FOREWORD INTRODUCITON

C.I. Pigment Yellow 53

CAS N°: 8007-18-9

SIDS Initial Assessment Report

For

SIAM 15

Boston, Massachussetts, 22 - 25 October 2002

1.	**Chemical Name:**	C.I. Pigment Yellow 53
2.	**CAS Number:**	8007-18-9
3.	**Sponsor Country:**	Japan
4.	**Shared Partnership with:**	Dr. Hubert Lendle BASF AG
5.	**Roles/Responsibilities of the Partners:**	
•	Name of industry sponsor /consortium	Dr. Hubert Lendle/ BASF AG E-mail : hubert.lendle@basf-ag.de
•	Process used	This substance is sponsored by Japan under the ICCA Initiative and is submitted for first discussion at SIAM 15.
6.	**Sponsorship History**	
•	How was the chemical or category brought into the OECD HPV Chemicals Programme ?	This substance is sponsored by Japan under the ICCA Initiative and is submitted for first discussion at SIAM 15.
7.	**Review Process Prior to the SIAM:**	The industry collected new data and prepared the updated IUCLID, and draft versions of the SIAR and SIAP. Japanese government peer-reviewed the documents, audited selected studies. no testing (X) testing ( )
8.	**Quality check process:**	
9.	**Date of Submission:**	
10.	**Date of last Update:**	
11.	**Comments:**	

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	8007-18-9
Chemical Name	C.I. Pigment Yellow 53
Structural Formula	Complex inorganic coloured pigment based on titanium oxide; in the rutile lattice, titanium ions are partially replaced by nickel (II) and antimony (V) ions. (Ti, Ni, Sb) O_2

SUMMARY CONCLUSIONS OF THE SIAR

C.I. Pigment yellow 53 is a solid, complex inorganic coloured pigment, based on titanium dioxide with nickel (II) and antimony (V) ions partially replacing titanium ions in the rutile lattice. It is practically inert and has a melting point above 1000 °C. The vapour pressure is estimated to be negligible. C.I. Pigment yellow 53 has an extremely low solubility in water; the concentration of nickel and antimony in filtrates (10 g/l) has been measured by atomic absorption to be <0.01 mg/l.

Human Health

No mortalities or clinical signs of toxicity were observed in male and female rats in an acute oral study; LD50 > 2000 mg/kg body weight [OECD TG 401].

C.I. Pigment Yellow 53 is minimally irritating to the rabbit skin immediately after application due to mechanical effects and slightly irritating to the rabbit eye for the same reason. No data are available on sensitisation. The substance contains nickel, however, which has been shown to be not biologically available following repeated inhalation and oral exposure in rats.

No signs of clinical toxicity or histopathological changes were seen in a 90 day feeding study in rats tested up to 450 mg/kg bw or in a combined repeat dose and/reproductive screening study conducted according to OECD TG 422. A NOAEL of 1000 mg/kg was identified in rats for repeated oral toxicity from the OECD 422 study. In a rat inhalation study, exposure to 60 mg/m^3 for 6 hr/day for 5 days produced no clinical signs of toxicity. However, the absence of histological examination prevents identification of a reliable NOAEC.

In *in vitro* genotoxicity tests no gene mutation in bacteria or mammalian cells and no clastogenic or aneugenic effects in mammalian cells were observed. There are no data available for *in vivo* genotoxicity. However, based on the *in vitro* data, there is no indication that C.I. Pigment Yellow 53 would exhibit genotoxic potential *in vivo*.

There are no specific studies on carcinogenicity.

No adverse effects on reproduction and development were observed in a reproductive/developmental toxicity screening test conducted according to OECD Guideline 422 using male and female rats treated via gavage up to 1000 mg/kg bw/day. The NOAEL for fertility for males and females = 1000 mg/kg bw/day (highest dose tested), the NOAEL for maternal toxicity = 1000 mg/kg bw/day (highest dose tested), and the NOAEL for development = 1000 mg/kg bw/day (highest dose tested). No histological changes on the gonads were observed in rats in the 90 d feeding study tested up to 450 mg/kg.

As for bioavailability of C.I. Pigment Yellow 53, in the same 90 day feeding study (see above) in rats, traces (below 30 µg/kg) of antimony were detected in liver and kidney of rats, but exclusively in the high dose group. These traces most likely originate from acid-soluble impurities. Anyhow, the traces of antimony detected in liver and kidney are considered to have no toxicological significance. No treatment related increase in nickel concentration was detected in liver and kidney at any dose level and exposure duration. The nickel and antimony concentration of liver and kidney in rats after inhalation exposure to 60 mg/m³ C.I. Pigment Yellow 53 was within the range of quantification limit or below. A bioavailability of nickel and antimony from the pigment was not demonstrated. The pigment dust

is eliminated from the lungs with a half-life of about 50 days which is typical for nuisance dusts.

Environment

The following aquatic effects concentrations (nominal) are available:

Tests with *Oryzias latipes*, *Daphnia magna* and *Selenastrum capricornutum* each show no toxic effects in the range of water solubility.

Investigations well above the water solubility show the following results:

Leuciscus idus: LC_{50} (96 h) > 10,000 mg/l; *Daphnia magna*: EC_{50} (48 h) > 100 mg/l; *Desmodesmus subspicatus*: EC_{50} (72 h)> 100 mg/l; *Pseudomonas putida*: EC_{50} (30 min) > 10,000 mg/l.

In a reproduction study with *Daphnia magna* a NOEC (21 d) >1 mg/l has been derived.

The substance is not acutely toxic to aquatic organisms (fish, invertebrates and algae) in tests with either aqueous extracts or suspensions prepared with nominal concentrations far exceeding its water solubility. Furthermore, no chronic effects towards *Daphnia magna* were observed.

No data are available on terrestrial organisms.

The substance is inorganic and thus not biologically degradable. According to the low water solubility and the structural properties of the pigment, bioaccumulation is not expected.

Exposure

Pigment yellow 53 is used for coloring plastics, ceramics, building materials and coatings. In 2001 the estimated world production amounts to 5,000 – 10,000 tonnes.

No data are available concerning exposure. Pigments released from production sites and not having been eliminated mechanically, will probably absorb to sewage sludge. In the endproducts, the pigments are fixed in the matrix and a release into the environment during use is not expected.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

This chemical is currently of low priority for further work based on a low hazard potential.

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number:	8007-18-9
Chemical Name:	C.I. Pigment Yellow 53
Empirical Formula:	(Ti, Ni, Sb) O_2
Structure:	Complex inorganic coloured pigment based on titanium dioxide; in the rutile lattice, titanium ions are partially replaced by 2 to 5 % nickel (II) and 9 to 12 % antimony (V) ions a typical analysis taken from a tested charge is: TiO2: 80%, Sb2O5: 14%, NiO: 4% According to the intended use, medium particle size varies between 0.5 and 1.5 µm.
Synonyms:	C. I. 77788 Nickel antimony titanium dioxide rutile Nickel antimony titanate yellow

1.2 Purity/Impurities/Additives

Substance type: inorganic

Physical status: solid

Purity: > 99% w/w (acid-soluble impurities amount to 10 –20 mg/kg antimony and 30 - 40 mg/kg nickel). These impurities are not fixed in the lattice and are extractable with HCl. After 2extractions with HCl, the acid soluble impurities are reduced to amounts below the detection limit (<1 mg/kg for Sb and <5 mg/kg for Ni)

1.3 Physico-Chemical properties

C.I. Pigment Yellow 53 has an extremely low solubility in water, the concentration of nickel and antimony in filtrates of a 10 g/l solution after 2h-stirring has been measured by atomic absorption to be <0.01mg/l (BASF AG, 2002a). The melting point is greater than 1000°C and the density reached 4-5 g/cm³ (DIN-ISO 787/10) (BASF AG, 2000). A negligible vapour pressure can be assumed for this mixed metal oxide. Nickel and antimony partially substituted titanium in the titanium dioxide lattice and are not available as metal ions or metal oxides (MAK-Begründung, 1983).

2 GENERAL INFORMATION ON EXPOSURE

In 2001 the estimated world production amounts to 5,000 – 10,000 tons, thereof in Europe 1,000 – 5,000 t/a (Germany 1,000 – 5,000 t/a), in the NAFTA 1,000 – 5,000 t/a and in Asia 1,000 to 5,000 t/a (Japan 1,000 to 5,000) (BASF AG, 2002b). Pigment yellow 53 is used for colouring plastics, ceramics, building materials and coatings. In the Swiss Product Register, about 60 products are listed (main category: “paint and dyes”, a few in the categories: “plastic moulding” and “ceramic colours”), about 10 of them are consumer products (“dyes for artists” and “ceramic colours”). The SPIN database lists for the year 2001 for Norway 30 products (651 tons), for Denmark 62 products (238 tons), for Finland 4 products (0 tons). For Sweden 44 products are given for the year 2000 (271 tons). The preparations listed for Norway and Sweden include products for consumer use, in Denmark and Finland, none of the products is for consumer use.

2.1 Environmental Exposure and Fate

Doped rutile pigments are manufactured by reacting finely divided metal oxides, hydroxides or carbonates in the solid state at a temperature of 1000 to 1,200 °C. The production is based on reactive anatase, or titanium dioxide hydrolysate containing sulfuric acid, and on the oxidation of trivalent antimony with oxygen in the form of nitric acid or air. For the production of C.I. Pigment Yellow 53 nickel metal oxide, hydroxide or carbonate is used. At the German production site, raw-material dust, and gases (e.g. SO3 and NOx), emitted during the calcination step are removed from the flue gas by dust separators and alkaline flue scrubbers. The raw-material dust is recycled. Soluble metal salts are removed by neutral precipitation in the waste-water treatment plant, and suspended pigment particles are mechanically separated from the water from washing and purification steps. Altogether, only a small amount of waste is produced with each tonne of product (Endriß H., 1998). In the end products, the pigments are fixed in the matrix and a release into the environment during the use phase is not expected (coatings) or impossible (coloured plastics and ceramics). Pigments released from production sites and not having been eliminated mechanically will probably absorb to sewage sludge.

Distribution modelling is not applicable since several physical parameters are not available.

C.I. Pigment Yellow 53 is an inorganic substance, biodegradation therefore is not assumed.

No data on bioaccumulation are available. However, regarding the extremely low water solubility, experiences from rodent investigations and the structure-related inert properties of the rutile, bioavailability and therefore bioconcentration is not expected.

(see also data on bioavailability in mammals after oral exposure [section 3.2.1 and 3.2.5])

2.2 Human Exposure

No data are available concerning exposure with the practically inert pigment. This pigment is produced as very fine powder and becomes respirable if it is airborne. The ACGIH recommends that airborne concentration in workplace should be kept below 3 mg/m3 for respirable biologically inert particles.

Migration tests with different plastics containing 1% of the pigment showed that in food stuff simulants, concentrations of Ni and Sb were below the detection limit (<0.3µg Ni/l and <0.25 µg Sb/l).

3 HUMAN HEALTH HAZARDS

3.1 Hazard Assessment Experience with Human Exposure

3.1.1 Experience with human exposure

No data are available.

3.2 Effects on Human Health

3.2.1 Toxicokinetics, Metabolism and Distribution

Concentration of nickel and antimony were analysed in liver and kidney of rats after oral exposure to C.I. Pigment Yellow 53 in a 90-days feeding study in monthly intervals (Bombard E. et al.,

1982). The administered doses were 0.45, 4.5, 45, and 450 mg/kg b.w./day. The detection limit for antimony was 5 µg/kg tissue and for nickel 10 µg/kg. In male and female rats the antimony concentrations in liver and kidney were below the detection limit at all doses measured after 1 and 2 months. After 3 months only in the high dose group antimony was detectable slightly above detection limit in liver (6 µg/kg) and kidney (5 µg/kg) of male rats and in females at levels of 6 (liver) and 10 (kidney) µg/kg. These traces most likely originate from the content of acid-soluble components (10 –20 mg antimony /kg pigment, that is 5 – 10 µg/kg b.w. or 125 - 250 µg/kg organ weight at the highest dose) and therefore do not indicate bioavailability of the pigment itself. No treatment related increase in nickel concentration was detected in liver and kidney at any dose level and exposure duration.

The bioavailability of nickel and antimony from inhaled C.I. Pigment Yellow 53 at an exposure level of 60 mg/m³ was studied in male rats (BASF AG, 1994). The nickel and antimony concentration in lung, liver and kidney were determined.

The mean nickel concentration in the liver was below the quantification limit in both exposed and in unexposed controls (but not held under comparable conditions like the exposed rats). In the kidney, the mean nickel concentration was below the detection limit in unexposed rats and above the detection limit but below the quantification limit in exposed animals, with the exception of an outlyer on day 3 post exposure presumably due to a contamination of the sample. In the liver, the mean antimony concentration (quantification limit 0.2 µg/kg) was 1.1 µg/kg in controls; maximal a 4-fold higher value was detected in exposed rats on post exposure day 3; but the concentration declined to control value with further observation. In the kidney, the antimony concentration in exposed rats was above the detection limit (1 µg/kg; controls below detection limit) but below the quantification limit (3 µg/kg); only on post exposure day 3 a concentration slightly above the quantification limit was detected (5.6 µg/kg).

During the post exposure period, the concentrations declined following first order kinetics. The muco-ciliar clearance half-life was about 50 days.

Conclusion

In a 90 day feeding study on rats (up to 450 mg C.I. Pigment Yellow 53 /kg b.w./day) no bioavailability was demonstrated. However, traces of antimony may be available from the acid-soluble impurities of the pigment.

There was also no detectable bioavailability after exposure to 60 mg/m³ C.I. Pigment Yellow 53. The pigment dust is eliminated from the lungs with a muco-ciliar clearance half-life of about 50 days which is typical for nuisance dusts.

3.2.2 Acute Toxicity

(Most recent Guideline Study according to OECD 401. Peer review was conducted by a Japanese Toxicological Expert Group in March 2001.)

LD_{50} rat (oral) (Ministry of Health, Labour and Welfare, 2002): > 2000 mg/kg body weight. The GLP study was performed according to OECD Guideline 401. No mortalities, growth depression, overt signs of toxicity or relevant autopsy findings at sacrifice after 14 days of observation.

Other acute oral studies in rat with LD50 values from >2,500 to > 10,000 mg/kg b.w. have been reported (TSCA a-c, BASF, 1978). Though the studies have been reported in less detail and have a restricted reliability they corroborate the low acute oral toxicity of the substance.

Conclusion

There was no acute toxicity at oral doses of 2000 mg/kg body weight and greater

3.2.3 Irritation

Skin Irritation

Occlusive patches loaded with 500 mg of the pigment resulted in minimal irritation (erythema and edema; mean score 0.7) of the abraded and intact skin of 6 rabbits when the patches were removed after 24 h exposure. Minimal irritation (mean score 0.3) was also observed one day after removal and no effects 2 days after removal (TSCA d).

