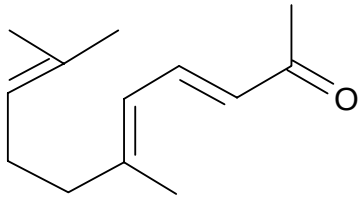
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	141–10–6
Chemical Name	Pseudoionone
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Pseudoionone has an acute oral mammalian LD_{50} (rat and mouse) above 2000 mg/kg bw, with most values greater than 5000 mg/kg bw. The acute dermal LD_{50} (rabbit) is above 5000 mg/kg bw. No inhalative or intraperitoneal toxicity data have been located.

Pseudoionone is severely to moderately irritating to the skin down to concentrations below 10%, based on studies in rabbit and guinea pig, but an 8% solution in petrolatum was not irritating to human volunteers. Pseudoionone produced transient irritant reactions of the eyes in a rabbit study. In a sensitisation test the reactions were judged to be of an irritant rather than a sensitising nature; however, a maximisation test with 8% pseudoionone in human volunteers resulted in 9 out of 108 subjects (8.3%) showing positive reactions.

The 28-day subchronic oral NOAEL of 50 mg/kg bw/d is based on minor, reversible effects (salivation kidney and liver weight gains) up to the highest dose of 1000 mg/kg bw/d. The same effects were observed in a one-generation reprotoxicity study in rat leading to a NOAEL for parental systemic toxicity of 120 mg/kg bw/d and a NOEL of 40 mg/kg bw/d, respectively.

Pseudoionone was not mutagenic in two bacterial Ames tests with and without metabolic activation nor in an *in vivo* OECD 474 mammalian micronucleus test. No carcinogenicity data have been located.

In a one-generation reproductive toxicity study in rats with an average exposure of 60 days for females and of 106 days for males, 120 mg/kg bw/d is the parental systemic toxicity NOAEL based on salivation, kidney and liver weight gains. Development of pups was unaffected up to the highest dose of 360 mg/kg bw/d leading to a developmental NOAEL of 360 mg/kg bw/d. Due to an increased rate in pup deaths during days 1–4 *post partum* in the highest dose group, the reproductive toxicity NOAEL is 120 mg/kg bw/d. A single application by gavage of 960 mg pseudoionone/kg bw to pregnant hamster dams caused no adverse effects on foetal development, in spite of reduced maternal bodyweight gain.

In several *in vitro* or *ex vivo* studies, pseudoionone was shown to have a potential for cytotoxicity at comparatively high concentrations.

In conclusion, the overall mammalian toxicity of pseudoionone is considered to be low. However, based on animal data, pseudoionone is a skin irritant and a weak eye irritant, and based on human data, there is a potential for sensitisation.

Environment

Pseudoionone is a liquid at room temperature, with a melting point of –75 °C, a boiling point of 265.4 °C, vapour pressure of 0.001741 hPa (20 °C), water solubility of 97 mg/l and a $logP_{OW}$ of 4.0. It has no ionisable groups at environmentally relevant *p*H. Due to the calculated $logK_{OC}$ values of 2.84 and 3.46 pseudoionone is predicted to adsorb moderately to organic carbon in soils and sediments. Based on standard Mackay distribution models, pseudoionone will mainly remain and be degraded in the environmental compartment of emission. Pseudoionone has no hydrolysable bonds. When exposed to atmospheric oxygen, pseudoionone is liable to slow autoxidation, but in case of exposure over large surfaces, *e.g.*, on cleaning rags, it may even self-ignite. The total atmospheric half-life due to indirect photodegradation is estimated at approximately 10 minutes. Based on the experimental $logP_{OW}$ and on QSAR-modelled $logK_{Ow}$ and BCF values (240-500), pseudoionone has a potential for bioaccumulation.

Pseudoionone attained 62% ready biodegradability in an OECD 301F test but failed the 10-day-window criterion; additional reports support aerobic biodegradability. Pseudoionone was not biodegradable under anaerobic conditions in an ISO 11734 test, being toxic to the sludge at the test concentration of 122 mg/l.

