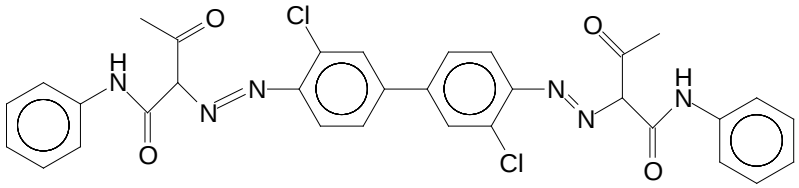
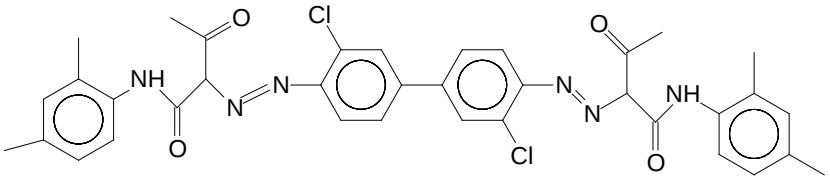
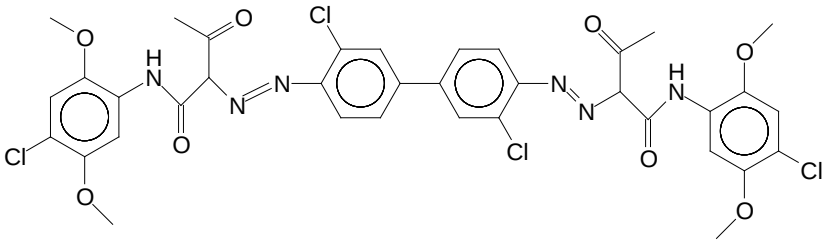
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	Pigment Yellow 12: 6358-85-6 Pigment Yellow 13: 5102-83-0 Pigment Yellow 83: 5567-15-7
Chemical Name	Pigment Yellow 12: Butanamide, 2,2'[(3,3'-dichloro[1,1'-biphenyl]-4,4'diyl)bis(azo)]bis[3-oxy-N-phenyl- Pigment Yellow 13: Butanamide, 2,2'[(3,3'-dichloro[1,1'-biphenyl]-4,4'diyl)bis(azo)]bis[N-(2,4-dimethylphenyl)-3-oxo- Pigment Yellow 83: Butanamide, 2,2'[(3,3'-dichloro[1,1'-biphenyl]-4,4'diyl)bis(azo)]bis[N-(4-chloro-2,5-dimethoxyphenyl)-3-oxo-
Structural Formula	Pigment Yellow 12:  Pigment Yellow 13:  Pigment Yellow 83: 

SUMMARY CONCLUSIONS OF THE SIAR

Category Rationale

The Diarylide Yellow Pigments category includes molecules with similar chemical structure; all contain the chloro-substituted biphenyl moiety, azo-moieties, keto groups and a substituted or non-substituted phenyl ring at both ends of the molecule, which is connected to the central part of the molecule via an amide bond. The only difference is in the substitution of the outer aniline rings, e.g. methyl, chloro and methoxy. They are expected to display essentially the same trend in environmental, ecotoxicological and toxicological behaviour based on the available data.

Physical-chemical properties

The substances are highly coloured solids which decompose before melting (>300 °C). Estimated vapour pressures range from 2.4^{-23} Pa to 2.9^{-19} Pa at 25 °C. Water solubilities are very low, with measured values between 0.35 µg/L (24 - 25 °C) and 8.1 µg/L (23 - 24 °C). The substances' solubility in n-octanol has been measured and ranges between 8.5 and 49.8 µg/L. Measured data on the log Kow are not available owing to testing being technically not feasible; modeling was used to fill this endpoint. The estimated log Kow values (KOWWIN v1.67) fall between 6.8 and 8.1 (although values estimated according to the ratio of the octanol solubility to the water solubility are $\leq$ 2.1). Dissociation constant, pKa, is not relevant for these very low water solubility substances.

