File No: **NA/3**

Date: 18 February 1991

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION
AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

CA-10

This Assessment has been compiled in accordance with the provisions of the Industrial Chemicals (Notification and Assessment) Act 1989 and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by Worksafe Australia which also conducts the occupational health & safety assessment. The assessment of environmental hazard is conducted by the Department of the Arts, Sport, the Environment, Territories and Tourism and the assessment of public health is conducted by the Department of Health, Housing and Community Services.

For the purposes of subsection 78(1) of the Act, copies of this full public report may be inspected by the public at the Library, Worksafe Australia, 92-94 Parramatta Road, Camperdown NSW 2050, between the hours of 10.00 a.m. and 12.00 noon and 2.00 p.m. and 4.00 p.m. each week day except on public holidays.

Please find enclosed order form for Full Public Reports.

For Enquiries please contact Ms Karen Bell at:

Street Address: 92 Parramatta Rd Camperdown, NSW 2050, AUSTRALIA
Postal Address: GPO Box 58, Sydney 2001, AUSTRALIA
Telephone: (61) (02) 565-9466 **FAX (61) (02) 565-9465**

Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

CA-10

1. IMPORTER

Kodak (Australasia) Pty. Ltd., 173 Elizabeth St, Coburg, Victoria, 3058.

2. IDENTITY OF THE CHEMICAL

Trade name: CA-10

Molecular weight: 590.86

3. PHYSICAL AND CHEMICAL PROPERTIES

At room temperature and atmospheric pressure, CA-10 is a non-volatile white crystalline solid with no discernible odour. Its physical and chemical properties include:

Melting point:	84-85°C
Density:	1144 kg/m^3 (at 20°C)
Vapour pressure:	1.17 x 10^{-3} Pa (at 55°C)
Autoignition temperature:	> 400°C
Thermal decomposition temperature:	>255°C
Thermal decomposition products:	carbon dioxide, and toxic fumes such as carbon monoxide and oxides of nitrogen and sulphur
Water solubility:	1.54 x 10^{-2} g/L ±1.7x 10^{-} g/L (at 25°C)
Hydrolytic stability:	No significant hydrolysis at 50°C and pH = 4 to 9
Partition coefficient log P (n-octanol/water):	0.79 ± 0.05

4. PURITY OF THE CHEMICAL

Degree of purity : 99.9% (by titration)

5. INDUSTRIAL USE

CA-10 is intended to be used exclusively as a charge control agent in commercial photocopier toner formulations (Kodak Coloredge Cyan Toner, Kodak Coloredge Magenta Toner, Kodak Coloredge Yellow Toner). The toner formulations will contain <2% by weight of CA-10. The formulations will be imported in sealed polyethylene cartridges each containing 350 gms of formulation.

Other ingredients of the formulations are polyester* (for Cyan, Magenta and Yellow Toner), CGH polymer* (for Cyan and Yellow Toner), cyan phthalocyanine pigment* (for Cyan Toner), magenta rhodamine pigment* (for Magenta Toner) and yellow azo pigment (for Yellow Toner).

The estimated quantity of CA-10 to be imported into Australia is less than 50 kgs per annum for the first five years.

* Note: full assessment reports and summary reports for these substances have been published by the Director of Chemicals Notification and Assessment under subsection 38(5) of the Industrial Chemicals (Notification and Assessment) Act 1989.

6. PUBLIC AND OCCUPATIONAL EXPOSURE

The formulations will be imported into Australia in sealed cartridges which are ready to be used in photocopiers. Only the seal of the cartridge needs to be broken immediately before use. No reformulation, packaging, bottling, filling or refilling of containers will be carried out in Australia. After use, the formulated product will be fused to paper in a water insoluble polymer matrix. Therefore it can be expected that there will be very low public and worker exposure to CA-10 and the formulated products under normal use conditions.

However, photocopier maintenance workers who frequently come into direct contact with the toner powder will experience higher exposure through skin contact and inhalation.

