

201-15138B

Robust Summaries for

Sunset Yellow

CAS No. 2783-94-0

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Consortium Registration Number

**Submitted to the EPA under the HPV Challenge Program by:
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Robust Summaries for Sunset Yellow

The evaluation of the quality of the following data uses a systematic approach described by Klimisch [Klimisch *et al.*, 1996]. Based on criteria relating to international testing standards for categorizing data reliability, four reliability categories have been established. The following categories are:

- Reliability code 1. Reliable without restrictions
- Reliability code 2. Reliable with restrictions
- Reliability code 3. Not reliable
- Reliability code 4. Not assignable

1 CHEMICAL AND PHYSICAL PROPERTIES

1.1 MELTING POINT

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
Remarks for substance	FD&C Yellow 6; 91.9% purity
Method/guideline	Measured
GLP	Yes
Year	1981
Remarks for Test Conditions	
Melting Point	
Decomposition	390 °C
Sublimation	
Remarks for Results	Decomposes without melting; decomposition begins at 390 °C

Conclusion Remarks

Data Qualities Reliabilities Reliability code 1. Reliable without restriction.

Remarks for Data Reliability Code 1. Guideline study.

References NTP (1981) National Toxicology Program. Carcinogenesis Bioassay of FD & C Yellow No. 6. NTP 80-33.

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
-----------------------	---------------

Remarks for substance FD&C Yellow 6

Method/guideline Calculated

GLP

Year

Remarks for Test Conditions

Melting Point 350 °C

Decomposition

Sublimation

Remarks for Results

Conclusion Remarks

Data Qualities Reliabilities Reliability code 4. Not assignable.

Remarks for Data Reliability Code 4. Calculated.

References MPBPVPWIN EPI Suite (2000) US Environmental Protection Agency.

1.2 BOILING POINT

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
-----------------------	---------------

Remarks for Substance FD&C Yellow 6

Method/guideline	Calculated
GLP	
Year	
Remarks for Test Conditions	
Boiling Point	837 °C
Pressure	
Pressure Unit	
Decomposition	
Remarks for Results	
Conclusion Remarks	
Data Qualities Reliabilities	Reliability code 4. Not assignable.
Remarks for Data Reliability	Code 4. Calculated.
References	MPBPVPWIN EPI Suite (2000) US Environmental Protection Agency.

1.3 VAPOR PRESSURE

CAS Numerical	2783-94-0
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Substance Name	Sunset Yellow
-----------------------	---------------

Remarks for substance	FD&C Yellow 6
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Method/guideline	Calculated/Mean of Antoine & Grain
-------------------------	------------------------------------

GLP	No
------------	----

Year

Remarks for Test Conditions

Vapor Pressure	1.43 X 10 ⁻²² mm Hg
-----------------------	--------------------------------

Temperature	25 °C
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Decomposition

Remarks for Results

Conclusion Remarks

Data Qualities Reliabilities Reliability code 4. Not assignable.

Remarks for Data Reliability Code 4. Calculated.

References MPBPVPWIN EPI Suite (2000) US Environmental Protection Agency.

1.4 N-OCTANOL/WATER PARTITION COEFFICIENTS

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
-----------------------	---------------

Remarks for substance FD&C Yellow No. 6

Method/guideline Calculated

GLP

Year

Remarks for Test Conditions

Log Pow -1.18

Temperature

Remarks for Results

Conclusion Remarks

Data Qualities Reliabilities Reliability code 4. Not assignable.

Remarks for Data Reliability Code 4. Calculated.

References KOWWIN EPI Suite (2000) US Environmental Protection Agency.

1.5 WATER SOLUBILITY

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	Purity not given
Method/guideline	Experimental
GLP	Ambiguous
Year	1991
Remarks for Test Conditions	Not given
Value (mg/L) at temperature	190,000 mg/L at 2 °C, 190,000 mg/L at 25 °C, and 200,000 mg/L at 60 °C
Description of Solubility	Not given
pH value and concentration at temp	
pKa value at 25 Celsius	
Remarks for Results	
Conclusion Remarks	
Data Qualities Reliabilities	Reliability code 4. Not assignable.
Remarks for Data Reliability	Code 4. Only secondary literature (review, tables, books, etc.).
References	Marmion D.M. (1991) Handbook of U.S. Colorants: Foods, Drugs, and Cosmetics and Medical Devices. 3rd Ed. New York, John Wiley & Sons, Inc.

2 ENVIRONMENTAL FATE AND PATHWAYS

2.1 PHOTODEGRADATION

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
-----------------------	---------------

Remarks for Substance Data are for structurally related sulfonic acid, 2-naphthalenesulfonic acid, 6-hydroxy-5-[(2-methoxy-5-methyl-4-sulfophenyl)azo]-, disodium salt (FD&C Red 40)

Method/guideline Not given

Test Type Experimental

GLP Ambiguous

Year 1991

Light Source 15-watt General Electric germicidal lamps

Light Spectrum (nm) Ultraviolet

Relative Intensity

Spectrum of Substance

Remarks for Test Conditions The concentration of the dye solution was measured before and after the photolysis using the Hewlett-Packard 8452A diode-array UV/Visible Spectrophotometer. Red 40 was prepared in an initial concentration of 5 mg/l. In the first part of the study, photolysis experiments were conducted using two 15-W (30 Watts total) General Electric germicidal lamps as the ultraviolet light source. The distance between the light source and the reaction vessels was approximately 2.5 cm. Both direct photolysis and indirect photolysis experiments were conducted. The indirect photolysis experiment used acetone as the sensitizer for indirect photodegradation.

Concentration of Substance 5 mg/L

Temperature

Direct photolysis 7% degradation after 50 minutes

Half-life t_{1/2}

Degradation % after

Quantum yield

Indirect photolysis 99% degradation after 20 minutes

Sensitizer Acetone

Concentration of sensitizer 5 mg/L

Rate constant

Degradation %after

Breakdown products

Remarks field for results

Conclusion remarks

Data Qualities Reliabilities Reliability code 2. Reliable with restriction.

Remarks for Data Reliability Code 2. Basic data given: comparable to guidelines/standards.

References Pasin B. and Rickabaugh J. (1991) Destruction of Azo Dyes by Sensitized Photolysis. Hazard. Ind. Wastes, 359-367.

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
-----------------------	---------------

Remarks for Substance FD&C Yellow 6

Method/guideline Calculation

Test Type AOPWIN

GLP

Year

Light Source

Light Spectrum (nm)

Relative Intensity

Spectrum of Substance

Remarks for Test Conditions

Concentration of Substance

Temperature

Direct photolysis

Half-life t_{1/2} 31.9 hours

Degradation % after

Quantum yield

Indirect photolysis

Sensitizer**Concentration of sensitizer****Rate constant****Degradation %after****Breakdown products****Remarks field for results****Conclusion remarks****Data Qualities Reliabilities** Reliability code 4. Not assignable.**Remarks for Data Reliability** Code 4. Calculated.**References** AOPWIN EPI Suite (2000) US Environmental Protection Agency.**2.2 BIODEGRADATION****CAS Numerical** 2783-94-0

Substance Name	Sunset Yellow
-----------------------	---------------

Remarks for Substance Data are for structurally related substance C.I. Acid Red No. 14**Method** Not given**Test Type****GLP** Ambiguous**Year** 1993**Contact time (units)** 24 hour**Innoculum** Activated sludge**Remarks for Test Conditions** Screened raw wastewater was used as the influent in three pilot scale activated sludge biological treatment systems. Each water soluble dye was tested at doses of 1 mg/L for low spike systems and 5 mg/L for high spike systems of influent flow. Before the data collection, dye analytical recovery studies were conducted by dosing the purified dye compound into organic free water, influent wastewater, and mixed liquor. These studies were run in duplicate and each recovery study was

repeated at least once to ensure that the dye compound could be extracted. Purified dye standards were analytically prepared from the commercial dye product by repeated recrystallization.

