File No: NA/22
11 February 1992

**NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME**

**FULL PUBLIC REPORT**

# MONOAZO RED TZ 2723

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Director
Chemicals Notification and Assessment

**FULL PUBLIC REPORT**

**MONOAZO RED TZ 2723**

## 1. IMPORTER

CIBA-GEIGY Australia Ltd., 140 Bungaree Road, Pendle Hill, NSW 2145.

## 2. IDENTITY OF CHEMICAL

**Trade name:** CIBACRON RED C-R

**Other name/s:** MONOAZO RED TZ 2723
F.A.T. 40'348/B
C335550

Monoazo Red TZ 2723 is classified as a non-hazardous chemical to humans because the toxicology data submitted suggest that it is unlikely to produce any toxic effects. For this reason, the chemical name, Chemical Abstract Registry Service Number (CAS No:) and the molecular and structural formulae have been exempted from publication.

## 3. PHYSICAL AND CHEMICAL PROPERTIES

At room temperature and atmospheric pressure, Monoazo Red TZ 2723 is a dark reddish/ brown powder of no discernible odour and negligible volatility. Its physical and chemical properties include:

**Melting point:** >300$^{O}$C

**Density:** 1.64 x $10^3$ kg/$m^3$ (at 23$^{O}$C)

**Vapour pressure:** negligible

**Water solubility:** >200 g/L (at 20$^{O}$C)

| | |
|---|---|
| **Hydrolysis:** | $t_{1/2}$ = 75 hrs (at pH 4; 25$^{O}$C)<br>$t_{1/2}$ = 2806 hrs (at pH 7; 25$^{O}$C)<br>$t_{1/2}$ = 332 hrs (at pH 9; 25$^{O}$C) |
| **Partition co-efficient:** | log $P_{O/W}$ = -13 |
| **Fat solubility:** | <0.05 mg/100g fat (at 37$^{O}$C) |
| **Surface tension:** | 10 $gL^{-1}$ solution = 72.5-72.7 $mN.m^{-1}$<br>(Water = 72 $mN.m^{-1}$) |
| **Particle size:**<br>(median mass distribution) | 21.3 µm |
| **Flammability:** | flammable |
| **Auto-iginition temperature:** | 320$^{O}$C |
| **Explosion potential:** | non-explosive |
| **Reactivity:** | stable at room temperature to 150$^{O}$ C; incompatible with reducing agents and alkalis; non-oxidising |

Comments on Physico-Chemical Properties

No data were provided for vapour pressure on the grounds that vapour pressure of a substance having a molecular weight of >1000 would be negligible and would have no relevance to toxicity or environmental fate. This is acceptable as it is also noted the notified chemical is a salt.

No data were provided for adsorption/desorption on the grounds that the probability and the level of entry of the notified chemical into the soil would be very low and also that such tests were not required by either the USA Environmental Protection Agency (EPA) or the European Economic Committee (EEC) in the respective notifications to these schemes. The high water solubility and low partition coefficient of the notified chemical suggest that adsorption will be low, but its chemical reactivity may result in binding to solid material.

No data were provided for dissociation constant on the grounds that (i) the notified chemical has multi-functional chemistry and is subject to complex dissociation modes in both its unreacted and hydrolysed form; (ii) the degree of dissociation is indicated by the very high water solubility; and (iii) such a test was not required by the US EPA and the EEC in the respective notifications to these schemes.

The above reasons for omission of data are acceptable.

## 4. METHODS OF DETECTION AND DETERMINATION

Infra-red spectroscopy; Nuclear Magnetic Resonance spectroscopy and Ultra-violet spectroscopy.

## 5. PURITY OF THE CHEMICAL

**Degree of purity:** 30-60% w/w

**Impurities:** by-products: 10-30%w/w

**Additives/ adjuvants:**

| | |
|---|---|
| sodium sulphate (CAS No: 7757-82-6) | 10-30% w/w |
| sodium tripolyphosphate (CAS No: 7758-29-4) | <10% w/w |
| sodium fluoride (CAS No: 7681-49-4) | <10% w/w |
| sodium chloride (CAS No: 7647-14-5) | <10% w/w |
| water (CAS No: 7732-18-5) | <10% w/w |

Monoazo Red TZ 2723 will make up >60% w/w of the formulated commercial product, CIBACRON RED C-R.

Sodium fluoride is present in Monoazo Red TZ 2723 at a concentration of 1.4% w/w and in the formulated commercial

product, CIBACRON RED C-R, at a concentration of 0.86% w/w. This value is comparable to the typical fluoride content of household toothpaste.