Pseudoionone was moderately toxic in acute aquatic ecotoxicity tests, with EC_{50} and LC_{50} values for freshwater fish, daphnids, green algae and cyanobacteria consistently between 1 and 10 mg/l : *Leuciscus idus*, 96-hour-LC_{50} = 4.64 mg/l, *Daphnia magna*, 48-hour-EC_{50} = 3.7 mg/l and *Scenedesmus subspicatus*, 72-hour-EbC_{50} = 1.11 mg/l respectively ErC_{50} = 2.02 mg/l, all data nominal concentrations. Pseudoionone had low toxicity to activated sludge with an EC_{50} > 1000 mg/l in a 30-minute OECD 209 test, moreover, it was not inhibitory in the ready biodegradability test at 45 mg/l. In contrast, it was toxic to anaerobic sludge bacteria at 122 mg/l and the LOEC to cyanobacteria was 3 mg/l. Based on very summary data for marine larvae and crustaceans, pseudoionone was toxic respectively inhibitory at unspecified low concentrations.

In a chronic and reproductive test with the common soil and sediment nematode *Caenorhabditis elegans* the NOEC of pseudoionone was a relatively high 100 mg/kg sediment (dry weight) for growth and egg production and 400 mg/kg for fertility, while the respective EC_{50} values were 2490, 821 and 1537 mg/kg. Pseudoionone showed juvenile-hormone-like activity in a number of insect species when applied topically at 10–80 µg per larva, which corresponds to a relatively weak effect in comparison with other terpenoids. Pseudoionone was toxic by oral uptake to mosquito larvae with an LC_{50} of 10.15 µg/l diet but it had no effect on honeybees at unspecified concentrations <1% in food. No avian data have been located.

Pseudoionone has been detected in a number of flowering plants and one mould, where it was made likely to be both a precursor and a metabolite of the common carotenoid lycopene. No phytotoxicity data have been located. Some sources show moderate toxicity towards certain fungi, moulds and bacteria, however, these data are difficult to quantify or to relate solely to the activity of pseudoionone.

In conclusion, pseudoionone is not readily biodegradable due to missing the 10-day window criterion, but expected to easily meet the criterion for inherent biodegradability, also based on a test with a closely related substance. Pseudoionone shows moderate toxicity towards aquatic and micro-organisms and low toxicity towards a common soil and sediment nematode. It has weak juvenile-hormone activity in several insects. There is an absence of toxicity studies examining terrestrial plants. However, pseudoionone has been identified as a biochemical intermediate and a metabolite in several plants. On the other hand, there may be some toxicity against fungi and bacteria.

Exposure

In Switzerland approximately 72 % of the produced pseudoionone are used on-site and processed in closed systems. Approximately 26 % are transferred by rail to a plant of the same group in Switzerland and processed in closed systems as well. Less than 1.5 % are shipped in barrels to three other companies. A similar situation applies to the coproducer in Germany.
Worldwide, approximately 40,000 tonnes pseudoionone per annum are estimated by industry to be produced. 99.9% of synthetic pseudoionone is used as an intermediate in the synthesis of vitamins A, E and K_1, of carotenoids and of terpenoid compounds. In addition, pseudoionone appears naturally in plants as an intermediate in the biosynthesis

and a metabolite in the degradation of lycopene. Lacking quantitative data, the amount of pseudoionone appearing from natural sources cannot be estimated, but it may be rather high.

Chemical production workers in the two production sites in Switzerland and in Germany and the main recipient companies are rarely exposed to pseudoionone, due to closed synthesis. Where direct contact is possible, *e.g.*, during sampling, filling of transport containers or maintenance work, standard occupational hygiene measures limit exposure. Some of the industrial pseudoionone is released to the atmosphere. Minor amounts are expected in industrial wastewater, no measured environmental concentrations have been located.

Pseudoionone is listed as a food ingredient in the European Union, but not in the United States, hence the public in the EU may be exposed to pseudoionone as an ingredient of food and beverages; while no quantitative data have been located, the actual use in food must be minimal. The use of pseudoionone as a fragrance compound in cosmetics was forbidden in the EU due to the sensitising potential and pseudoionone is only tolerated as an impurity at less than 2% in pure ionone fragrance compounds, hence exposure through cosmetics must also be minimal.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health:

The only hazards identified are irritation to skin and slight irritation to eyes as well as sensitisation. Given the main use as a chemical intermediate and the low content of the substance in consumer products in the Sponsor country, the substance is considered to be of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.

Environment:

The chemical possesses properties indicating a hazard for the environment. Based on data presented by the Sponsor country, exposure to the environment is anticipated to be low, and therefore this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor.