
***p-tert*-Butyltoluene**

(CAS reg no: 98-51-1)

Health-based Reassessment of Administrative
Occupational Exposure Limits

Committee on Updating of Occupational Exposure Limits,
a committee of the Health Council of the Netherlands

No. 2000/15OSH/030, The Hague, 7 March 2002

Preferred citation:

Health Council of the Netherlands: Committee on Updating of Occupational Exposure Limits. *p-tert*-Butyltoluene; Health-based Reassessment of Administrative Occupational Exposure Limits. The Hague: Health Council of the Netherlands, 2002; 2000/15OSH/030.

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1 Introduction

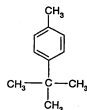
The present document contains the assessment of the health hazard of *p-tert*-butyltoluene by the Committee on Updating of Occupational Exposure Limits, a committee of the Health Council of the Netherlands. The first draft of this document was prepared by A Wientjes, M.Sc. and H Stouten, M.Sc. (TNO Nutrition and Food Research, Zeist, the Netherlands).

The evaluation of the toxicity of *p-tert*-butyl toluene has been based on the review by the American Conference of Governmental Industrial Hygienists (ACG99). Where relevant, the original publications were reviewed and evaluated as will be indicated in the text. In addition, literature was retrieved from the online data bases Medline, Toxline, and Chemical Abstracts covering the period 1966 to 26 April 1999 (19990426/UP), 1965 to 29 January 1999 (19990129/ED), and 1967 to 24 April 1999 (19990424/ED; vol 130, iss 18), respectively, and using the following key words: *tert*-butyltoluene, methyl-butylbenzene, and 98-51-1. HSDB and RTECS, data bases available from CD-ROM, were consulted as well (NIO99, NLM99). The final literature search has been carried out in April 1999.

In July 2001, the President of the Health Council released a draft of the document for public review. Comments were received from the following individuals and organisations: A Aalto (Ministry of Social Affairs and Health, Tampere, Finland). These comments were taken into account in deciding on the final version of the document.

2 Identity

| | | |
|------------------------------------|---|---|
| name: <i>p-tert</i> -butyl toluene | : | <i>p-tert</i> -butyl toluene |
| synonyms | : | 4- <i>t</i> -butyltoluene; 1-methyl-4- <i>tert</i> -butylbenzene; <i>p</i> -methyl- <i>tert</i> -butylbenzene; <i>tertiary</i> butyltoluene |
| molecular formula | : | C ₁₁ H ₁₆ |
| CAS reg no | : | 98-51-1 |
| structural formula | : | |



Data from ACG99, Ric92

3 Physical and chemical properties

| | | |
|--------------------------------|---|----------------------------------|
| molecular weight | : | 148,18 |
| boiling point | : | 192.8°C |
| melting point | : | -52.4°C |
| flash point | : | 68.3°C (open cup) |
| vapour pressure | : | at 20°C: 70 Pa; at 25°C: 86.7 Pa |
| solubility in water | : | insoluble |
| Log P _{octanol/water} | : | 4,35 |
| conversion factors | : | 1 ppm = 6.1 mg/m ³ |
| (20°C, 101.3 kPa) | : | 1 mg/m ³ = 0.16 ppm |

Data from ACG99, Ano86a.

p-tert-Butyltoluene (*p*-TBT) is a clear flammable liquid with a distinct, aromatic, gasoline-like odour (ACG99). Odour thresholds of 0.067 and 0.011 mg/m³ (0.01 and 0.002 ppm) have been reported (Ano83). Human volunteers exposed to several concentrations ranging between 30 and 975 mg/m³ (5-160 ppm), for 5 minutes, immediately recognized the odour of the compound at concentrations as low as 5 ppm. Olfactory agnosia was experienced in a few subjects (Hin54).

p-TBT can react with strong oxidisers to cause explosion and fire (ACG99).

4 Uses

p-TBT is used primarily as an intermediate in the production of *tert*-butylbenzoic acid which is utilised in the manufacture of unsaturated polyesters and alkyd resins, and furthermore as a solvent, and as a perfume fixative (ACG99, NLM99).

5 Biotransformation and kinetics

Uptake, distribution, and elimination of *p*-TBT were studied by exposing outbred albino male NMRI-mice to 6100 mg/m³ (1000 ppm), for up to 8 hours. After 30 minutes of exposure, concentrations of *p*-TBT in kidney, brain, and mesenteric fat were roughly 5 times those in blood. Thereafter, kidney:blood concentration ratios remained about the same, while the brain:blood concentration ratios declined to about 2-3 at 8 hours. At this latter time point, mesenteric fat concentrations increased to about 9 times those in blood. The ratio of the

liver: blood concentration was nearly constant: about 1.5 and about 3 at 30 minutes and 8 hours, respectively. Elimination curves for *p*-TBT of blood, brain, liver, kidney, and mesenteric fat after a 4-hour exposure showed nonlinearity indicative of a kinetic model with at least 2 compartments. The data did not suggest accumulation of the compound in fat or nervous tissue. This was confirmed by the lack of detectable amounts of *p*-TBT in mesenteric fat 24 hours after a single 4-hour exposure to 6100 mg/m³ (1000 ppm). Barely detectable amounts were found after 5 subsequent daily 4-hour exposures to 6100 mg/m³ (1000 ppm) (Ras80).

The distribution of *p*-TBT was studied by exposing male Wistar rats to [methyl-¹⁴C]*p*-*tert*-butyltoluene, for 15 minutes. Results from whole-body autoradiography showed that radioactivity was rapidly distributed throughout the body with relatively high amounts in the brain and the spinal cord (white matter), the liver, lungs, kidneys, bone marrow, and Harderian gland. The radioactivity in the brain rapidly declined to trace levels at 4 hours. In lungs and kidneys, trace levels were found at 12 and 48 hours, respectively, while in the liver, radioactivity was still present at 96 hours. Radioactivity was detected in bile and intestinal contents from 1 to 96 hours, in adrenals from immediately after exposure up to 8 hours, and in blood, intestinal mucosa, and bone marrow up to 12 hours. Radioactivity was present at all time points in the skin, adipose tissue, and the Harderian gland at levels increasing with time, and in subcutaneous and mesenteric fat at levels decreasing with time (Ing82).

Metabolism was studied in male Wistar rats and male Dunkin Hartley guinea pigs by oral (gavage) administration of 100 mg radiolabelled *p*-TBT/kg bw or by inhalation of trace concentrations for 24 hours. There were no route-dependent differences in metabolism. The *tert*-butyl group was oxidised to alcohol and carboxylic acid derivatives. The majority of the radioactivity was eliminated in urine and faeces (ratio: 3.5:1) over the first 3 days and a recovery of 83% was achieved (over 10 days). The major urinary metabolites in rats were *p*-*tert*-butylbenzoic acid and its alcohol derivative 2-(*p*-carboxyphenyl)-2-methylpropan-1-ol, whereas *p*-*tert*-butylbenzoylglycine was the most prominent in the guinea pig urine. Based on these data, the authors proposed a metabolism scheme as presented in Annex II (Wal83).

6 Effects and mechanism of action

Human data

When human volunteers were exposed to 30, 61, 122, 244, 366, 488, and 975 mg/m³ (10-160 ppm) (n=4-9/group), for 5 minutes, 1/9, 1/4, 1/6, 0/4, 3/5, 2/5, and 2/4 volunteers complained of eye irritation. The degree of irritation was not classified, but irritation was generally mild except for 2 cases of moderate irritation at 488 mg/m³ (80 ppm). Occasionally, nose - 1 or 2 cases at levels of 61 mg/m³ (10 ppm) and higher - and throat - 2 cases at 366 and 975 mg/m³ (60, 160 ppm) each - irritation were noted. Other incidental complaints included metallic or menthol taste (at 122, 366, and 488 mg/m³), nausea, and giddiness and increased breathing (at 975 mg/m³). Except for the highest concentration of 975 mg/m³ (160 ppm), these exposure levels were not experienced as objectionable (Hin54).

Reviewing health records of 33 operators exposed to *p*-TBT over the past 3 years revealed that 8 of them had volunteered specific complaints of symptoms such as nasal irritation, nausea, malaise, headache, and weakness. Objective findings were: a cardiovascular symptom characterised by decreased blood pressure, increased pulse rates, and failure to respond satisfactorily to the Master's test in 8 persons, tremor and anxiety in 4, and evidence of a chemical irritation from contact with *p*-TBT in 2. Laboratory findings showed evidence of peripheral blood changes. These changes included decreased haemoglobin values (in 8 persons; lowest value obtained: 78%), decreased erythrocyte count (in 2), leucopenia (in 7), eosinophilia (in 13), prolonged clotting time (in 5), and an elevated icterus index (in 2). The changes were of a mild and transient nature. There were no indications of abnormal kidney functioning. Generally, exposure concentrations were 60 mg/m³ (10 ppm) or less, but at specific operations, exposure could amount to 2135 mg/m³ (350 ppm) (Hin54).

Animal data

Irritation and sensitisation

When *p*-TBT was applied to the clipped intact and scarified skin of rabbits, the Draize irritation score was less than 0.5 (maximum possible score: 8.0). Further, it was reported that erythema was more pronounced in the intact than in the

scarified skin and that oedema at the application site was found in 1/6 animals. A subcutaneous injection of 1 mL/kg caused extensive skin ulcerations in 2/3 rabbits (Hin54).

In the Magnusson-Kligman maximisation test performed according to OECD guidelines, intracutaneous administration at a concentration of 20% and subsequent epidermal administrations at concentrations of 100 and 50%, respectively, did not induce sensitisation in female guinea pigs (Hül87).

When installed into the eyes of rabbits, average total Draize's scores were 9.3, 6.6, and 4.0 at 1, 24, and 72 hours, respectively (maximum possible score: 110). The most consistent sign of irritation was a moderate to heavy discharge. At 24 hours, slight chemosis was seen but this had disappeared before the next reading at 48 hours (Hin54).

Some eye and respiratory tract irritation was seen in rats exposed for 8 hours to 363 mg/m³ (60 ppm), the lowest concentration tested in a study on the acute toxicity of *p*-TBT (Hin54).

Sensory irritation of the upper respiratory tract was evaluated in mice (male Swiss-Webster) during a 30-minute oronasal exposure to increasing concentrations of *p*-TBT. The airborne concentration resulting in a 50% decrease in the respiratory rate (RD₅₀) was 2200 mg/m³ (360 ppm). No pulmonary irritation was found in cannulated mice exposed to a concentration eliciting a 50% decrease in the respiratory rate due to sensory irritation in normal mice (*i.e.*, 2000 mg/m³ or 330 ppm)(Nie82).

Acute toxicity

In female rats (Long-Evans), an 8-hour LC₅₀ of 1000 mg/m³ (165 ppm) has been estimated while 1-, 2-, and 4-hour LC₅₀s were 5660, 4448, and 1503 mg/m³ (934, 734, 248 ppm), respectively. In male mice, the 4-hour LC₅₀ was 1503 mg/m³ (248 ppm). The principle effects were impairment of the nervous system and the respiratory tract (among others, spastic and flaccid paralysis, clonic and tonic convulsions, epileptoid seizures, extreme respiratory difficulty, nasal discharge, salivation). Apart from slight dyspnea at the higher concentration, no effects were seen in rabbits exposed to 2727 or 6060 mg/m³ (450, 1000 ppm) for 4 hours. No systemic effects were seen in rats exposed to 363 mg/m³ (60 ppm), for 8 hours. At *postmortem* examinations, pulmonary tract irritation, enlargement and yellowish discolouration of the liver, and engorgement of the abdominal viscera were generally observed. Microscopic lesions were described in a general way and not clearly in relation to exposure levels and exposure routes. They included

amongst others centrilobular or diffuse fatty infiltration in the liver, fine granular changes in renal tubular epithelium, pulmonar emphysema, diffuse pulmonary oedema and severe haemorrhage. Lesions in the brain obviously found in animals exposed to levels of 1210 mg/m^3 (200 ppm) were summarily characterised by oedema of the meninges and white matter, myelin degeneration, and reactive gliosis (Hin54; see also Ung55). Exposure to *ca.* $24,000 \text{ mg/m}^3$ (4000 ppm), for 30 and 50 minutes, or to *ca.* 6100 mg/m^3 (1000 ppm), for 60 minutes, caused mortality in 8/8 and 4/7 male rats (Long-Evans), respectively. One of the survivors showed residual neurologic signs after 24 hours (Fur58).

In male rats (Wistar) exposed to 0, 305, and 915 mg/m^3 (50, 150 ppm), for 6 hours, statistically significant differences were found lasting for 5 days in animals exposed to 305 mg/m^3 and for at least 12 days in animals exposed to 915 mg/m^3 (Lun93).