The notifier has stated that the treatment of the formulated commercial product in the sewer system will dilute the NaF content to ppb levels. This would have no significant effect on aquatic invertebrates and algae (*Daphnia magna* $LC_{50}$ = 340 $mgL^{-1}$ and *Scenedesmus* $LC_{50}$ = 43 $mgL^{-1}$) (1).

## 6. INDUSTRIAL USE

Monoazo Red TZ 2723, present as >60% w/w of the formulated commercial product, CIBACRON RED C-R, will be imported for use solely as a reactive dye for the colouration of cellulosic textiles by the cold pad-batch or pad-steam method.

## 7. OCCUPATIONAL EXPOSURE

Monoazo Red TZ 2723 will be imported and distributed to users in sealed robust 30 kg drums, therefore, significant risk of exposure from accidental spillage during transit is unlikely.

Occassionally, repacking of the dyestuff may take place at CIBA-GEIGY, Thomastown, Victoria. The notifier estimates that a total quantity of 60 kg per year would be repacked. It is stated that 2 workers could be exposed to the powder dye during repacking. In spite of the use of anti-dusting agents, if engineering controls and personal protection measures are not implemented exposure of these workers to the powder dye could be high.

Monoazo Red TZ 2723 will be used in the textile industry in New South Wales, Victoria, South Australia and Tasmania. The notifier states that three workers at each site could be exposed to the dye during the weighing and dissolving process. If engineering controls and personal protection measures are not implemented the exposure of these workers to the powder dye could be high. Once a solution of the dye has been formed, the potential for exposure will be significantly reduced. After dyeing has occurred, the dye is permanently fixed to the cellulosic textiles, thus presenting little occupational risk.

Thus under correct handling and dyeing procedures, the potential for occupational exposure to this dye should be minimal.

## 8. PUBLIC EXPOSURE

Monoazo Red TZ 2723 has good fastness properties (88% fixation), is not likely to bioaccumulate and will be imported in secure robust containers, therefore, it is anticipated that public exposure to this dye will be minimal under correct handling and dyeing procedures. The notifier states that with a higher degree of fixation (88%) than existing dyes, up to 30% less of unfixed dye will pass into the effluent in the washing-off operation. It is estimated by the notifier that about 14 kg/annum of the dyestuff will be lost to each user's treatment plant (or municipal water system) from the dyeing operations. The maximum average daily discharge into municipal sewage works is estimated by the notifier to be between 0.18 to 11.25 ppb. No bioaccumulation is expected in the foodchain because the product has very low fat solubility, and the hydrolysed form is not expected to be a significant public hazard.

## 9. ENVIRONMENTAL EXPOSURE

### . Release

The notifier indicates that as the notified chemical will replace existing dyestuffs and the use pattern of dyed textiles is expected to remain unchanged, there will be no increase in the release of dyestuff to the environment. The notifier projects that an even use of 234 kg of the notified chemical per customer and a dye fixation rate of 88% (measured by colorimetric analysis of the liquors from the dyeing process), will result in about 14 kg per year of the notified chemical being lost to each user's treatment plant or municipal water system.

The notified chemical will be highly diluted in wastes from dye factories which are treated by sewage plants that dispose their effluents into the ocean. However, the dilution will be significantly lower and can be very low in dry or drought conditions in the case of dye factories which have their wastes treated by sewage treatment plants that dispose their effluents into inland waters.

Appendix 1 provides two detailed cases for receiving water concentrations. The calculations are based on:

. discharges from dyeworks solely involved with pad-batch operation (the dyeing technique most suited for use with Monoazo Red TZ 2723);

. receiving river volumes (which is a major factor in determining dye concentrations in the environment);

. expected annual total sales of 2500 kg of Monoazo Red TZ 2723;

. an even use at seven dyeworks;

. a 88% fixation level; and

. 50% removal at the municipal sewage plant.

The sewage plant removal is a coarse estimate as the notified chemical is likely to either not absorbed or shows very variable adsorptive properties to sludge as indicated in dye absorption sludge tests using dyes similar to the notified chemical (2). However, even if there is no dye removal in sewage treatment, the resulting dye concentration to receiving waters is less than the "worst case" concentration as stated below.

The notifier states that discharges from all sites likely to use the notified chemical will be to the municipal sewage works where it is estimated that municipal stream volumes vary from several to 500 ML per day. The notifier predicts the concentration in receiving waters to be 11.25 ppb under low flow conditions and 0.18 ppb under high flow conditions (Appendix 1).

