TC NES SUBGROUP ON IDENTIFICATION OF PBT AND VPVB SUBSTANCES

RESULTS OF THE EVALUATION OF THE PBT/VPVB PROPERTIES OF:

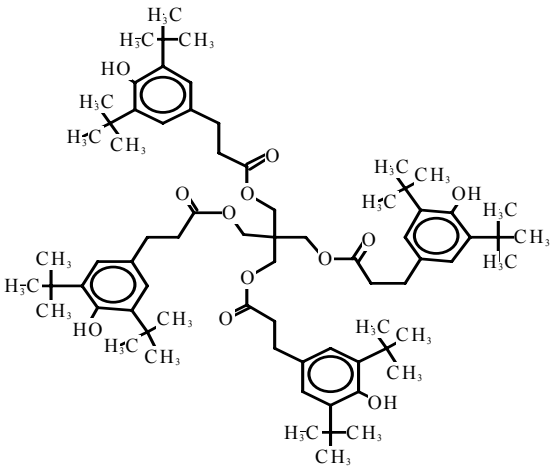
Substance name: Pentaerythritol tetrakis(3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate)

EC number: 229-722-6

CAS number: 6683-19-8

Molecular formula: C73 H108 O12

Structural formula:



Summary of the evaluation:

Pentaerythritol tetrakis(3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate) is not considered as a PBT –substance. It meets the P/vP criteria according to screening data, although it cannot be excluded, that the substance would degrade with an unknown (very slow) rate. B criterion is not met based on indicators of limited bioconcentration. No assessment of ecotoxicity was carried out.

The potential degradation products are benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydroxy- (“Metilox acid”; CAS 20170-32-5) and pentaerythritol (CAS 115-77-5). Both degradation products fulfill the P/vP criteria based on screening data, but they do not meet the B criterion.

JUSTIFICATION

1 IDENTIFICATION OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES

Name: Pentaerythritol tetrakis(3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate)
EC Number: 229-722-6
CAS Number: 6683-19-8
IUPAC Name:
Molecular Formula: C73 H108 O12
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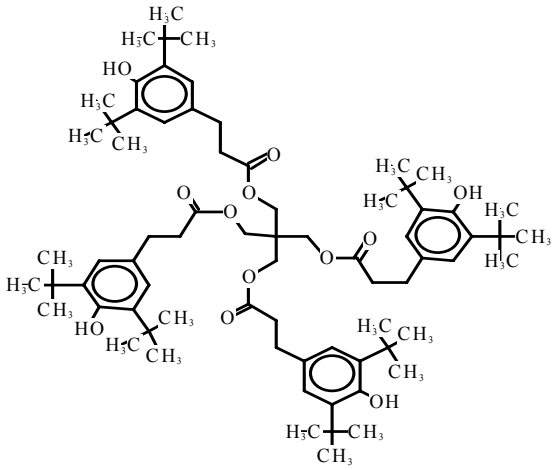

Molecular Weight: 1177.81
Synonyms: Hydrocinnamic acid, 3,5-di-tert-butyl-4-hydroxy-,neopentanetetrayl ester (8CI)
Neopentanetetrayl 3,5-di-tert-butyl-4-hydroxyhydrocinnamate
Pentaerythritol tetrakis (3,5-di-tert-butyl-4-hydroxyhydrocinnamate)
Phenosane 23
RA 1010
Ralox 630
Sumilizer BP 101
For full list of synonyms, see European Commission (2000)
Smiles c1(C(C)(C)C)cc(CCC(=O)OCC(COC(=O)CCc3cc(C(C)(C)C)c(O)c(C(C)(C)C)c3)(COC(=O)CCc4cc(C(C)(C)C)c(O)c(C(C)(C)C)c4)COC(=O)CCc2cc(C(C)(C)C)c(O)c(C(C)(C)C)c2)cc(C(C)(C)C)c1O

1.1 Purity/Impurities/Additives

No data available.

1.2 Physico-Chemical properties

Table 1 Summary of physico-chemical properties. For details and references, see European Commission (2000). It is noted, that the study reports were not available to the Rapporteur for evaluation.