7. ENVIRONMENTAL EXPOSURE

7.1 Release

Minimal environmental release of CA-10 is expected to occur through its use in office copying machines and from the disposal of empty cartridges. However, releases to the environment may occur through processing waste paper onto which CA-10 is fixed through the photocopying process.

7.2 Fate

Paper to which the polymer matrix is fixed will ultimately be incinerated, disposed of in a landfill or recycled.

When incinerated, CA-10, will be degraded to oxides of carbon, nitrogen and sulphur.

The polymer matrix is not expected to degrade in landfill and therefore CA-10 encapsulated in the polymer matrix is likely to persist.

In recycling, wastepaper is usually repulped using a number of alkalis, dispersing agents, wetting agents, water emulsifiable organic solvents and bleaching agents. These chemicals enhance fibre separation, ink detachment from the fibres, pulp brightness and whiteness of the paper. After pulping, the contaminants and the ink are separated from the fibres by pumping the stock through various heat washing, screening, cleaning, flotation and dispersion stages (1). In view of its hydrolytic stability CA-10 is not likely to degrade in the recycling process, and its relatively low partition coefficient indicates that it is likely to be discharged in the aqueous waste stream.

8. EVALUATION OF TOXICOLOGICAL DATA

8.1 Acute Toxicity Studies

Table 1. Summary of acute toxicity of CA-10

Test	Species	Outcome
Oral (2) (M&F)	Rat	LD_{50}: 3536 mg/kg
Dermal (3) (M&F)	Rat	LD_{50}: >2000 mg/kg
Skin irritation (4)	Rabbit	moderate irritant
Eye irritation (5)	Rabbit	severe irritant
Skin sensitisation (6)	Guinea pig	non-sensitising

8.1.1 Oral Toxicity (2)

CA-10 was administered by gavage to CD(SR)BR rats at dose levels of 1250, 2500 and 5000 mg/kg. Five rats of each sex were used at each dose level. Clinical signs noted included diarrhoea, slight to moderate weakness, rough hair coat, faecal staining of inguinal hair and dehydration. In the intermediate dose group, one female death was noted. At the highest dose level, eight deaths, four of each sex were noted. Necropsy of those animals which died during the study revealed atrophy of the thymus, accessory male sex organs and adipose tissue; small spleens; porphyrin stains on the hair of the face; faecal staining of the inguinal hair and in two female rats, haemorrhage in the glandular gastric mucosa. An acute oral LD_{50} for male and female rats of 3536 mg/kg was observed.

It has also been reported (7) that Magenta Toner (the toner product which contains less than 2% by weight of CA-10) exhibited very low acute oral toxicity (LD_{50} in rats: >5000 mg/kg)

8.1.2 Dermal Toxicity (3)

A single dose of 2000 mg/kg of CA-10 moistened with distilled water was applied to the shaven backs of five male and five

female CD(SD)BR rats. Clinical observations were made over a period of 14 days. Erythema was initially observed in all 10 animals, but by Day 8 it had subsided. No other signs of treatment-related organ toxicity were noted. A dermal LD_{50} of >2000 mg/kg was observed.

It has also been reported (7) that Magenta Toner (the toner product which contains less than 2% by weight of CA-10) exhibited very low dermal toxicity (LD_{50} in guinea pigs: >2000 mg/kg).

8.1.3 **Skin Irritation** (4)

A single dose of 0.5 gm of CA-10 moistened with distilled water, was placed on a fibre pad which was applied to the clipped back of each of nine New Zealand White rabbits. Clinical observations were made at 1, 24, 48 and 72 hours and 5, 6, 7 and 14 days after treatment. Slight to well-defined erythema, slight to moderate oedema and eschar formation were noted. The intensity of these reactions decreased by the seventh day and by the end of the study very slight erythema was observed in all animals. The test results indicate that the chemical is moderately irritating to rabbit skin.