In the "worst case" scenario, assuming no loss in the treatment works, 30% of expected sales and 750 kg per year are used at one inland site, the expected concentration at the treatment works (based on the low volume of 4 megaL per day) is assessed to be 76.5 ppb. Further dilution will result in receiving water concentrations of 26.5 ppb (1:3 dilution) and 7.8 ppb (1:10 dilution).

. **Fate**

The notified chemical will be released in the effluents from the sewage treatment works which treat the wastes produced by the dyeworks.

In general, dyestuffs are practically not biologically degraded during the short residence time characteristic of most sewage treatment plants (3). A study which mimicks the mixing of dye wastes with the biomass in an activated sludge plant shows that dyes similar to the notified chemical either do not adsorb or show variable adsorptive properties to sludge (2).

It should be noted that in Appendix 1, the notifier assumes that 50% of the notified chemical will be removed during the sewage treatment process, suggesting that it expects the notified chemical to undergo abiotic hydrolysis due to alkalinity typical of effluent from sewage works (4). This level of removal is unlikely due to the short residence time of most sewage treatment plants (3) and the hydrolytic half-life ($t_{1/2}$ = 2 weeks) of the notified chemical in alkaline conditions. Despite its water solubility, the dye may bind to sediment due to its reactivity.

The notified chemical can enter the soil compartment when effluents containing the notified chemical is used for irrigation of agricultural or municipal land (eg. golf courses, racecourses). The likely concentration of the notified chemical in effluent irrigation waters is likely to be in the order of ppb based on the notifier's predicted concentration of 11.25 ppb in sewage treatment works (Appendix 1).

. **Bioaccumulation**

The high water solubility, very low partition coefficient (octanol/water) and low fat solubility of the notified chemical indicate that it is unlikely to bioaccumulate. Therefore, the omission of bioaccumulation studies by the notifier, based on the chemical's extremely low partition coefficient, is acceptable.

. **Biodegradation**

Table 1 Summary of biodegradation of Monoazo Red TZ 2723

| Test | Result | Reference |
|---|---|---|
| Dissolved organic carbon ($mgL^{-1}$) | 0% (28 d) | 5 |
| Biological oxygen demand | 0 mg/g $O_2$ | 6 |
| Respirated inhibition | IC50 (3h)>100 | $7^{-1}$ |

As indicated in the table above, the dissolved organic carbon study (5) and the biological oxygen demand study (6) show that Monoazo Red TZ 2723 is not readily biodegradable. The activated sludge respiration inhibition test (7) shows that Monoazo Red TZ 2723 does not inhibit respiration of micro-organisms.

Many dyes, especially the azo dyes are degraded under anaerobic conditions and form sulphonated or other hydrophilic aromatic amines or lipophilic aromatic amines (8). In general, aromatic amines are degraded under aerobic conditions but not under anaerobic conditions. Desorption of aromatic amines back into the aerobic environment does not occur resulting in further biodegradation and complete mineralisation (8).

Due to the reactivity of the azo dye, the unfixed dye when discharged with sewage effluent may bind to waterway sediment and in the long term, undergoes gradual long-term anaerobic biodegradation. Biodegradation under anaerobic conditions is expected to be an important environmental fate mechanism for azo dyes (9).

## 10. ASSESSMENT OF TOXICOLOGY DATA

### 10.1 Acute Toxicity

Table 2 Summary of acute toxicity of Monoazo Red TZ 2723

| Test | Species | Outcome | Reference |
|---|---|---|---|
| Oral | Rat | $LD_{50}$: 4936 mg/kg | 10 |
| Dermal | Rat | $LD_{50}$: >2000 mg/kg | 11 |
| Skin | Rabbit | non-irritant | 12 |
| Eye | Rabbit | slight irritant | 13 |
| Skin | Guinea pig | non-sensitising | 14 |

#### 10.1.1 Oral toxicity (10)

This study was carried out in accordance with the *OECD Guidelines for Testing of Chemicals* No: 401 (15).

Monoazo Red TZ 2723 in water was administered by single gavage to three groups of *KFM-Han. Wistar (outbred, SPF-Quality)* rats (five males and five females per group) at dose levels of 2000 mg/kg; 3500 mg/kg and 5000 mg/kg. These animals were observed for 15 days. Reddish discoloured extremities were observed at all dose levels. In the 3500 mg/kg dose group, slight sedation, dyspnoea, hunched posture, diarrhoea and ruffled fur were also observed. All the animals in the lower dose groups (2000 and 3500 mg/kg) recovered during the study and necropsy revealed no pathological changes. In the 5000 mg/kg dose group, symptoms observed were slight to moderate sedation, dyspnoea, hunched posture, emaciation, diarrhoea and ruffled fur. A death rate of 60% was recorded in this high dose group. At this dose level, except for the reddish discoloured extremities, the surviving animals were observed to have recovered from the other symptoms by the end of the study. Necropsy of this dose group revealed general reddish discoloration in all animals; and in one animal which died during

the study, its lungs and stomach had also been discoloured red. Gain in bodyweight was unaffected at all dose levels.