A dermal LD_{50} of 19.6 mL/kg (*ca.* $17,000 \text{ mg/kg}$) has been estimated in rabbits. In the treatment-related deaths, mainly effects on the nervous system were seen. No effects were seen at a dose of 10.7 mL/kg (*ca.* $9,200 \text{ mg/kg}$) (Hin54).

Oral LD_{50} s of 1500, 800, and 1800 mg/kg bw have been reported for male rats (Long-Evans), male mice (Webster), and male albino rabbits, respectively. As with inhalation and dermal exposure, signs of impairment of the nervous system were predominant (Hin54).

Repeated dose toxicity

When rats (Long-Evans) were exposed to air saturated with vapours of *p*-TBT (*ca.* 5185 mg/m^3 or 850 ppm) for 1 hour/day, 5 days/week, for 5 (n=5/sex), 7 (n=10/sex), or 10 (n=5/sex) days, clonic convulsions and tremors were induced in 30% of the animals followed by dyspnea and paralysis after the second and third exposure. After 10 exposures, mortality amounted to 80%. In most animals, death was caused by pulmonary oedema and pneumonia (Hin54).

When male rats (Long-Evans; n=10) were exposed to 6100 mg/m^3 (1000 ppm) gradually increasing from 12 minutes/day (on day 1) to 2 hours/day (on days 10-17) over a 17-day period, mean body weight gain was decreased when compared to controls, but no mortality occurred. At day 17, the rats were so weak, lethargic, and poorly coordinated that the exposures were terminated. At autopsy, no changes were found in the nervous system tissues of exposed animals (Fur58).

In male Wistar rats (n=9) exposed to 132 mg/m^3 (20 ppm), 6 hours/day, for 14 days, significant changes were found in the amplitudes of flash evoked

potentials on day 2, 19, and 26 after cessation of the exposure, but not on days 5 and 12. The authors considered these effects as adverse since they were thought to be indicative of impairment of an important function of the brain, namely selective control and reduction of the stream of information from the sensory organs. There were no significant differences in body weight gain during and after exposure between the exposed and control group (Lun95).

Female rats (Long-Evans; n=10/group) were exposed to *ca.* 175 and 350 mg/m³ (25-30 and 50-60 ppm) of *p*-TBT for 1, 2, 4, or 7 hours/day, 5 days/week. Half of the animals of the 50-60-ppm and 25-30-ppm group were killed after 5 and 10 weeks, respectively, while the remaining animals were exposed for 26 weeks. In the animals exposed for 5 or 10 weeks, no mortality, statistical significant body weight gain changes, or unusual behaviour were observed. During exposure, eye irritation (blinking, closing lids, encrustation) and slightly lowered respiration rate occurred. Relative organ weight changes which were determined for liver, kidneys, lungs, spleen, and heart included increases in liver weights in animals exposed to 175 mg/m³ for 2, 4, or 7 hours and in animals exposed to 350 mg/m³ for 7 hours, in kidney weights in animals exposed to 350 mg/m³ for 2 hours, and in spleen weights in animals exposed to 175 mg/m³ for 1 hour. There were no effects on mean haemoglobin, erythrocyte, and leucocyte values. Apart from moderate brown-mottled discolouration of the liver of the animals exposed for 7 hours, no gross or histological changes were found in the low-concentration group. In the high-concentration group, there were effects on the liver (brown-mottled discolouration; mild peripheral fatty changes), the lungs (patchy emphysema; oedema of tracheal mucosa with partial desquamation of the surface epithelium), kidneys (fat deposits in renal tubular epithelium), and the heart (focal necrosis in the myocardium). As to the nervous system, no lesions were found at exposures for 1 or 2 hours while those in animals exposed for 4 or 7 hours were not concentration related and of identical severity. They were stated to be essentially those of chronic encephalomeningitis characterised by accumulation of neuroglial cells around the damaged neurons of the deep cortical areas, *striatum*, and *medulla oblongata*. Diffuse demyelination of the *corpus callosum* and *pedunculi cerebri* were observed as well. In the animals exposed for 26 weeks, no signs of toxicity were observed except for 3 rats exposed to 350 mg/m³, 7 hours/day. One of these animals died in week 9, while the other animals showed transient effects on fore- or hindlegs. Although growth curves indicated a concentration- and exposure-duration-related increased growth retardation, these changes did not attain statistical significance, probably because of the original within-group weight variation. Relative organ weight changes included

