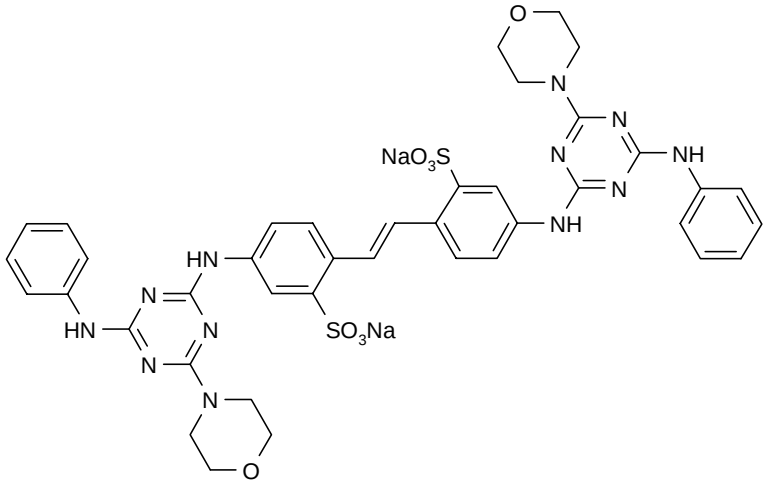
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	16090-02-1 56776-30-8
Chemical Name	Disodium 4,4'-bis[(4-anilino-6-morpholino-1,3,5-triazin-2-yl)amino]stilbene-2,2'-disulfonate
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Analogue Rationale

Fluorescent Brightener FWA-1 is a technical product which belongs to a group of stilbene type brighteners. As the active ingredient of C.I. Fluorescent Brightener 339 this compound is the most important member of this group of chemicals whose properties have been evaluated. The commercial forms of Fluorescent Brightener FWA-1 (CAS No. 16090-02-1) are granules/powders that may contain added salts or are aqueous slurries that contain small amounts of dispersants. Few tests are based on a commercial form that contains 82.5 % FWA-1, water, sodium chloride and sulfate.

Environmental fate or monitoring studies refer to the anionic form of FWA-1 due to the fact that the salt dissociates completely. Some toxicity tests have been performed with a surrogate (C.I. Fluorescent Brightener 220), that has identical structural characteristics but different substituents.

The compound is registered under the CAS Numbers 56776-30-8, with double bond geometry defined as (E). In dilute aqueous solutions, when irradiated with daylight, FWA-1 photo-isomerizes to a compound with double bond geometry defined as (Z). A further CAS Number is 60650-94-4 (no structure diagram available, referring to the names “C.I. Fluorescent Brightener 339” and “Tinopal AMS-GX”). The free acid is registered with the CAS Number 32466-46-9. There are two additional C.I. names for the compound with CAS-No. 16090-02-1: C.I. Fluorescent Brightener 71 is defined by this CAS-No., the CA Index Name. C.I. Fluorescent Brightener 71 replaces the generic name C.I. Fluorescent Brightener 260 which is discontinued.

All types of FWA-1 are based on the identical organic diamino stilbenedisulfonate (DAS) which determines the ecological and toxicological properties.

Human Health

After oral exposure, rats excreted FWA-1 almost completely in the feces within 48 hours. There was no measurable

skin penetration of FWA-1 when topically applied in a detergent solution to rats. When applied at 0.43 mg/ml in ethanol, approximately 0.01 µg/cm^2 penetrated rat skin within 2 days.

The acute oral LD_{50} in rats was greater than 5000 mg/kg bw. Clinical signs were unspecific and included sedation, dyspnea, ruffled fur, and curved body position. The acute dermal LD_{50} in rats was greater than 2000 mg/kg bw. No systemic toxicity was observed after dermal exposure. No reliable studies were available on the acute inhalation toxicity of FWA-1.

FWA-1 was slightly irritating to the skin and eyes of rabbits. The chemical was not a skin sensitizer in animal studies or in human repeat insult patch tests.

No substance-related effects were found in a comprehensive oral 28-day study on rats up to and including the highest tested dose of 825 mg/kg bw/day (= No-Observed-Adverse-Effect-Level, NOAEL). The No-Observed-Effect-Level (NOEL) in a combined 2 year chronic toxicity / carcinogenicity feeding study was 1000 ppm (corresponding to 51 mg/kg bw/day for male animals and to 78 mg/kg bw/day for female animals) based on increased kidney weights. In the absence of histopathological kidney changes and in the absence of accompanying hematological or biochemical changes, the effects on kidney weights are considered treatment related but not toxicologically relevant. Therefore, 10 000 ppm (corresponding to 524 and 791 mg/kg bw/day for males and females, respectively) can be established as a NOAEL for the 2-year study.