Results of this study indicate an acute oral $LD_{50}$ of 4936 mg/kg in rats of both sexes for Monoazo Red TZ 2723.

### 10.1.2 Dermal toxicity (11)

This study was carried out in accordance with the *OECD Guidelines for Testing of Chemicals* No: 402 (16).

A single dose of 2000 mg/kg of Monoazo Red TZ 2723 moistened with water was applied by occlusive application to the shaved backs of ten (five males and five females) *KFM-Han. Wistar (outbred, SPF-Quality)* rats. Twenty-four hours post-exposure, the dressings were removed and the skin reaction assessed (17). The animals were observed for 15 days. Slight necroses were observed in both male and female rats from Day 2 to Day 12. Red discolouration of the application area by the dye, was also observed in these animals from Day 2 and this was seen to have persisted till the termination of the study. No erythema was observed but it should be noted that the red discolouration of the application site could hinder the observation of erythema but the effect would have to be slight for it to be masked. No deaths occurred, gain in bodyweight was unaffected and no adverse clinical signs were observed. Necropsy revealed no macroscopic organ changes.

Results from this study indicate an acute dermal $LD_{50}$ of >2000 mg/kg in rats of both sexes for Monoazo Red TZ 2723 .

### 10.1.3 Skin irritation (12)

This study was carried out in accordance with the *OECD Guidelines for Testing of Chemicals* No: 404 (18).

A single dose of 0.5g of Monoazo Red TZ 2723 moistened with water was applied by occlusive application to the shaven backs of 3 (2 males and 1 female) *New Zealand White, KFM (SPF-Quality)* rabbits. Four hours post-exposure, the dressings were removed and the skin reactions assessed according to the scoring system described in (18). Thereafter, skin reactions were assessed at 1, 24, 48 and 72 hours intervals after the removal of the dressing. Apart from the red discolouration of the application area by the dye, no skin reactions were observed. It should be noted however that

the reddish skin discolouration by the dye could hinder the observation of erythema but the effect would have to be slight for it to be masked. Gain in bodyweight was unaffected, no deaths occurred and no adverse clinical signs were observed. Necropsy was not performed on any of these animals.

The results of this study suggest that Monoazo Red TZ 2723 is not a skin irritant in rabbits at the concentration tested.

### 10.1.4 Eye irritation (13)

This study was carried out in accordance with the *OECD Guidelines for Testing of Chemicals* No: 405 (19).

A single dose of 0.1 g of Monoazo Red TZ 2723 was instilled in the conjunctival sac of the left eye of each of three *New Zealand White, KFM (SPF-Quality)* rabbits. The right eye remained untreated and served as the control. The eyes were examined 1, 24, 48 and 72 hours post-exposure. Irritation was scored according to the scoring system described in (19). A slight discharge and chemosis were observed in all three animals in the first hour after exposure. Red staining of the conjunctivae and sclera by the dye was observed in two animals from one hour to 72 hours and in one animal from 24 to 72 hours. Also observed was the red staining of the nictitating membranes and eyelashes of the treated eyes from one hour to 72 hours, in all three animals. Although no redness due to conjunctival irritation was noted, this effect could have been masked by the reddish discolouration caused by the dye. However, the irritation would have to be slight for it to be masked. No corrosion was observed. No deaths occurred during the study and no systemic toxicity was evident. Necropsy was not performed on these animals.

The results of this study suggest that Monoazo Red TZ 2723 is a slight eye irritant in rabbits.

### 10.1.5 Skin sensitisation (14)

This study was carried out in accordance with the *OECD Guidelines for Testing of Chemicals* No: 406 (20).

The Guinea Pig Maximisation Test (21) was used. Skin reactions were assessed according to the scoring system described in (18).

The positive control used was DNCB (1-chloro-2,4-dinitro-benzol). Water was used as the negative control.

In the preliminary study, aqueous solutions of Monoazo Red TZ 2723 at concentrations of 0.1, 0.3, 0.5, 1, 3, and 5%, were administered by intradermal injection to the clipped flanks of each of two *Dunkin-Hartley* albino guinea pigs. Twenty-four hours post-exposure, the skin reactions were assessed. Very slight to moderate oedema was observed with the 3 and 5% solutions, in both animals. No erythema was observed but this might have been masked by the reddish dicolouration of the skin by the dye at the application sites. The same two animals were later subjected to occlusive epidermal administration of Monoazo Red TZ 2723 at concentrations of 3, 5, 10 and 25%. No skin reactions were observed 24, 48 and 72 hours post exposure, however, the observation of slight erythema could have been hindered by the reddish discolouration of the skin at the application sites.

In the induction and challenge study, 30 *Dunkin-Hartley* albino guinea pigs (15 males and 15 females) were used of which 10 (5 males and 5 females) served as controls.

Induction

In the control group, water, instead of the test substance was administered intradermally and epidermally to the control animals . The 20 test animals were each induced by an intradermal injection of a 3% aqueous solution of Monoazo Red TZ 2723. One week later, these test animals were subjected to occlusive epidermal application of a 25% aqueous solution of the test substance for 48 hours. Twenty-four hours prior to the epidermal application, animals in both the test and control groups were treated epidermally with a 10% solution of sodium lauryl sulphate to enhance sensitisation by provoking a mild inflammatory reaction. The application sites were assessed for erythema and oedema immediately after the removal of the dressings and then at 24 and 48 hours thereafter. One animal from the test group died on Day 8 of the study; but the notifier indicates that this death was unrelated to treatment. Reddish skin discolouration of the application areas by the dye and slight erythema were observed in both the control (8/10) and test (16/20) groups. As sodium lauryl sulphate is capable of producing an inflammatory reaction, it is possible that the slight erythema observed in both the control and test animals could have been caused by exposure to sodium lauryl sulphate.

Challenge

Two weeks following the epidermal induction application, the animals in both the treated and control groups were challenged with a 25% aqueous solution of Monoazo Red TZ 2723 on the left flank. Water as the control was applied to the right flank of these animals. The animals were exposed for 24 hours. The application sites were assessed for erythema and oedema 24, 48 and 72 hours following challenge. Slight erythema was observed in one animal (1/20) from the test group following challenge with Monoazo Red TZ 2723. No other positive reactions were noted. However, reddish discolouration of the application areas was noted which could have hindered the observation of erythema. Bodyweight was unaffected and no adverse clinical signs were observed.

Results from this study suggest that Monoazo Red TZ 2723 is not a skin sensitiser in guinea pigs under the experimental conditions reported.

## 10.2 Five-day oral toxicity (22)

Monoazo Red TZ 2723 in water was administered to three groups of six *Wistar KFM-Han. outbred, SPF-Quality* rats (3 males and 3 females) by gavage for a five-day period at dose levels of 0, 200 and 1000 mg/kg/day. No deaths occurred during the study. Gain in bodyweight was unaffected by treatment. Synechia was noted in two male rats, one of the 200 mg/kg dose group and the other, a control. Therefore, it is unlikely for these ophthalmic reactions to be treatment-related. Necropsy revealed dark red foci in the stomach of two male rats and one female rat of the 1000 mg/kg dose group; and dilation of the horns of the uterus in two female rats, one of the 200 mg/kg dose group and the other of the 1000 mg/kg dose group.

From the results of this study, the dose levels for the 28-day short-term repeated dose oral study were set at 0, 50, 200 and 1000 mg/kg bodyweight of Monoazo Red TZ 2723.

## 10.3 Twenty-eight day short term repeated dose oral toxicity (23)

This study was carried out in accordance with the *OECD Guidelines for Testing of Chemicals* No: 407 (24).

Monoazo Red TZ 2723 in water was administered by gavage once daily to groups of male and female *Wistar, KFM-Han., outbred, SPF-Quality*, rats at dose levels of 0 mg/kg (control, 20 rats), 50 mg/kg (10 rats), 200 mg/kg (10 rats) and 1000 mg/kg (20 rats). The duration of treatment was 28 days. Ten rats each from the control and the high dose group were subjected to a 14-day treatment-free recovery period.

One female rat of the high dose group died after four weeks of treatment; necropsy revealed diaphragmatic hernia and this death was considered to be non-treatment related.

At necropsy, treatment-related red discolouration was noted in rats (19/20) of the high dose group, including the recovery group. The organs affected were the stomach, intestine, kidneys, urinary bladder, testes, skin, mysenteric lymph nodes, uterus and the vagina. Treatment-related microscopic findings were observed in the kidneys of rats in the middle and high dose groups and in the stomach of rats in all treated groups. The renal findings were characterised by minimal to moderate red pigment deposits in the proximal tubular epithelium in males and females, slight to moderate vacuolation of tubular epithelium in females, and slight to marked increase in tubular hyaline droplets in males; a dose-response relationship was observed for these effects. Except for the tubular hyaline droplets, the other two effects were not observed in any control animals. The gastric findings were characterised by eosinophilic cytoplasmic inclusions in the glandular mucosa of the fundic area, and vacuolation of the squamous mucosa of the forestomach; a dose-response relationship was seen with effects occuring at the lowest dose level of 50 mg/kg/day. The gastric findings were not observed in any of the non-recovery group of control animals. The significance of these findings are unclear.

In the recovery group, cytoplasmic inclusions were observed in two control animals and in all 10 high dose animals, whilst epithelial vacuolation was observed in one control and one high dose animal. Low and mid dose groups were not held for a recovery period which did not allow comparison of incidences in these groups at this time point. Also observed in the recovery group were renal findings relating to five cases of hyaline droplets in the high dose group, three in the control; five cases of tubular vacuolation, and 10 cases of tubular pigmentation both found in the high dose group. Reversal of the changes did not take place during the 14-day treatment-free recovery period.

In the high dose group (both sexes), a three to four fold increase in bilirubin was observed but, this returned to normal during the recovery phase. Urinalysis detected the presence of bilirubin in both male and female rats of the middle and high dose groups and also in low dose females; as well as proteinuria in the high dose males. In the high dose group, these changes persisted to the end of the recovery period. The increase in bilirubin was claimed by the notifier to be a false positive result relating to interference of the test compound or metabolites with the test procedure. No sign of liver damage was evident.

At all dose levels, food consumption and gain in bodyweight were unaffected by treatment; no ophthalmic findings were observed and hematological, biochemical and urinalysis data indicated no changes of toxicological significance at the termination of treatment nor at the end of the treatment-free recovery period. However, statistically significant increased kidney to bodyweight ratios were observed in male and female rats of the high dose group at terminal sacrifice which persisted in females to the end of the recovery period.

The notifier states that a further 28-day repeated dose oral toxicity study has been conducted to help clarify the observations made in this study and these results would be available for assessment shortly.

## 10.4 Genotoxicity

Table 3. Summary of genotoxicity of Monoazo Red TZ 2723

| Test | Dose range | Outcome | Reference |
|---|---|---|---|
| *Salmonella typhimurium* Reverse Mutation Assay | 10 - 5000 µg/plate | negative | 25 |
| Chromosome Aberration Assay in Chinese Hamster V79 cells | 0.01 - 7 mg/ml | positive | 26 |
| in-vivo mouse micronucleus assay | 4000 mg/kg | negative | 27 |

### 10.4.1 Salmonella typhimurium reverse mutation assay (25)

This study was carried out in accordance with the *OECD Guidelines for Testing of Chemicals* No: 471 (28).

Monoazo Red TZ 2723 at concentrations of 10, 100, 333.3, 1000 and 5000 µg/plate was tested in two independent experiments for gene mutation according to the direct plate incorporation method using *Salmonella typhimurium* strains TA 1535, TA 1537, TA 1538, TA 98 and TA 100, both in the presence and absence of microsomal activation. Untreated strains and strains treated with the solvent (water) were used as negative controls. Positive controls used were sodium azide, 4-nitro-o-phenylene-diamine and 2-aminoanthracene. No dose-related increase in the number of revertant colonies was observed in any of the strains exposed to Monoazo Red TZ 2723, both in the presence and absence of microsomal activation. In contrast, the positive controls showed marked increases in the number of revertant colonies.

The results of this study indicate that Monoazo Red TZ 2723 was not mutagenic under the experimental conditions reported.

### 10.4.2 Chromosome aberration assay in chinese hamster V79 cells in-vitro (26)

This study was carried out in accordance with the *OECD Guidelines for Testing of Chemicals* No: 473 (29).

