

PHENOLPHTHALEIN

(Group 2B)

For definition of Groups, see [Preamble Evaluation](#).

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CAS No.: 77-09-8

Chem. Abstr. Name: 3,3-Bis(4-hydroxyphenyl)-1-(3*H*)-isobenzofuranone

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Phenolphthalein has been widely used as a laxative for nearly a century. Generally available without prescription, it is now being withdrawn from the market in many countries because of recent toxicological concern. Phenolphthalein has also long been used in the laboratory as an indicator in acid–base titrations.

5.2 Human carcinogenicity data

In the few available studies, there was no consistent association between the occurrence of colon cancer or adenomatous colorectal polyps and use of phenolphthalein-containing laxatives. Cancers at other sites have not been studied.

5.3 Animal carcinogenicity data

Phenolphthalein was tested for carcinogenicity by oral administration in two experiments in mice and in one experiment in rats. In one experiment in mice, it induced histiocytic sarcomas and lymphomas in both males and females and benign ovarian tumours in females. In an experiment in mice lacking one allele of the *p53* tumour suppressor gene, it increased the incidence of lymphomas. This result was confirmed in a separate study reported as an abstract. It induced benign renal tumours in male rats and benign phaeochromocytomas in males and females.

5.4 Other relevant data

Phenolphthalein is absorbed in the small bowel and is conjugated in the liver to form phenolphthalein glucuronide, which is eliminated in the bile. As it passes through the small intestine, it is partially deconjugated and reabsorbed.

Phenolphthalein and its glucuronide enhance oxygen radical production and cause oxidative damage *in vitro*. Phenolphthalein has also been shown to have low oestrogenic activity in some model systems. Phenolphthalein induced micronucleated erythrocytes in mice given multiple but not single treatments by gavage or in feed. Abnormal spermatozoa were induced in male mice but not male rats treated with phenolphthalein in the feed for 13 weeks. The malignant thymic lymphomas induced by phenolphthalein in female heterozygous *p53*-deficient mice showed loss of the normal *p53* allele.

Phenolphthalein induced chromosomal aberrations, *Hprt* gene mutations and morphological transformation but not aneuploidy or ouabain-resistant mutations or sister chromatid exchange in cultured mammalian cells. It did not induce gene mutations in bacteria.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of phenolphthalein.

There is sufficient evidence in experimental animals for the carcinogenicity of phenolphthalein.

Overall evaluation

Phenolphthalein is possibly carcinogenic to humans (Group 2B).

For definition of the italicized terms, see [Preamble Evaluation](#).

P>Synonyms

- 3,3-Bis(4-hydroxyphenyl)phthalide
 - 3,3-Bis(*para*-hydroxyphenyl)phthalide
 - α -(*para*-hydroxyphenyl)- α -(4-oxo-2,5-cyclohexadien-1-ylidene)-*ortho*-toluic acid
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