In studies following the experimental design according to Federal Register 38, No. 187, § 1500.41, S. 27019, 27. Sept. 1973, the application of 50% C.I. Pigment Yellow 53 in water to the skin of 6 rabbits resulted also only in slight erythema (primary irritation value 0.2; no edema) of abraded skin but no irritation with intact skin after 72 hr, although evaluation of erythema after 24 hr was impossible due to treatment related colouring of the skin (Ministry of Health, 2002).

Conclusion

C.I. Pigment Yellow 53 is considered to be minimally irritating to the rabbit skin due to both the slight degree and the reversibility of the effects after 8 days.

Eye Irritation

Instillation of 100 mg C.I. Pigment Yellow 53 into the conjunctival sac of 3 rabbits resulted in no effects on mucous membrane, cornea or iris 1-7 days after application. In additional experiments, treated eyes of rabbits were rinsed 30 sec after instillation and 1 out of 3 animals showed erythema (mean reaction score 0.7; no further effects) 24 h after treatment but not at later time points (TSCA e).

Following the experimental design according to Federal Register 38, No. 187, § 1500.42, S. 27019, 27. Sept. 1973, no effects on cornea and iris but slight (in 5/6 rabbits) or clear (in 1/6 animals) erythema were observed 24 h after instillation of the test substance. These effects were reversible; 48 h after treatment slight erythema was seen in 3/6 animals and after 72 h in 2/6 rabbits (BASF, 1978).

The results indicate a mechanical irritation of the mucous membrane due to the instillation of test substance particles.

Conclusion

C.I. Pigment Yellow 53 may lead to slight irritation in the rabbit eye after instillation.

3.2.4 Sensitisation

No data available. The substance contains nickel, which has been proven to be not bioavailable following a repeat oral and a repeat inhalation study in the rat.

3.2.5 Repeated Dose Toxicity

(These studies were selected as a Key Studies as they present results of substance application by different routes of application. In their majority they are GLP compliant Guideline Studies or of equivalent validity.)

In a feeding study (Bombard E et al., 1982)- rats received 0, 10, 100, 1000, 10000 mg C.I. Pigment Yellow 53 per kg diet (corresponding to 0, 0.45, 4.5, 45, 450 mg/kg b.w./day) for 90 days. 15 animals per dose per gender were used for toxicological investigations (30 animals per gender in the control group) and additionally 10 animals per dose and gender for analytical investigations (control 20 animals per gender). Rats were observed daily; food consumption and body weight gain were determined once per week. Haematology, urinalysis and clinical and biochemical investigations were conducted after one month and at the end of the study (no post exposure observation period). Organ weights were determined at necropsy (thyroid gland, thymus, heart, lung, liver, spleen, kidneys, adrenal glands, and gonads). Complete histopathological investigations (above mentioned organs studied plus aorta, eyes, intestine, femur, brain, urinary bladder, pituitary, cervical lymph nodes, stomach, oesophagus, epididymides, pancreas, prostate, seminal vesicle, bone marrow of sternum, trachea, uterus, and skeletal muscles) were performed on 5 rats per gender of control and high dose group. Concerning the toxicity of C.I. Pigment Yellow 53 no treatment related effects were observed in male and female rats in any parameter described above. The NOAEL determined in this study was 450 mg/kg b.w./day.

In a combined repeated dose and reproductive toxicity screening test on male and female rats according to OECD guideline 422 (see also section 3.2.8 for further details) doses of 250, 500 and 1000 mg/kg b.w./day given by gavage for 41-46 days C.I. Pigment Yellow 53 resulted in no significant effects on growth, clinical signs, body weight gain, food consumption, haematology and biochemistry. No gross pathological changes and no effects on organ weight were observed at necropsy. Furthermore no alterations were seen in histopathology (Ministry of Health, 2002). The NOAEL determined in this study was 1000 mg/kg b.w./day.

In an inhalation study on male rats (BASF, 1994), the bioavailability of nickel and antimony from inhaled C.I. Pigment Yellow 53 was investigated (for details see section 3.2.1). Rats exposed 6 hours per day to 60 mg C.I. Pigment Yellow 53 per m³ for 5 days showed no clinical signs of poisoning, no effects on body weight and no mortality during exposure and in post exposure observation period of up to 60 days. The exposure level was set to a ten fold higher level than the limit level for inert dusts set at that time by the German MAK Commission. It was further selected to warrant a sufficiently high Ni deposition in the lung in relation to the relative Ni content in the pigment and in relation to the analytical detection limit. A NOAEL could not be derived from this study because of no examinations on hematology, blood biochemistry, organ weight and histopathology were carried out.

Conclusion

In a 90 day feeding study on rats doses up to 450 mg/kg b.w./day resulted in no adverse effects. In a combined repeated dose and reproductive toxicity screening test on male and female rats according to OECD guideline 422, no adverse effects were observed:

NOAEL = 1000 mg/kg b.w./day (highest dose tested).

In an inhalation study on male rats, no clinical signs of poisoning and no effects on body weight were observed during 5 days inhalation exposure to 60 mg/m³ for 6 hours per day and in the post exposure observation period of up to 60 days.

3.2.6 Mutagenicity

(The studies reported were either OECD Guideline studies or of comparable quality.)

In vitro studies following the current guideline standards have shown that C.I. Pigment Yellow 53 has no activity at different genotoxic endpoints. A suspension of the insoluble test substance induced no gene mutation in the bacterial reverse mutation test (OECD guideline 471 & 472; max.

concentration 5 mg/plate; no cytotoxicity) on Salmonella typhimurium strain TA98, TA100, TA1535, TA1537,and TA1538 (Corning Hazelton, 1995), and on E. coli WP2uvrA (BASF, 1994; Ministry of Health, 2002), and in the mouse lymphoma assay (comparable to OECD guideline 476; max. concentration 100 µg/ml; no cytotoxicity)(Corning Hazelton, 1996), each with and without metabolic activation. Furthermore, no clastogenic activity and no polyploidy was observed in the chromosomal aberration test (OECD guideline 473) on Chinese hamster lung cells with and without metabolic activation (Ministry of Health, 2002), although cytotoxicity was observed in different experimental designs. In the Chromosomal Aberration Test the maximal test concentrations were 78.1, 1250, and 78.1 µg/ml (-S9 mix, +S9 mix; both short term treatment, and –S9 mix, continous treatment). Cytoxicity was observed at mone than 39.1, 78.1 and 19.5 µg/l (-S9 mix, +S9 mix; both short term treatment, and –S9 mix, continous treatment).

Conclusion

C.I. Pigment Yellow 53 induced, with or without addition of a metabolic activation system, no gene mutation in bacteria or mammalian cells and no clastogenic or aneugenic effects in mammalian cells. There are no in-vitro data to indicate that C.I. Pigment Yellow 53 would exhibit a genotoxic potential in vivo. There are no data available for in-vivo genotoxicity.

3.2.7 Carcinogenicity

No data available.

3.2.8 Toxicity for Reproduction

(This study was selected as a recent Guideline Study. No other studies to this endpoint are available. The study is valid without restriction.)

In a combined repeated dose (see also section 3.2.5) and reproductive/ developmental toxicity screening test according to OECD guideline TG 422 12 male and 12 female rats per group received 0, 250, 500, 1000 mg/kg bw/day (Ministry of Health, 2002) by gavage. The exposure period for males was 46 days and for females 41-45 days throughout mating and pregnancy up to day 4 post natal. The premating exposure period for both gender was 14 days. The treatment was without any effects on reproductive parameters (estrous cycle, copulation index, fertility index, gestation index, gestation length, nursing index, number of pregnant females, number of corpora lutea and implantation sites, implantation index and delivery index). Furthermore, no effects were observed on live birth index, sex ratio of pups, number of pups alive on day 4 of lactation, viability index, body weight of live pups on day 0 and 4 post natal. The full macroscopic examination of all pups revealed no external anomalies or any other necropsy findings. The NOAEL for Reproduction and for Development were determined as 1000 mg/kg b.w./day in this study. No effects on gonads were observed in the 90 day feeding study on rats at doses up to 450 mg/kg b.w./day (see section 3.2.5).

Conclusion

No adverse effects on reproduction and development were observed in a reproductive / developmental toxicity screening test according to OECD guideline TG 422 on male and female rats treated via gavage with up to 1000 mg/kg bw/day.

NOAEL males = 1000 mg/kg b.w./day (highest dose tested)

NOAEL females = 1000 mg/kg b.w./day (highest dose tested)

3.2.9 Developmental Toxicity

(This study was selected as a recent Guideline Study. No other studies to this endpoint are available. The study is valid without restriction.)

Data on the study according to OECD guideline 422 are presented in section 3.2.8.

NOAEL maternal = 1000 mg/kg b.w./day (highest dose tested)

NOAEL development = 1000 mg/kg b.w./day (highest dose tested)

3.2.10 Initial Assessment for Human Health

There is no acute toxicity of C.I. Pigment Yellow 53 after oral exposure, based on the following data: No death of male and female rats up to 2000 mg/kg body weight with no toxic signs [OECD TG 401].

C.I. Pigment Yellow 53 is not irritating to the rabbit skin and slightly irritating to the rabbit eye.

No data are available on sensitisation; the non-bioavailability of the nickel (potential sensitising component of the pigment) via the oral and inhalative route indicated no sensitising potential.

In a 90 day feeding study on rats doses up to 450 mg/kg b.w./day resulted in no adverse effects in clinical observation, haematology, urine analysis, clinical chemistry and macro- and microscopical pathology. In a combined repeated dose and reproductive toxicity screening test on male and female rats according to OECD guideline 422, no adverse effects were observed at doses of up to 1000 mg/kg b.w./day given by gavage for 41-46 days. In a bioavailability study on male rats, no clinical signs of poisoning and no effects on body weight were observed during 5 days inhalation exposure to 60 mg/m³ for 6 hours per day and in the post exposure observation period of up to 60 days.

In vitro genotoxicity tests indicated that the substance has no genotoxic activity. In-vivo genotoxicity tests are not available.

There are no specific studies on carcinogenicity.

No adverse effects on reproduction and development were observed in a reproductive/ developmental toxicity screening test according to OECD guideline 422 on male and female rats treated via gavage with up to 1000 mg/kg b.w./day.

As for bioavailability of C.I. Pigment Yellow 53, in the 90 day feeding study (see above) on rats using doses up to 450 mg/kg b.w./day, traces below 30 µg/kg tissue of antimony were detected in liver and kidney of rats but exclusively in the high dose group. These traces are considered to have no toxicological significance. No treatment related increase in nickel concentration was detected in liver and kidney at any dose level and exposure duration. The nickel and antimony concentration of liver and kidney in rats after inhalation exposure to 60 mg/m³ C.I. Pigment Yellow 53 was within the range of quantification limit or below. A bioavailability of nickel and antimony from the pigment was not demonstrated. The pigment dust is eliminated from the lungs with a half-life of about 50 days which is typical for nuisance dusts.

4 HAZARDS TO THE ENVIRONMENT

The following acute toxicity tests with aquatic organisms are available:

Oryzias latipes	LC_{50} (96h) >1 mg/l	Limit-test, semistatic, aqueous extract tested (stock 1 mg/l). Analytical monitoring. Data refer to nominal concentrations.	MOE (2001)
Leuciscus idus	LC_{50} (96 h) > 10000 mg/l NOEC (96 h) = 10000 mg/l	Tested above the water solubility. No analytical monitoring. Data refer to nominal concentrations.	BASF (1988)
Daphnia magna	EC_{50} (48h) > 1 mg/l	Limit-test, semistatic, aqueous extract tested (stock 1 mg/l). Analytical monitoring. Data refer to nominal concentrations.	MOE (2001)
Daphnia magna	EC_{50} (48 h) > 100 mg/l EC_0 (48 h) ≥ 100 mg/l	Aqueous extract tested (stock 100 mg/l, centrifugation after 20 hours of stirring). No analytical monitoring. Data refer to nominal concentrations.	BASF AG (1999)
Selenastrum capricornutum	ErC_{50} (72h) > 1 mg/l EbC_{50} (72h) > 1 mg/l NOEC (72h) > 1 mg/l	Limit-test, aqueous extract tested (stock 1 mg/l). Analytical monitoring. Data refer to nominal concentrations.	MOE (2001)
Desmodesmus subspicatus	ErC_{50} (72 h) > 100 mg/l ErC_{10} (72 h) > 100 mg/l EbC_{50} (72 h) > 100 mg/l EbC_{10} (72 h) = 64.1 mg/l NOEC (72 h) = 25 mg/l	Aqueous extract tested (stock 100 mg/l, centrifugation after 20 hours of stirring). No analytical monitoring. Data refer to nominal concentrations.	BASF AG (2001)
Pseudomonas putida	EC_{50} (30 min) > 10000 mg/l; EC_{10} (30 min) = 5680 mg/l	Tested above the water solubility. No analytical monitoring. Data refer to nominal concentrations.	BASF AG (1997)

The ecotoxicities shown in this table are greater than the water solubility which seems to be very low. In the three tests with *Orizias latipes*, *Daphnia magna* and *Selenastrum capricornutum* (MOE, Japan, 2001) the test condition was not clear concerning the preparation of the test solution. Therefore the toxicity value should be used with caution; however these test results may show that no effects are observed at the concentration of water solubility of C.I. Pigment Yellow 53.

A slight effect on the growth (based on biomass) was observed in the algae *Desmodesmus subspicatus* (= *Scenedesmus subspicatus*) at a threshold value below nominal 100 mg/l [EbC_{10} (72 h) = 64.1 mg/l], which probably is due to depletion of light intensity for coloration or cloud in test water at high concentrations. The name of genus *Desmodesmus* have been used as a part of *Scenedesmus* species as a different genus by some researchers or as subgenus of *Scenedesmus*.

Detectable effects on bacteria in the oxygen consumption test at high concentrations were also reported.

However, based on short-term tests from each of the four trophic levels, C.I. Pigment Yellow 53 can be regarded as acutely not harmful to aquatic organisms.

A chronic test with *Daphnia magna* showed no effect on reproduction. For this test also the procedure for preparation of the test solution was not shown in the original report (MOE, 2001), it should be used with caution.

Daphnia magna	NOEC (21 d) >1 mg/l	Limit-test, semistatic, aqueous extract tested (stock 1 mg/l). Analytical monitoring. Data refer to nominal concentrations.	MOE (2001)

No data are available on terrestrial organisms.

The cited studies are carried out according to nationally and/or internationally accepted guidelines and are considered as valid.

4.1 Initial Assessment for the Environment

C.I. Pigment yellow 53 is a solid, complex inorganic coloured pigment, based on titanium dioxide with nickel (II) and antimony (V) ions partially replacing titanium ions in the rutile lattice. It is practically inertand has a melting point above 1000 °C. The vapour pressure is estimated to be negligible. C.I. Pigment yellow 53 has an extremely low solubility in water; the concentration of nickel and antimony in filtrates (10 g/l) has been measured by atomic absorption to be <0.01 mg/l.