increases in liver weights in animals exposed to 175 mg/m³ for 4 and 7 hours and in all animals exposed to 350 mg/m³, and in kidney weights in animals exposed to 350 mg/m³ for 2, 4, or 7 hours. Except for a decreased leucocyte count in animals exposed to 350 mg/m³ for 2, 4, or 7 hours, there were no statistically significant changes in haemoglobin, erythrocyte, and leucocyte values. At necropsy, there were no remarkable consistent changes in the animals exposed to 175 mg/m³. In the high-concentration group, only occasional gross findings were reported including 2 cases of bronchiectasis, 2 cases of friable liver, 1 case of discoloured kidneys and abnormally pale liver. Microscopic examinations only showed infrequent mild peripheral fatty changes in the liver, and there was no evidence of cirrhosis or renal tubular changes. Nervous system lesions were similar to those found at 5- and 10-week exposures (Hin 54; see also Ung55).

Following oral (gavage) administration, no mortality was seen in male rats (SPF; n=8/group; controls: n=4) given 0, 12.5, 25, 50, or 100 mg/kg bw (vehicle: rape oil), once a day, for 5 days. Clinical signs were seen in the animals of the 2 highest dose groups and included loss of hair, shaggy fur, hunched posture, lethargy, and diarrhoea. In these groups, body weight gain was severely affected. At autopsy, only the liver, kidneys, and testes were examined. No changes were seen in the animals given 12.5 or 25 mg/kg. In the other 2 groups, delineation of hepatic lobules and structural changes of germinal epithelium (degenerated spermatids and spermatocytes, reduced spermatozoa, sporadic occurrence of giant cells) were observed. In the animals of the 100 mg/kg group, testes weight were decreased (*ca.* 23%) when compared to controls. In a similar experiment in male mice (SPF; n=6) given 100 mg/kg bw, minor damage of germinal epithelium was found, while in guinea pigs (Himalayan spotted SPF; n=5) and dogs (Beagle; n=2), administration of 100 mg/kg bw caused moderate germinal epithelial damage and very slight seminiferous tubular atrophy in one guinea pig and one dog, respectively (Ano86b).

Mutagenicity and genotoxicity

p-TBT was found negative when adequately tested with and without metabolic activation in *S. typhimurium* strains TA1535, TA1537, TA1538, TA98, and TA100 (Bro81, Dea85, Hül87, Zei87) and *E. coli* strain WP2 and WP2 *uvrA* (Bro81, Dea85). In liquid cultures of the yeast *S. cerevisiae* JD1, *p*-TBT did not induce gene conversions (Bro81, Dea85). As to mammalian cell systems, the compound did not cause chromosome damage (chromatid gaps, breaks) when tested in cultured rat liver (RL₁) cells (Bro81, Dea85).

Reproduction toxicity

In rats, 5 daily doses of 50 or 100 mg/kg bw of *p*-TBT caused structural changes of the germinal epithelium while testes weights were decreased by 23% at the high dose. No such effects were seen at doses of 12.5 and 25 mg/kg bw. When mice, guinea pigs, and dogs were given 100 mg/kg bw (the only dose tested), minor germinal epithelial damage was found in mice, while there was moderate damage in 1/5 guinea pigs and very slight atrophy in 1/2 dogs (see also section on repeated dose toxicity) (Ano86b).

When pregnant rats (Mol:WIST; number not reported) were exposed to 132 mg/m³ (20 ppm) *p*-TBT, 6 hours/day, on gestational days 7-20, no maternal toxicity was induced. In the offspring, viability was not decreased, but lower pup body weight until day 10 and delayed ontogeny of reflexes, also after correction for body weight, was observed. Learning and memory abilities were investigated at the age of 3, 17, and 22 months using the Morris water maze. In this test, rats have to spatially navigate using distal extramaze cues to locate a small platform under the water surface in a large pool. At 3 months, latencies and swim length were increased in the learning period in the female offspring of the exposed group ($p=0.6\%$). When tested 3 weeks later, there were some indications of impaired memory, but increases in latency and swim length did not reach statistical significance ($p=8.7\%$). At 17 months, no impairment was seen. At 22 months, memory impairment of the female offspring of the exposed animals was observed, but it was not clear whether this was the consequence of prenatal exposure to the test substance or to an interaction of prenatal exposure and aging (only an abstract available) (Has96).