FWA-1 was not mutagenic in several bacterial tests (Ames tests) with and without metabolic activation. The chemical did not induce structural chromosome aberrations in V79 Chinese hamster cells. No increase in micronuclei was induced by FWA-1 in a mouse bone marrow micronucleus assay.

No indication of a carcinogenic effect of FWA-1 was found, neither after dermal administration (3 times/week for one year, up to 30 µl, 0.01 %) to mice on irradiated skin, nor after chronic oral administration (24 months, up to 10 000 ppm = 524 mg/kg bw/day for males, 791 mg/kg bw/day for females) to rats, respectively.

In the absence of any valid reproductive or developmental toxicity studies with FWA-1, results from modern guideline studies with a structurally very similar compound (Fluorescent Brightener C.I. 220), as well as results from a pilot developmental study with the free acid form of FWA-1 were used to evaluate the reproductive and developmental toxicity.
With Fluorescent Brightener C.I. 220, the NOAEL for parental toxicity in a 2-generation study was at 300 mg/kg bw/day. At 1000 mg/kg bw/day (highest dose tested) an increase in kidney weight was observed; in the same study, the NOAEL for parental reproductive performance was established at 1000 mg/kg bw/day; for offspring growth and development, the NOAEL was also at 1000 mg/kg bw/day.
The developmental toxicity study with Fluorescent Brightener C.I. 220 on rabbits revealed NOAELs for maternal and developmental toxicity at 100 mg/kg bw/day each (LOAEL, maternal and developmental toxicity: 400 mg/kg bw/day, based on clinical signs and bloody intestinal contents in the dams, and reduced fetal weight). In a similar study, performed on rats, the NOELs for both maternal and developmental toxicity were 1000 mg/kg bw/day (highest dose tested). Pilot oral prenatal developmental toxicity studies on rabbits and on rats were performed with the free acid form of FWA-1 and resulted in maternal and developmental NOAELs of 1000 mg/kg bw/day (highest dose tested) for both species. Based on the available data, it can be concluded that the potential of FWA-1 to induce reproductive or developmental toxicity is probably very low.

Environment

FWA-1 is a yellowish solid compound with a melting point of 337°C and a relative density of 1.54 g/cm^3 at 22 °C. It has a water solubility of 1.9 g/l (at 20 °C and at pH = 10.5) and an extrapolated vapor pressure of $4 * 10^{-18}$ hPa at 25 °C. The measured log K_{OW} is -1.58 (at 25 °C and at pH = 6.6).

In the atmosphere FWA-1 is degraded by photochemically produced OH radicals. The half-life is calculated to be about 1 hour. Due to the negligible vapor pressure this degradation process is not relevant. In natural water (Lake Greifensee, Switzerland) photodegradation half-live was measured as 4.1 – 5.1 hours. Under natural winter time

conditions, 70 % photolysis was calculated within 28 days for the same lake. FWA-1 is hydrolytically stable in water in the dark; the hydrolytic half-lives are more than one year.
Like many other FWAs also FWA-1 is not readily biodegradable. However, elimination by adsorption is significant as it was conducted in a Modified Zahn-Wellens Test (OECD TG 302 B) to a level of 98.8 % on day 28 and earlier.
In sewage treatment plants, adsorption onto sludge was observed up to a rate of 85 %, but no evidence was found for biodegradation during aerobic biological treatment and anaerobic-mesophilic digestion of sewage sludge.

The calculation of the distribution of FWA-1 between the environmental compartments according to the Mackay Fugacity Level I model and of the Henry´s law constant does not seem appropriate as the substance is ionized under environmental conditions. From the physico-chemical properties (in specific a high water solubility and a low log K_{OW}) it might be concluded that the sole target compartment for FWA-1 is water. However, as a high adsorption to soil was calculated, it might be assumed that the substance will strongly adsorb also to the sediment and soil compartment. K_{OC} values were calculated as $9.545 * 10^9$ but might be overestimated. In an adsorption/desorption study according OECD TG 106 without distinguishing between isomers, K_{oc} values have been measured for three soil types: K_{oc} = 1040 l/kg sand, K_{oc} = 860 l/kg loamy sand and K_{oc} = 2240 l/kg sandy loam. All these values will lead to a high adsorption potential to soil, sediment and suspended solids.
The measured BCF values of 1.4 to 28 give no indication for a significant bioaccumulation potential.