The following aquatic effect concentrations (nominal) are available:

Tests with *Oryzias latipes*, *Daphnia magna* and *Selenastrum capricornutum* each show no toxic effects in the range of water solubility.

Investigations well above the water solubility show the following results:

Leuciscus idus: LC_{50} (96 h) > 10000 mg/l; *Daphnia magna*: EC_{50} (48 h) > 100 mg/l; *Desmodermus subspicatus*: EC_{50} (72 h)> 100 mg/l; *Pseudomonas putida*: EC_{50} (30 min) > 10000 mg/l.

In a reproduction study with *Daphnia magna* a NOEC (21 d) >1 mg/l has been derived.

The substance is not acutely toxic to aquatic organisms (fish, invertebrates and algae) in tests with either aqueous extracts or suspensions prepared with nominal concentrations far exceeding its water solubility. Furthermore, no chronic effects towards Daphnia magna were observed.

No data are available on terrestrial organisms.

The substance is inorganic and thus not biologically degradable. According to the low water solubility and the structural properties of the pigment, bioaccumulation is not expected.

5 RECOMMENDATIONS

This chemical is currently of low priority for further work based on a low hazard potential.

6 REFERENCES

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TSCA (a), OTS0001087, Doc ID FYI-OTS-0794-1087 submitted by Dry Colour MFGS Assn (tests performed at Ro Rosner-Hixon Laboratories, Basel, Switzerland

TSCA (d), OTS0001087, Doc ID FYI-OTS-0794-1087 submitted by Dry Colour MFGS Assn (tests performed at Ciba-Geigy Laboratories, Basel, Switzerland; GU Project No. 821126)

TSCA (b), OTS0001087, Doc ID FYI-OTS-0794-1087 submitted by Dry Color MFGS Assn (tests performed at Duke Laboratories)

TSCA (e), OTS0001087, Doc ID FYI-OTS-0794-1087 submitted by Dry Colour MFGS Assn (tests performed at Ciba-Geigy Laboratories, Basel, Switzerland; GU Project No. 821125)

TSCA (c), OTS0001087, Doc ID FYI-OTS-0794-1087 submitted by Dry Colour MFGS Assn (tests performed at Ciba-Geigy Laboratories, Basel, Switzerland

ANNEX

Date of the literature search (August 27, 2001)

Toxicology

JETOC
RTECS
AGRICOLA
CABA
CANCERLIT
TOXCENTER
TOXLINE
JICST-EPLUS
LIFESCI
TOXLIT
EMBASE
ESBIOBASE
EMBAL
HEALSAFE
CSNB
MEDLINE
IRIS
ATSDR TOX. PROFILES
ATSDR TOX: FAQS
CHEMFINDER
CIVS
GESTIS
GINC
NICNAS
NTP

Oecology

AQUASCI
BIOSIS
EMBASE
ESBIOBASE.
LIFESCI
OCEAN
POLLUAB
SCISEARCH
TOXCENTER
TOXLINE
ULIDAT
DATALOG
CHEMFATE
BIODEG
AQUIRE
HSDB

I U C L I D

D a t a S e t

Existing Chemical ID: 8007-18-9
CAS No. 8007-18-9
EINECS Name C.I. Pigment Yellow 53
EC No. 232-353-3

Producer Related Part
Company: BASF AG
Creation date: 22-FEB-1994

Substance Related Part
Company: BASF AG
Creation date: 22-FEB-1994

Memo: master

Printing date: 01-DEC-2004
Revision date:
Date of last Update: **21-APR-2004**

Number of Pages: **65**

Chapter (profile): Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile): Reliability: without reliability, 1, 2, 3, 4
Flags (profile): Flags: without flag, SIDS

1.0.1 Applicant and Company Information

Type: lead organisation
Name: BASF AG
Contact Person: Product Safety **Date:**
c/o Dr. Hubert Lendle
GUP/CL - Z570
Street: Carl-Bosch-Strasse
Town: 67056 Ludwigshafen
Country: Germany
Phone: + 49 621 60 44712
Telefax: + 49 621 60 6644712
Email: hubert.lendle@basf-ag.de
Homepage: www.basf-ag.de

Flag: Critical study for SIDS endpoint
01-APR-2004

Type: cooperating company
Name: Bayer AG
Country: Germany

Flag: Critical study for SIDS endpoint
14-MAR-2003

Type: cooperating company
Name: Broll Buntpigmente GmbH
Country: Germany

Flag: Critical study for SIDS endpoint
14-MAR-2003

Type: other: cooperating organisation
Name: Color Pigments Manufacturers Ass. (CMPA), Inc.
Country: United States

Flag: Critical study for SIDS endpoint
14-NOV-2002

Type: cooperating company
Name: Dr. Hans Heubach GmbH & Co. KG
Country: Germany

Flag: Critical study for SIDS endpoint
14-MAR-2003

Type: cooperating company
Name: Ishihara Sangyo Kaisha, Ltd.
Country: Japan

Flag: Critical study for SIDS endpoint
14-MAR-2003

Type: cooperating company
Name: Kawamura Chemical Co., Ltd.
Country: Japan

Flag: Critical study for SIDS endpoint
14-MAR-2003

1.0.2 Location of Production Site, Importer or Formulator

1.0.3 Identity of Recipients

1.0.4 Details on Category/Template

1.1.0 Substance Identification

Mol. Formula: unspecified

Flag: non confidential, Critical study for SIDS endpoint
14-NOV-2002

1.1.1 General Substance Information

Substance type: inorganic
Physical status: solid
Purity: > 99 - % w/w
Colour: yellow
Odour: odourless

Flag: non confidential, Critical study for SIDS endpoint
12-MAR-2003 (1)

1.1.2 Spectra

1.2 Synonyms and Tradenames

Antimony nickel titanium oxide yellow

Flag: non confidential, Critical study for SIDS endpoint
27-AUG-1996

C.I. 77788

Flag: non confidential, Critical study for SIDS endpoint
27-AUG-1996

C.I. Pigment Yellow 53 (8CI, 9CI)

Flag: non confidential, Critical study for SIDS endpoint
27-AUG-1996

Nickel antimony titanate yellow

Flag: non confidential, Critical study for SIDS endpoint
27-AUG-1996

Nickel antimony titanium yellow rutile

Flag: non confidential, Critical study for SIDS endpoint
27-AUG-1996

Pigment Yellow 53

Flag: non confidential, Critical study for SIDS endpoint
27-AUG-1996

1.3 Impurities

1.4 Additives

1.5 Total Quantity

Remark: Production quantity (year of reference: 2001):

Europe : 1000 - 5000 t/a
includes Germany: 1000 - 5000 t/a

USA : 1000 - 5000 t/a

Asia : 1000 - 5000 t/a
includes Japan : 1000 - 5000 t/a

World : approx. 7000 t/a
Flag: non confidential, Critical study for SIDS endpoint
04-DEC-2001

1.6.1 Labelling

Labelling: no labelling required (no dangerous properties)

Flag: non confidential, Critical study for SIDS endpoint
14-NOV-2002 (1)

1.6.2 Classification

Classified: no classification required (no dangerous properties)

Flag: non confidential, Critical study for SIDS endpoint
14-NOV-2002 (1)

1.6.3 Packaging

1.7 Use Pattern

Type: type
Category: Use resulting in inclusion into or onto matrix

Flag: non confidential, Critical study for SIDS endpoint
14-MAR-1996

Type: industrial
Category: Paints, lacquers and varnishes industry

Flag: non confidential, Critical study for SIDS endpoint
14-MAR-1996

Type: industrial
Category: Polymers industry

Flag: non confidential, Critical study for SIDS endpoint
14-MAR-1996

Type: industrial
Category: other: Ceramics industry

Flag: non confidential, Critical study for SIDS endpoint
26-NOV-2001

Type: use
Category: Colouring agents

Flag: non confidential, Critical study for SIDS endpoint
14-MAR-1996

1.7.1 Detailed Use Pattern

1.7.2 Methods of Manufacture

Type: Production

Remark: Doted rutile pigments are manufactured by reacting finely divided metal oxides, hydroxides or carbonates in the solid state at a temperature of 1000 to 1,200 °C. The production is based on reactive anatase, or titanium dioxide hydrolysate containing sulfuric acid, and on the oxidation of trivalent antimony with oxygen in the form of nitric acid or air. For the production of C.I. Pigment Yellow 53 nickel metal oxide, hydroxide or carbonate is used.
The reactions proceed more readily if the components are reactive, finely divided and intimately mixed. Adding mineralizers promotes solid-state reaction during calcination, which is performed either continuously in a rotary, annular or tunnel furnace, or batchwise in a directly fired car-bottom or rotary-hearth furnace. After calcination, the resulting clinker is wet-ground and any soluble salts are washed out. The product is dried either in a spray-drying tower, when low-dusting, free-flowing grades are required, or by standard means, which, however, necessitates subsequent grinding to a pigment powder.

Raw-material dust, and gases (e.g. SO3 and NOx), emitted during the calcination step are removed from the flue gas by dust separators and alkaline flue scrubbers. The raw-material dust can be recycled. Soluble metal salts can be removed by neutral precipitation in the waste-water treatment plant, and suspended pigment particles can be mechanically separated from the water from washing and purification steps. Altogether, only a small amount of waste is produced with each tonne of product.

Flag: non confidential, Critical study for SIDS endpoint
15-NOV-2002 (2)

Type: Production

Remark: The finished C.I. Pigment Yellow 53 contains about 2 to 5 % nickel(II) and 9 to 12 % antimony (V) (all data calculated as metal).
Flag: non confidential, Critical study for SIDS endpoint
15-NOV-2002 (3)

1.8 Regulatory Measures

1.8.1 Occupational Exposure Limit Values

Type of limit: MAK (DE)
Limit value: other: no MAK- or BAT-value established

Remark: There are no adequate information from human and animal testing for the placement of an MAK value.
Flag: non confidential, Critical study for SIDS endpoint
14-FEB-2003 (4)

1.8.2 Acceptable Residues Levels

1.8.3 Water Pollution

Classified by: KBwS (DE)
Labelled by: KBwS (DE)
Class of danger: 0 (generally not water polluting)

Remark: ID-Number: 1956
Flag: non confidential, Critical study for SIDS endpoint
21-APR-2004 (5)

Classified by: other: VwVwS (Germany) of 17.05.1999, Annex 3
Labelled by: other: VwVwS (Germany) of 17.05.1999, Annex 3
Class of danger: 0 (generally not water polluting)

Flag: non confidential, Critical study for SIDS endpoint
14-NOV-2002 (1)

1.8.4 Major Accident Hazards

1.8.5 Air Pollution

1.8.6 Listings e.g. Chemical Inventories

Type: TSCA

Flag: non confidential, Critical study for SIDS endpoint
13-NOV-2001 (6)

Type: DSL

Flag: non confidential, Critical study for SIDS endpoint
13-NOV-2001 (6)

Type: ENCS
Additional Info: ENCS-No. 1-517X
ENCS-No. 1-543X
ENCS-No. 1-558X

Flag: non confidential, Critical study for SIDS endpoint
21-FEB-2002 (6)

Type: PICCS

Flag: non confidential, Critical study for SIDS endpoint
13-NOV-2001 (6)

Type: EINECS
Additional Info: EINESCS-No. 232-353-3

Flag: non confidential, Critical study for SIDS endpoint
21-FEB-2002 (6)

Type: AICS

Flag: non confidential, Critical study for SIDS endpoint
13-NOV-2001 (6)

Type: ECL
Additional Info: ECL Serial No. KE-08034

Flag: non confidential, Critical study for SIDS endpoint
21-FEB-2002 (6)

1.9.1 Degradation/Transformation Products

EINECS-Name: No hazardous decomposition products if stored and handled as prescribed/indicated.

Flag: non confidential, Critical study for SIDS endpoint
14-NOV-2002 (1)

1.9.2 Components

1.10 Source of Exposure

1.11 Additional Remarks

1.12 Last Literature Search

1.13 Reviews

2.1 Melting Point

Value: > 1000 degree C

Reliability: (4) not assignable
Manufacturer/producer data without proof
Flag: Critical study for SIDS endpoint
11-DEC-2001 (7)

2.2 Boiling Point

2.3 Density

Type: density
Value: = 4 - 5 g/cm³ at 20 degree C

Method: other: DIN-ISO 787/10
GLP: no

Reliability: (4) not assignable
Manufacturer/producer data without proof
Flag: Critical study for SIDS endpoint
14-FEB-2003 (7)

2.3.1 Granulometry

2.4 Vapour Pressure

Remark: A negligible vapour pressure can be assumed for this mixed metal oxide.
Flag: Critical study for SIDS endpoint
12-MAR-2003 (8)

2.5 Partition Coefficient

2.6.1 Solubility in different media

Solubility in: Water

GLP: no

Remark: C.I. Pigment Yellow 53 has an extremely low solubility in water, the concentration of nickel and antimony in filtrates of a 10 g/l solution after 2h-stirring has been measured by atomic absorption to be <0.01mg/l
Flag: Critical study for SIDS endpoint
14-FEB-2003 (9)

Solubility in: Water
pH value: = 7 - 8
Conc.: 50 g/l at 20 degree C
Descr.: not soluble

Method: other: DIN-ISO 787/9

Result: The pH-value has been determined from a pigment suspension having a concentration of 50 g/l.
Reliability: (4) not assignable
Manufacturer/producer data without proof
Flag: Critical study for SIDS endpoint
14-FEB-2003 (7)

2.6.2 Surface Tension

2.7 Flash Point

Remark: not applicable
Reliability: (4) not assignable
Manufacturer/producer data without proof
Flag: Critical study for SIDS endpoint
11-DEC-2001 (7)

2.8 Auto Flammability

2.9 Flammability

2.10 Explosive Properties

2.11 Oxidizing Properties

2.12 Dissociation Constant

2.13 Viscosity

2.14 Additional Remarks

3.1.1 Photodegradation

Remark: no data are available
Flag: Critical study for SIDS endpoint
12-MAR-2003

3.1.2 Stability in Water

3.1.3 Stability in Soil

3.2.1 Monitoring Data (Environment)

3.2.2 Field Studies

3.3.1 Transport between Environmental Compartments

Type: other

Remark: no data are available
Flag: Critical study for SIDS endpoint
11-DEC-2001

3.3.2 Distribution

Media: air - biota - sediment(s) - soil - water
Method: Calculation according Mackay, Level I

Remark: Distribution modelling is not applicable since several physical parameters (molecular weight, water solubility, vapour pressure, partition coefficient) are not available.
Flag: Critical study for SIDS endpoint
11-DEC-2001

3.4 Mode of Degradation in Actual Use

3.5 Biodegradation

Method: other

Remark: C.I. Pigment Yellow 53 is an inorganic substance, biodegradation is therefore not assumed.
Flag: Critical study for SIDS endpoint
12-MAR-2003 (8)

3.6 BOD5, COD or BOD5/COD Ratio

3.7 Bioaccumulation

Year: 2002
Test substance: as prescribed by 1.1 - 1.4

Remark: No data on bioaccumulation are available. However, regarding the extremely low water solubility, experiences from rodent investigations and the structure-related inert properties of the rutil, bioavailability and therefore bioconcentration is not expected.
Flag: Critical study for SIDS endpoint
14-FEB-2003 (8)

3.8 Additional Remarks

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: semistatic
Species: Oryzias latipes (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** yes
LC50: > 1
Limit Test: yes
Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year: 2001
GLP: yes
Test substance: other TS
Method: -Test Organisms:
a) Size (length and weight): 1.64 cm (1.51 - 1.80 cm) in length; 0.064 g (0.044 - 0.089 g) in weight
b) Age: Not described
c) Any pretreatment: Acclimated for several days before testing, any groups showing > 5 % mortality were not used for testing. Not fed for 24 hours before the test started.