Human Health

Standard single exposure toxicokinetics studies indicate essentially no potential for uptake via the oral and dermal routes. However, following repeated oral exposure at high dose levels, there is some evidence that a very limited uptake of the compound (or its impurities) could occur, based on observations of staining of the mucosal surfaces of internal organs (although the possibility of contamination during necropsy cannot be excluded). In an oral reproductive developmental screening study, staining of the pups could indicate a potential for limited placental transfer, again at a high dose level. Given that the pigment yellows are essentially not absorbed into the body, metabolism is not relevant. However, the presence of very low levels of 3,3'-dichlorobenzidine has been demonstrated in two studies using very sensitive techniques following oral administration of some yellow pigment compounds. It seems likely that this is due to the presence of a mono-azo impurity in some of the yellow pigment parent compounds, which is absorbed and subsequently metabolised. No 3,3'-dichlorobenzidine was found in the urine of experimental animals after exposure orally or via the lungs in long term studies. Following ingestion, the vast majority of the pigments are excreted unchanged in the faeces.

The acute oral LD50 values for rats are >3000 mg/kg bw for Pigment Yellow 13 and >1,750 mg/kg bw for Pigment Yellow 83. The acute oral LD50 values derived from studies in experimental animals are >1,750 mg/kg bw for the three Diarylide Yellow Pigments. For acute dermal toxicity a single LD50 of >3,000 mg/kg bw is available for Pigment Yellow 13. No deaths or clinical signs of toxicity were observed following oral or dermal exposure. The inhalation LC50 available is >4,448 mg/m^3 for Pigment Yellow 13. Tachypnoea, dyspnoea, exophthalmos, ruffled fur and curved or ventral body position were observed, although all animals recovered and no gross abnormalities were observed at necropsy.

All three pigments may be minimally irritating when in contact with the skin. Based on the available data the pigments have a minimal to slight potential for eye irritation. There is no indication that the three pigments are sensitisers.

No adverse effects were seen after 4-7 weeks oral administration of Pigment Yellow 12 at 1000 mg/kg/day (NOAEL), the highest dose tested in a well conducted and reported test of repeated dose toxicity (OECD TG422) study. Furthermore, in the cases of Pigment Yellow 12 and 83, no toxicologically significant effects were observed in a range of chronic toxicity studies of lesser quality (in terms of reporting) in rats and mice at doses up to 6500 mg/kg/day. Based on the kinetics of the three pigments and the chemical similarities, it can be concluded that these findings can be extrapolated to all three pigments.

For the inhalation route the effects seen are related to the deposition of dust particles in the lungs, leading to

Pigment Yellow 13 related effects even at the lowest exposure concentration of 54 mg/m^3 (local LOAEL). Systemically no effects were observed at the highest concentration tested, 410 mg/m^3 (systemic NOAEL).

All three pigments are not genotoxic in bacterial tests. Pigment Yellow 12 did not induce clastogenic effects in mammalian cells. Based on the chemical similarities between the three pigments, it is predicted that all three Yellow Pigments will not induce chromosomal changes in mammalian cells. There are no *in vitro* data to suggest that the pigments are genotoxic *in vivo*.

No increased tumour incidence after treatment with Pigment Yellow 12 and 83 were observed in several long-term studies in rats and mice (NOAEL (rat) > 630 mg/kg; NOAEL (mouse) > 1,960 mg/kg). Based on chemical similarity it can be concluded that the three pigments are not carcinogenic.

It can be concluded that Pigment Yellow 12 does not have any adverse effects on reproductive parameters. There was no evidence of teratogenicity. The NOAEL for maternal and reproductive toxicity is >1,000 mg/kg bw. Supporting evidence is also available from the fact that no changes on the reproductive organs were observed in the studies of repeat dose toxicity and carcinogenicity study with Pigment Yellow 83. In view of the structural similarities and similar kinetics no effects on reproduction or development are expected from Pigment Yellow 13 and Pigment Yellow 83.

The substances in this category do not present a hazard for human health due to their low hazard profile. Adequate screening-level data are available to characterize the human health hazard for the purposes of the OECD Cooperative Chemicals Assessment Programme.

