellow K-3GL is not associated with an increase in micronucleus formation in mice.

9.3 28 Day repeated dose study. OECD Guideline 407

Groups of 5 male and 5 female Wistar rats, (KFM Han), were gavaged with 0, 50, 200 and 1,000mg/kg/day of Cartasol Yellow K-3GL for 28 days. Cartasol Yellow K-3GL was dissolved in 4% carboxymethyl cellulose in distilled water.

Animals were observed twice daily. At the end of the 4 week period the following examinations were carried out

- haematology;
- clinical biochemistry;
- urinalysis; and
- ophthalmoscopic examination.
- histopathologic examination of the adrenal glands, heart, kidneys, liver and any gross lesions for the control group and the high dose group.

Females receiving 1000mg/kg/day showed a decreased weight gain over the period of the study. No change was noted in any of the parameters in haematology or urinalysis at the end of the study. Rats in the high dose group, both male and female, showed increased cholesterol values. At autopsy, the liver weight/body weight ratio was found to be increased in high dose males and in all female dose groups. The kidney weight/body weight ratio was similarly increased in high dose males and the medium and high dose females. The adrenal gland/body weight ratios were increased in the high dose group of both sexes.

The only clinical symptom observed during the study was slight diarrhoea in the high dose group.

9.4 OVERALL ASSESSMENT OF TOXICOLOGICAL DATA

Cartasol Yellow K-3GL showed low acute oral and dermal toxicity in test animals. In rats, the oral LD_{50} was found to be > 5,000mg/kg and dermal LD_{50} > 2,000mg/kg. Cartasol Yellow K-3GL was not irritant to the skin. Cartasol Yellow K-3GL was found to be a slight eye irritant. It is not expected to be a respiratory irritant of significant problems. Cartasol Yellow K-3GL was not mutagenic towards *Salmonella typhimurium* on repeat testing. The mouse micronucleus test was also negative.

In the 28 day repeated oral dose study in rats, Cartasol Yellow K-3GL exhibited low systemic toxicity. The only effects noted were a decreased weight gain over the period of the study in females in the high dose group, diarrhoea and a minor effect on liver and kidney relative weights.

10 Environmental Effects

Environmental effects testing is not required for small volume chemicals (< 1 tpa), but the company provided the following test results in its possession, as required under subsection 23(10) of the Act.

Test	Species	Result
96h acute	Carp (*Cyprinus carpio*)	LC_{50} = 10.7 mg.L^{-1}
96h acute	Rainbow trout (*Salmo gairdneri*)	LC_{50} = 3.8 mg.L^{-1}
24h immobilisation	*Daphnia magna*	EC_{50} = 299 mg.L^{-1}

The above results show the dye to be moderately toxic to fish and essentially nontoxic to daphnids. The fish result should be regarded with some caution as static conditions and nominal concentrations were used. While the dye proved stable in distilled water for 72 h, monitoring of the test medium for carp revealed that dissolved concentrations declined from 63-87% of theoretical before treatment to 20-37% after the test. Losses were explained in terms of reaction or adsorption of the dye to slime particles and faeces, and this explanation was supported by the observation of coloured sedimentation and turbidity. Most deaths occurred in the first 48 h of exposure when measured concentrations remained at or above 50% of applied, indicating that toxicity based on measured concentrations would not exceed that quoted above by more than a factor of two.

Quaternary ammonium compounds, if tested for fish toxicity in deionised water will, through ionic interactions, bind readily to gills. This can give rise to toxic effects due to reduction of oxygen transfer across damaged membranes or through effects on the ionic balance. However, toxicity is greatly reduced in the environment because of preferential binding to dissolved organics in surface water (10).

11. Environmental Hazard

The cationic nature of Cartasol Yellow K-3GL entails its ready removal from solution by binding to organic matter. At the proposed level of importation, this should ensure a low environmental exposure to the free dye.

The dye is not expected to impact on the environment when bound to paper or leather. In its free state, the dye proved moderately toxic to fish in laboratory tests, but toxicity should be reduced by at least an order of magnitude in natural surface waters because of microbial degradation and preferential binding to dissolved organics. Under worst case conditions, the predicted concentration in paper mill effluent is 10 ppb, more

than two orders of magnitude lower than concentrations which produced toxic effects on aquatic organisms in the laboratory. Environmental concentrations resulting from formulation wastes would be expected to be even lower because of dilution by other waste streams entering sewage treatment works and subsequent dilution by the receiving ocean. Accordingly, the environmental hazard appears minimal.