-Test substance: C. I. Pigment Yellow 53;(Ti, Sb, Ni)O2
Main Ingredients
TiO2: 80%
SbO5: 14%
NiO: 4%
Acceesorry Ingredients
CaO: 0.8%
SiO2: 0.6%
ZnO: 0.2%
Al2O3: 0.1%

-Test Conditions:
a) Dilution Water Source: Dechlorinated tap water
b) Dilution Water Chemistry:pH: = 7.6 (25°C)
Electric conductivity: = 150 uS/cm
Total hardness (as CaCO3): = 63mg/L
Alkalinity (as CaCO3): = 43mg/L
c) Exposure Vessel Type: 5 L test solution in a 5 L GlassBeaker
d) Nominal Concentrations: control and 1.00mg/L; C. I. Pigment Yellow 53 was almost insoluble in water and showed a low toxicity by preliminary test. Consequently, the experiments were carried out with 1.00 mg/L at which precipitates and floating substances were not observed. However, it was likely that the test substance was not dissolved, because the presence of the test substance in the filtrate (The test solution was filterd with 0.45um membrane filter.) was below the detectably limit of ICP-MS operating condition.
e) Vehicle/Solvent and Concentrations: Not used
f) Stock Solutions Preparations and Stability: 1,000mg/L stock solution was prepared for 1.0mg/L tests, in the following way: 100mg-test substance was added in 100mL-dilution water. The test substance was not dissolved but dispersed in the stock solution.
g) Number of Replicates: 1

h) Fish per Replicates: 10
i) Renewal Rate of Test Water: Every 24 hours
j) Water Temperature: 23.5 - 23.8°C
k) Light Condition: 16:8 hours, light-darkness cycle (<1,000 lux)
l) Feeding: No

- Analytical Procedure: Test concentrations were mesured by Inductively Coupled Plasma-Mass Spectrometer.

-Statistical Method: Binomial
a) Data Analysis: The LC50 value and its 95% confidence limits were not determined, a limit test (OECD TG 203) was conducted.
b) Method of Calculating Mean Measured Concentrations (i.e. arithmetic mean, geometric mean, etc.): Geometric Mean

Remark: The procedure of preparation of test solution was not shown in the report, therefore it was not clear whether a sufficient effort was made to obtain a saturated solution. However in the document it was well described that the concentration was measured with the whole sample containing undissolved test substance without filtration and that the toxicity value was seen to be above the water solubility in the present test.

Result: - Measured Concentrations : The tested concentrations were measured at 0 hour and 24 hours later (before exchange of test solution) . The tested concentration at 24 hours was showed as 71% of nominal concentration, however it was likely that the measured comcentration did not reflect really C. I. Pigment Yellow 53 content in the tested solution due to the low water solubility.

Nominal concentration mg/L	Measured concentration mg/L	Mean* measured concentration mg/L
	0 Hour (new)	24 Hours (old)
Control	<0.07	<0.07 -
1.00	0.98	0.71 0.83

*: Geometric Mean

- Water chemistry in test (pH and DO): pH 7.2 - 7.5(control), DO 7.3 - 8.5 mg/L

-Effect Data(mortality):
96hr LC50 > 1.00 mg/L

- Cumulative Mortality: No death occurred to the tested fish during the test period, except one fish at 96 hr period for 1.00 mg/L (nominal concentration).

Nominal	Mean* Meas.

Concentr. mg/L	Concentr. mg/L	Cumulative Mortality (% Mortality) 24hr	48hr	72hr	96hr
Control	-	0 (0)	0 (0)	0 (0)	0 (0)
1.00	0.83	0 (0)	0 (0)	0 (0)	1 (10)

*:Geometric Mean

-Other Effect: No toxicological symptom was observed during the test period.

Nominal Concentr. mg/L	Mean* Meas. Concentration mg/L	Symptoms (Symptom-number of fish) 24hr	48hr	72hr	96hr
Control	-	Normal	Normal	Normal	Normal
1.00	0.83	Normal	Normal	Normal	Normal

*:Geometric Mean

- Calculation of toxic values: Based on the nominal concentrations, however the measured concentrations did not seem to reflect really C. I. Pigment Yellow 53 content being dissolved in the tested solution.

Source: National Institute of Environmental Studies, Environment Agency Tsukuba-Ibaraki
Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint
29-MAR-2004 (10)

Type: static
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no
NOEC: = 10000
LC50: > 10000

Method: other: DIN 38412 Part 15
Year: 1982
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: TS insoluble; coloured and cloudy test solution; undissolved TS visible on the bottom of aquaria; results on the basis of nominal concentrations.
Result: RESULTS: EXPOSED
- No mortality after 96 h
- No symptoms observed at 1, 4, 24, 48, 72, 96h
RESULTS: CONTROL
- No animals showed adverse effects
- Positive control conducted with Chloroacetamide, LC50 (48h) =32 mg/l
Test condition: DILUTION WATER
according to DIN 38412, part 11 (Oct. 1982)
TEST SYSTEM
- concentrations: 0, 5000, 10000 mg/l

- Number of animals per test concentration: 10
- Loading: 4.7 g fish/l test water
- Test temperature: 21 degree C
- pH 7.5-7.9 during exposure in all 3 groups
- Oxygen content: 7.0-8.4 in all 3 groups
- Test parameter: mortality and symptoms
- Effects checked after directing the fish towards the front pane of aquaria (cloudy content, see remark); at the end of test period (96h) fish transfered into clean water for determination of symptoms.

Reliability: (1) valid without restriction
Comparable to OECD 203
Flag: Critical study for SIDS endpoint
12-MAR-2003 (11)

4.2 Acute Toxicity to Aquatic Invertebrates

Type: semistatic
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** yes
NOEC: > 1
EC50: > 1
Limit Test: yes

Method: OECD Guide-line 202
Year: 2001
GLP: yes
Test substance: other TS

Method: - Test Organisms:
a) Age: < 24 hours old
b) Supplier/Source: National Institute for Environmental Studies (JAPAN)

-Test substance: C. I. Pigment Yellow 53;(Ti, Sb, Ni)O2
Main Ingredients
TiO2: 80%
SbO5: 14%
NiO: 4%
Acceesorry Ingredients
CaO: 0.8%
SiO2: 0.6%
ZnO: 0.2%
Al2O3: 0.1%

- Test Conditions:
a) Dilution Water Source: Elendt M4 (OECD Guide-line 211)
b) Dilution Water Chemistry (pH, EC, Total hardness ,Alkalinity, etc.): Not described
c) Exposure Vessel Type: 100 mL test solution in a 100 mLGlass Beaker with Teflon-lined sheet cap
d) Nominal Concentrations: control and 1.00mg/L; C. I. Pigment Yellow 53 was almost insoluble in water and showed a low toxicity by preliminary test. Consequently, the experiments were carried out with 1.00 mg/L at which precipitates and floating substances were not observed. However, it was likely that the test substance was not dissolved, because the presence of the test substance in the

filtrate (The test solution was filterd with 0.45um membrane filter.) was below the detectably limit of ICP-MS operating condition.
e) Vehicle/Solvent and Concentrations: Not used
f) Stock Solutions Preparations and Stability: 1,000mg/L stock solution was prepared for 1.0mg/L tests, in the following way: 100mg-test substance was added in 100mL-dilution water. The test substance was not dissolved but dispersed in the stock solution.
g) Number of Replicates: 4
h) Individuals per Replicates: 5
i) Renewal Rate of Test Water: Every 24 hours
j) Water Temperature: 20.4 - 20.5°C
k) Light Condition: 16:8 hours, light-darkness cycle (<= 800 lux)
l) Feeding: No

- Analytical Procedure: Test concentrations were mesured by Inductively Coupled Plasma-Mass Spectrometer.

- Statistical Method: Binomial
a) Data Analysis: The EC50 value and its 95% confidence limits were not determined, a limit test (OECD TG 202) was conducted.
b) Method of Calculating Mean Measured Concentrations (i.e.arithmetic mean, geometric mean, etc.): Geometric Mean

Remark: The procedure of preparation of test solution was not shown in the report, therefore it was not clear whether a sufficient effort was made to obtain a saturated solution. However in the document it was well described that the concentration was measured with the whole sample containing undissolved test substance without filtration and that the toxicity value was seen to be above the water solubility in the present test.

Result: - Measured Concentrations : The tested concentrations were measured at 0 hour and 24 hours later (before exchange of test solution) . The tested concentration at 24 hours was showed as 48% of nominal concentration, however it was likely that the measured comcentration did not reflect really C. I. Pigment Yellow 53 content in the tested solution due to low solubility.

Nominal concentration mg/L	Measured concentration mg/L		Mean* measured concentration mg/L
	0 Hour (new)	24 Hours (old)	
Control	<0.05	<0.05	-
1.00	0.92	0.48	0.63

*:Geometric Mean

- Water chemistry in test (pH and DO): pH 8.2 - 8.4(control), DO 8.5 - 8.7 mg/L

-Effect Data(immobilization):

48hr EC50 > 1.00mg/L (95% C. I.: not available)
48hr NOEC > 1.00mg/L (95% C. I.: not available)

- Calculation of toxic values: Based on the nominal concentrations, however the measured concentrations did not seem to reflect really C. I. Pigment Yellow 53 content being dissolved in the tested solution.

Source: National Institute of Environmental Studies, Environment Agency Tsukuba-Ibaraki
Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint
29-MAR-2004 (10)

Type: static
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no
EC0: >= 100
EC50: > 100
EC100: > 100

Method: other: EEC-Directive 92/32/EEC, Annex V, Part C.2
Year: 1992
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Result: RESULTS: EXPOSED
- Nominal concentrations: 0, 12.5, 25, 50, 100 mg/l
- Effect data (Immobilisation):
1 out of 20 animals showed immobilisation in high and in low dose group after 48 h;
- Other effects: no
RESULTS CONTROL: valid negative (immobility 0%) and positive control

Test condition: STOCK AND TEST SOLUTION AND THEIR PREPARATION
Unsoluble TS (water solubility < 1 mg/l) stirred in the M4 medium (see dilution water) for ca. 20 h at ca. 20 °C; undissolved TS removed by centrifugation; nominal concentration of the eluate 100 mg/l; further dilution of this eluate with M4 medium;
prepared nominal concentrations:
control, 12.5, 25, 50, 100 mg/l.

DILUTION WATER
M4 medium

TEST SYSTEM
- Exposure vessel type: 20 ml glass tubes with flat bottom
- Number of replicates (individuals per replicate): 4 (5)
- Test temperature: 20.3-20.4 °C
- Dissolved oxygen: 7.6-8.3 mg/l
- pH: 8.0-8.1
The concentration control analysis was not performed. It is known from similar anorganic pigments (e.g. C.I. Pigment Brown 24) that the expected concentration of the substance is beyond the detection limit of the analytical method.

STATISTICS:

Results allowed no statistical evaluation of the data.
Reliability: (1) valid without restriction
guideline study
Flag: Critical study for SIDS endpoint
12-MAR-2003 (12)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Selenastrum capricornutum (Algae)
Endpoint: biomass
Exposure period: 72 hour(s)
Unit: mg/l **Analytical monitoring:** yes
NOEC: > 1
EC50: > 1
Limit Test: yes

Method: OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year: 2001
GLP: yes
Test substance: other TS

Method: - Test Organisms:
a) Method of Cultivation: axenic Gorham medium
b) Stain Number: ATCC22662
c) Supplier/Source: American Type Culture Collection

-Test substance: C. I. Pigment Yellow 53;(Ti, Sb, Ni)O2
Main Ingredients
TiO2: 80%
SbO5: 14%
NiO: 4%
Acceesorry Ingredients
CaO: 0.8%
SiO2: 0.6%
ZnO: 0.2%
Al2O3: 0.1%

- Test Conditions:
a) Medium: OECD medium
b) Exposure Vessel Type: 100 mL Medium in a 500 mL Erlenmeyer Flask with glass cap
c) Nominal Concentrations: control and 1.00mg/L; C. I. Pigment Yellow 53 was almost insoluble in water. Consequently, the experiments were carried out with 1.00 mg/L at which precipitates and floating substances were not observed. However, it was likely that the test substance was not dissolved, because the presence of the test substance in the filtrate (The test solution was filterd with 0.45um membrane filter.) was below the detectably limit of ICP-MS operating condition.
d) Vehicle/Solvent and Concentrations: Not used.
e) Stock Solutions Preparations and Stability: 100mg/L stock solution was prepared for 1.0mg/L tests, in the following way: 100mg-test substance was added in 1000mL-OECD medium. The test substance was not dissolved but dispersed in the stock solution.
f) Number of Replicates: 3
g) Initial Cell Number: 10,000 cells/mL
h) Water Temperature: 22.7 - 23.5°C

i) Light Condition: 4,000 lux (+/- 20%), continues
j)Shaking: 100 rpm

- Analytical Procedure: Test concentrations were mesured by Inductively Coupled Plasma-Mass Spectrometer.

- Statistical Method: t-test
a) Data Analysis: Student's t-Test was used on comparison between means in control and treated(1mg/L).
b) Method of Calculating Mean Measured Concentrations (i.e.arithmetic mean, geometric mean, etc.): Not described

Remark: NOEC was determined based on growth inhibition.
The procedure of preparation of test solution was not shown in the report, therefore it was not clear whether a sufficient effort was made to obtain a saturated solution. However in the document it was well described that the concentration was measured with the whole sample containing undissolved test substance without filtration and that the toxicity value was seen to be above the water solubility in the present test.

Result: - Measured Concentrations : The tested concentrations were measured at 0 hour and 72 hours. The test substance concentration at 72 hours was lower than that of detection limit. It appeared that most test chemical precipitated inadvertently with algal cells during centrifugation due to its low water solubility.