The INF, primary effluent (PE), and ASE were filtered and the filtrate was passed through a column packed with resin. The filter paper and resin were soaked in an ammonia acetonitrile solution and then Soxhlet extracted with ammonia-acetonitrile. The extract was concentrated and brought up to 50 mL volume with a methanol/dimethylformamide solution. The mixed liquor samples were separated into two components, the filtrate or soluble fraction (SOL) and the residue (RES) fraction. The SOL fraction was processed similar to these samples but the resin adsorption step was omitted. All extracted samples were analyzed by HPLC with an ultraviolet-visible detector. Total suspended solids analyses were also performed on the INF, PE, ML, and ASE samples.

All systems were operated for at least three times the solids retention time to ensure acclimation prior to initiation of data collection. All samples were 24 hr. composites made up of 6 grab samples collected every 4 hr. and stored at 4 degrees Celsius.

Degradation % after time

Results

Percent recovery as measured: Organic Free Water: 101% at 1 mg/L and 90% at 5 mg/L; Wastewater: 98% at 1mg/L and 97% at 5 mg/L; Mixed Liquor: 88% at 1mg/L and 92% at 5 mg/L
Mass Balance Data Summary: Low spike: 116% recovered, 1% adsorbed; High spike: 148% recovered, less than 1% adsorbed.

Kinetic

**Time required for 10% degradation
10 day window criteria**

Total degradation

Classification

Breakdown products (transient or stable?)

Remarks fields for results

Since the majority of the test substance was recovered, the authors assumed that this compound was not biodegraded. The authors based this assumption on preliminary data indicating little or no problems in recovering the compounds from the sample matrix. Additionally, the results also indicate that the material was not adsorbed. The authors attributed the high sulfonic acid substitution on the test substance as the reason why the material was not removed by the microbial cells or cell byproducts and subject to aerobic biodegradation.

Conclusion remarks

Data Qualities Reliabilities

Reliability code 1. Reliable without restriction.

Remarks for Data Reliability Code 1. Comparable to guideline study.

References Shaul G.M., Holdsworth T.J., Dempsey C.R., and Dostal K.A. (1990) Fate of water soluble azo dyes in the activated sludge process. Chemosphere 22, p107-119.

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
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Remarks for Substance FD & C Yellow 6

Method BIOWIN

Test Type Calculated

GLP

Year

Contact time (units)

Innoculum

Remarks for Test Conditions

Degradation % after time

Results

Kinetic

**Time required for 10%
degradation
10 day window criteria**

Total degradation

Classification Not readily biodegradable

**Breakdown products
(transient or stable?)
Remarks fields for results**

Conclusion remarks

Data Qualities Reliabilities Reliability code 4. Not assignable.

Remarks for Data Reliability Code 4. Calculated.

References BIOWIN EPI Suite (2000) US Environmental Protection Agency.

2.3 FUGACITY

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
-----------------------	---------------

Remarks for Substance FD&C Yellow No. 6

Model Conditions 25 C, 100,000 lbs.

Test Type Environmental Equilibrium Partitioning Model

Method Mackay

Model Used (title, version, date) EQC V 2.70 Level III

Input parameters MW, log Kow, water solubility, MP & VP

Year

Remarks for Test Conditions

Media Air

absorption coefficient

Desorption

Volatility

Model data and results

Estimated Distribution and Media Concentration 0.00219%

Remarks

Conclusion remarks

Data Qualities Reliabilities Reliability code 4. Not assignable.

Remarks for Data Reliability Code 4. Calculated.

References EPIWIN EPI Suite (2000) US Environmental Protection Agency. Level III. Fugacity.

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
-----------------------	---------------

Remarks for Substance FD&C Yellow No. 6

Model Conditions 25 C, 100,000 lbs.

Test Type	Environmental Equilibrium Partitioning Model
Method	Mackay
Model Used (title, version, date)	EQC V 2.70 Level III
Input parameters	MW, log Kow, water solubility, MP & VP
Year	
Remarks for Test Conditions	
Media	Soil
absorption coefficient	
Desorption	
Volatility	
Model data and results	
Estimated Distribution and Media Concentration	50.1%
Remarks	
Conclusion remarks	
Data Qualities Reliabilities	Reliability code 4. Not assignable.
Remarks for Data Reliability	Code 4. Calculated.
References	EPIWIN EPI Suite (2000) US Environmental Protection Agency. Level III. Fugacity.
CAS Numerical	2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	FD&C Yellow No. 6
Model Conditions	25 C, 100,000 lbs.
Test Type	Environmental Equilibrium Partitioning Model
Method	Mackay
Model Used (title, version, date)	EQC V 2.70 Level III
Input parameters	MW, log Kow, water solubility, MP & VP
Year	
Remarks for Test Conditions	
Media	Water

absorption coefficient

Desorption

Volatility

Model data and results

Estimated Distribution and Media Concentration 49.8%
Remarks

Conclusion remarks

Data Qualities Reliabilities Reliability code 4. Not assignable.

Remarks for Data Reliability Code 4. Calculated.

References EPIWIN EPI Suite (2000) US Environmental Protection Agency. Level III. Fugacity.

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
-----------------------	---------------

Remarks for Substance FD&C Yellow No. 6

Model Conditions 25 C, 100,000 lbs.

Test Type Environmental Equilibrium Partitioning Model

Method Mackay

Model Used (title, version, date) EQC V 2.70 Level III

Input parameters MW, log Kow, water solubility, MP & VP

Year

Remarks for Test Conditions

Media Sediment

absorption coefficient

Desorption

Volatility

Model data and results

Estimated Distribution and Media Concentration 0.0918%
Remarks

Conclusion remarks

Data Qualities Reliabilities Reliability code 4. Not assignable.

Remarks for Data Reliability

Code 4. Calculated.

References

EPIWIN EPI Suite (2000) US Environmental Protection Agency. Level III. Fugacity.

3 ECOTOXICITY

3.1 ACUTE TOXICITY TO FISH

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	Data are for sulfonic acid derivative, 2,2'-(1,2-ethene-diyl)bis(5-amino)-benzenesulfonic acid
Method/guideline	
Test Type	Experimental
GLP	Ambiguous
Year	Not given
Species/Strain/Supplier	Fish
Analytical monitoring	
Exposure period (unit)	48 hour
Remarks for Test Conditions	
Observations on precipitation	
Nominal concentrations as mg/L	
Measured concentrations as mg/L	
Unit	
Endpoint value	LC50 = 200 mg/L
Reference substances (if used)	
Remarks fields for results	
Conclusion remarks	
Data Qualities Reliabilities	Reliability code 4. Not assignable.
Remarks for Data Reliability	Code 4. Only secondary literature (review, tables, books, etc.).
References	Alstoffe, (1992) Daten zur Beurteilung der Wirkung auf Mensch and Umwelt-Satensätze, Verband der Chemischen Industrie, Frankfurt 1992. Schön N. (1991) Altsoff-Grunddatensätze-Liste der bisher publizierten Grunddatensätze UWSF-Z. Umwelchem. Ökotox, 3(3), 183-185.

Schön N. (1992) Altsoff-Grunddatensätze-Liste der bisher publizierten Grunddatensätze UWSF-Z. Umwelchem. Ökotox, 4(6), 343-345.