REACH ref Annex, §	Property	Value	Comments
VII, 7.1	Physical state at 20 C and 101.3 Kpa	solid	European Commission 2000
VII, 7.2	Melting / freezing point	110-125 °C	Great Lakes Chemicals, Italia, Milan (Internal reference)
VII, 7.3	Boiling point	-	Not applicable
VII, 7.5	Vapour pressure	0.0000000000013 hPa at 20 °C	MSDS, Ciba
VII, 7.7	Water solubility	$<10^{-4}$ g/l at 20 ºC < 0.001 g/l at 20 °C 0.3 g/l at 20 °C < 1mg/l at 20 °C 1.368×10^{-18} mg/l at 25 °C	Measured, Ciba, 1985; Dir. 84/449/EEC A.6 Ciba Additive GmbH, 1989 Bennox MSDS MSDS Ciba, 1990 Estimate from Log Kow (WSKOW v1.41):
VII, 7.8	Partition coefficient n-octanol/water (log value)	22.7 19.60	Calculated CLOGP 3, Ciba-Geigy Ltd., 1985 Estimate (KOWWIN v1.67)
	Fat solubility	1700 mg/100 g fat at 37 ºC	
	Dissociation constant	No dissociation in relevant range	

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2 MANUFACTURE AND USES

Eight producers/importers have provided data under Regulation 93/793/EEC with a total volume of 10,000 – 50,000 tonnes per year. Reported uses include the use as a stabilizer and the use as an antioxidant. CibaRS (2004) reported, that the substance is used as antioxidant in polyolefins, other polymers and lubricants and it is approved for use in indirect contact with food and cosmetics. Typical application concentration is according to CibaRC (2004) in polyolefins is 500-1000 ppm and in lubricans 0.1-0.5 %.

3 CLASSIFICATION AND LABELLING

The substance is not classified under Directive 67/548/EEC.

4 ENVIRONMENTAL FATE PROPERTIES

4.1 Degradation (P)

4.1.1 Abiotic degradation

Indirect photochemical degradation in the atmosphere is considered to be fast based on the estimated half-life of 2.61 hours for the reaction with OH-radicals using AOP v1.91 (24 h day^{-1}; $5*10^5$ OH^- cm^{-3}).

The estimations of hydrolysis (HYDROWIN v 1.67) show very slow DT_{50}'s, greater than 2.years and greater than70 days at pH 7 and 8 respectively.

4.1.2 Biotic degradation

According to the record of Ciba Additive GmbH, the substance is not readily nor inherent biodegradable

Regulatory Services (2004) reported additionally on a result of a modified sturm test with 10 and 20 mg/l test concentrations, 4-5 % of degradation was observed respectively in 28 days (Ciba-Geigy Ltd., 1981).

Furthermore, Ciba Regulatory Services (2004) informed on a modified MITI-test with 30 and 100 mg/l test concentrations. In this test 0 % in 28 was degraded. It is noted, that this study report was not available to the Rapporteur for evaluation.

An inherent test OECD 302B was done in 1985, the substance concentration was 20 mg/l, the result showed a 4% of degradation after 28 days (IUCLID data file), and the substance was considered as not inherent degradable.

BIOWIN v4.02 provides following predictions: BIOWIN2 = 0.00; BIOWIN3 = -0.83 and BIOWIN6 = 0.00, being in agreement with the experimental data.

A 45.2 % of the substance was "bio-eliminated" in a simulation test aerobic sewage treatment OECD 303A: Activated sludge units (Ciba-Geigy Ltd., 1985), but in this study the substance concentrations were not measured in the sludge and the "bio elimination" could be attributed to sludge adsorption due to the high value of the calculated log Kow (PCKOC v 1.66 estimates a log Koc of $1x10^{10}$). Furthermore, the pass level was not reached.

Two other substances with a (3,5-di-tert-butyl-4-hydroxyphenyl)propionate fragment have also been assessed for their PBT properties. These are methyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate (CAS 6386-38-5; PBT candidate nr. 65) and octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate (CAS 2082-79-3; PBT candidate nr. 74).

Octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate, is based on several OECD 301 –tests considered as not readily biodegradable, but the substance shows rapid primary degradation, depending of the biodegradation test used the metabolites are benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydroxy- ("Metilox acid"; CAS 20170-32-5; an identified product) from a modified MITI OECD 301 C or metilox acid and 1-octadecanol (an assumed product) from a modified Zahn Wellens test. Octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate has a higher predicted water solubility (6.088×10^{-9} mg/l) and a lower logKow (13.4) than pentaerythritol tetrakis(3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate) and hence the former is expected to be more available to biodegradation. The cleavage of the esther bonds of pentaerythritol tetrakis(3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate) can be expected to be also possible, but the rate of biodegradation is likely to be considerably suppressed by mass-transfer limitations.

