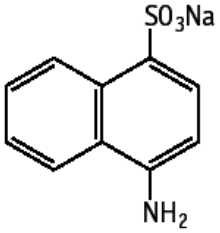
INITIAL TARGETED ASSESSMENT PROFILE

CAS No.	130-13-2
Chemical Name	4-Amino-1-naphthalenesulfonic acid sodium salt
Structural Formula	

SUMMARY CONCLUSIONS OF THE TARGETED ASSESSMENT

NOTE: The present assessment was targeted to address only the following endpoint(s): Human Health: acute toxicity, repeated dose toxicity, *in vitro* mutagenicity and developmental toxicity. It cannot be considered as a full SIDS Initial Assessment. Summary information on exposure is also reported here. Other endpoints for human health and the environment have not been presented to OECD member countries, and thus are not included in this profile.

Rationale for targeting the assessment

Under the Japanese Chemical Substances Control Law (CSCL), risk assessment of existing chemical substances has been conducted by the government. The CSCL was amended in 2010 and 2011 and shifted toward risk-based management from hazard-based management. Chemical substances are classified as follows from April 1, 2011: (1) Class I Specified Chemical Substances (persistent, highly bioaccumulative, has long-term toxicity for humans or long-term toxicity for predator animals at higher trophic level), (2) Class II Specified Chemical Substances (has long-term toxicity for humans or flora and fauna in the human living environment, has risk), (3) Monitoring Chemical Substances (persistent, highly bioaccumulative, long-term toxicity unknown), (4) Priority Assessment Chemical Substances (suspected long-term toxicity for humans or flora and fauna in the human living environment, suspected risk) and (5) General Chemical Substances (risk to humans or flora and fauna in the human living environment is sufficiently low).

4-Amino-1-naphthalenesulfonic acid sodium salt is classified as a General Chemical Substance based on degrees of hazard intensity and exposure estimates at the priority assessment meeting.

This targeted assessment document was originally based on the material of the priority assessment meeting provided from the chemical assessment council of Ministry of Health, Labour and Welfare (MHLW), Japan, and the toxicological profile was re-assessed for the OECD Cooperative Chemicals Assessment Programme.

Physical-Chemical Properties

4-Amino-1-naphthalenesulfonic acid sodium salt is a brown crystalline solid at room temperature. Melting point is 280 °C, and boiling point is calculated to be 634.6 °C by MPBPWIN (version 1.43). However, this chemical may be decomposed before the temperature reaches 634.6 °C. Partition coefficient between octanol and water (log K_{ow}) is -2.34. Vapour pressure is estimated to be 2.07×10^{-12} Pa at 25 °C. Water solubility is 1×10^{6} mg/L at 25 °C.

Human Health

In a limited and old toxicokinetics study with rabbits, 4-amino-1-naphthalenesulfonic acid sodium salt (50mg/mL) or inulin were administered by rapid intravenous injection into a median ear vein. Blood samples were taken at frequent intervals. Urine was collected for 3 - 5 days. It was found that 4-amino-1-naphthalenesulfonic acid bound strongly to blood and was not fully released by the protein precipitant. 4-Amino-1-naphthalenesulfonic acid had a greater clearance value compared with inulin. It was concluded that 4-amino-1-naphthalenesulfonic acid is actively secreted into the renal tubule.

No acute toxicity study is available for 4-amino-1-naphthalenesulfonic acid sodium salt. However, in a 7-day dose range finding study for a 28-day repeated dose toxicity test, no deaths or clinical signs of toxicity were observed at a dose as high as 1000 mg/kg bw/day in rats. Therefore, the oral LD_{50} for 4-amino-1-naphthalenesulfonic acid sodium salt was considered to be greater than 1000 mg/kg bw in rats.

A 28-day repeated dose toxicity study was conducted in accordance with the Japanese guideline (similar to OECD Guideline 407). In this study, 4-amino-1-naphthalenesulfonic acid sodium salt was administered to rats by gavage at 0 (vehicle control: water for injection listed in the Japanese Pharmacopoeia), 100, 300 or 1000 mg/kg bw/day. The test substance did not cause any treatment-related changes in general conditions, food consumption, body weights, urinary findings, results of hematological analysis or pathological findings. Blood chemical analysis revealed increases in GPT activity in males and in the creatinine and calcium levels in females in the 1000 mg/kg bw/day group. Since these biochemical changes were slight and no related changes were found for the organ weight or histopathology, the NOAEL for 4-amino-1-naphthalenesulfonic acid sodium salt is considered to be 1000 mg/kg bw/day in male and female rats in the 28-day repeated dose oral toxicity test.

In bacterial mutation studies using *Salmonella typhimurium* and *Escherichia coli* [including OECD guideline study (TG471 and 472)], 4-amino-1-naphthalenesulfonic acid sodium salt was negative in all tested strains with and without metabolic activation. In an *in vitro* chromosome aberration test using CHL/IU cells (OECD TG 473), 4-amino-1-naphthalenesulfonic acid sodium salt was also negative for structural chromosomal aberration or polyploidy induction with and without metabolic activation. *In vivo* genotoxicity data are not available. Based on these results, 4-amino-1-naphthalenesulfonic acid sodium salt is considered to be non genotoxic *in vitro*.

As for the developmental toxicity, one prenatal toxicity study was available. 4-Amino-1-naphthalenesulfonic acid sodium salt was administered by gavage to female rats at 0 (vehicle: distilled water), 15, 30, 100 or 200 mg/kg bw/day during days 0 - 19 of pregnancy. None of the animals died during the treatment period, neither were any adverse clinical signs observed, although no information on the body weight, food and water consumption and histopathological findings in dams were available. No significant effects were found on total number of corpora lutea and implantations, number of corpora lutea per dam, and the percentage of implantation loss. In the 200 mg/kg bw/day group, the number of resorption per litter and the incidence of total litter loss were increased. There were no significant differences in the total number of fetuses per litter, the number of live fetuses per litter or the mean weight of the fetuses between the control and 4-amino-1-naphthalenesulfonic acid sodium salt-treated groups. No dose-related increase was found in the number of offspring with external, skeletal, sternebral or soft-tissue abnormalities. Based on these findings, the NOAEL for developmental toxicity of 4-amino-1-naphthalenesulfonic acid sodium salt was considered to be 100 mg/kg bw/day in rats.

Agreed Hazard Conclusions

Based on the available information, 4-amino-1-naphthalenesulfonic acid sodium salt posseses properties indicating a hazard for one human health endpoint (developmental toxicity) targeted in this assessment.

Available Exposure

Production and/or import volume of 4-amino-1-naphthalenesulfonic acid sodium salt was reported to be less than 1,000 tones/year in fiscal year 2010 in Japan. Production volumes in other countries are not available. 4-Amino-1-naphthalenesulfonic acid sodium salt is used as an intermediate for azo-dyes.