Results on acute aquatic toxicity are available for fish (*Oryzias latipes* 48-hour LC_{50}: 50 mg/l; *Danio rerio*: 96-hour LC_{50}: 337 mg/l for the E-isomer; 14-day LC_{50}: 165 mg/l (geometric mean of the LC_0 and the LC_{100})), invertebrates (*Ceriodaphnia cf. dubia*; EC_{50} (48 hours): 6.9 mg/l; *Daphnia magna*; EC_{50} (24 hours): > 1000 mg/l), and algae (*Desmodesmus subspicatus*; EC_{50} (96 hours): 41.1 mg/l). In a chronic toxicity test on reproduction of the water flea *Daphnia magna*, the NOEC (21 days) was 0.8 mg/l, indicating potential to cause long-term adverse effects in the aquatic environment.
The toxicity of FWA-1 to micro-organisms and earthworms was determined to be low: the $L(E)C_{50}$ values were > 100 mg/l and > 1000 mg/kg dw, respectively.
According to the EU risk assessment procedure, a $PNEC_{aqua}$ of 0.008 mg/l was obtained by applying an assessment factor of 100 on the lowest endpoint, the result of the chronic *Daphnia* test.

Exposure

There are several producers of FWA-1 in Europe and world-wide. The total production volume for FWA-1 is estimated by the European Commission to 10 000 – 50 000 tonnes/a in 1999. In the Sponsor country the annual production volume is in the range of 500 to 600 tonnes/a by only one producer.
The chemical is produced in a closed system. From the manufacturing site of the Sponsor Country releases into the atmosphere do not exceed legally limiting values (< 25 kg/a). Releases into the hydrosphere may occur during manufacture, formulation and processing as well as during widespread usage due to the relatively low removal efficiency in sewage treatment.
The total European usage was estimated to be approximately 2100 tonnes of active ingredient in 2001. More than 90 % of this brightener is used in household detergents in concentrations ranging from 0.05 to 0.35 %. It is also used to a far lesser extent (< 10 % in total) in textiles and paper. It is used also in combination with distyrylbiphenylsulfonate (DSBP)-type FWAs. FWA-1 behaves like colorless direct cotton dyes, i.e., during the washing process, FWA-1 penetrates the textile fibers by diffusing on the surface of the pore walls. Measurements have shown that up to 72 % of FWA-1 of the end-use concentration may be adsorbed on to the fiber.
FWA-1 can be found in water, sludge, sediment and soil.
The range of concentrations was 20 - 337 ng/l for 3 West-German rivers and 123 - 2097 ng/l for two East-German rivers.
In a monitoring program in Switzerland, the range of concentrations in rivers was 6 - 986.2 ng/l.
The maximum concentration in sediment cores of Lake Greifensee (Switzerland) were 1.2 mg FWA-1/kg sediment in the 1970's and leveled out at 0.7 mg/kg sediment from 1983 onward (no indication of wet or dry weight basis).The 90th percentile value is 1.597 mg/kg sediment.
A point of high concentrations is the river Rhine below the production site of FWA-1 with a 90th percentile of 740 ng/l and an average of 549 ng/l.
The seawater and freshwater monitoring of 16 sites in Tokyo Bay and adjacent rivers demonstrated that FWA-1 is

widely distributed in the riverine environments of Tokyo. Dissolved FWA-1 concentrations in the rivers were around 1 µg/l. The concentration ranges of FWA-1 detected in Tokyo Bay were 21.3 - 127.4 ng/l At most stations the concentrations were several tens of ng/l.
Exposure of workers to FWA-1 may occur during manufacture, use, transport and disposal of FWA-1, mainly through the respiratory and dermal routes of exposure. Exposure of workers is controlled by personal protective equipment, local exhaust ventilation techniques and regular workplace surveys. FWA-1 is widely used in household detergents, with a maximum FWA-1 concentration in these products of ca. 0.35 %. The maximum total systemic exposure of consumers via direct or indirect skin contact, inhalation of detergent dust or via the oral route has been estimated to be about 0.23 mg/kg bw/day.

RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health: The chemical is currently of low priority for further work due to its low hazard profile.

Environment: The chemical is a candidate for further work. The chemical possesses properties indicating a hazard for the environment (chronic toxicity to daphnia). Therefore, an exposure assessment and, if then indicated, an environmental risk assessment is recommended.

Note: There is a HERA (Human and Environmental Risk Assessment) Report for FWA-1 available, produced by A.I.S.E. and Cefic in 2004 (http://www.heraproject.com).