It has also been reported (7) that Magenta Toner (the toner product which contains less than 2% by weight of CA-10) appeared to be a slight skin irritant in guinea pigs.

8.1.4 **Eye Irritation** (5)

A single dose of 0.1 gm of CA-10 was instilled in one eye of each of six New Zealand White rabbits, with the other untreated eyes acting as controls. Following treatment, three of the treated eyes were immediately washed with running tap water. In all three unwashed eyes, corneal opacity, redness and swelling were observed one hour after treatment. Other ocular lesions noted included moderate discharge, slight erythema and moderate oedema of the lids. At 24 hours, the symptoms worsened with necrosis of the conjunctiva and nictitating membrane. Similar effects though less serious were also observed in the three washed eyes. No systemic effects were observed. The test was terminated after 24 hours as a result of distress to the animals. CA-10 is a severe

eye irritant and washing did not appear to reduce the irritation significantly.

It has been reported (7) that Magenta Toner (the toner product which contains less than 2% by weight of CA-10) appeared to be a slight eye irritant in rabbits.

8.1.5 Skin Sensitisation (6)

In the primary irritation study, 0.5 gm of CA-10 moistened with water was applied to the shaven backs of three (HA)BR Hartley female guinea pigs for a period of six hours. Observations at 24 and 48 hours revealed no signs of irritation. The maximum non-irritant dose observed (100% concentration) was 0.5 gm.

In the Induction and Challenge study, 0.5 gm of CA-10 moistened with water to give a 100% concentration solution (the maximal non-irritant concentration) was applied to the shaven backs of 10 (HA)BR Hartley guinea pigs. This was repeated once a week for three weeks. Two weeks after the last induction exposure, the maximal non-irritant concentration was again applied to the backs of the 10 treated animals. To differentiate dermal irritation from sensitisation, 10 untreated animals were subjected to the same challenge. The animals were then examined for signs of erythema and oedema at 24 and 48 hours after the challenge application. Evaluation of the observations was based on Buehler's method (8, 9). No signs of irritation were observed in any of the irritation control or induction and challenge groups of animals. These results indicate that CA-10 is essentially a non-sensitiser in guinea pigs. No positive controls were used in the study.

8.2 31-day Short Term Repeated Dose Study (10)

CA-10 was given by gavage in corn oil to groups of five male and five female CD(SD)BR rats at dose levels of 0, 100, 300 and 1000 mg/kg/day, five days a week over a 31-day period. However, due to high rates of mortality in these groups, additional dose groups of 10 and 30 mg/kg/day were added to the study.

At the 100 mg/kg dose level, deaths occured in one male (day 21) and two females (days 2 and 21). At 300 mg/kg, three females were euthanised *in extremis* on day 4, as was one male on day 14, and another female on day 15. All animals in the 1000 mg/kg group

either died or were euthanised in moribund condition after 3 or 4 days. Clinical signs observed in the 100, 300 and 1000 mg/kg groups included diarrhoea, dehydration, hypothermia, unkempt haircoats, abdominal distention, alopecia, porphyrin nasal discharge and depressed general activity.

A dose-related decrease in mean bodyweight associated with decreased food consumption was noted in animals receiving CA-10 at dose levels of 100, 300 and 1000 mg/kg.

In both male and female rats, dosed with 100 and 300 mg/kg CA-10, increases in serum alanine aminotransferase and aspartate aminotransferase levels were noted. At 300 mg/kg, significant increases in serum albumin levels, haemoglobin concentration and haematocrit were also noted. These effects were consistent with dehydration and stress on the test animals.

Kidney, liver and thymus weights were significantly reduced in the 300 mg/kg males, and the same applies to thymus weight in the 100 mg/kg females, when compared to the control groups. This was not evident in the 0, 10 or 30 mg/kg/day groups.