Environment

The pigments have a calculated half-life for photo-oxidation of 1.7 – 4.5 hours (indirect reaction with OH-radical) and are expected to be hydrolytically stable. Fugacity modelling (Mackay Level III) predicts that the pigments will partition primarily to sediment (>98%) if released to the aquatic compartment only. Fugacity modelling for these substances is uncertain and the results should be treated with caution, because it is not clear that the substances fall within the applicability domain of the model. Based on the QSAR estimated log Kows the pigments have high potential for adsorption to soil (predicted Log Koc 5.61 – 5.77). The experimental data indicate that the pigments are not biodegradable (OECD 301C, Pigment Yellow 13 (36.6% dispersion in water) did not degrade during the 28-day incubation period).

The results of calculations of bioaccumulation potential are contradictory, given the high predicted log Kow values of the substances. No definitive experimental data on bioaccumulation are available. However based on the low measured solubilites in n-octanol, which may serve as an indicator for uptake into organisms and partitioning to lipids, and together with the molecular dimensions of the substances it can be concluded that these substances are unlikely to be of concern with regard to bioaccumulation. (Note: two of these substances were considered in the EU Technical Committee for New and Existing Substances PBT working group. The conclusion that they did not meet the criteria for a B (BCF $\geq$ 2000) or vB (BCF $\geq$ 5000) substance was drawn based on this information).

The acute LC50/EC50 of the pigments to fish and daphnia are above the water solubility limit. In 72h algal tests with Pigment Yellow 12 and 83, the ErC50s were also above the water solubility limit. Although some effects on biomass were reported in one algal study for Pigment Yellow 12 (below 50%), significant fluctuations were observed in the algal results. Further algal testing on Pigment Yellow 12 indicated no effects at solubility and these are considered key studies based on a weight of evidence approach. The NOEC in a daphnia chronic reproduction study was set at the water solubility limit as no effects were reported at the nominal concentration of 1 mg/L. No toxicity towards micro-organisms was observed at the solubility limit. Overall, available studies revealed no acute or chronic toxicity at concentrations orders of magnitude above the water solubility limit and at, or near, the water solubility limit. Based on the very low water and n-octanol solubility, exposure of aquatic organisms to the pigments is expected to be low. Partitioning to sediment may be possible based on the high sorptive potential (log Koc = 5.61 – 5.77). Two reliable long term studies in sediment dwelling organisms are available on pigment yellow 12 and 83 (both according to OECD 225: Sediment-Water Lumbriculus Toxicity Test Using Spiked Sediment); in both studies no effects were seen at the (limit) concentration tested, hence the 28-day NOEC was 1000 mg/kg sediment dry weight (nominal). Two reliable long term studies in earthworms are available on pigment yellow 12 and 83 (according to OECD Guideline 222:

Earthworm (*Eisenia fetida*) Reproduction Test); in both studies no statistically significant differences were observed between test group and controls at the one concentration tested (limit test), hence the 28-day (for mortality and biomass) and 56-day (for reproduction) NOECs were 1000 mg/kg soil dry weight (nominal).

The diarylide pigments do not present a hazard to the environment due to their low hazard profile. They have a low potential for bioaccumulation but are not readily biodegradable. Adequate screening-level data are available to characterize the environmental hazard for the purposes of the OECD Cooperative Chemicals Assessment Programme.

Exposure

For the year 2001 the global market for the three diarylide yellow pigments under evaluation was about 50,000 tonnes. The pigments are used as colouring agents in industrial and decorative paints, inks and plastics (polymers), cosmetics (Pigment Yellow 13 and 83) and textiles (Pigment Yellow 12).

Worker exposure to the pigments can occur during handling and cleaning operations. The principal route of exposure is by inhalation. Skin contact may be possible. Consumer exposure is expected to be negligible as consumer products only contain the pigments in a matrix. Exposure to consumers from PY13 and PY83 might be expected as the substances are approved cosmetic ingredients in Europe, however no information on the quantities used for this application are available.

There is potential environmental exposure arising from the production and processing of the substances. In addition exposure after paper recycling can not be excluded.