Nominal concentration mg/L	Measured concentration mg/L		% of nominal concentration mg/L	
	0 Hour	72 Hours	0 Hour	72 Hours
Control	<0.07	<0.07	-	
1.00	1.08	<0.07	108	0

Water chemistry in test (pH and DO): pH 7.7 at thestart of the test, pH 10.1 at the end of the test
-Effect Data:
area method
EbC50(0-72hr) >1.0 mg/L (95% C. I.: not available)
NOEC >1.0 mg/L
rate method
ErC50(24-48hr) >1.0 mg/L (95% C. I.: not available)
NOEC >1.0 mg/L
ErC50(24-72hr) >1.0 mg/L (95% C. I.: not available)
NOEC >1.0 mg/L
- Percent Growth Inhibition of Selenastrum capricornutum

Nominal Concentration mg/L	No.	Area under the growth curves Area A (0-72hr)	Inhibition (%)*1 IA (0-72hr)
Control	1	44,754,000	
	2	44,447,000	
	3	44,912,000	
	Average	44,704,000	-
	SD	236,0001.00	
	1	45,355.000	
	2	47,551,000	

		3	52,121,000		
		Average	48,342,000	-8.1	
		SD	3,452,000		

Nominal Concentr. mg/L	Growth rate Rate No.	u(24-48hr)	Inhibition(%)*1 Im(24-48hr)	Rate u(24-72hr)	Inhibition(%)*1 m(24-72hr)
Control	1	0.0768		0.0761	
	2	0.0782		0.0756	
	3	0.0777		0.0754	
	Average	0.0776	-	0.0757	-
	SD	0.0007		0.0004	
1.00	1	0.0776		0.0767	
	2	0.0823		0.0779	
	3	0.0820		0.0783	
	Average	0.0806	-3.9	0.0776	-2.5
	SD	0.0026		0.0008	

*1: Values are the percent inhibition relative to the control
SD: Stadard devation

- Growth Curves: Log phase during the test period

Source: National Institute of Environmental Studies, Environment Agency Tsukuba-Ibaraki
Reliability: (2) valid with restrictions

Flag: Critical study for SIDS endpoint
30-MAR-2004 (10)

Species: other algae: Desmodesmus subspicatus Chodat SAG 86.81
Endpoint: growth rate
Exposure period: 72 hour(s)
Unit: mg/l **Analytical monitoring:** no
NOEC: = 25
LOEC: = 50
EC10: > 100
EC50: > 100
EC90 : > 100

Method: OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year: 1984
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Testing also according to EEC Directive 92/69/EEC, Annex V, Part C.3 (1992)
Remark: The concentration control analysis was not performed. It is known from similar anorganic pigments (e.g. C.I. Pigment Brown 24) that the expected concentration of the substance is lower than the detection limit of the analytical method.
Result: CONTROL
In negative control cell multiplication factor after 72h: 124-fold; positive control with potassium dichromate EC50 (72h)= 0.37 mg/l

INHIBITION OF ALGAL BIOMASS AFTER 72h

	Concentration in mg TS/l					
	0	6.25	12.5	25	50	100
Inhibition in % of control	0.0	-7.9	-3.4	-4.1	5.1	18.7

EbC10 (72h) = 64.1 mg/l (nominal)
EbC50 (72h) > 100 mg/l (nominal)

INHIBITION OF GROWTH RATES AFTER 72h

	Concentration in mg TS/l					
	0	6.25	12.5	25	50	100
Inhibition in % of control	0.0	-3.3	-2.6	-2.3	0.3	2.8

ErC10 (72h) > 100 mg/l (nominal)
ErC50 (72h) > 100 mg/l (nominal)

Test condition: STOCK SOLUTION AND DILUTION
The test was performed with an aqueous extract (eluate) of the test substance (water solubility < 1mg/l); TS stirred in demineralized water for ca. 20h at 20°C, undissolved TS removed by centrifugation, nominal concentration of the eluate 125 mg/l, further dilution to nominal concentrations: 100, 50, 25, 12.5, 6.25 mg/l.

TEST MEDIUM
prepared according to guideline (see above)

PERFORMANCE OF THE TEST
test vessels 250 ml Erlenmeyer flasks plugged with siliconsponge caps; test volume 100 ml;
pH values in uninoculated tests 7.8-8.0 at start of experiments and 8.0-8.1 after 72 h, in inoculated tests pH 7.9-8.0 after 72 h;
test parameter: in vivo chlorophyll-a-fluorescence at 435 nM wavelength after 0, 24, 48, 72 h; control culture: additionally cell counting after 72 h in a counting chamber

STATISTICS
EC values calculated by linear regression analysis from dose-response relationship; NOEC and LOEC: Duncan multiple range test at 95% significance level,
LOEC and NOEC are determined by comparing directly the means of the fluorescence measurement of the various concentration levels with the control.

Reliability: (1) valid without restriction
guideline study

Flag: Critical study for SIDS endpoint

21-APR-2004 (13)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: Pseudomonas putida (Bacteria)
Exposure period: 30 minute(s)
Unit: mg/l **Analytical monitoring:** no
EC10: = 5680
EC50: > 10000

EC90 : > 10000

Method: other: DIN 38412 Part 27 (draft)
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: Bacterial oxygen consumption test according to Robra, K.H., gwf. Wasser-Abwasser 117, 80-86 (1976)
Result: The results show the nominal concentrations of the TS that inhibited oxygen consumption of the microorganisms.

Concentration in mg/l	mean oxygen consumption in % of control
10000	69.2
5000	94.7
2500	100.8
1250	99.2
625	100.8
312	99.2

Test condition:
- Test solution stirred for 17 h at 293 °K and than used as dispersion (unsoluble in water) in the oxygen consumption test
- test volume 100 ml (5 ml glucose [198 g/l] and 95 ml test substance including bacterial suspension)
- assay batch aerated for 30 min
- decline in concentration of dissolved oxygen measured in a flow cell
- pH of the test mix: 7.2-7.4
- temperature: 25°C
- tested concentrations: control, 312, 625, 1250, 2500, 5000, 10000 mg/l (nominal)

Reliability: (2) valid with restrictions
Acceptable, well documented study report which meets basic scientific principles.
Flag: Critical study for SIDS endpoint
12-MAR-2003 (14)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

4.5.2 Chronic Toxicity to Aquatic Invertebrates

Species: Daphnia magna (Crustacea)
Endpoint: reproduction rate
Exposure period: 21 day(s)
Unit: mg/l **Analytical monitoring:** yes
NOEC: > 1
LOEC: > 1
EC50: > 1
LC50 : > 1

Method: other: OECD Guide-line 211
Year: 2001

GLP: yes
Test substance: other TS

Method:
- Test Organisms:
 a) Age: < 24 hours old
 b) Supplier/Source: National Institute for Environmental Studies (JAPAN)

-Test substance: C. I. Pigment Yellow 53;(Ti, Sb, Ni)O2
Main Ingredients
 TiO2: 80%
 SbO5: 14%
 NiO: 4%
Acceesorry Ingredients
 CaO: 0.8%
 SiO2: 0.6%
 ZnO: 0.2%
 Al2O3: 0.1%

- Test Conditions:
 a) Dilution Water Source: Elendt M4 (OECD Guide-line 211)
 b) Dilution Water Chemistry (pH, EC, Total hardness ,Alkalinity, etc.): Not described
 c) Exposure Vessel Type: 80 mL test solution in a 100 mLGlass Beaker with Teflon-lined sheet cap
 d) Nominal Concentrations: control and 1.00mg/L; C. I. Pigment Yellow 53 was almost insoluble in water. Consequently, the experiments were carried out with 1.00 mg/L at which precipitates and floating substances were not observed. However, it was likely that the test substance was not dissolved, because the presence of the test substance in the filtrate (The test solution was filterd with 0.45um membrane filter.) was below the detectably limit of ICP-MS operating condition. As a result of acute toxicity test for invertebrates, a limit test (OECD 211) was conducted.
 e) Vehicle/Solvent and Concentrations: Not used
 f) Stock Solutions Preparations and Stability: 1,000mg/L stock solution was prepared for 1.0mg/L tests, in the following way: 100mg-test substance was added in 100mL-dilution water. The test substance was not dissolved but dispersed in the stock solution.
 g) Number of Replicates: 10
 h) Individuals per Replicates: 1
 i) Renewal Rate of Test Water: Every 24 hours
 j) Water Temperature: 19.6 - 20.3°C
 k) Light Condition: 16:8 hours, light-darkness (<800 lux)
 l) Feeding: 0.2 mg carbon/day/individual (ChlorellaVulgaris: Green Algae)

- Statistical Method:
 a) Data Analysis: LC50 of parental mortality: Binomial
 NOEC and LOEC: t-test.
 b) Method of Calculating Mean Measured Concentrations (i.e.arithmetic mean, geometric mean, etc.): Not described

Remark: NOEC was determined based on the cumulative number of juveniles produced per adult alive for 21 days.
The procedure of preparation of test solution was not shown in the report, therefore it was not clear whether a sufficient effort was made to obtain a saturated solution. However in the document it was well described that the concentration was

measured with the whole sample containing undissolved test substance without filtration and that the toxicity value was seen to be above the water solubility in the present test.

Result: - Effect: reproduction- Measured Concentrations (as mg/L):

Nominal Concentration (mg/L)	Measured Concentration (mg/L) on day: 0 new	1 old	8 new	9 old	14 new	15 old
Control	<0.07	<0.07	<0.07	<0.07	<0.07	<0.07
1.00	0.88	0.83	0.90	0.15	0.94	0.88

- Water chemistry in test (pH and DO): pH 7.3 - 8.4(control), pH 8.70 - 8.83 (63.2 mg/L), DO 7.5 - 8.7 mg/L

- Total hardness: 240 - 265 mg/L

-Effect Data(reproduction):
21days LC50 >1.00mg/L (95% C. I.: not available)
21days EC50 >1.00mg/L (95% C. I.: not available)
21days NOEC >1.00mg/L
21days LOEC >1.00mg/L

- Cumulative Number of Died Parental daphnids:

Nominal Concentration (mg/L)	Cumulative Number of Died Parental daphnids (days) 1	2	3	4	5	6	7	8	9	10
Control	0	0	0	0	0	0	0	0	0	0
1.00	0	0	0	0	0	0	0	0	0	0

Nominal Concentration (mg/L)	Cumulative Number of Died Parental daphnids (days) 11	12	13	14	15	16	17	18	19	20	21
Control	0	0	0	0	0	0	0	0	0	0	0
1.00	0	1	1	1	1	1	1	1	1	1	1

- Time (days) of the First Brood Production: Mean;
Control : 8 days
1.00mg/L: 8 days

- Mean Cumulative Number of Offsprings Produced per Adult:
21days;
Control:102.8
1.00mg/L: 95.2

- Calculation of toxic values: Based on the nominal concentrations, however the measured concentrations did not seem to reflect really C. I. Pigment Yellow 53 content being dissolved in the tested solution.

Source: National Institute of Environmental Studies, Environment

Agency Tsukuba-Ibaraki
Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint
30-MAR-2004 (10)

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Sediment Dwelling Organisms

4.6.2 Toxicity to Terrestrial Plants

4.6.3 Toxicity to Soil Dwelling Organisms

4.6.4 Toxicity to other Non-Mamm. Terrestrial Species

4.7 Biological Effects Monitoring

4.8 Biotransformation and Kinetics

4.9 Additional Remarks

5.0 Toxicokinetics, Metabolism and Distribution

In Vitro/in vivo:	In vivo
Type:	Toxicokinetics
Species:	rat
No. of animals, males:	5
No. of animals, females:	5
Doses, males:	10; 100; 1000; 10,000 ppm in feed (0.45; 4.5; 45; 450 mg/kg bw/ day)
Doses, females:	10; 100; 1000; 10,000 ppm in feed (0.45; 4.5; 45; 450 mg/kg bw/ day)
Route of administration:	oral feed
Exposure time:	90 day(s)

Test substance: other TS: technical grade Nickel

Remark: The detected traces of antimony (see results) most likely originate from the acid-soluble impurities of the pigment (10-20 mg antimony/kg pigment, that is 5-10 microgram/kg bw or 125-250 microgram/kg organ weight at the highest dose) and therefore do not indicate bioavailability of the pigment itself.

Result: No deaths, no overt signs of reactions to the treatment, no effects on body weight gain (similar food consumption in all groups) or organ weight, no treatment related findings from haematological or biochemical investigations and urinalysis.
No macroscopic pathological changes attributable to treatment. No treatment related effects observed in histopathology.
No nickel concentrations related to the treatment detectable in liver and kidneys at any time and dose.
No antimony detectable in liver and kidneys after 1 and 2 months at any dose.
After 3 months treatment with 10000 ppm TS in the diet antimony was detectable in liver (6 ppb) and kidney (5 ppb) of males slightly above the detection limit and in females at levels of 6 (liver) and 10 (kidney) ppb.

Test condition: EXPERIMENTAL DESIGN
15 animals per dose per gender for toxicological investigations and 30 animals per gender in the control group;
additionally 10 animals per dose and gender for analytical investigations and 20 animals per gender in the control group.
Tests started at the age of 4- 5 weeks; TS given in powdered food (Altromin); feed and tap water ad libitum.

General observations:
Rats observed daily; food consumption and body weight gain determined once per week.
Haematological, clinical and biochemical investigations:
RBC, reticulocytes, platelets, haemoglobin, haematocrit, total and differential WBC, MCV, ALP, GOT, GPT, creatinine, urea, glucose, cholesterol, total plasma proteins and urine proteins, urinalysis conducted after one month and at the end of the study on 5 males and 5 females of each group; in addition thromboplastin time and glutamate dehydrogenase activity measured after three months.

Gross and histopathological investigations:
organ weight determined from thyroid gland, thymus, heart, lung, liver, spleen, kidneys, adrenal glands, and gonads and histopathology performed together with aorta, eyes, intestine, femur, brain, urinary bladder, pituitary, cervical lymph nodes, stomach, oesophagus, epididymides, pancreas, prostate, seminal vesicle, bone marrow of sternum, trachea, uterus, skeletal muscles from 5 animals per gender of control and top dose group.

Statistics:
Data on weight determinations, hematology and clinical chemistry compared by Wilcoxon U-test, level of significance p<=0.05.

Chemical Analysis
After 1, 2 and 3 months liver and kidneys from 5 animals per gender and dose group analysed for their nickel and antimony contents by AAS.
The detection limit for antimony was 5 ppb and for nickel 10 ppb.

Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint
14-MAR-2003 (15) (16)

In Vitro/in vivo: In vivo
Species: rat
Route of administration: inhalation
Exposure time: 5 day(s)

Method: other
GLP: yes
Test substance: other TS

Remark: The exposure level was set to a ten fold higher level than the limit level for inert dusts set at that time by the German MAK Commission and to ensure a sufficient measureable Ni-deposition in the lung.
Though a control group was not studied through the course of the experiment, the results obtained appear internally consistent and interpretable in relation to toxicity for the following reasons:
-mortality: no deaths were observed during exposure and post exposure period
-clinical examination: no clinical signs were observed which were different from normal
-body weight: weight gain not affected compared with historical controls.
With respect to the observed levels of Ni and Sb in liver, kidneys and lung the non-bioavailability of the pigment has been clearly demonstrated.