Gross pathology in animals which died during the study revealed distention of the gastrointestinal tract with gas and/or watery mucoid contents, congestion of the intestinal vasculature and haemorrhage of the gastric mucosa. In surviving animals in the 300 mg/kg group, distention of portions of the intestinal tract with watery contents and gas was observed. No treatment-related changes were observed in surviving animals from the 100 mg/kg dose group or in any animals in the 30 or 10 mg/kg groups.

Histopathology of animals which died prior to study termination revealed necrosis, haemorrhage, vascular congestion and atrophy of the gastrointestinal mucosae; liver inflammation and atrophy of organs including the spleen, thymus, adipose tissues, lymph nodes, bone marrow and testes. Gastrointestinal distention was observed in surviving animals in the 300 mg/kg dose group. Surviving animals in the 100 mg/kg dose group experienced no treatment related changes. No treatment related changes were seen in the 10 mg/kg and 30 mg/kg dose groups.

The data indicate that CA-10 is severely irritating to the gastrointestinal tract and may cause organ toxicity. The no-observable effect level was 10 mg/kg for both male and female animals.

8.3 Genotoxicity

Table 2. Summary of genotoxicity studies with CA-10

Test Type	Dose Range	Outcome
Salmonella/microsome reverse mutation assay (11)	1-500 ug/plate	Negative
In vivo mouse micronucleus assay (12)	150-1500 mg/kg	Negative

8.3.1 Ames Salmonella/Microsome Reverse Mutation Assay (11)

CA-10 was tested for genotoxicity using *Salmonella typhimurium* strains TA-1535, TA-1537, TA-1538, TA-98 and TA-100, in both the presence and absence of a mammalian metabolic activation mixture (S9 mix). Under the test conditions, CA-10 was not genotoxic towards *Salmonella typhimurium*.

8.3.2 In Vivo Mouse Micronucleus Assay (12)

CA-10 was suspended in corn oil and administered by gavage to male and female ICR mice at dose levels of 150, 500 and 1500 mg/kg. Cyclophosphamide treated mice served as positive controls. Administration of CA-10 was not associated with a significant increase in micronuclei in bone marrow polychromatic erythrocytes.

8.4 Overall Assessment of Toxicological Data

CA-10 has low acute oral and dermal toxicities (oral LD_{50} in rats: 3536 mg/kg; dermal LD_{50} in rats: >2000 mg/kg). Animal tests show that CA-10 is severely irritating to the eyes, and moderately irritating to the skin. It is anticipated that CA-10 if inhaled will also severely irritate the upper respiratory tract. CA-10 is not sensitising to the skin. In a short term repeated dose study, high concentrations of CA-10 were severely irritating to the gastrointestinal tract.

CA-10 was not genotoxic in either the *Salmonella typhimurium* reverse mutation test or the mouse micronucleus assays.

It has also been reported (7) that Magenta Toner which contains less than 2% of CA-10, exhibited very low acute oral and dermal toxicities in test animals (oral LD_{50} in rats: >5000 mg/kg; dermal LD_{50} in guinea pigs: >2000 mg/kg). It also appeared to be a slight skin and eye irritant. It is anticipated that the toner dust if inhaled will also slightly irritate the upper respiratory tract.

9. ENVIRONMENTAL ASSESSMENT

9.1 Assessment of Environmental Effects

CA-10 has high aquatic toxicity [LC_{50} *(Fathead minnow)*: 0.36 ppm ; *(Daphnia magna)*: 0.25 ppm] but is practically non-toxic to the rat (LD_{50} in rats: 3536 mg/kg).

9.2 Assessment of Environmental Hazard

The main environmental hazard from use of CA-10 would appear to be from the treatment and disposal of waste paper, particularly recycling. The chemical proved resistant to hydrolysis in Company tests and therefore might be expected to survive the recycling process and be discharged in the aqueous waste stream from recycling plants. However, only small volumes are to be used annually, so it is unlikely that toxic concentrations would result, even before dilution of any discharges by the receiving water.

10. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

CA-10 is a severe eye irritant and a moderate skin irritant. If inhaled, it is likely that CA-10 will also cause irritation to the upper respiratory tract. However, due to the small proportion (<2%) of CA-10 in the toner formulations and the very low public and worker exposure under normal use conditions, the formulated products should not pose any significant acute health and safety hazard to the public and workers. Under these circumstances, the

recommendations specified in Section 12 should be sufficient to minimise exposure.

However, should the proportion of CA-10 in the formulated products be changed to exceed 2% by weight or a change in use practices cause higher public and worker exposure to CA-10, stricter control measures should be implemented.

11. RECOMMENDATIONS FOR THE CONTROL OF PUBLIC AND WORKER EXPOSURE

To minimise public and worker exposure to the formulated products which contain less than 2% of CA-10, in general, the following guidelines and precautions should be observed:

.as good work practice, photocopiers should be located in well ventilated areas to control the accumulation of dusts, gases or fumes;

.a copy of the Material Safety Data Sheet for each of the formulated products should be available to all personnel who may be exposed to the toners; and

.photocopier maintenance workers who frequently come into direct contact with the toner formulations should:

-wear appropriate gloves (for example cotton or impervious gloves);

-avoid the generation of a dust cloud; and

-observe good personal hygiene practices at work.

Note: Guidance on general working practices associated with the operation of office copying machines is detailed in Worksafe Australia *Guide on Office Copying Machines (13).*

However, should the proportion of CA-10 in the formulated products be changed to exceed 2% by weight or a change in use practices cause higher public and worker exposure to CA-10, stricter control measures should be implemented (for example local exhaust ventilation and appropriate personal protection).

12. REQUIREMENTS FOR SECONDARY NOTIFICATION

Under the Industrial Chemicals (Notification and Assessment) Act 1989 (the Act), secondary notification of CA-10 shall be required by Kodak (Australasia) Pty Ltd if any of the circumstances stipulated under subsection 64(2) of the Act arise. No other specific conditions are prescribed.

13. REFERENCES

1. Forestry Canada, Industry/ Trade and Technology Directorate, and Environment Canada, Final Report, *Waste Paper Recycling Study (to end of 1989)*, p56-57.

2. Acute Oral Toxicity of CA-10. Data on file, Eastman Kodak, USA. Report TX-88-163, 1988.

3. Acute Dermal Toxicity of CA-10. Data on file, Eastman Kodak, USA. Report TX-88-164, 1988.

4. Acute Skin Irritation of CA-10. Data on file, Eastman Kodak, USA. Report TX-88-165, 1988.

5. Acute Eye Irritation of CA-10. Data on file, Eastman Kodak, USA. Report TX-88-167, 1988.

6. Skin Sensitisation Study (Buehler Method) of CA-10. Data on file, Eastman Kodak, USA. Report TX-88-166, 1988.

7. National Industrial Chemicals Notification and Assessment Scheme Assessment Report No.: NA/7, 1991.

8. Buehler E.V.. *Delayed contact hypersensitivity in the guinea pig*. Arch. Dermatol., 91: 171-175, 1965.

9. Ritz H.L. and Buehler E.V.. *Planning, conduct and interpretation of guinea pig sensitisation patch tests*. In: Current Concepts in Cutaneous Toxicity, (V.A. Drill and D. Lazar, eds.), pp 25-40. Academic Press, New York, 1980.

10 Four-weeks oral toxicity study of CA-10 in the rat. Data on file, Eastman Kodak, USA. Report TX-88-187, 1989.

11. Mutagenicity Test on CA-10 in Ames Salmonella/Microsome Reverse Mutation Assay. Data on file, Eastman Kodak, USA. Study No.: 10412-0-401, 1989.

12. Mutagenicity Test on CA-10 in *In-vivo* Mouse Micronucleus Assay. Data on file, Eastman Kodak, USA. Study No.: 10412-0-455, 1989.

13. National Occupational Health and Safety Commission, *Office Copying Machines*, AGPS, Canberra, December, 1989.