Monoazo Red TZ 2723 was tested for its potential to induce structural chromosome aberrations in *Chinese hamster V79* cells *in-vitro* at dose levels of 0.01, 3, 4, 5 and 7 mg/ml in the presence and absence of metabolic activation. Positive controls used were ethylmethanesulphonate and cyclophosphamide. The solvent served as the negative control. Monoazo Red TZ 2723 was found to induce structural chromosome aberrations at concentrations of 3, 4 and 5 mg/ml but not at 0.01 mg/ml in the absence of metabolic activation, and at 5 and 7 mg/ml but not 0.01 mg/ml in the presence of metabolic activation. Statistically significant increases in the number of cells with chromosome aberrations were observed at 7 hrs (4 mg/ml without activation), 18 hrs (7 mg/ml with activation and 3 and 5 mg/ml without activation) and 28 hrs (5 mg/ml without activation) after exposure. The positive controls used showed marked increases in the number of cells with chromosome aberration. A reduction of the mitotic index, was observed at 3, 4 and 5 mg/ml with or without activation.

The results of this study indicate that Monoazo Red TZ 2723 was mutagenic under the experimental conditions reported.

### 10.4.3 Micronucleus assay in bone marrow cells of the mouse (27)

This study was carried out in accordance with the *OECD Guidelines for Testing of Chemicals* No: 474 (30).

Monoazo Red TZ 2723 in aqua dest.. was administered orally as a single 4000 mg/kg bodyweight dose to a group of ten (5 males and 5 females) NMRI mice. The solvent, aqua dest.., served as the negative control and cyclophosphamide was used as the positive control. Four animals treated with Monoazo Red TZ 2723 (3 males and 1 female) died during the study. When compared to the negative control, Monoazo Red TZ 2723 did not show any increase in the number of polychromatic cells with micronuclei; in contrast, the positive control, showed a marked increase. The ratio of polychromatic to normochromatic erythrocytes was unchanged by treatment, indicating no cytotoxic effects.

Results of this study indicate that Monoazo Red TZ 2723 was not mutagenic under the experimental conditions reported.

### 10.5 Overall assessment of toxicology data

Monoazo Red TZ 2723 has low acute oral toxicity (oral $LD_{50}$ in rats: 4936 mg/kg) and low acute dermal toxicity (dermal $LD_{50}$ in rats : >2000 mg/kg). Animal tests show that it is not a skin irritant nor a skin sensitiser but it has been found to be a slight eye irritant. A short-term repeated dose study in rats by gavage shows red discolouration of various organs in rats of the high dose group (1000 mg/kg/day) and treatment-related microscopic findings in the kidneys of rats in the middle (200 mg/kg/day) and high dose group and in the stomach of rats in all treated groups (50 mg/kg/day - 1000 mg/kg/day). Monoazo Red TZ 2723 was found to be non-genotoxic in the *Salmonella typhimurium* reverse mutation assay and the *in-vivo* mouse micronucleus assay, but at high concentrations *in-vitro* in the presence and absence of metabolic activation, it induced chromosome aberrations in *Chinese hamster V79* cells. Since Monoazo Red TZ 2723 only tested positive in the chromosome aberration test and not in the *Salmonella typhimurium* reverse mutation assay or the *in-vivo* mouse micronucleus assay, it is considered to be weakly genotoxic, and is unlikely to pose a significant genotoxic hazard.

## 11. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Animal tests have revealed that Monoazo Red TZ 2723 is not a skin sensitiser. No acute inhalation study has been carried out, however, this chemical is not respirable as its particle size is above the respirable range of 7 µm (31). In spite of these properties, inhalation and skin contact should be avoided as reactive dyes have been linked with respiratory sensitisation and contact dermatitis in humans (32). Monoazo Red TZ 2723 has been found to be a slight eye irritant in rats, therefore, eye contact should also be avoided. The notifier states that no adverse effects on human health have been reported with the use of this chemical overseas.

Monoazo Red TZ 2723 is stable at room temperature and pressure. It is highly soluble in water, has negligible volatility and is not easily flammable nor is it explosive. Therefore, it should not pose any risk to the safety of workers in the work environment.

Due to low public and occupational exposure under correct handling and dyeing procedures, it is unlikely that this chemical will pose any significant health or safety hazard to the public or workers.

## 12. ASSESSMENT OF ENVIRONMENTAL EFFECTS

Table 4 Summary of ecotoxicity of Monoazo Red TZ 2723

| Test | Species | Outcome | Reference |
|---|---|---|---|
| Acute toxicity | *Zebrafish* | 96 hr $LC_{50}$: 870 ppm | 33 |
| Acute immobilisation | *Daphnia magna* | 24 hr $EC_{50}$: >1000 $mgL^{-1}$ | 34 |

The results from the above-mentioned studies indicate that the notified chemical is slightly toxic to the species tested. The reports made no comment about the clarity of the test solutions. Assuming a safety factor of 1000 for acute immobilisation, the predicted chronic toxicity for *Daphnia magna* would be >1ppm, which is about two orders of magnitude higher than the "worst case" predicted environmental concentration in water of the notified chemical.