In an abstract on screening a number of compounds - selected as representatives of chemical classes - for possible teratogenic effects, it was reported that *p*-TBT was teratogenic - defined as producing either a gross abnormality or a significant change in body weight and certain bone lengths - when tested in the rat fetus and the chick embryo (no details given) (Roc68).

7 Existing guidelines

The current administrative occupational exposure limit (MAC) for *p*-TBT in the Netherlands is 6.1 mg/m³ (1 ppm), 8-hour TWA.

Existing occupational exposure limits for *p*-TBT in some European countries and in the USA are summarised in Annex I.

8 Assessment of health hazard

p-TBT is readily absorbed from the respiratory and gastrointestinal tract, rapidly distributed throughout the body, and after being metabolised excreted in urine and faeces within a few days.

Following exposure to 30 mg/m³ (5 ppm) of *p*-TBT, for 2 minutes, one out of 9 volunteers complained of eye irritation. At higher levels, eye, nose, and throat irritation, metallic/menthol taste, nausea, and giddiness were occasionally complained of, and a concentration of 975 mg/m³ (160 ppm) was experienced as objectionable. Reviewing health records of operators considered to be exposed to average levels of *p*-TBT of 60 mg/m³ (10 ppm) with peak levels of 2135 mg/m³ (350 ppm) revealed subjective symptoms (nasal irritation, nausea, malaise, headache, weakness) and objective findings (cardiovascular effects, tremor and anxiety, chemical irritation, and changes in peripheral blood), generally of mild and transient nature.

Based on experimental animal data, the committee concludes that liquid *p*-TBT is at most slightly irritating to eyes and skin. The compound did not show sensitising properties when tested in the maximisation test in guinea pigs. In rats, concentrations of *ca.* 360 mg/m³ (60 ppm) were found to be irritating to the eyes and respiratory tract.

From acute lethality data (4-hour LC₅₀ rat: 1500 mg/m³; oral LD₅₀ rat: 1500 mg/kg bw), the committee considered *p*-TBT as toxic by inhalation and as harmful if swallowed, while no such qualification is warranted as to dermal exposure (LD₅₀ rabbit: *ca.* 17,000 mg/kg bw).

Acute and repeated inhalation experiments in rats and rabbits showed that irritation of eyes and respiratory tract and effects on the nervous system are predominant and that chronic exposure may induce slight effects on the liver. In a generally poorly reported and limitedly designed 26-week study in which rats were exposed to concentrations of *ca.* 175 or 350 mg/m³ (25-30, 50-60 ppm, resp), no NOAEL could be established since at the lower concentration increased relative liver weights and lesions in nervous system tissues were found. In a 14-day study with only one concentration, namely 132 mg/m³ (20 ppm), sensory-evoked potentials were affected suggesting impairment of controlling information from sensory organs by the brain.

p-TBT did not induce mutations in bacteria (*S. typhimurium*, *E. coli*), gene conversions in yeast (*S. cerevisiae*), or chromosome damage in mammalian cells

(rat liver RL₁ cells). The committee did not find data on *in vivo* genotoxicity testing.

The committee did not find adequate studies on the potential reproduction toxicity of *p*-TBT, but the available data indicate that exposure to *p*-TBT may induce developmental toxicity. In rats, germinal epithelial damage was seen after 5 daily oral doses of 50 and 100 mg/kg bw, but not at 25 mg/kg bw. Similar damage was observed in mice and to a lesser degree in guinea pigs and dogs at doses of 100 mg/kg bw (no other doses were tested).

The committee did not find data on the potential carcinogenicity of *p*-TBT.

The committee considers the toxicological data base on *p*-*tert*-butyltoluene too poor to justify recommendation of a health-based occupational exposure limit.

The committee concludes that the limited information from 14-day and 26-week rat inhalation studies in which effects were found at levels of 132 and *ca.* 175 mg/m³ (20 and 25-30 ppm, resp.) suggests that the present MAC-value of 6.1 mg/m³ (1 ppm), 8-hour TWA, may be too high.

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Annex I

Occupational exposure limits for *p-tert*-butyltoluene in various countries.

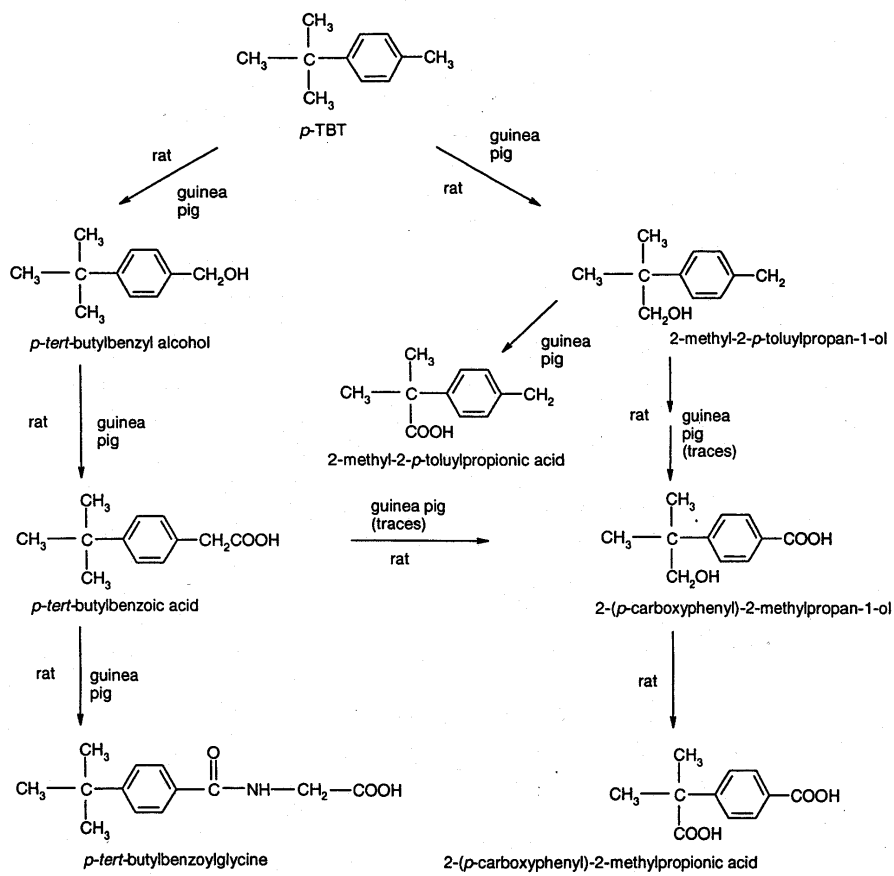
| country -organisation | occupational exposure limit | | time -weighted average | type of exposure limit | note ^a | lit ref ^b |
|---|--------------------------------|-------------------|---------------------------|---------------------------|-------------------|----------------------|
| | ppm | mg/m ³ | | | | |
| the Netherlands | | | | | | |
| -Ministry of Social Affairs and Employment | 1 | 6.1 | 8 h | administrative | | SZW01 |
| Germany | | | | | | |
| -AGS | 10 | 60 | 8 h | | | TRG00 |
| | 10 | 60 | 15 min | | | |
| -DFG MAK-Kommission | - ^c | - ^c | | | | DFG01 |
| Great-Britain | | | | | | |
| -HSE | - | - | | | | HSE01 |
| Sweden | - | - | | | | Arb00b |
| Denmark | 1 | 6,1 | 8 h | | | Arb00a |
| USA | | | | | | |
| -ACGIH | 1 | 6.1 | 8 h | TLV | | ACG01 |
| -OSHA | 10 | 60 | 8 h | PEL | | ACG00 |
| -NIOSH | 10 | 60 | 10 h | REL | | ACG00 |
| | 20 | 120 | 15 min | | | |
| European Union | | | | | | |
| -SCOEL | - | - | | | | CEC00 |

^a S = skin notation; which means that skin absorption may contribute considerably to the body burden; sens = substance can cause sensitisation

^b Reference to the most recent official publication of occupational exposure limits

^c Listed among substances for which studies of the effects in man or in experimental animals have yielded insufficient information for the establishment of MAK values

Annex II



Proposed metabolism of *p*-*tert*-butyltoluene (*p*-TBT) in rats and guinea pigs (from Wal83).