

CAS N°	102-06-7
CHEMICAL NAME	1,3-Diphenylguanidine
Structural formula	

RECOMMENDATIONS OF THE SPONSOR COUNTRY

This chemical is a candidate for further work

SUMMARY CONCLUSIONS OF THE SIAR

Exposure

Diphenylguanidine is a solid with a melting Point in the region of 145-150°C. Its boiling point is greater than 170°C. Vapour pressure is relatively low (174×10^{-6} kPa at 20°) and solubility in water varies greatly with the pH of the medium from 475 mg/l to 1 g/l at pH 7 and 25° C, to 519 g/l at strongly acid pH and 20°C. At higher pHs the solubility does not appear to decrease significantly. The change in solubility is due to the ionisation state of the substance. There are two protonation steps. The log pKa of the first protonation occurs at 10.12 but the second is unknown. The log Kow is measured as 1.69 but the pH of test is unknown. Probably this result relates to the protonated molecule but whether in cationic or dicationic form not known. A calculated value is 2.9

The expected production volume of 1,3-Diphenylguanidine in year 2000 is 2400 tonnes/year in Europe, 2400 tonnes/year in the USA, an amount of 5300 tonnes/year for Asia and 11100 tonnes per year for the world.

1,3-diphenylguanidine is used as a primary accelerator in vulcanisation of rubber, as secondary accelerator for sulfur-containing compounds such as thiazoles, sulfenamides and thiram and as a minor use as a primary material for standardising acids.

Depending on the specific application, the concentration of 1,3-diphenylguanidine used in the production of rubber compounds may vary from 0.25% to 2.0% by weight.

Health effects

1,3-Diphenylguanidine is absorbed rapidly after oral uptake but only slowly after dermal application. The substance is metabolised quickly and eliminated in the urine and faeces. No information is available on the mode of action.

1,3-diphenylguanidine is moderately toxic by ingestion, the oral LD50 is 350-850 mg/kg b.w. for the rat. By dermal route, 1,3-diphenylguanidine is practically non toxic, the dermal LD0 is > 2,000 mg/kg b.w. in the rabbit. After oral administration, the symptoms were normally of a nervous character, but post mortem examination revealed liver effects (dark colour) and severe irritation of the gastro-intestinal tract.

Three sub-chronic 13-week toxicity feeding studies in rats or mice have shown an increase of the mortality rate in rats at high dose (3000 ppm) and a decrease of food consumption in rats (as of 500-750 ppm) and body weight gain in rats and mice (as of 500-750 ppm) due to the poor palatability of the 1,3-Diphenylguanidine-treated feed. Treatment-related effects on the organs and the haematological, clinical-chemical parameters and urinalysis were not observed. The NOAEL/LOAEL lies at 500/750 ppm (32/50 mg/kg bw/d) and 150/500 ppm (11/37 mg/kg bw/d) for rats and 500/750 ppm (75/114 mg/kg bw/d) in mice. Based on these data, a conservative NOAEL can be established at 32 mg/kg bw/d for rats and 75 mg/kg/d for mice.

Most of the *in vitro* and *in vivo* investigations available give no indication of a genotoxic effect.

A carcinogenicity study which would meet present standards is not available.

Previous and unreliable reproductive toxicity studies in male mice and hamsters indicated a negative influence on fertility of 1,3-diphenylguanidine, which may have been due to impurities in the test substance. Taken into account the reliable studies, where 1,3-diphenylguanidine was tested with a purity of 97.7% to 99.9%, representative of the industrial product, 1,3-diphenylguanidine did not affect the fertility of male mice when administered by gavage up to the maximal tested dose level of 16 mg/kg/d. In addition to the results of the feeding sub-chronic studies on the rat and mouse, special studies for recognising reproductive toxic effects were also performed. Comparisons of the parameter changes with the results of tests with feed withdrawal infer that the effects observed in the 1,3-Diphenylguanidine-treated animals in high concentration groups are a result of the

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poor general state of health (malnutrition, exhaustion) of the animals and not a direct toxic effect on the reproductive organs. Very conservative NOAELs, based on the effects on the reproductive organs, secondary to malnutrition and exhaustion, can be established at 32 mg/kg bw/d for rats and from 16 to 231 mg/kg bw/d for mice.

In female rats and mice foetotoxic, but not teratogenic, effects were seen after the oral administration of maternotoxic doses. In the rat study the NOEL was given as 5 mg/kg bw for the dams and 25 mg/kg bw for the foetuses. In the mouse study the NOEL was given as 4 mg/kg bw for the dams and > 10 mg/kg bw for the foetuses.

1,3-Diphenylguanidine is irritating to the eye and non-irritating to the skin.

Human cases have shown that contact dermatitis patients, for whom a rubber intolerance was often present, occasionally reacted positively to 1,3-diphenylguanidine in the patch test. Taken into account the negative Guinea pig maximisation assay, it can be inferred that the positive reactions observed in human patients with contact dermatitis reflected cross-reactions rather than a direct sensitising effect of 1,3-diphenyl guanidine.

In man, earlier and unconfirmed studies described the following symptoms after workplace exposures to 1,3-Diphenylguanidine : eye and mucous membrane irritation, gastric and bilious complaints and disturbed liver metabolism.

Environment

1,3-diphenylguanidine has three forms: unionised, primarily protonated and secondarily protonated. The pKa at which the first protonation occurs is 10.12 while the pKa for the second protonation is unknown and as this will be less than 10.12 it is not known whether this state will be reached at normal environmental pHs between 6 and 8. This leads to problems in determining the environmental fate of the substance.

Due to the relatively high solubility (approx. 0.5 g/l) at environmental pHs (6 to 9), low octanol water partition coefficient (<3) and low volatility of 1,3-Diphenylguanidine the substance is not expected to adsorb to sediment and will mainly be present in the aqueous phase. A bioconcentration test on fish provided a BCF of <2. The substance is therefore likely to remain bioavailable and, although not readily biodegradable, has been shown to mineralise rapidly in the presence of adapted micro-organisms. Based on the above the substance can be considered inherently biodegradable. Bioaccumulation in biota is not expected for this substance.

1,3-diphenylguanidine has been shown to be toxic to fish and algae and harmful to daphnia in several acute studies (fish : 96 h LC50 = 4.2-11 mg/l; algae : EC50 = 1.7-7.5 mg/l; daphnid : 48 h EC50 = 17-62.4 mg/l).

The PNEC can be determined using the NOECs from the algae (0.3 mg/l) and daphnid chronic (1.9 mg/l) studies (excluding the EbC50 results), by applying an uncertainty factor of 50. The resulting PNEC would be 6 µg/l.

A terrestrial plant study conducted on monocotyledons and dicotyledons did not show a high level of concern for DPG in these species

Due to its main use as a vulcanisation activator during which process it is incorporated in the rubber compound but much reverts after processing, leaching of DPG may occur from rubber compounds but the substance represents a relatively low percentage of content in the finished product (1-2%). DPG may be of concern locally in aqueous discharge from production and downstream use sites as well as due to releases from rubber articles containing DPG.

NATURE OF FURTHER WORK RECOMMENDED

Human health

No further works are recommended

Environment

Based on current information no clear conclusion can be drawn. While the fate properties suggest that the substance will not bioaccumulate in the environment and that degradation will occur, the PNEC, be it based on flora or fauna is relatively low and the downstream use is such that the substance is likely to be found (within or outside polymer matrix) in the environment mainly due to abrasion from car tyres.

In the absence of knowledge on the leaching behaviour of the substance from abraded rubber compounds, further work to provide a reasonable estimate of the environmental concentration is considered necessary.