No data were provided for algae growth inhibition on the grounds that the notified chemical will colour alga strongly, and any growth changes will be masked by this effect and render the test unreliable.

While there are other methods of measuring changes in algal growth, a survey of fish toxicity data on over 3000 commercial products by the Ecological and Toxicological Association of the

Dyestuffs Manufacturing Industry (ETAD) indicates that the majority of dyes are not very toxic to fish (8). Algal growth inhibition tests of 56 dyestuffs show close parallels with fish toxicity data (8). Based on the above information and fish toxicity result for the notified chemical, it is unlikely that the notified chemical will be toxic to algae, therefore, such a test will not be required.

## 13. ASSESSMENT OF ENVIRONMENTAL HAZARD

The main route of environmental exposure for the notified chemical will occur when unfixed dye in the effluents from sewage plants are released to the aquatic compartment where it may persist owing to its lack of biodegradation under aerobic conditions. It is unlikely to undergo volatilisation given its negligible vapour pressure.

The effluents from the dyeworks that are discharged to rivers or streams may present a greater hazard to the environment than the effluents from dyeworks which are discharged to the ocean. Thus the potential hazard is greater in inland areas because of the lower volume of the receiving waters.

Ecotoxicity results indicate that Monoazo Red TZ 2723 is unlikely to present either an acute or chronic hazard to aquatic invertebrates, freshwater fish and micro-organisms at the likely environmental levels indicated in Section 9 of this report. As explained in Section 12 of this report, although no algal toxicity studies were carried out, the notified chemical is unlikely to present a hazard to algae. While Monoazo Red TZ 2723 may persist in the aquatic compartment, its very high water solubility and very low partition coefficient (octanol/water) both indicate that bioaccumulation to toxic levels is extremely unlikely.

If the notified chemical does bind to sediment to some extent, the hazard presented to benthic organisms is unclear. However, it is unlikely that significant toxic levels of the notified chemical will be reached due to its high water solubility and lack of bioaccumulation potential.

Therefore, whether the notified chemical passes through the sewage treatment works without being removed or is partially removed as assumed by the notifier, the amount of Monoazo Red TZ

2723 that will reach the environment is likely to be in the order of ppb, a level that is unlikely to present a hazard to the environment, based on the ecotoxicity data submitted.

## 14. RECOMMENDATIONS FOR SAFETY PROCEDURES TO CONTROL OCCUPATIONAL EXPOSURE

To minimise occupational exposure to the formulated commercial product containing the notified chemical, Monoazo Red TZ 2723, the following guidelines and precautions should be observed:

. the workplace should be well ventilated and local exhaust ventilation should be employed in areas where the powder dye will be handled;

. suitable personal protective equipment which comply with Australian standards (AS) should be worn such as:

  . safety glasses (AS 1337) - *Eye Protectors for Industrial Applications* (35),

  . impervious elbow length gloves (AS 2161) - *Industrial Safety Gloves and Mittens (excluding Electrical and Medical Gloves)* (36),

  . appropriate protective clothing and

  . disposable dust masks. When ventilation is insufficient, approved dust respirators should be worn (AS 1716) - *Respiratory Protective Devices* (37);

. as good work practice, the product should be handled with care to avoid spillage, the generation of a dust cloud or splashings. Containers of powder dye should only be opened during weighing. The handling of powder dye should be minimised for example by making a paste or a solution from the powder as quickly as possible after weighing;

. good housekeeping and maintenance should be practised. Wet methods or vacuum cleaning which do not lead to dispersion of the settled dust should be used for plant maintenance and sanitation. Spillages should be attended to immediately;

. personal hygiene should be observed; and

. a copy of the Material Safety Data Sheet (MSDS) for both the notified chemical and the commercial product should be easily accessible to employees.

## 15. RECOMMENDATIONS FOR MATERIAL SAFETY DATA SHEET (MSDS)

The MSDSs for Monoazo Red TZ 2723 (Attachment 1) and CIBACRON RED C-R (Attachment 2) have been compiled in accordance with Worksafe Australia format (38).

## 16. REQUIREMENTS FOR SECONDARY NOTIFICATION

Under the Industrial Chemicals (Notification and Assessment) Act 1989 (the Act), secondary notification of Monoazo Red TZ 2723 shall be required by CIBA-GEIGY Australia Ltd. if any of the circumstances stipulated under subsection 64(2) of the Act arise. No other specific conditions are prescribed.

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