12. RECOMMENDATIONS FOR THE CONTROL OF PUBLIC AND WORKER EXPOSURE

To minimise public and worker exposure to Cartasol Yellow K-3GL the following guidelines and precautions should be observed:

. As good work practice, all precaution should be taken to minimise splashing and to minimise skin contact with Cartasol Yellow K-3GL while mixing and applying.

  Workers engaged in operations where splashing is possible should wear goggles which conform to *Australian Standard 1337 - 1984* (11) to prevent eye contact.

. Workers handling leather and other products on which the pigment has not dried should wear appropriate gloves which conform to *Australian Standard number 2161-1978* (12) and any other protective clothing required to prevent skin contact.

. Material safety data sheets should be available to all workers using Cartasol Yellow K-3GL and products containing Cartasol Yellow K-3GL.

13. material safety data sheet

The material safety data sheet for Cartasol Yellow K-3GL is in accordance with the Worksafe Australia format (13).

14. REQUIREMENTS FOR SECONDARY NOTIFICATION

Under the *Industrial Chemicals Notification and Assessment Act 1989* (the Act) secondary notification of Cartasol Yellow K-3GL shall be required if any of the circumstances stipulated under

section 64 (2) of the Act arise. If the volume imported or manufactured increases above one tonne per year, secondary notification with additional information on environmental fate is required. If there is an increase in public exposure, then secondary notification and further information may be required to assess public health hazard.

References

(1) Acute Oral Toxicity Study with Cartasol Gelb K-3 Lactat Konz in Rats. Data on file, Sandoz AG, Division Chemikalien, Basel, SWITZERLAND

(2) Acute Dermal Toxicity Study with Cartasol Gelb K-3 Lactat Konz in Rats. Data on file, Sandoz AG, Division Chemikalien, Basel, SWITZERLAND

(3) Primary Skin Irritation Study with Cartasol Gelb K-3 Lactat Konz in Rabbits (4 hour occlusive application). Data on file, Sandoz AG, Division Chemikalien, Basel, SWITZERLAND

(4) Primary Eye Irritation Study with Cartasol Gelb K-3 Lactat Konz in Rabbits Data on file, Sandoz AG, Division Chemikalien, Basel, SWITZERLAND

(5) Test for Delayed Contact Hypersensitivity in the Albino Guinea Pig with Cartasol Gelb K-3 Lactat Konz. Maximisation Test. Data on file, Sandoz AG, Division Chemikalien, Basel, SWITZERLAND

(6) Salmonella / mammalian microsome mutagenicity test with Cartasol Gelb K-3 Lactat Konz Data on file, Sandoz AG, Division Chemikalien, Basel, SWITZERLAND

(7) Salmonella typhimurium reverse mutation assay with Cartasol Gelb K-3 Lactat Konz. Data on file, Sandoz AG, Division Chemikalien, Basel, SWITZERLAND

(8) Mouse micronucleus Assay with Cartasol Gelb K-3 Lactat Konz. Data on file, Sandoz AG, Division Chemikalien, Basel, SWITZERLAND

(9) Subacute 28 day oral toxicity (gavage) study with Cartasol Gelb K-3 GL Lactat Konz. Data on file, Sandoz AG, Division Chemikalien, Basel, SWITZERLAND

(10) M S Goodrich, L H Dulak, M A Friedman and J J Lech, Environmental Toxicology and Chemistry, 1991, **10**, 509515.

(11) Australian Standard 1337-1984 *Eye Protectors for Industrial Applications*, Standards Association of Australia Publ, Sydney 1984.

(12) Australian Standard 2161-1978 *Industrial Safety Gloves and Mittens (excluding Electrical and Medical Gloves)*, Standards Association of Australia Publ, Sydney 1978.

(13) National Occupational Health and Safety Commission, *Guidance Note for Completion of a Material Safety Data Sheet* 2nd Edition, AGPS, Canberra, 1990