# SIDS INITIAL ASSESSMENT PROFILE

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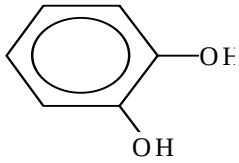
| **CAS No.** | 120-80-9 |
| **Chemical Name** | 1,2-Dihydroxybenzene (pyrocatechol, catechol), |
| **Structural Formula** |  |

## SUMMARY CONCLUSIONS OF THE SIAR

### Human Health

Catechol is absorbed by oral and dermal route as well as by the respiratory tract. A part of catechol is metabolized to o-benzoquinone by enzymatic oxidation. After oral administration catechol is conjugated with glucuronic acid and sulfuric acid and eliminated mainly and rapidly via urine.
The acute oral toxicity by gavage in rats is: LD50 = 300 mg/kg bw. The body weight gain increased and the animals that died during the observation period revealed hyperaemia of the stomach and intestine. In an acute inhalation study with rats the LC0 value was ≥ 2.8 mg/L, signs of intoxication observed were irritation and persisting tremors. Loss of distal portions of the tail and digits at doses of 2.8 mg/L and 2.0 mg/L were dose-related. The dermal acute toxicity is moderate: $LD_{50}$ in rats is 600 mg/kg bw.

Catechol produced slight to moderate erythema and slight oedema after 24 hours on the intact skin of rabbits, and was highly irritating to the eyes of rabbits. An epidemiology study on human workers exposed to catechol and phenol vapors, indicated irritation for the respiratory tract (cough, sputa, throats). Skin sensitisation tests with guinea pigs were positive.

None of the available publication on repeated dose toxicity was reliable. However, the carcinogenicity studies allow an estimation of the toxicity level after prolonged exposure. No clinical abnormalities or deaths related to catechol were observed during exposure via the diet, (in contrast to acute gavage). Body weight gain was clearly delayed (about 15%) in male rats exposed to 0.8% (318 mg/kg bw/day) catechol from week 1 to the termination (week 34 or 104) but not in those given 0.4% (141 mg/kg bw/day) or less. Slight thickening of the pyloric region was apparent in the 0.8% and 0.4% groups at week 34. Marked to moderate thickening was also found in rats fed 0.2% (65 mg/kg bw/day) and above, at the end of the study. Other gross lesions observed in the present study were considered to be of spontaneous nature and typical of this strain of rat. The NOAEL can be estimated to be 0.1% (33 mg/kg bw/day) at 34 weeks and LOAEL = 0.1% (33 mg/kg bw/day) at 104 weeks. Another study with male and female rats by oral feeding during 104 weeks at 0.8% indicated no differences between both sexes.

Regarding genetic toxicity with catechol *in vitro*, 8 reverse mutation assays with *Salmonella typhimurium* were negative with and without metabolic activation. In one mutoxitest with *Escherichia coli*, a positive result was obtained without metabolic activation and the result was negative with metabolic activation. Addition of metabolic activation completely inhibited the mutagenesis of catechol. Four gene mutation assays in cultured mammalian cells without metabolic activation were positive. . In chromosome aberration assays *in vitro*, catechol induced positive results without metabolic activation, and with S9 the toxicity of catechol was decreased. *In vitro* tests on damaging effects of catechol were positive only without metabolic activation in different cell lines. Positive results were obtained in a Sister chromatid exchange assay, without metabolic activation, at concentrations that were not cytotoxic (10 and 30

µM). Additional testing on cell transformation *in vitro* indicated that catechol at the concentration levels of 1 and 3 µM may induce morphological transformation in Syrian Hamster Embryo. An *in vivo* genetic toxicity spot test in mice was negative. *In vivo* micronucleus assays with mice were positive, indicating that administration of catechol at doses of 40 mg/kg by gavage and by intraperitoneal route at 10, 20, and 30 mg/kg bw induced chromosomal aberrations.
Results from an i*n vivo* replicative DNA synthesis test were positive. Two UDS tests gave opposite results and a test on DNA breaks was negative. In conclusion, *in vitro* tests were positive without metabolic activation and negative with metabolic activation, indicating ambiguous results concerning the mutagenic potential of catechol. *In vivo*, a positive micronucleus assay with mice, and a replicative DNA synthesis test indicated a potentially mutagenic effect of catechol.

Regarding carcinogenicity, several studies by oral route reported catechol to induce positive responses in rat stomachs. Tumours are mainly caused by local irritation, inflammation, and ulceration leading to regenerative hyperplasia. Only studies by the oral route are available, but concerns for carcinogenicity at other sites of first contact cannot be dismissed.
At low levels of catechol no promoting effects were described, probably because any hydroxyl radicals, formed by oxidation-reduction cycles through metabolism, are detoxified and there is no cytotoxicity and therefore, no increase in cell duplication. Carcinogenic responses of catechol occur, at a high dose (0.8%), at cytotoxic effects, leading in turn to inflammatory responses, increased DNA synthesis and cell duplication rates. Overall, these phenomena might select cells with altered gene structure, typical of neoplasia, generally in the point of application of the substance (forestomach in rats). In conclusion catechol can be considered as an animal carcinogen at high doses while it is not at low doses. Although there is some evidence that catechol is mutagenic, the exact mechanism of carcinogenicity is uncertain; however results of carcinogenicity studies tend to indicate that catechol acts by a non-genotoxic mechanism as there seems to be a threshold level.