CAS Numerical	2783-94-0
Substance Name	Sunset Yellow
Remarks for Substance	Data are for sulfonic acid derivative,2,2'-(1,2-ethene-diyl)bis(5-amino)-benzenesulfonic acid, disodium salt
Method/guideline	
Test Type	Experimental
GLP	Ambiguous
Year	Not given
Species/Strain/Supplier	Fish
Analytical monitoring	
Exposure period (unit)	72 hour
Remarks for Test Conditions	
Observations on precipitation	
Nominal concentrations as mg/L	
Measured concentrations as mg/L	
Unit	
Endpoint value	LC50 greater than 1000 mg/L
Reference substances (if used)	
Remarks fields for results	
Conclusion remarks	
Data Qualities Reliabilities	Reliability code 4. Not assignable.
Remarks for Data Reliability	Code 4.Only secondary literature (review, tables, books, etc.).
References	<p>Alstoffe, (1992) Daten zur Beurteilung der Wirkung auf Mensch and Umwelt-Satensätze, Verband der Chemischen Industrie, Frankfurt 1992.</p> <p>Schön N. (1991) Altsoff-Grunddatensätze-Liste der bisher publizierten Grunddatensätze UWSF-Z. Umwelchem. Ökotox, 3(3), 183-185.</p> <p>Schön N. (1992) Altsoff-Grunddatensätze-Liste der bisher publizierten Grunddatensätze UWSF-Z. Umwelchem. Ökotox, 4(6), 343-345.</p>

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	Data are for sulfonic acid derivative, 2,2'-(1,2-ethene-diyl)bis(5-amino)-benzenesulfonic acid, dipotassium salt
Method/guideline	
Test Type	Experimental
GLP	Ambiguous
Year	Not given
Species/Strain/Supplier	Fish
Analytical monitoring	
Exposure period (unit)	96 hour
Remarks for Test Conditions	
Observations on precipitation	
Nominal concentrations as mg/L	
Measured concentrations as mg/L	
Unit	
Endpoint value	LC50 greater than 10000 mg/L
Reference substances (if used)	
Remarks fields for results	
Conclusion remarks	
Data Qualities Reliabilities	Reliability code 4. Not assignable.
Remarks for Data Reliability	Code 4.Only secondary literature (review, tables, books, etc.).
References	Alstoffe, (1992) Daten zur Beurteilung der Wirkung auf Mensch and Umwelt-Satensätze, Verband der Chemischen Industrie, Frankfurt 1992. Schön N. (1991) Altsoff-Grunddatensätze-Liste der bisher publizierten Grunddatensätze UWSF-Z. Umwelchem. Ökotox, 3(3), 183-185. Schön N. (1992) Altsoff-Grunddatensätze-Liste der bisher publizierten Grunddatensätze UWSF-Z. Umwelchem. Ökotox, 4(6), 343-345.

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
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Remarks for Substance FD&C Yellow 6

Method/guideline ECOSAR

Test Type Calculated

GLP

Year

Species/Strain/Supplier Fish

Analytical monitoring

Exposure period (unit) 96 hour

Remarks for Test Conditions Input parameters: Molecular weight, Water solubility, 190,000 mg/L at 25 °C; melting point 390 °C

Observations on precipitation

Nominal concentrations as mg/L

Measured concentrations as mg/L

Unit

Endpoint value LC50 = 6044 mg/L

Reference substances (if used)

Remarks fields for results

Conclusion remarks

Data Qualities Reliabilities Reliability code 4. Not assignable.

Remarks for Data Reliability Code 4. Calculated.

References ECOSAR EPI Suite (2000) U.S. Environmental Protection Agency (Nabholz V. and G. Cash, 1998).

3.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	Data are for sulfonic acid derivative, 2,2'-(1,2-ethene-diyl)bis(5-amino)-benzenesulfonic acid
Method/guideline	
Test Type	Experimental
GLP	
Year	
Analytical procedures	
Species/Strain	<i>Daphnia magna</i>
Test details	24 hour
Remarks for Test Conditions	
Nominal concentrations as mg/L	
Measured concentrations as mg/L	
Unit	
EC50, EL50, LC0, at 24,48 hours	EC50 = 100 mg/L
Biological observations	
Control response satisfactory?	
Appropriate statistical evaluations?	
Remarks fields for results	
Conclusion remarks	
Data Qualities Reliabilities	Reliability code 4. Not assignable.
Remarks for Data Reliability	Code 4. Only secondary literature (review, tables, books, etc.).
References	Alstoffe, (1992) Daten zur Beurteilung der Wirkung auf Mensch and Umwelt-Satensätze, Verband der Chemischen Industrie, Frankfurt 1992. Schön N. (1991) Altsoff-Grunddatensätze-Liste der bisher publizierten Grunddatensätze UWSF-Z. Umwelchem. Ökotox, 3(3), 183-185. Schön N. (1992) Altsoff-Grunddatensätze-Liste der bisher publizierten Grunddatensätze UWSF-Z. Umwelchem. Ökotox, 4(6), 343-345.

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	FD&C Yellow 6
Method/guideline	ECOSAR
Test Type	Calculated
GLP	
Year	
Analytical procedures	
Species/Strain	<i>Daphnia magna</i>
Test details	48 hours
Remarks for Test Conditions	Input parameters: Water solubility, 190,000 mg/L at 25 °C; Molecular weight 452.37; Melting point 390 °C
Nominal concentrations as mg/L	
Measured concentrations as mg/L	
Unit	
EC50, EL50, LC0, at 24,48 hours	EC50 = 486.5 mg/L
Biological observations	
Control response satisfactory?	
Appropriate statistical evaluations?	
Remarks fields for results	
Conclusion remarks	
Data Qualities Reliabilities	Reliability code 4. Not assignable.
Remarks for Data Reliability	Code 4. Calculated.
References	ECOSAR EPI Suite (2000) U.S. Environmental Protection Agency (Nabholz V. and G. Cash, 1998).

3.3 ACUTE TOXICITY TO AQUATIC PLANTS

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	The test substance was an unidentified sulfonic acid substituted azo dye.
Method/guideline	
Test Type	Experimental
GLP	Ambiguous
Year	1996
Species/Strain/Supplier	Green algae, <i>Selenastrum capricornutum</i>
Endpoint basis	
Exposure period (duration)	96 hour
Analytical monitoring	
Remarks for Test Conditions	Algal chronic toxicity test were performed according the method of EPA, 1988. Three replicates were performed for each dye at a nominal concentration of 1 mg/l for the active colorant. One ml of dye stock solution was added to 50 mg/l of algal assay medium in 125 ml Erlenmeyer flasks. <i>S. capricornutum</i> in continuous culture provided the initial inoculum (10,000 algal cells/ml). The cells were incubated in the solution for 96 hours. The diluent and negative control were algal assay medium. AAM was prepared by adding 1 ml from each of five stock solutions to 900 ml of deionized water. After spiking, the total volume was brought to 1 liter with deionized water. Population growth was used to establish potential toxicity. If the dye inhibited algal growth by more than 50% of that of the negative controls, a definitive test using several dilutions of the dye was performed to allow for determination of an EC50 concentration.
Nominal concentrations as mg/L	
Measured concentrations as mg/L	
Unit	
Endpoint value	Average yield: 36.6% with 95% C.I. (34.9-38.4).
NOEC, LOEC or NOEL, LOEL	
Biological observations	26.4% stimulation of population growth compared to control.
Control response satisfactory?	Yes
Appropriate statistical evaluations?	Yes, Dunnett's test
Remarks fields for results	Not statistically significant.

Conclusion remarks**Data Qualities Reliabilities** Reliability code 2. Reliable with restriction.**Remarks for Data Reliability** Code 1. Comparable to guideline study.**References** Greene J. C. and Baughman G.L. (1996) Effects of 46 dyes on population-growth of fresh-water green-alga *Selenastrum-capricornutum*. *Textile Chemist And Colorist*, 28, 23-30.

Green J.D. et al. (1988) Protocols for short term toxicity screening of hazardous w

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	FD&C Yellow 6
Method/guideline	ECOSAR
Test Type	Calculated
GLP	
Year	
Species/Strain/Supplier	Green algae
Endpoint basis	
Exposure period (duration)	96 hour
Analytical monitoring	
Remarks for Test Conditions	Input parameters: Water solubility - 190,000 mg/L at 25 °C; Molecular weight 452.37; Melting point 390 °C
Nominal concentrations as mg/L	
Measured concentrations as mg/L	
Unit	
Endpoint value	EC50 = 146,000 mg/L
NOEC, LOEC or NOEL, LOEL	
Biological observations	
Control response satisfactory?	
Appropriate statistical evaluations?	
Remarks fields for results	
Conclusion remarks	

Data Qualities Reliabilities	Reliability code 4. Not assignable.
Remarks for Data Reliability	Code 4. Calculated.
References	ECOSAR EPI Suite (2000) US Environmental Protection Agency (Nabholz V. and G. Cash, 1998).

4 HUMAN HEALTH TOXICITY

4.1 ACUTE TOXICITY

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	Not given
Method/guideline	Not given
Test Type	Acute Toxicity LD50
GLP	No
Year	1964
Species/Strain	Rats/Wistar
Sex	Male
# of animals per sex per dose	6
Vehicle	Water
Route of administration	Oral-Gavage
Remarks for test conditions	Wistar adult male rats were administered 2000 mg/kg bw <i>via</i> stomach tube.
Value LD50 or LC50 with confidence limits	Greater than 2000 mg/kg bw
Number of deaths at each dose level	0 deaths
Remarks for results	
Conclusion remarks	The oral LD50 for sunset yellow is greater than 2000 mg/kg bw.
Data Qualities Reliabilities	Reliability code 2. Reliable with restriction.
Remarks for Data Reliability	Code 2. Basic data given: comparable to guidelines/standards.
References	Lu F. and Lavallo C. (1964) The acute toxicity of some synthetic colours used in drugs and foods. Canadian Pharmaceutical Journal 9.
CAS Numerical	2783-94-0
Substance Name	Sunset Yellow
Remarks for Substance	Greater than 85% purity
Method/guideline	LD50 calculated by Weil (1952)

Test Type	Acute Toxicity LD50
GLP	No
Year	1967
Species/Strain	Rats/Carworth Farm E strain
Sex	Male and Female
# of animals per sex per dose	5
Vehicle	Water
Route of administration	Oral
Remarks for test conditions	Groups of five male and female rats each (body weights: males 200-250 g; females 150-200 g) were administered the test substance in aqueous solution. Animals were fasted for 18 hours prior to treatment and observed for 7 days following treatment. Necropsies were performed on animals that died and some survivors.
Value LD50 or LC50 with confidence limits	Greater than 10,000 mg/kg
Number of deaths at each dose level	No deaths at up to 10,000 mg/kg bw.
Remarks for results	Slight diarrhea reported for 24 hours following treatment. Feces and urine were colored orange. No macroscopic changes reported upon necropsy.
Conclusion remarks	
Data Qualities Reliabilities	Reliability code 2. Reliable with restriction.
Remarks for Data Reliability	Code 2. Basic data given: comparable to guidelines/standards.
References	Gaunt I.F., Farmer M., Grasso P., and Gangolli .D. (1967) Acute (Rat and Mouse) and Short-term (Rat) Toxicity Studies on Sunset Yellow FCF. Fd Cosmet Toxicol 5, pp. 747-754.
CAS Numerical	2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	Greater than 85% purity
Method/guideline	LD50 calculated by Weil (1952)
Test Type	Acute Toxicity LD50
GLP	No
Year	1967
Species/Strain	Mice/ICI Alderley Park strain
Sex	Male and Female

# of animals per sex per dose	5
Vehicle	Water
Route of administration	Oral
Remarks for test conditions	Groups of five male and female mice each (body weights: 20-25 kg) were administered the test substance in aqueous solution. Animals were fasted for 18 hours prior to treatment and observed for 7 days following treatment. Necropsies were performed on animals that died and some survivors.
Value LD50 or LC50 with confidence limits	Greater than 6000 mg/kg bw
Number of deaths at each dose level	No deaths at up to 6000 mg/kg bw
Remarks for results	Slight diarrhea reported for 24 hours following treatment. Feces and urine were colored orange. No macroscopic changes reported upon necropsy.
Conclusion remarks	
Data Qualities Reliabilities	Reliability code 2. Reliable with restriction.
Remarks for Data Reliability	Code 2. Basic data given: comparable to guidelines/standards.
References	Gaunt I.F., Farmer M., Grasso P., and Gangolli .D. (1967) Acute (Rat and Mouse) and Short-term (Rat) Toxicity Studies on Sunset Yellow FCF. Fd Cosmet Toxicol 5, pp. 747-754.

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	Greater than 85% purity
Method/guideline	LD50 calculated by Weil (1952)
Test Type	Acute Toxicity LD50
GLP	No
Year	1967
Species/Strain	Rats/Carworth Farm E strain
Sex	Male and Female
# of animals per sex per dose	5
Vehicle	Water
Route of administration	Intraperitoneal
Remarks for test conditions	Groups of five male and female rats each (body weights: males 200-250 g; females 150-200 g) were administered the test substance in aqueous solution. Animals were fasted for 18 hours prior to treatment and observed for 7 days following treatment. Necropsies were performed on animals that died

	and some survivors.
Value LD50 or LC50 with confidence limits	3800 mg/kg bw (2900-4600 mg/kg bw)
Number of deaths at each dose level	Not given
Remarks for results	Slight diarrhea reported for 24 hours following treatment. Skin, feces and urine were colored orange. Deaths were preceded by comas, and in some animals convulsions. No macroscopic changes reported upon necropsy.
Conclusion remarks	
Data Qualities Reliabilities	Reliability code 2. Reliable with restriction.
Remarks for Data Reliability	Code 2. Basic data given: comparable to guidelines/standards.
References	Gaunt I.F., Farmer M., Grasso P., and Gangolli .D. (1967) Acute (Rat and Mouse) and Short-term (Rat) Toxicity Studies on Sunset Yellow FCF. Fd Cosmet Toxicol 5, pp. 747-754.

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	Greater than 85% purity
Method/guideline	LD50 calculated by Weil (1952)
Test Type	Acute Toxicity LD50
GLP	No
Year	1967
Species/Strain	Mice/ICI Alderley Park strain
Sex	Male and Female
# of animals per sex per dose	5
Vehicle	Water
Route of administration	Intraperitoneal
Remarks for test conditions	Groups of five male and female mice each (body weights: 20-25 kg) were administered the test substance in aqueous solution. Animals were fasted for 18 hours prior to treatment and observed for 7 days following treatment. Necropsies were performed on animals that died and some survivors.
Value LD50 or LC50 with confidence limits	5500 (95% C.I.: 4600-6700) mg/kg bw (Males) 4600 (95% C.I.: 3900-5300) (Females)
Number of deaths at each dose level	Not given
Remarks for results	Slight diarrhea reported for 24 hours following treatment. Skin, feces and urine were colored orange. Deaths were preceded by comas, and in some animals convulsions. No macroscopic

changes reported upon necropsy.

Conclusion remarks

Data Qualities Reliabilities Reliability code 2. Reliable with restriction.

Remarks for Data Reliability Code 2. Basic data given: comparable to guidelines/standards.

References Gaunt I.F., Farmer M., Grasso P., and Gangolli .D. (1967) Acute (Rat and Mouse) and Short-term (Rat) Toxicity Studies on Sunset Yellow FCF. *Fd Cosmet Toxicol* 5, pp. 747-754.

4.2 GENETIC TOXICITY

4.2.1 *In vitro* Genotoxicity

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	FD&C Yellow No. 6; Purity not given
Method/guideline	Ames plate incorporation and liquid pre-incubation
Test Type	Reverse mutation
System of Testing	Bacterial
GLP	Ambiguous
Year	1981
Species/Strain	<i>Salmonella typhimurium</i> TA1535, TA 1537, TA1538, TA98, TA100
Metabolic Activation	Rat liver microsome fraction S9 from Aroclor induced rats
Doses/concentration levels	.005- 5.0 mg/plate
Statistical Methods	Not given
Remarks for test conditions	Reverse mutation tests were carried out using <i>S. typhimurium</i> strains TA1535, TA 1537, TA1538, TA98, TA100. Plate incorporation tests were conducted according to Ames et al., with the Andrews et al. modifications. Duplicates were performed at each of the six concentrations of the test substance. Mutagenic compounds were assayed using duplicate plates. A substance was considered positive when

the number of revertants above background was at least twice the value of the historical control mean or twice the value of the current control mean, whichever was greater and a dose response curve could be generated.

Positive controls without metabolic activation were sodium azide (TA1535 and TA100), 9-aminoacridine (TA97 and TA1535), and 4-nitro-o-phenylenediamine (TA98). The positive controls were sodium azide, 9-aminoacridine, 2-nitrofluorene, and 2-aminoanthracene.

Result	Negative
Cytotoxic concentration	5.0 mg/plate for plate-incorporation, and .5 mg/ml for pre-incubation test
Genotoxic effects	Negative
Appropriate statistical evaluations?	None given
Remarks for results	Negative
Conclusion remarks	The test substance was negative in the AMES assay for reverse mutation using <i>Salmonella typhimurium</i> TA1535, TA 1537, TA1538, TA98, TA100.
Data Qualities Reliabilities	Reliability code 1. Reliable without restriction.
Remarks for Data Reliability	Code 1. Guideline study.
References	Chung K.T., Fulk G.E., & Andrews A.W. (1981) Mutagenicity testing of some commonly used dyes. <i>Applied and Environmental Microbiology</i> 42, 641-648.

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	FD&C Yellow No. 6; Purity not given
Method/guideline	Ames, McCann and Yamasaki (1975)
Test Type	Reverse mutation
System of Testing	Bacterial
GLP	Ambiguous
Year	1984
Species/Strain	<i>Salmonella typhimurium</i> TA1535, TA 1537, TA98, TA100, TA92, TA94
Metabolic Activation	Rat liver microsome fraction S9 from Aroclor induced rats
Doses/concentration levels	up to 5.0 mg/ml
Statistical Methods	Not given
Remarks for test conditions	Reverse mutation tests were carried out using <i>S. typhimurium</i> strains TA92, TA1535, TA100, TA1537, TA94 and TA98. Cells

cultured overnight were pre-incubated with the test substance and the S-9 mix for twenty minutes at 37 degrees Celsius prior to plating. Duplicates were performed at each of the six concentrations of the test substance. The number of revertant colonies were counted following incubation for two days. Negative controls were either untreated plates or solvent. Positive results were determined if the number of colonies found was twice the number in the control. If the test was positive and a dose response relationship was not detected, additional experiments at different doses or induced mutation frequency assays were performed.

Result	Negative
Cytotoxic concentration	5.0 mg/ml was the highest non-cytotoxic dose used in the experiment.
Genotoxic effects	Negative
Appropriate statistical evaluations?	None given
Remarks for results	Negative
Conclusion remarks	Sunset Yellow was negative in the AMES assay for reverse mutation using <i>Salmonella typhimurium</i> TA1535, TA 1537, TA98, TA100, TA92, TA94.
Data Qualities Reliabilities	Reliability code 2. Reliable with restriction.
Remarks for Data Reliability	Code 2. Acceptable, well-documented publication/study report which meets basic scientific principles.
References	Ishidate, M., Sofuni, T., Yoshikawa, K., Hauashi, M., Nohmi, T., Sawada, M. and Matsuoka. (1984). Primary Mutagenicity Screening of Food Additives Currently Used in Japan. <i>Fd. Chem. Toxic.</i> 22(8) 623-636.

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	FD&C Yellow No. 6; Purity not given
Method/guideline	Ames
Test Type	Reverse mutation
System of Testing	Bacterial
GLP	No
Year	1979
Species/Strain	<i>Salmonella typhimurium</i> TA1535, TA 1537, TA98, TA100
Metabolic Activation	Rat liver microsome fraction S9 from Aroclor induced rats
Doses/concentration levels	10-250 mg/plate
Statistical Methods	Not given

Remarks for test conditions	The test substance was dissolved in DMSO. The test was considered positive if 2 fold increase in revertants was observed. Positive controls included 9-aminoacridine; 2-aminoflourine; and N-methyl-N-nitrosoguanidine.
Result	Negative
Cytotoxic concentration	Not given
Genotoxic effects	Negative
Appropriate statistical evaluations?	None given
Remarks for results	Negative
Conclusion remarks	No evidence of genotoxicity was reported.
Data Qualities Reliabilities	Reliability code 2. Reliable with restriction.
Remarks for Data Reliability	Code 2. Basic data given: comparable to guidelines/standards.
References	Muzzall J.M. and Cook W.I. (1979) Mutagenicity test of dyes used in cosmetics with the Salmonella/mammalian microsome test. Mutations Research 67, 1-8.a

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	FD&C Yellow No. 6; Purity 91.8%
Method/guideline	Sister Chromatid Exchange test was carried out using a Chinese hamster ovary (CHO).
Test Type	Sister Chromatid Exchange
System of Testing	Chinese hamster ovary cells
GLP	Ambiguous
Year	1989
Species/Strain	Chinese hamster ovary cells (CHO)
Metabolic Activation	With and without metabolic activation
Doses/concentration levels	up to 5,000 micrograms/mL
Statistical Methods	Trend test.
Remarks for test conditions	Sister chromatid exchange tests were carried out using the Chinese hamster ovary cells. Cells were exposed to the test substance for 25 hr. With metabolic activation, the cells were exposed to the test chemical plus the metabolic activation for 2 hr. For both tests (with and without metabolic activation) 10 micromolar bromodeoxyuridine (BrdUrd) was added 2 hours following initiation of the test. Colcemid was present for the last 2-2.5 hours of the incubation. Without metabolic activation, the total incubation time was 27.5-28 hr and the cells were washed

Result	prior to the addition of the Colcemid. The cultures with metabolic activation were washed to remove the test substance and the metabolic activation 2 hours following initial exposure. In one trial without activation, SCE's were induced at 30 and 25% respectively at 1,667 and 5,000 micrograms/ml. With activation, the test substance did not induce SCE's at concentrations up to 5000 micrograms/mL.
Cytotoxic concentration	Not given
Genotoxic effects	Equivocal.
Appropriate statistical evaluations?	Yes, trend test
Remarks for results	Equivocal without activation. Negative with activation.
Conclusion remarks	The SCE response to FD&C Yellow No. 6 was judged to equivocal without activation and negative with activation.
Data Qualities Reliabilities	Reliability code 2. Reliable with restriction.
Remarks for Data Reliability	Code 2. Acceptable, well-documented publication/study report which meets basic scientific principles.
References	Ivett J.L., Brown B.M., Rodgers C., Anderson B.E., Resnick M.A., and Zeigler, E. (1989) Chromosomal aberrations and sister chromatid exchange tests in Chinese Hamster Ovary Cells in Vitro. IV. Results with 15 chemicals. Environmental and Molecular Mut

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	FD&C Yellow No. 6; Purity 91.8%
Method/guideline	Chromosomal aberration test was carried out using a Chinese hamster ovary cell line, CHL.
Test Type	Chromosomal aberration test
System of Testing	Chinese hamster ovary cells
GLP	Ambiguous
Year	1989
Species/Strain	Chinese hamster ovary cells (CHO)
Metabolic Activation	With and without metabolic activation
Doses/concentration levels	up to 5,000 micrograms/L
Statistical Methods	
Remarks for test conditions	Chromosomal aberration tests were carried out using the Chinese hamster ovary cells. Cells were exposed to the test substance for 8 hr. With metabolic activation, the cells were exposed to the test chemical plus the metabolic activation for 2 hr, washed, incubated for 8 hr., and then treated with Colcemid for 2-2.5 hr. The cells were prepared for viewing on slides.