Result: TOXIC EFFECTS:-mortality: no deaths during exposure and post exposure period-clinical examination: no clinical signs different from normal-body weight: weight gain not affected compared with historical controls.

CONTENT OF Ni AND Sb IN
LIVER:
Mean Sb concentration (quantification limit 0.2 ng/g)

in unexposed animals was 1.1 ng/g; directly post-exposure and on day 3-post-exposure the concentration was about 4-fold higher in exposed animals, during further observation the concentration was similar to unexposed animals (1.3 ng/g on day 10).
Mean Ni-concentration was in the same range in exposed and unexposed animals (however, below the quantification limit of 10 ng/g; outliers not considered).

KIDNEYS:
Mean Sb concentration in unexposed animals was below the detection limit (1 ng/g), in exposed animals it was above the detection limit but below the quantification limit (3 ng/g), only the day 3 post exposure group reached a value of 5.6 ng/g (2-3-fold increase compared with other observation days).
Mean Ni concentration was below the detection limit (1 ng/g) in unexposed animals and above detection limit but below quantification limit (25 ng/g) in exposed animals, except on day 3 post-exposure 94 ng/g were determined (10-fold more than in other exposure groups; authors comment: presumably due to contamination of the sample).
However, the data neither demonstrate that the Ni content was
significantly increased nor that it was unchanged by exposure to the pigment dust.

LUNG:
Directly post-exposure the mean Ni and Sb concentration was 79 and 202 µg/lung , respectively (corresponding to 2 mg of pigment/lung). The concentration declined during the post-exposure period, following first order kinetics; the clearance half-life was 50 days.

AUTHORS CONCLUSION

No signs of toxicity have been observed.
The Ni and Sb concentration of liver and kidney after exposure was 3-5 orders of magnitude lower than in the lung and in most cases below quantification limits but above detection limits.
Pigment dust is eliminated from the lungs with a half-life of 50 days (typical for nuisance dusts), a bioavailibility of Ni and Sb from the pigment was not demonstrated.

Test condition: TEST ORGANISMS
- Age: 7 weeks on delivery (June 24, 1991; last sacifice Sept. 10, 1991)
- Weight at study initiation: 230-232 g body weight in all 5 test groups (see post exposure observation period)
- Number of animals: 10 rats per goup

EXPOSURE:
Head-nose exposure system; 5 d preflow period to accustom rats to exposure conditions; target conc: 60 mg/m3, measured conc. 59.6 +-2.51 mg/m3 (mean of daily means from 6 individual analysis per exposure); particle size analysis on test day 3 and 5: mass median aerodynamic diameter (MMAD) 0.6 - 1.0 µm (99-98% respirability); control group sacrificed on the day of arrival for analysis.

CLINICAL EXAMINATIONS:
body weight (at the beginning of pre-flow, at the beginning of exposure period and the morning of the last exposure, then once weekly), behaviour and state of health (daily three times on exposure, once during pre-flow- and post-exposure-period), mortality (daily).

ANALYSIS:
Ni and Sb concentration in lung, liver and kidneys determined; Food analysis: contamination in the used commercial feed was was 1.42 mg Ni/kg and 13 µg Sb/kg.

Statistics:
no statistical evaluation because no concurrent control.

Test substance: Lichtgelb 8G (Batch No.: Pt 8817; BASF Aktiengesellschaft; CAS 8007-18-9).
Chem. analysis:

TiO2	76.8%
Sb2O5	13.6%
NiO	5.0%
SiO2 (amorphous)	2.4%
Pb	31 ppm
As	16 ppm
other heavy metals	< 5 ppm
Ni soluble in 0.1 n HCl	46 ppm

Reliability: (3) invalid
Significant methodological deficiencies. Onyl one dose and no concurrent control limit validity of data on toxicity.
14-MAR-2003 (17) (16)

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Sex: male
Vehicle: other: 0.2% agar and 0.1% Tween 80
Value: > 5000 mg/kg bw

Method: other
GLP: no data
Test substance: other TS: Solfast Titan Yellow AURL 7536

Reliability: (2) valid with restrictions
No GLP, Insufficient Documentation
19-FEB-2003 (18)

Type: LD50
Species: rat
Sex: female
No. of Animals: 8
Vehicle: water
Value: > 10000 mg/kg bw

Method: other
GLP: no
Test substance: other TS: Inorganic Yellow (Ferro Corporation)

Test condition: 8 animals per dose
Reliability: (2) valid with restrictions
No GLP, No guideline study
19-APR-2001 (19)

Type: LD50
Species: rat
Sex: male/female
No. of Animals: 5
Vehicle: water
Value: > 2500 mg/kg bw

Method: OECD Guide-line 401 "Acute Oral Toxicity"
GLP: no data
Test substance: other TS: TK 13005, no further data

Result: 1 female died at 5000 mg/kg bw, no further mortality
Test condition: doses > 5000 mg/kg bm were not applicable
Reliability: (2) valid with restrictions
No details about the TS
25-OCT-2001 (20)

Type: LD50
Species: rat
Vehicle: water
Value: > 10000 mg/kg bw

Method: other: BASF-Test
GLP: no
Test substance: other TS: Sicotangelb AMFG (fest)

Test substance: TiO2: 78.9%
Sb2O5: 15.5%
NiO 4.1%
SiO2: 1.5% (crosscontamination with material from ball mill)
As: 40 ppm
Pb: 130 ppm
Cu: 4 ppm
Zn: 10 ppm
Cr: 2 ppm
Reliability: (2) valid with restrictions
13-MAR-2003 (21)

Type: LD50
Species: other: Crj; CD(SD) IGS rat
Sex: male/female
No. of Animals: 5
Vehicle: other: aqueous suspension with 1% sodium carboxylmethyl cellulose
Value: > 2000 mg/kg bw

Method: OECD Guide-line 401 "Acute Oral Toxicity"
Year: 2000
GLP: yes
Test substance: other TS

Remark: The chemical was given by gavage at 0 and 2,000 mg/kg bw and the observation period was 1,2,3,4,5 and 6 hours, and once daily up to 14 days after administration. All of animals

were sacrified for autopsy findings at 14 days.
Result: Any mortality, general appearance, growth depression and autopsy finding were not observed.
Test substance: Purity 100% C.I. Pigment Yellow 53 (LotNo. 4879) from Ishihara Sangyo, Japan
Reliability: (1) valid without restriction
Guideline study accordingto OECD 401. Peer review was conducted by a Japanese toxicological expert group at March 5, 2001.
Flag: Critical study for SIDS endpoint
13-MAR-2003 (22)

5.1.2 Acute Inhalation Toxicity

Type: other: Inhalation Risk Test
Species: rat
Strain: no data
Sex: no data
No. of Animals: 12
Vehicle: other: air
Exposure time: 7 hour(s)

Method: other: Smyth et al., 1962, Am Ind Hyg Ass J, 23, 95-107
Year: 1962
GLP: no
Test substance: other TS: Sicotangelb AMFG (fest)

Result: No mortality after 7 hour exposure, no symptoms of poisoning; no macroscopical findings at autopsy.
Test substance: TiO_2: 78.9%
Sb_2O_5: 15.5%
NiO 4.1%
SiO_2: 1.5% (crosscontamination with material from ball mill)
As: 40 ppm
Pb: 130 ppm
Cu: 4 ppm
Zn: 10 ppm
Cr: 2 ppm
Test condition: 200 l of air were passed through a 5 cm bed height of the test substance to create an atmosphere enriched with the volatile parts of the test article at room temerature.
Reliability: (3) invalid
unsuitable test system
03-MAR-2003 (21)

5.1.3 Acute Dermal Toxicity

5.1.4 Acute Toxicity, other Routes

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration: undiluted

Exposure: Occlusive
Exposure Time: 24 hour(s)
No. of Animals: 6
Result: not irritating

Test substance: other TS:Solfast Titan Yellow AURL 7536, no further data

Reliability: (3) invalid
Insufficient Documentation
20-FEB-2003 (18)

Species: rabbit
Concentration: undiluted
Exposure: Occlusive
Exposure Time: 24 hour(s)
No. of Animals: 6
PDII: .3
Result: not irritating
EC classificat.: not irritating

Method: other: EPA §163.81-5; Federal Register 43, 163, 22. Aug. 1978
Year: 1978
GLP: no data
Test substance: other TS: TK 13005 (Batch NO. 41635-121081)

Result: AVERAGE SCORE;
-mean reaction score erythema & edema:

	0h	24h	48h	72h	144h
intact skin	0.7	0.3	0.0	0.0	0.0
abraded skin	0.7	0.3	0.0	0.0	0.0

REVERSIBILITY: reversibility of minimal irritation
OHTER EFFECTS: no

Test condition: TEST ANIMALS;
- strain: New Zealand White
- Sex: male and female
- Source: Kleintierfarm Madoerin AG, CH-4414 Fuellinsdorf
- Age; no data
- Weight at study initation: 2-3 kg
- Number of animals; 3 males and 3 females

ADMINISTRASTION/Exposure
- Preparation of test substance: no further preparation
- Area of exposure; 6 cm2 of shaved skin,
a) intact an db) abraded (slight scarified by a
"Schroepfschnaepper", Aesculap)
- Occlusion: loaded gauze patch (0.5 g TS) applied to a)
intact and b) abraded skin; patches covered with impermeable
material and fastened to the body with adhesive tape
- vehicle: no
- total amount applied: 0.5 g of the TS
- removal of test substance: after 24 h

EXAMINATIONS
- Scoring system:

Erythema/eschar formation

no erythema	0
very slight erythema (barely perceptible)	1
well defined erythema	2
moderate to severe erythema	3

severe erythema to slight eschar formation 4

Edema formation
no edema 0
ver slight edema (barely perceptible) 1
slight edema (edges of area well defined) 2
moderate edema (raised > 1mm) 3
severe edema (raised > 1mm, extending beyond area of exposure) 4

Examination time points: 0, 24, 48, 72, 144 h after patch removal

Reliability: (2) valid with restrictions
Valid with restrictions
no details about the TS
Flag: Critical study for SIDS endpoint
14-MAR-2003 (23)

Species: rabbit
Concentration: 50 %
Exposure: no data
No. of Animals: 6
Result: not irritating

Method: other: Federal Register 38, 187 § 1500.41, 27. Sept. 1973
Year: 1973
GLP: no
Test substance: other TS: Sicotangelb AMFG (fest)

Result: Intact skin:
evaluation of erythema after 24 h not possible due to treatment related colouring of the skin: no erythema after 72 h and 8 d; no edema after 24 h, 72 h or 8d.

Abraded skin:
Erythema: no data after 24h; after 72 h slight erythema in 3 animals (1 animal evaluation impossible, see above), primary irritation value 0.2; scaling in 4 animals after 8 d.

Edema: no effects
Test condition: Effects scored after 24h, 72 h an d8 days.
Test substance: TiO2: 78.9%
Sb2O5: 15.5%
NiO 4.1%
SiO2: 1.5% (crosscontamination with material from ball mill)
As: 40 ppm
Pb: 130 ppm
Cu: 4 ppm
Zn: 10 ppm
Cr: 2 ppm
Reliability: (1) valid without restriction
Valid without restriction
Flag: Critical study for SIDS endpoint
14-MAR-2003 (21)

5.2.2 Eye Irritation

Species: rabbit
Dose: 100 other: mg

No. of Animals: 3
Result: slightly irritating
Method: other: EPA §163.81-5, Federal Register 43, 163, 22. Aug. 1978
Year: 1978
GLP: no data
Test substance: other TS: TK 13005 (Batch No. 41635-121081), no further data
Result: Only one rabbit (female, rinsed) showed definetely injected vessels of conjunctiva above normal after 24 h but not at later time points (no effects on cornea and iris); no further effects in any other rabbit.

Primary irritation index
a) in unrinsed eyes 0.0
b) in rinsed eyes 0.1

Conclusion:
No irritation when applied to the rabbit eye mucosa.
Test condition: TEST ANIMALS:
- Strain: New Zealand White
- Sex: males and female
- Source: Kleintierfarm Madoerin AG, CH-4414 Fuellinsdorf
- Age: no data
- Weight at study initiation: 2-3 kg
- Number of animals: a) 3 males (unrinsed) & b) 3 females (rinsed)
- control: right eye of each animal served as an untreated control

ADMINISTRATION/EXPOSURE
- 100 mg of substance instilled in the conjunctival sac of the left eye of 6 animals; lids gently closed for 15 s; in 3 out of 6 animals ca. 30 s after instillation treated eye flushed with 10 ml sterile physiological saline
- Vehicle: no

EXAMINATIONS
- Ophtalmoscopic examination: prior to the study animals checked for normal ophthalmic conditions; eye irritation assessed with a slit lamp 24, 48, 72 h and 4 and 7 d after treatment
- Scoring system: effects on cornea, iris and conjunctivae evaluated and calculation of primary eye irritation index according to above mentioned guideline; documentation of individual results.
Reliability: (2) valid with restrictions
No details about the TS
Flag: Critical study for SIDS endpoint
13-MAR-2003 (24)

Species: rabbit
Concentration: undiluted
No. of Animals: 6
Result: slightly irritating

Method: other: Federal Register 38, 187 §1500.42, 27. Sep. 1973
Year: 1973
GLP: no
Test substance: other TS: Sicotangelb AMFG (fest)

Result: No effects on cornea and iris.
Slight conjunctival erythema (no further effects on conjunctiva) in 5/6 and clear erythema in 1/6 rabbits after 24 h; after 48 h slight erythema in 3/6 animals and after 72 h in 2/6; mean primary irritation value 1.33.
Test condition: Application form: unchanged; readings after 24, 48, 72 h.
Test substance: TiO2: 78.9%
Sb2O5: 15.5%
NiO 4.1%
SiO2: 1.5% (crosscontamination with material from ball mill)
As: 40 ppm
Pb: 130 ppm
Cu: 4 ppm
Zn: 10 ppm
Cr: 2 ppm
Reliability: (1) valid without restriction
Valid without restriction
Flag: Critical study for SIDS endpoint
14-MAR-2003 (21)

5.3 Sensitization

5.4 Repeated Dose Toxicity

Species: rat **Sex:** male
Strain: other: Wistar/Chbb:THOM
Route of administration: inhalation
Exposure period: 5 days
Frequency of treatment: 6 hours/day, daily
Post exposure period: 0, 3, 10, 31, 60 days
Doses: 60 mg/m3 (0.06 mg/l)
Control Group: other: unexposed control rats sacrificed and examined directly after being supplied from the breeder

Method: other
GLP: yes
Test substance: other TS

Method: The bioavailability of Ni and Sb from inhaled C.I. Pigment Yellow 53 was investigated.
Remark: The exposure level was set to a ten fold higher level than the limit level for inert dusts set at that time by the German MAK Commission and to ensure a sufficient measureable Ni-deposition in the lung.
Though a control group was not studied through the course of the experiment, the results obtained appear internally consistent and interpretable in relation to toxicity for the following reasons:
-mortality: no deaths were observed during exposure and post exposure period
-clinical examination: no clinical signs were observed which were different from normal
-body weight: weight gain not affected compared with historical controls.
With respect to the observed levels of Ni and Sb in liver, kidneys and lung the non-bioavailability of the pigment has been clearly demonstrated.
Result: TOXIC EFFECTS:

-mortality: no deaths during exposure and post exposure period
-clinical examination: no clinical signs different from normal
-body weight: weight gain not affected compared with historical controls.
CONTENT OF Ni AND Sb IN
LIVER:
Mean Sb concentration (quantification limit 0.2 ng/g) in unexposed animals was 1.1 ng/g; directly post-exposure and on day 3-post-exposure the concentration was about 4-fold higher in exposed animals, during further observation the concentration was similar to unexposed animals (1.3 ng/g on day 10).
Mean Ni-concentration was in the same range in exposed and unexposed animals (however, below the quantification limit of 10 ng/g; outliers not considered).
KIDNEYS:
Mean Sb concentration in unexposed animals was below the detection limit (1 ng/g), in exposed animals it was above the detection limit but below the quantification limit (3 ng/g), only the day 3 post exposure group reached a value of 5.6 ng/g (2-3-fold increase compared with other observation days).
Mean Ni concentration was below the detection limit (1 ng/g) in unexposed animals and above detection limit but below quantification limit (25 ng/g) in exposed animals, except on day 3 post-exposure 94 ng/g were determined (10-fold more than in other exposure groups; authors comment: presumably due to contamination of the sample).
However, the data neither demonstrate that the Ni content was
significantly increased nor that it was unchanged by exposure to the pigment dust.
LUNG:
Directly post-exposure the mean Ni and Sb concentration was 79 and 202 µg/lung , respectively (corresponding to 2 mg of pigment/lung). The concentration declined during the post-exposure period, following first order kinetics; the clearance half-life was 50 days.
AUTHORS CONCLUSION
No signs of toxicity have been observed.
The Ni and Sb concentration of liver and kidney after exposure was 3-5 orders of magnitude lower than in the lung and in most cases below quantification limits but above detection limits.
Pigment dust is eliminated from the lungs with a half-life of 50 days (typical for nuisance dusts), a bioavailibility of Ni and Sb from the pigment was not demonstrated.

Test condition: TEST ORGANISMS
- Age: 7 weeks on delivery (June 24, 1991; last sacifice Sept. 10, 1991)
- Weight at study initiation: 230-232 g body weight in all 5 test groups (see post exposure observation period)
- Number of animals: 10 rats per goup

EXPOSURE:
Head-nose exposure system; 5 d preflow period to accustom rats to exposure conditions; target conc: 60 mg/m3, measured conc. 59.6 +-2.51 mg/m3 (mean of daily means from 6

individual analysis per exposure); particle size analysis on test day 3 and 5: mass median aerodynamic diameter (MMAD) 0.6 - 1.0 µm (99-98% respirability); control group sacrificed on the day of arrival for analysis.

CLINICAL EXAMINATIONS:
body weight (at the beginning of pre-flow, at the beginning of exposure period and the morning of the last exposure, then once weekly), behaviour and state of health (daily three times on exposure, once during pre-flow- and post-exposure-period), mortality (daily).

ANALYSIS:
Ni and Sb concentration in lung, liver and kidneys determined; Food analysis: contamination in the used commercial feed was was 1.42 mg Ni/kg and 13 µg Sb/kg.

Statistics:
no statistical evaluation because no concurrent control.

Test substance: Lichtgelb 8G (Batch No.: Pt 8817; BASF Aktiengesellschaft; CAS 8007-18-9).
Chem. analysis:

TiO2	76.8%
Sb2O5	13.6%
NiO	5.0%
SiO2 (amorphous)	2.4%
Pb	31 ppm
As	16 ppm
other heavy metals	< 5 ppm
Ni soluble in 0.1 n HCl	46 ppm

Reliability: (3) invalid
Significant methodological deficiencies. Only one dose and no concurrent control limit validity of data on toxicity.

Flag: Critical study for SIDS endpoint

14-MAR-2003 (17)

Species: rat **Sex:** male/female
Strain: other: Wistar TNO W74
Route of administration: oral feed
Exposure period: 90 days
Frequency of treatment: continously
Post exposure period: no
Doses: 10, 100, 1000 and 10,000 ppm in feed (0.45, 4.5, 45, 450 mg/kg bw)
Control Group: yes, concurrent vehicle
NOAEL: = 450 mg/kg bw

Method: other
GLP: no data
Test substance: other TS: technical grade Nickel rutile yellow (C.I. Pigment yellow 53) characterized on a molar base as (Ti 0.88, Sb 0.05, Ni 0.075)O2 and as ca. 80% TiO2, 15% Sb2O5, 5% NiO on a weight % base

Remark: The detected traces of antimony (see results) most likely originate from the acid-soluble impurities of the pigment (10-20 mg antimony/kg pigment, that is 5-10 microgram/kg bw or 125-250 microgram/kg organ weight at the highest dose) and therefore do not indicate bioavailability of the pigment

itself.

Result: No deaths, no overt signs of reactions to the treatment, no effects on body weight gain (similar food consumption in all groups) or organ weight, no treatment related findings from haematological or biochemical investigations and urinalysis.
No macroscopic pathological changes attributable to treatment. No treatment related effects observed in histopathology.
No nickel concentrations related to the treatment detectable in liver and kidneys at any time and dose.
No antimony detectable in liver and kidneys after 1 and 2 months at any dose.
After 3 months treatment with 10000 ppm TS antimony was detectable in liver (6 ppb) and kidney (5 ppb) of males slightly above the detection limit and in females at levels of 6 (liver) and 10 (kidney) ppb.

Test condition: EXPERIMENTAL DESIGN
15 animals per dose per gender for toxicological investigations and 30 animals per gender in the control group;
additionally 10 animals per dose and gender for analytical investigations and 20 animals per gender in the control group.
Tests started at the age of 4- 5 weeks; TS given in powdered food (Altromin); feed and tape water ad libitum.

General observations:
Rats observed daily; food consumption and body weight gain determined once per week.

Haematological, clinical and biochemical investigations:
RBC, reticulocytes, platelets, haemoglobin, haematocrit, total and differential WBC, MCV, ALP, GOT, GPT, creatinine, urea, glucose, cholesterol, total plasma proteins and urine proteins, urinalysis conducted after one month and at the end of the study on 5 males and 5 females of each group; in addition thromboplastin time and glutamate dehydrogenase activity measured after three months.

Gross and histopathological investigations:
organ weight determined from thyroid gland, thymus, heart, lung, liver, spleen, kidneys, adrenal glands, and gonads and histopathology performed together with aorta, eyes, intestine, femur, brain, urinary bladder, pituitary, cervical lymph nodes, stomach, oesophagus, epididymides, pancreas, prostate, seminal vesicle, bone marrow of sternum, trachea, uterus, skeletal muscles from 5 animals per gender of control and top dose group.

Statistics:
Data on weight determinations, hematology and clinical chemistry compared by Wilcoxon U-test, level of significance $p<=0.05$.

Chemical Analysis
After 1, 2 and 3 months liver and kidneys from 5 animals per gender and dose group analysed for their nickel and antimony contents by AAS.
The detection limit for antimony was 5 ppb and for nickel 10

ppb.
Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint
14-MAR-2003 (15) (16)

Species: rat **Sex:**
Route of administration: oral feed
Exposure period: 90 days
Frequency of treatment: continously
Post exposure period: no
Doses: 1, 5, 10% in the feed (100, 500, 1000 mg/kg bm, as determined by the authors)
Control Group: yes, concurrent vehicle
NOAEL: >= 4500 mg/kg bw

Method: other
GLP: no
Test substance: other TS: Titani Yellow (TiO_2 82.5%, NiO 1.7%, Sb_2O_3 8.5%) (Ishihara Sangyo KK)

Result: No toxic action was observed.
Test condition: 10 Rats per dose, 4 control groups

Investigations:
Growth rate, haematology, organ masses (all organs including gonades), histopathology (stomach, intestine, liver, kidneys), clinical observations
01-OCT-2001 (25)

Species: rat **Sex:** male/female
Strain: other: Crj; CD(SD)IGS
Route of administration: gavage
Exposure period: males: 46 days; females 41-45 days from 14 days before mating to the day before autopsy (day 4 of lactation)
Frequency of treatment: once daily
Post exposure period: 1 day
Doses: 0, 250, 500, 1000 mg/kg (males & females)
Control Group: yes, concurrent vehicle
NOAEL: = 1000 mg/kg bw

Method: other: OECD TG 422 combined repeated dose and reproductive/developmental toxicity screening test
Year: 2000
GLP: yes
Test substance: other TS

Remark: Groups of 12 males(355-387g) and females(247-217g) were given the test article by gavage. General appearance was observed once a day, and body weight and food consumption were measured at day 1,2,3,5,7,10 and 14, then after weekly. Hematology, biochemistry, gross pathological changes and organ weight were examined at necropsy for all animals. Histopathological examination was conducted for control and high dose animals.
Result: The substance did not cause any significant effect on growth, food consumption, clinical signs, hematology, biochemistry, organ weight and pathological examination.
Test substance: Purity 100% C.I. Pigment Yellow 53 (LotNo. 4879) from Ishihara Sangyo, Japan
Reliability: (1) valid without restriction

Guideline study accordingto OECD 422. Peer review was conducted by a Japanese toxicological expert group at March 5, 2001.
Flag: Critical study for SIDS endpoint
13-MAR-2003 (22)

Species: cat **Sex:**
Route of administration: oral unspecified
Exposure period: 14 days
Frequency of treatment: daily?
Post exposure period: no
Doses: 0.5 - 2 gram

Test substance: other TS: Titani Yellow (TiO2 82.5%, NiO 1.7%, Sb2O3 8.5%) (Ishihara Sangyo KK)

Result: no abnormal changes, normal body mass gain, however, decreased appetite on day 1 and 2, transient diarrhea
Reliability: (3) invalid
Insufficient documentation
13-MAR-2003 (25)

Species: dog **Sex:**
Route of administration: oral unspecified
Exposure period: 7 days
Frequency of treatment: daily
Doses: 1 - 3 gram

Test substance: other TS: Titani Yellow (TiO2 82.5%, NiO 1.7%, Sb2O3 8.5%) (Ishihara Sangyo KK)

Result: no abnormal changes, normal body mass gain, however, temporarily decreased appetite, yellow substance was excreted
Reliability: (3) invalid
Insufficient documentation
13-MAR-2003 (25)

5.5 Genetic Toxicity 'in Vitro'

Type: Mouse lymphoma assay
System of testing: Mouse Lymphoma Cells L5178Y
Concentration: 3.13, 6.25, 12.5, 25, 50, 100 µg/ml with and without metabolic activation
Cytotoxic Concentration: no cytotoxicity at any concentration (compare with solubility of the TS in the freetext)
Metabolic activation: with and without
Result: negative

Method: other: Clive et al., 1987, Mutation Research, 189, 143-156
Year: 1987
GLP: yes
Test substance: other TS: Nickel Antimony Titanate, no further data

Method: Test comparable to OECD guideline 476.
Result: With metabolic activation (MA):
Trial 1 not acceptable because of cell culture problems, but no mutagenicity observed; in trial 2 no significant increase in mutant frequency (minimum criterion: 2-fold vehicle control) and no dose-related response, weak to no

cytotoxicity (relative growths 60.5% to 93.3%);
Without MA:
In Trial 1 excessive cytotoxicity in positive control but no mutagenicity of the TS; in trial 2 weak cytotoxicity of TS (59.7-92.9% relative growth) but no treatment induced mutant frequency that exceeded minimum criterion and no dose related trend was observed.

Valid positive controls with and without MA, mutant frequency in controls within acceptable range. Acceptable cloning efficiencies in controls (87.9% without MA, 92.9% with MA).

AUTHORS EVALUATION
TS was negative with and without activation under the conditions of testing; there was no cytotoxicity; the TS was insoluble and was tested at concentrations where it was possible to remove the TS at the end of exposure period.

Test condition: METABOLIC ACTIVATION (MA) SYSTEM
S-9 mix with liver homogenate from male Sprague-Dawley rats treated with 500 mg/kg Aroclor1254 5 d prior to sacrifice

CONTROLS
Untreated (negative) control (only in cytotoxicity test) and vehicle control (DMSO); positive control methyl methanesulfate (without MA) and methylcholanthrene (with MA)

MEDIA
- culture medium: RPMI 1640 supplemented with PluronicF68, L-glutamine, sodium pyrovate, antibiotics and 10% horse serum
- treatment medium: Fischers medium with same supplements but 5% horse serum
- cloning medium: like culture medium but 20% horse serum and without PluronicF68 and addition of BBL purified agar (0.24%)
- selection medium: cloning medium containing 3 µg/ml of 5-trifluorothymidine

PERFORMANCE OF TEST
TS formed a suspension in DMSO at concentrations from 0.195 to 100 mg/l; higher concentrations not included because of the insolubility of the TS (visible precipitates could not be removed by washing and dosing period could therefore not be controlled); in preliminary rangefinding tests no cytotoxicity at 1000 µg/ml; 2 independent trials; 3 vehicle controls and 2 positive controls in each trial; exposure period 4 h; expression period 2 d; selection period 10-14 d.

Since the TS was negative, colony sizing was not performed (total mutant colonies documented).

Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint
28-SEP-2001 (26)

Type: Ames test
System of testing: Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538
Concentration: 100, 250, 500, 1000, 2500, 5000 µg/plate with and without metabolic activation (see also freetext)

Cytotoxic Concentration: no cytotoxicity (see also freetext)
Metabolic activation: with and without
Result: negative

Method: other: Maron and Ames, 1983, Mutation Research, 113, 173-215
Year: 1983
GLP: yes
Test substance: other TS: Nickel Antimony Titanate, no further data

Method: Comparable to OECD guideline 471
Result: In preliminary dose range-finding study (TA100, 6.8-5000 µg/plate, 10 doses) no cytotoxicity with and without S9-mix as evidenced by no decrease in revertants/plate; precipitates at 1000 µg/plate (background lawn could not be evaluated).
GENOTOXIC EFFECTS:
- With and without metabolic activation: no positive results at any dose level in all tested strains.
CYTOTOXIC CONCENTRATION:
- No cytotoxicity of the TS at any dose level; precipitates influenced evaluation of background lawn at 1000 µg/plate.
CONTROLS:
spontaneous revertants in negative controls within the normal range; valid positive controls.
Evaluation:
Under the condition of this study the TS did not cause an increase in the number of revertants of any tester strain either with or without metabolic activation.
Test condition: SYSTEM OF TESTING
- Type: plate incorporation method
- Metabolic activation system: S9-mix, liver microsomes prepared from male Sprague-Dawley rats i.p. injected with 500 mg/kg Aroclor1254.
- number of plates per concentration/control: 3
- Solvent: DMSO, insoluble TS formed suspension which remained in all dilutions
- Controls: negative (vehicle control and sterility control) and positive control:
-S9 mix: 2-nitrofluorene (TA98), sodium azide (TA1535, TA100), ICR-191 (TA1537) and 4-nitroquinoline-N-oxide (WP2uvrA)
+S9 mix: 2-Aminoanthracene (five strains)
- Cytotoxicity: evaluated via bacterial background lawn and reduction in revertant colonies

CRITERIA FOR EVALUATING RESULTS:
TA98 and TA100 considered positive if the TS produced at least a 2-fold increase in revertants per plate over vehicle control and a dose response to increasing concentrations; same criteria for the other strains but 3-fold increase.
Reliability: (2) valid with restrictions
No 2nd independent trial
Flag: Critical study for SIDS endpoint
13-MAR-2003 (27)

Type: Bacterial reverse mutation assay
System of testing: Salmonella typhimurium TA100, TA98, TA1537, TA1535; E. coli WP2uvrA
Concentration: 156, 313, 625, 1250, 2500, 5000 µg/plate
Metabolic activation: with and without
Result: negative

Method: OECD Guide-line 471
Year: 2000
GLP: yes
Test substance: other TS

Remark: The substance was suspended in distilled water.
Precipitation was observed at the concentration of 2500 and 5000 µg/plate.

Metabolic activation:
with and without S9 derived from rat liver induced with phenobarbital and 5,6-benzoflavone

Pos.Cont.:
-S9 mix: 2-(2-Furyl)-3-(5-nitro-2-furyl)acrylamide (TA100, TA98,WP2), Sodium azide (TA1535) and 9-Aminoacridine (TA1537)
+S9 mix: 2-Aminoanthracene (five strains)

Result: Cytotoxic concentration:
Not observed up to 5000 µg/plate in the five strains with or without metabolic activation.

Genotoxic effects:
Negative with and without metabolic activaton.

Test substance: Purity 100% C.I. Pigment Yellow 53 (LotNo. 4879) from Ishihara Sangyo, Japan

Reliability: (1) valid without restriction
Guideline study according to OECD 471. Peer review was conducted by a Japanese genotoxicological expert group at March 22, 2001.

Flag: Critical study for SIDS endpoint

24-JUN-2002 (22)

Type: other: chromosomal aberration test
System of testing: Chinese hamster lung (CHL/IU) cells
Concentration: short-term treatment (-S9 mix): 4.88, 9.77, 19.5, 39.1, 78.1 µg/ml; short-term treatment (+S9 mix): 19.5, 39.1, 78.1, 156, 313, 625, 1250 µg/ml; continuous treatment (-S9 mix): 4.88, 9.77, 19.5, 39.1, 78.1 µg/ml
Metabolic activation: with and without
Result: negative

Method: OECD Guide-line 473
Year: 2000
GLP: yes
Test substance: other TS

Result: Cytotoxicity was observed at more than 39.1, 78.1, and 19.5 µg/ml in -S9mix, +S9mix and continuous treatments, respectively.

Negative in clastogenicity and polyploidy with and without metabolic activation.

Test condition: Test Design:
Pos. Cont.: -S9: Mitomycin C
+S9: Cyclophosphamide
Metabolic activation:
with and without S9 derived from rat liver induced with phenobarbital and 5,6-benzoflavone.

Solvent: distilled water
Criteria for evaluating results:
No. of cells/concentration: 200; Dose selection according to survival curve

Test substance: Purity 100% C.I. Pigment Yellow 53 (LotNo. 4879) from Ishihara Sangyo, Japan

Reliability: (1) valid without restriction
Guideline study according to OECD 473. Peer review was conducted by a Japanese toxicological expert group at March 22, 2001.

Flag: Critical study for SIDS endpoint
19-FEB-2003 (22)

Type: Bacterial reverse mutation assay
System of testing: E. coli WP2uvrA
Concentration: 100, 250, 500, 1000, 2500, 5000 µg/plate with and without metabolic activation (see also freetext)
Cytotoxic Concentration: no cytotoxicity (see also freetext)
Metabolic activation: with and without
Result: negative

Method: other: Maron and Ames, 1983, Mutation Research, 113, 173-215
Year: 1983
GLP: yes
Test substance: other TS: Nickel Antimony Titanate, no further data

Method: Comparable to OECD guideline 472
Result: In preliminary dose range-finding study (6.7-5000 µg/plate, 10 doses) no cytotoxicity with and without S9-mix as evidenced by the number of revertants per plate; precipitates at 1000 µg/plate (background lawn could not be evaluated).
GENOTOXIC EFFECTS:
- With and without metabolic activation: no positive results at any dose level.
-CYTOTOXIC CONCENTRATION:
- No cytotoxicity of the TS at any dose level; precipitates at 1000 µg/plate influenced evaluation of background lawn.
CONTROLS:
spontaneous revertants in negative controls within the normal range; valid positive controls.

Evaluation:
Under the condition of this study the TS did not cause an increase in the number of revertants of the tester strain either with or without metabolic activation.

Test condition: SYSTEM OF TESTING
- Type: plate incorporation method
- Metabolic activation system: S9-mix, liver microsomes prepared from male Sprague-Dawley rats i.p. injected with 500 mg/kg Aroclor1254.
- number of plates per concentration/control: 3
- Solvent: DMSO, insoluble TS formed suspension which remained in all dilutions
- Controls: negative (vehicle control and sterility control) and positive control with (2-aminoanthracene) and without S9-mix (4-nitroquinoline-N-oxide).
- Cytotoxicity: evaluated via bacterial background lawn and reduction in revertant colonies

CRITERIA FOR EVALUATING RESULTS:
Considered positive if the TS produced at least a 2-fold increase in revertants per plate over vehicle control and a dose response to increasing concentrations.

Reliability: (2) valid with restrictions
No 2nd independent trial

Flag: Critical study for SIDS endpoint

15-OCT-2001 (27)

5.6 Genetic Toxicity 'in Vivo'

5.7 Carcinogenicity

5.8.1 Toxicity to Fertility

Type:	other: Fertility/Development
Species:	rat
Sex:	male/female
Strain:	other: Crj; CD(SD)
Route of administration:	gavage
Exposure Period:	male: 46 days from 14 days prior to mating; female: 41-45 days from 14 days prior to mating to day 4 postpartum throughout mating and pregnancy
Frequency of treatment:	Once daily
Premating Exposure Period	
male:	14 days
female:	14 days
Duration of test:	male: 47 days; female: 42-46 days
Doses:	0, 250, 500, 1000 mg/kg/ b. w. (males & females)
Control Group:	yes, concurrent vehicle
NOAEL Parental:	= 1000 mg/kg bw
NOAEL F1 Offspring:	= 1000 mg/kg bw

Method: other: OECD TG 422 combined repeated dose and reproductive/developmental toxicity screening test
Year: 2000
GLP: yes
Test substance: other TS

Remark: Groups of 12 males (355-387g) and females (247-217g) were given the test article by gavage. Estrous cycle was determined before mating. Male/female per cage (1/1) was cohabitated for the most 4 days, until proof of pregnancy (formation of vaginal closing or sperm detection in vagina). The following reproductive parameters and developmental parameters were measured.
Reproductive parameters:
Estrous cycle, copulation index (number of pairs with successful copulation/number of pairs mated X 100), fertility index (number of pregnant animals/number of pairs with successful copulation X 100), gestation index (number of females with live pups/number of living pregnant females X 100), gestation length, nursing index, number of pregnant females, corpora lutea and implantation sites, implantation index (number of implantation sites/number of corpora lutea X 100), delivery index (number of pups born/number of

implantation sites X 100), live birth index (number of live pups on day 0/number of pups born X 100) sex ratio (total number of male pups/total number of female pups).
Developmental parameters:
Number of pups alive on day 4 of lactation, viability index (number of live pups on day 4/number of live pups on day 0 X 100), body weight of live pups (on day 0 and 4), full macroscopic examination on all of pups.

Result: There were no effects of administration of the test article on the estrous cycle, copulation index, fertility index, length of gestation, delivery, the gestation index, numbers of corpora lutea and implantation sites or implantation index. With regard to the pups, there were no effects of administration of the test article on the number of pups born, number of dead pups, live birth index, sex ratio, external anomalies, viability index, body weight or necropsy findings.

NOAEL:
Reproduction: 1000 mg/kg bw/day
Development: 1000 mg/kg bw/day

Test substance: Purity 100% C.I. Pigment Yellow 53 (LotNo. 4879) from Ishihara Sangyo, Japan

Reliability: (1) valid without restriction
Guideline study according to OECD 422. Peer review was conducted by a Japanese toxicological expert group at March 5, 2001.

Flag: Critical study for SIDS endpoint

13-MAR-2003 (22)

5.8.2 Developmental Toxicity/Teratogenicity

Species: rat **Sex:** male/female
Strain: Crj: CD(SD)
Route of administration: gavage
Exposure period: 46 days for males; 41-45 days for females
Frequency of treatment: once daily
Duration of test: male: 47 days; female: 42-46 days
Doses: 0, 250, 500, 1000 mg /kg bw/day
Control Group: yes, concurrent vehicle
NOAEL Maternal Toxity: = 1000 mg/kg bw
NOAEL Teratogenicity: = 1000 mg/kg bw

Method: other: OECD TG 422 combined repeated dose and reproductive/developmental toxicity screening test
Year: 2000
GLP: yes
Test substance: other TS

Result: No adverse effects on reproduction and development were observed in a reproductive/developmental toxicity screening test according to OECD guideline TG 422

Test substance: Purity 100% C.I. Pigment Yellow 53 (LotNo. 4879) from Ishihara Sangyo, Japan

Reliability: (1) valid without restriction
Guideline study according to OECD 422. Peer review was conducted by a Japanese toxicological expert group at March 5, 2001.

Flag: Critical study for SIDS endpoint

05-MAR-2003 (22)

5.8.3 Toxicity to Reproduction, Other Studies

In Vitro/in vivo: In vivo
Species: rat
Strain: Crj: CD(SD) **Sex:** male/female
Route of administration: gavage
Exposure period: 46 days for males; 41-45 days for females
Frequency of treatment: once daily
Duration of test: male: 47 days; female; 42-46 days
Doses: 0, 250, 500, 1000 mg/kg b.w./day
Control Group: yes, concurrent vehicle

Method: other: OECD TG 422 combined repeated dose and reproductive/developmental toxicity screening test
Year: 2000
GLP: yes
Test substance: other TS

Result: no adverse effects on reproduction and development were observed in a reproductive/developmental toxicity screening test according to OECD guideline TG 422
Test substance: Purity 100% C.I. Pigment Yellow 53 (LotNo. 4879) from Ishihara Sangyo, Japan
Reliability: (1) valid without restriction
valid without restriction
Guideline study according to OECD 422. Peer review was conducted by a Japanese toxicological expert group at March 5, 2001
Flag: Critical study for SIDS endpoint
14-MAR-2003 (22)

5.9 Specific Investigations

5.10 Exposure Experience

Remark: no data available
24-AUG-2001

5.11 Additional Remarks

6.1 Analytical Methods

6.2 Detection and Identification

7.1 Function

7.2 Effects on Organisms to be Controlled

7.3 Organisms to be Protected

7.4 User

7.5 Resistance

8.1 Methods Handling and Storing

Safe Handling: Breathing must be protected when large quantities are decanted without local exhaust ventilation.
Fire/Exp. Prot.: Avoid dust formation.
Storage Req.: Keep container tightly closed.
Transport Code: Not classified as hazardous under transport regulations.

Flag: non confidential, Critical study for SIDS endpoint
14-NOV-2002 (1)

8.2 Fire Guidance

Prot. Equipment: Wear a self-contained breathing apparatus.
Ext. Medium: water spray, dry extinguishing media, foam, carbon dioxide
Add. Information: The degree of risk is governed by the burning substance and the fire conditions. Contamined extinguishing water must be disposed in accordance with official regulations.
Products arising: Evolution of fumes/fog. Harmful vapours can be released in case of fire.

Flag: non confidential, Critical study for SIDS endpoint
14-NOV-2002 (1)

8.3 Emergency Measures

Type: other: general advice

Remark: Remove contaminated clothing.
Flag: non confidential, Critical study for SIDS endpoint
14-NOV-2002 (1)

Type: injury to persons (skin)

Remark: Wash thoroughly with soap and water.
Flag: non confidential, Critical study for SIDS endpoint
14-NOV-2002 (1)

Type: injury to persons (eye)

Remark: Wash affected eyes for at least 15 minutes under running water with eyelids held open.
Flag: non confidential, Critical study for SIDS endpoint
14-NOV-2002 (1)

Type: injury to persons (oral)

Remark: Rinse mouth and then drink plenty of water.
Flag: non confidential, Critical study for SIDS endpoint
14-NOV-2002 (1)

Type: injury to persons (inhalation)

Remark: If difficulties occur after dust has been inhaled, remove to fresh air and seek medical attention.
Flag: non confidential, Critical study for SIDS endpoint
14-NOV-2002 (1)

Type: accidental spillage

Remark: Personal precautions:
Avoid dust formation. Use personal protective clothing

Environmental precations:
Contain contamined water/firefighting water. Do not discharge into drains/surface waters/groundwater.

Methods for cleaning up or taking up:
For small amounts: Pick up with suitable appliance and dispose of.
For large amounts: Contain with dust binding material and dispose of.
Avoid raising dust.

Flag: non confidential, Critical study for SIDS endpoint
14-NOV-2002 (1)

8.4 Possib. of Rendering Subst. Harmless

8.5 Waste Management

Memo: other: Must be dumped or incinerated in accordance with local regulations.

Flag: non confidential, Critical study for SIDS endpoint
14-NOV-2002 (1)

8.6 Side-effects Detection

8.7 Substance Registered as Dangerous for Ground Water

8.8 Reactivity Towards Container Material

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(18) TSCA, OTS0001087, Doc ID FYI-OTS-0794-1087 submitted by Dry Color MFGS Assn (tests performed at Rosner-Hixon Laboratories)

(19) TSCA, OTS0001087, Doc ID FYI-OTS-0794-1087 submitted by Dry Color MFGS Assn (tests performed at Duke Laboratories)

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(26) Corning Hazelton, unpublished data, CHV 16702-0-431, 2. Apr. 1996, sponsored by Color Pigment Manufacturers Assoc.

(27) Corning Hazelton, unpublished data, CHV Study No.: 16702-0-409, 16. June, 1995, sponsored by Color Pigment Manufacturers Assoc.