No studies were performed to assess the effect of catechol on fertility. In the carcinogenicity studies where reproductive organs were examined, no lesions, no alteration or abnormalities were described after long term exposure (34 and 104 week) at concentrations of 0.1, 0.2, 0.4, 0.8% (respectively 33, 65, 141, 318 mg/kg bw/day).
In one developmental study with rats, one generation, with a single day administration by gavage at the $11^{th}$ day of gestation , maternal toxicity was described at each dose tested (333, 667, 1000 mg/kg bw) by reducing body weight gains. Mortality in the dams at 1000 mg/kg was 67%. Litter size decreased at 667 mg/kg bw in postnatal day 6 and at 1000 mg/kg in postnatal day 1. Litter biomass decreased in postnatal day 1 at 667 mg/kg bw. A syndrome of malformation involving the limb, tail and urogenital system was observed. The litter incidence regarding hindlimb paralysis and/or short kinky tails was 21.4%, 66.7% and 80.0% for 333, 667 and 1000 mg/kg respectively.
As this study is not a standardized study (single day administration) and it is the only one available for catechol, analogy with a parent product, hydroquinone (para-diphenol), presenting similar antioxidant properties, similar metabolism, and a similar toxicological profile, was used. In a developmental toxicity study with hydroquinone, doses up to 300 mg/kg were given to pregnant rats during organogenesis. Hydroquinone was not selectively toxic to the developing conceptus. The NOEL for both maternal and developmental toxicity was 100 mg/kg bw, based, in the 300 mg/kg group, on a decrease in body weight gain and feed consumption in dams and on an increase in the incidence of total common vertebral variations in foetuses.

Neurotoxicity was studied with application of catechol on the external surface of an isolated dorsal root ganglion cell of American bull frog. Catechol inhibited specifically fast K+ current, but not the slow Ca+, Na+ currents. The ED50 for the prolongation of action potential was estimated from Lineweaver-Burk and Eadie-Hofsee plots of the data to be about 71.6 mg/L
In an immunotoxicity test, catechol was reported to inhibit the mitogenesis of B-cells in a dose dependent manner, and cytotoxicity was observed on T-cells.
Studies on hematotoxicity of Catechol reported effects on hematopoietic and human blood cell.
In *in vitro* hepatotoxicity studies, no influence of catechol was observed on cytochrome P450 of rats and on human liver microsomes at a dose of 110 mg/L.

**Environment**

Catechol has a low vapor pressure (0.03 hPa at 25 °C) and a high water solubility (median value of 449 g/l at 20°C).

Since it has a pKa of 9.23, catechol reactivity and transfer between environmental compartments could be affected by pH. The measured log Kow is 0.84-1.01 at 20°C.

According to the Mackay level I model, the preferred targeted compartment of catechol will be water (99.2%). Based on its vapor pressure and its Henry's law constant ($7.35\ 10^{-4}$ $Pa.m^3.mol^{-1}$), catechol is expected to have a low volatility from dry soil surfaces and aqueous media. Removal of catechol from surface water by means of photodegradation should not be expected for the non-ionized form, whereas it could occur for the ionized form (absorption maximum at 313 nm in basic solution). Atmospheric oxidation half-life has been estimated by QSAR to be 0.6 days. Hydrolysis is not expected to occur: phenols are generally resistant to hydrolysis. Catechol has shown a high potential to polymerize with humic acids present in soil; the polymers formed were highly stable. In a clay loam soil, catechol has been found to be very mobile.

Biodegradation studies have shown that catechol was readily biodegradable in aerobic conditions. In anaerobic conditions, biodegradation is also possible. With an estimated bioconcentration factor of 3, catechol is not expected to bioconcentrate in aquatic organisms.

In acute aquatic toxicity studies, the lowest $EC/LC_{50}$ values were 8.9 mg/L (96 h) for freshwater fish, 1.7 mg/L (24 h) for *Daphnia magna*, 22 mg/L (96 h) for algae and 19.6 mg/L (48 h) for micro-organisms. No chronic toxicity tests were performed with aquatic organisms. This leads to a derived PNECaqua of 1.7 µg/L, using an assessment factor of 1000.

**Exposure**

The production volume in the Sponsor country is 10 000- 50 000 metric tonnes/year.

The principal use of catechol is as an intermediate for chemical synthesis for 97%, 3% is used as an etching agent in the electronic engineering industry. Use of catechol in leather industry is only suspected but as the consortium does not sell the substance to leather industry, this information is not verifiable.
Occupational exposure can occur at production (during sampling, conditioning, during operations on the machine making flakes), at processing (chemical or electronic industries); monitoring data are not available, but as appropriate occupational hygiene practices are used, including personal protective equipment, occupational exposure is kept as minimal as possible. Knowledge of production and processing schemes suggests that the final marketed products (aroma products, agrochemicals and pharmaceuticals) do not contain catechol. Therefore, consumer exposure is not expected.
From catechol chemical industry, environmental exposure would be from production and processing. At the production site, the effluents, containing about 500 ppm of catechol, are driven to a biological waste water treatment plant (Consortium companies, internal data). No measurements have been performed in the STP effluent. Based on its biodegradability, a model estimate indicates that 87% is removed during waste water treatment.
In electronic industry, for surface treatment, given the potential toxicity of other treatment products, the effluents are expected to be all collected and destroyed in the Sponsor country (Lead company, internal data).
Human exposure via the environment is expected to be low since catechol is readily biodegradable and non bioaccumulative.

**RECOMMENDATION**

The chemical is currently of low priority for further work

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

**Human Health** :
The chemical possesses properties (irritant, skin sensitizing agent, anti-oxidant, mutagenic, carcinogenic at high dose levels and possibly developmental toxicant) indicating a hazard for human health. Based on data presented by the Sponsor country, exposure to humans 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 country.

**Environment** :

The chemical possesses properties indicating a hazard for aquatic organisms. Although these hazards do not warrant further work as they are related to acute toxicity which may become evident only at a high exposure level, it should nevertheless be noted by chemical safety professionals and users.