Result	Negative with and without metabolic activation.
Cytotoxic concentration	Not given
Genotoxic effects	Negative
Appropriate statistical evaluations?	Yes, trend test
Remarks for results	Negative
Conclusion remarks	Sunset Yellow tested negative in the chromosomal aberration test using Chinese hamster ovary cells.
Data Qualities Reliabilities	Reliability code 2. Reliable with restriction.
Remarks for Data Reliability	Code 2. Acceptable, well-documented publication/study report which meets basic scientific principles.
References	Ivett J.L., Brown B.M., Rodgers C., Anderson B.E., Resnick M.A., and Zeigler, E. (1989) Chromosomal aberrations and sister chromatid exchange tests in Chinese Hamster Ovary Cells in Vitro. IV. Results with 15 chemicals. Environmental and Molecular Mut
CAS Numerical	2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	FD&C Yellow No. 6; Purity not given
Method/guideline	Chromosomal aberration test was carried out using a Chinese hamster fibroblast cell line, CHL. The cells were exposed to 3 different doses for 24 and 48 hours. No metabolic activation system was applied.
Test Type	Chromosomal aberration test
System of Testing	Chinese hamster fibroblast cell line CHL.
GLP	Ambiguous
Year	1984
Species/Strain	Chinese hamster fibroblast cell line CHL.
Metabolic Activation	None
Doses/concentration levels	up to 6.0 mg/ml
Statistical Methods	
Remarks for test conditions	Chromosomal aberration tests were carried out using the Chinese hamster fibroblast line. Cells were exposed to the test substance at three different doses for 24 and 48 hr. No metabolic activation was employed. The maximum dose used for each test substance was found in a preliminary test to determine the dose required for 50% cell-growth inhibition. Colcemid at a final concentration of 0.2 ug/ml was added to the culture two hours prior to cell harvesting. The cells were prepared for viewing on slides. One hundred visible

metaphases were observed under the microscope and the incidence of polyploid cells and structural chromosomal aberrations (including chromosome and chromatid gaps, breaks, exchanges, ring formations, fragmentations and others) were recorded. Negative controls included untreated cells and solvent treated cells. The incidence of aberrations in the negative controls was generally less than 3.0%. The results were considered negative if less than 4.9%, equivocal if between 5.0-9.9%, and positive if more than 10%. If dose response relationships were not observed, additional experiments were carried out at similar dose levels.

The maximum dose for positive results represents the dose at which the maximum effect was obtained.

For quantitative evaluation of the clastogenic potential, the D20 was calculated, which is the dose (mg/ml) at which structural aberrations (including gaps) were detected in 20% of the metaphases observed. In addition, the TR value was calculated, which indicates the frequency of cells with exchange-type aberrations per unit dose (mg/ml). These values are relatively high for chemicals that show carcinogenic potential in animals.

Result	The test substance was shown to be positive (20% total incidence of cells with aberrations) in chromosomal aberration test at 48 hours. TR value was 1.8 and D20=2.0. It was also positive at 2.0 mg/ml at 24 hour and 48 hour, (23.0 and 18%, total incidence of cells with aberrations) The results were considered positive if the total incidence of cells with aberrations (including gaps) was 10.0% or more.
Cytotoxic concentration	Not given
Genotoxic effects	Positive
Appropriate statistical evaluations?	None given
Remarks for results	Positive
Conclusion remarks	Sunset Yellow tested positive in the chromosomal aberration test using Chinese hamster fibroblasts.
Data Qualities Reliabilities	Reliability code 2. Reliable with restriction.
Remarks for Data Reliability	Code 2. Acceptable, well-documented publication/study report which meets basic scientific principles.
References	Ishidate, M., Sofuni, T., Yoshikawa, K., Hauashi, M., Nohmi, T., Sawada, M. and Matsuoka. (1984). Primary Mutagenicity Screening of Food Additives Currently Used in Japan. <i>Fd. Chem. Toxic.</i> 22(8) 623-636.

4.2.2 *In vivo* Genotoxicity

CAS Numerical	2783-94-0
Substance Name	Sunset Yellow
Remarks for Substance	FD&C Yellow No. 6
Method/guideline	Rodent Micronucleus Test
Test Type	Rodent Micronucleus
GLP	Ambiguous
Year	1991
Species/Strain	Rat/PVG
Sex	Male
Route of administration	Oral-Gavage
Doses/concentration levels	10 ml/kg bw
Exposure period	Single dose
Remarks for test conditions	Male PVG rats received a single oral dose of 500, or 1000 mg/kg of the test substance. Bone marrow samples were taken at 24 and 48 hours later.
Effect on mitotic index or PCE/NCE ratio by dose level and sex	
Genotoxic effects	No significant increase in the frequency of micronucleated polychromatic erythrocytes at either time point and in either species was reported. Additionally, there was reported increase in the % PE (polychromatic erythrocytes).
NOEL (C)/ LOEL (C)	
Appropriate statistical evaluations?	Yes.
Remarks for results	No effects.
Conclusion remarks	
Data Qualities Reliabilities	Reliability code 2. Reliable with restriction.
Remarks for Data Reliability	Code 2. Acceptable, well-documented publication/study report which meets basic scientific principles.
References	Westmoreland C. and Gatehouse D.G. (1991) The differential clastogenicity of Solvent Yellow 14 and FD & C Yellow No. 6 in vivo in the rodent micronucleus test (observations on species and tissue specificity). Carcinogenesis 12 (8), 1403-8.
CAS Numerical	2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	Data are for structurally related substance, C.I. Acid Yellow 23, 94% purity
Method/guideline	Mirsalis and Butterworth, 1980
Test Type	Unscheduled DNA Synthesis
GLP	Ambiguous
Year	1985
Species/Strain	Rat/Sprague Dawley
Sex	Male
Route of administration	Oral-Gavage
Doses/concentration levels	500 mg/kg bw
Exposure period	2 hour; 15 hour
Remarks for test conditions	<p>Six to eight male Sprague-Dawley rats weighing 200-300 g were administered 500 mg acid yellow 23/kg bw via gavage. The control animal was administered corn oil only. Animals were killed at two timepoints, 2 hr and 15 hr. If negative results were obtained at timepoint 1 and timepoint 2, the in vivo testing was terminated and considered to be negative. If the initial test at timepoint 1 yielded a positive response, the test substance was retested at that timepoint. If another positive response was observed, the test was considered positive. Timepoints are the time the test substance was administered prior to the start of liver perfusion and isolation of hepatocytes.</p> <p>Hepatocytes from rats were isolated and cultured according to the two step in situ liver perfusion model (Malansky and Williams, 1982). Viable hepatocytes (2×10^5) were seeded in wells and incubated for 4 hours with [3H]-thymidine (10 uCi/ml) and the test substance (prepared in either DMSO or water) according to a procedure similar to Williams, 1977. Control incubations were conducted with and without DMSO. The authors state that DMSO had no effect on DNA repair.</p> <p>DNA repair was quantified by the autoradiographic determination of incorporated [3H]-thymidine. Net nuclear grains (NNG) were determined by counting the number of grains in each nuclei and subtracting the average number of grains present in the three equal size adjacent cytoplasmic areas. Average NNG counts of 5 or more were assumed to constitute a positive response, because these differed from the control response by greater than 2 standard deviations. In the negative controls, NNG counts ranged from -0.6- to -2.8 and from -0.9 to -2.1 for no solvent and 1% DMSO incubations, respectively. The proportion of cells with greater than or equal to 5 NNG was less than or equal to 8.1% for all control incubations. Therefore NNG below zero were considered negative responses. Concentrations of dyes producing 90% or greater detachment of the hepatocytes from the coverslips</p>

were assumed to be toxic and not counted.

Effect on mitotic index or PCE/NCE ratio by dose level and sex

The positive control was Solvent Yellow 3 (o-aminoazotoluene).
Experiment 1

Dose (mg/kg bw)	Time	Avg NNG	% >5NNG
500	2 hr	-2.6 (+/-3.7)	2
	15 hr	-1.3 (+/-2.6)	2

Genotoxic effects

Negative

NOEL (C)/ LOEL (C)

Greater than 500 mg/kg bw

Appropriate statistical evaluations?

None given

Remarks for results

Negative

Conclusion remarks

C.I. Acid Yellow 23 did not induce unscheduled DNA synthesis in an *in vivo* assay using rat hepatocytes isolated from the livers of Sprague Dawley rats.

Data Qualities Reliabilities

Reliability code 2. Reliable with restriction.

Remarks for Data Reliability

Code 2. Basic data given: comparable to guidelines/standards.

References

Kornbrust D. and Barfknecht T. (1985) Testing Dyes in HPC/DR systems. Environmental Mutagenesis 7, 101-120.

4.3 REPEATED DOSE TOXICITY

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	91.9% purity; 5.05% water; 2.77% sodium chloride
Method/guideline	National Toxicology Program. Carcinogenesis bioassay NTP 80-33
GLP	Yes
Year	1981
Species/Strain	Rats/F344/N
Sex	Male and Female
Route of administration	Oral-Diet

Doses/concentration levels	0, 12,500 or 25,000 ppm
Exposure period	103 weeks
Frequency of treatment	Daily
Control Group	Yes
Post exposure observation period	1 week
Remarks for test conditions	Groups of fifty male and fifty female rats each were administered 12,500 or 50,000 ppm FD & C Yellow No. 6 in the diet daily for 103 weeks. Ninety male and female rats each served as concurrent controls. Animals were housed five per cage and fed the test diet ad libitum. The animals were observed twice per day and weighed at least monthly. Necropsies were performed on all animals. Gross and histopathological examinations were performed on all animals. Tissues examined included adrenal glands, brain, cecum, colon, duodenum, epididymus or uterus, esophagus, eyes, femur including marrow, tissue masses, heart, ileum, jejunum, kidneys, liver, lungs and bronchi, mammary gland, lymph nodes, pancreas, parathyroids, pituitary gland, rectum, skin, spleen, stomach, thigh muscle, thymus, thyroid gland, trachea, and urinary bladder.
NOAEL(NOEL)	25,000 ppm (females); 12,500 ppm (males)
LOAEL(LOEL)	Greater than 25,000 ppm (females); 25,000 ppm (males)
Actual dose received by dose level and sex	not determined
Toxic response/effects by dose level	The mean body weights of male rats administered the high dose were slightly lower than the control animals throughout the study. The survival of male and female rats was similar between treated animals and controls (males: control 70/90 (78%); low dose 36/50 (72%); and high dose 38/50 (76%) and females: control 66/88 (75%); low dose 40/50 (80%) and high dose 37/50 (74%)). Histopathological examination revealed no evidence of carcinogenicity related to treatment with the test material. No other effects were reported.
Appropriate statistical evaluations?	Yes, Cox and Taron
Remarks for results	See Toxic response/effects by dose level.
Conclusion remarks	The authors reported that under the conditions of the bioassay, there was no clear evidence of carcinogenicity of FD & C Yellow No. 6 in F344/N rats.
Data Qualities Reliabilities	Reliability code 1. Reliable without restriction.
Remarks for Data Reliability	Code 1. Guideline study.
References	NTP (1981) National Toxicology Program. Carcinogenesis Bioassay of FD & C Yellow No. 6. NTP 80-33.
CAS Numerical	2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	91.9% purity; 5.05% water; 2.77% sodium chloride
Method/guideline	National Toxicology Program. Carcinogenesis bioassay NTP 80-33
GLP	Yes
Year	1981
Species/Strain	Mice/B6C3F1
Sex	Male and Female
Route of administration	Oral-Diet
Doses/concentration levels	0, 12,500 or 25,000 ppm
Exposure period	103 weeks
Frequency of treatment	Daily
Control Group	Yes
Post exposure observation period	1 week (female mice)
Remarks for test conditions	Groups of fifty male and fifty female mice each were administered 12,500 or 50,000 ppm FD & C Yellow No. 6 in the diet daily for 103 weeks. Fifty male and female mice each served as concurrent controls. Animals were housed five per cage and fed the test diet ad libitum. The animals were observed twice per day and weighed at least monthly. Necropsies were performed on all animals. Gross and histopathological examinations were performed on all animals. Tissues examined included adrenal glands, brain, cecum, colon, duodenum, epididymus or uterus, esophagus, eyes, femur including marrow, tissue masses, heart, ileum, jejunum, kidneys, liver, lungs and bronchi, mammary gland, lymph nodes, pancreas, parathyroids, pituitary gland, rectum, skin, spleen, stomach, thigh muscle, thymus, thyroid gland, trachea, and urinary bladder.
NOAEL(NOEL)	12,500 ppm
LOAEL(LOEL)	25,000 ppm
Actual dose received by dose level and sex	not determined
Toxic response/effects by dose level	The mean body weights of male and female mice administered the high dose were slightly lower than the control animals throughout most of the study. The survival of male and female mice was similar between treated animals and controls (males: control 38/50 (76%); low dose 40/50 (80%); and high dose 33/50 (66%) and females: control 38/50 (76%); low dose 35/50 (70%) and high dose 43/50 (86%)). An increased incidence in hepatocellular carcinomas was reported among males in the low (46%) and high (32%) dose groups compared to the control males (26%), but was only a significant difference in the low

Appropriate statistical evaluations?	dose mice. No significant differences were observed in the female animals. The increased incidence in hepatocellular carcinomas reported for male mice was not considered clearly related to administration of the test material given the variability in tumour occurrence in control male B6C3F1 mice and because the incidence of these tumours was not significantly increased in the high dose male mice.
Remarks for results	Yes, Cox and Taron
Conclusion remarks	The authors reported that under the conditions of the bioassay, there was no clear evidence of carcinogenicity of FD & C Yellow No. 6 in B6C3F1 mice.
Data Qualities Reliabilities	Reliability code 1. Reliable without restriction.
Remarks for Data Reliability	Code 1. Guideline study.
References	NTP (1981) National Toxicology Program. Carcinogenesis Bioassay of FD & C Yellow No. 6. NTP 80-33.
CAS Numerical	2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	91.9% purity; 5.05% water; 2.77% sodium chloride
Method/guideline	12 week range finding study. National Toxicology Program. Carcinogenesis bioassay NTP 80-33
GLP	Yes
Year	1981
Species/Strain	Rat/F344/N
Sex	Male and Female
Route of administration	Oral-Diet
Doses/concentration levels	0, 6000, 12,500, 25,000, 50,000 or 100,000 ppm
Exposure period	12 weeks
Frequency of treatment	Daily
Control Group	Yes
Post exposure observation period	1 week
Remarks for test conditions	Groups of ten male and ten female rats each were administered 0, 6000, 12,500, 25,000, 50,000 or 100,000 ppm FD & C Yellow No. 6 in the diet daily for 12 weeks followed by one week of control diet only. Animals were housed five per cage and fed the test diet ad libitum. The animals were observed twice per day and weighed weekly. Necropsies were performed on all animals. Gross and histopathological examinations were performed on all animals.

NOAEL(NOEL)	6000 ppm (females); 12,500 ppm (males)
LOAEL(LOEL)	12,500 ppm (females); 25,000 ppm (males)
Actual dose received by dose level and sex	not determined
Toxic response/effects by dose level	No animals died during the study. Decreases in mean body weight gain were reported for male rats at the 25,000, 50,000 or 100,000 ppm intake levels. For female rats, decreases in mean body weight gain were reported at the 12,500, 25,000, 50,000 or 100,000 ppm intake levels. Bone marrow hyperplasia was reported in all examined animals at the 50,000 or 100,000 ppm intake levels.
Appropriate statistical evaluations?	Yes, Cox and Taron
Remarks for results	See Toxic response/effects by dose level.
Conclusion remarks	
Data Qualities Reliabilities	Reliability code 1. Reliable without restriction.
Remarks for Data Reliability	Code 1. Guideline study.
References	NTP (1981) National Toxicology Program. Carcinogenesis Bioassay of FD & C Yellow No. 6. NTP 80-33.

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	91.9% purity; 5.05% water; 2.77% sodium chloride
Method/guideline	12 week range finding study. National Toxicology Program. Carcinogenesis bioassay NTP 80-33
GLP	Yes
Year	1981
Species/Strain	Mice/B6C3F1
Sex	Male and Female
Route of administration	Oral-Diet
Doses/concentration levels	0, 6000, 12,500, 25,000, 50,000 or 100,000 ppm
Exposure period	12 weeks
Frequency of treatment	Daily
Control Group	Yes
Post exposure observation period	1 week
Remarks for test conditions	Groups of ten male and ten female mice each were administered 0, 6000, 12,500, 25,000, 50,000 or 100,000 ppm FD & C Yellow No. 6 in the diet daily for 12 weeks followed by

	one week of control diet only. Animals were housed five per cage and fed the test diet ad libitum. The animals were observed twice per day and weighed weekly. Necropsies were performed on all animals. Gross and histopathological examinations were performed on all animals.
NOAEL(NOEL)	50,000 ppm (male); less than 6000 ppm (female)
LOAEL(LOEL)	100,000 ppm (male); 6000 ppm (female)
Actual dose received by dose level and sex	not determined
Toxic response/effects by dose level	Mean body weight gain was decreased compared to controls among male mice receiving the 100,000 ppm intake level. Decreases in body weight gain were also reported for female mice at all intake levels, and was dose related from 12,500 ppm to 100,000 ppm. Gross and histopathological examinations revealed no treatment related lesions in male or female mice at any intake level.
Appropriate statistical evaluations?	Yes, Cox and Taron
Remarks for results	
Conclusion remarks	
Data Qualities Reliabilities	Reliability code 1. Reliable without restriction.
Remarks for Data Reliability	Code 1. Guideline study.
References	NTP (1981) National Toxicology Program. Carcinogenesis Bioassay of FD & C Yellow No. 6. NTP 80-33.

4.4 DEVELOPMENTAL TOXICITY

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	FD&C Yellow No. 6
Method/guideline	Teratogenicity study
Test Type	
GLP	Ambiguous
Year	1974

Species/Strain	Rat/Charles River CD
Sex	Female
Route of administration	Oral-Gavage
Duration of test	20 days
Doses/concentration levels	0, 100, 300 or 1000 mg/kg bw/day
Exposure period	9 days
Frequency of treatment	Daily
Control Group and treatment	Yes, three negative control groups were maintained and administered 0.5% methocel, while one positive control group was maintained and administered 7.5% mg/kg bw/day of retinoic acid.
Remarks for test conditions	FD&C Yellow No. 6 was administered by gavage at dose levels of 100, 300 or 1000 mg/kg bw/day to 140 female Charles River CD rats. Three negative control groups (20/group) received the vehicle control while one control group received the positive control (7.5% mg/kg bw/day retinoic acid). All females were dosed on days 6-15 of gestation. Cesarean sections were performed on the 20th day of gestation.
NOAEL(NOEL) maternal toxicity	
LOAEL(LOEL) maternal toxicity	Not given
NOAEL (NOEL) developmental toxicity	100 mg/kg bw/day
LOAEL (LOEL) developmental toxicity	300 mg/kg bw/day
Actual dose received by dose level and sex	Not given
Maternal data with dose level	
Fetal data with dose level	The mean weights of the offspring from the 300 and 1000 mg/kg bw/day groups were decreased when compared to the average fetus weight of the combined negative controls. There were no compound related effects on early or late resorptions, empty implantation sites, body weight or numbers of live or dead fetuses. No teratogenicity was observed among the offspring.
Appropriate statistical evaluations?	Not given
Remarks for results	
Conclusion remarks	
Data Qualities Reliabilities	Reliability code 2. Reliable with restriction.
Remarks for Data Reliability	Code 2. Basic data given: comparable to guidelines/standards.
References	International Research and Development Corporation (1972) Teratology study in rats. Compound FD&C Yellow No. 6. Unpublished report no. 306-004.

4.5 REPRODUCTIVE TOXICITY

CAS Numerical 2783-94-0

Substance Name	Sunset Yellow
Remarks for Substance	FD&C Yellow No. 6
Method/guideline	3-generation reproductive study
Test Type	
GLP	Ambiguous
Year	1974
Species/Strain	Rat/Charles River CD
Sex	Male and Female
Route of administration	Oral-Diet
Duration of test	
Doses/concentration levels	5, 50, 150 or 500 mg/kg bw/day
Premating Exposure period for males	
Premating Exposure period for females	
Frequency of treatment	Daily
Control Group and treatment	Yes.
Remarks for test conditions	One hundred twenty Charles River CD rats (10 males and 20 females/group/generation) received 5, 50, 150 or 500 mg/kg bw/day of the test substance as a dietary admixture in a three-generation study. Ten males and twenty females received no compound and served as controls.
NOAEL(NOEL)	500 mg/kg bw/day
LOAEL(LOEL)	Not determined
Actual dose received by dose level and sex Parental data and F1 as appropriate	Not given

Offspring toxicity F1 and F2

Appropriate statistical evaluations?

Remarks for results

There were no compound related effects on fertility, gestation, pup viability or lactation indices, on reproductive organs of females, or on organ weights among parents and offspring. There were no compound related lesions in any tissue examined histologically, including kidneys and adrenal glands from parental rats or from offspring.

Conclusion remarks

Data Qualities Reliabilities

Reliability code 2. Reliable with restriction.

Remarks for Data Reliability

Code 2. Basic data given: comparable to guidelines/standards.

References

International Research and Development Corporation (1974) Multi-generation reproduction study in rats. Compound FD&C Yellow No. 6. Unpublished report no. 306-005.