Biodegradability of the main degradation product metilox acid was tested by CiBa-Geigy (1989) in an OECD 301B –test. At test concentrations of 10.27 and 20.33 mg/l, 7% and 3%, respectively,

were mineralized within 28 days based on carbon dioxide formation. The substance was emulsified with nonylphenol polyethoxylate in order to achieve a better distribution in the medium. Based on the result, metilox acid is considered not readily biodegradable. It is noted, that the study report was not available to the Rapporteur for evaluation. BIOWIN v4.02 provides for metilox acid following predictions: BIOWIN2 = 0.094; BIOWIN3 = 2.51; BIOWIN6 = 0.081.

The other product of the possible ester cleavage is expected to be pentaerythritol (CAS 115-77-5). BIOWIN v4.02 provides following predictions: BIOWIN2 = 0.98, BIOWIN3 = 3.33 and BIOWIN6 = 0.99. Biodegradation data are presented in OECD SIAR (OECD, 1998) and the substance is considered as not readily biodegradable based on an OECD 301C –test (13.2 % degraded in 25 days). Additionally, the substance is hydrolytically stable.

4.1.3 Other information [1]

No data available.

4.1.4 Summary and discussion of persistence

According to the QSAR –predictions and the available records on biodegradability, pentaerythritol tetrakis(3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate) is expected to be persistent in environmental conditions. Biodegradation is possible at the ester bond based on data on structurally similar substance octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate (CAS 2082-79-3). However, biodegradation rate of pentaerythritol tetrakis(3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate) can be expected to be very slow if not negligible due to mass-transfer limitations. The potential degradation products are “Metilox acid” (CAS 20170-32-5), and pentaerythritol (CAS 115-77-5), which both are based on standard ready biodegradability tests considered as not readily biodegradable.

4.2 Environmental distribution

Data not reviewed for this report.

4.2.1 Adsorption

4.2.2 Volatilisation

4.2.3 Long-range environmental transport

4.3 Bioaccumulation (B)

[1] For example, half life from field studies or monitoring data

4.3.1 Screening data

The logKow estimated values are 22.7 and 19.6 (CLOPGP v3 and KOWWIN v1.67 respectively). BCFWIN v2.15 predicts a BCF of 3.2. The cross sectional diameter is at equilibrium 19.5 Å based on the calculation of CibaSC (2005) using Molecular Modeling Pro. The fat solubility of the substance (1700 mg/100 g fat) was used to calculate the octanol solubility, this value is 13940 mg/l.

4.3.2 Measured bioaccumulation data

CERI (2003) reported on an OECD 305 flow through test with *Cyprinus carpio*. The substance was tested at two exposure levels, 1 and 0.1 mg/l, introduced to the test systems with solvent (HCO-40). Exposure duration was 6 weeks. The measured concentrations during the test in water were very close to the nominal concentrations (analysed with HPLC). BCFs based on the relation of measured concentrations in water and fish were during the test < 0.2 for the higher exposure level and < 2.3 for the lower exposure level. The test is not considered to be reliable, as the test concentrations were far beyond the predicted water solubility (measured water solubility < 1 mg/l). In order to re-evaluate the study, water solubility should be determined precisely.

Two older studies are available regarding the bioaccumulation potential of the possible metabolite **Metilox acid** (CAS 20170-32-5):

Gakushuin University (1986) carried out a bioconcentration study with 3-(3-tert.-butyl-4-hydroxy-5-methyl-phenyl)-propionic acid in accordance to OECD 305C. The substance is closely related to metilox acid. At the end of an 8-week exposure period, the BCF at a test concentration of 0.5 mg/l was <0.4, and at a test concentration of 0.05 mg/l the BCF was <4.3.

Gakushuin University (1988) performed also a bioconcentration test with a hindered phenol derivative reaction mass. In this study, a bioconcentration factor was also determined for metilox acid that occurred in the test water as a metabolite. This bioconcentration factor was based on the metilox acid concentration in test water and should be considered worst-case as metilox acid was additionally formed from parent substance in fish body. The bioconcentration factor was determined to be 94-108 at high exposure concentration (1 mg/l of parent) and 373-532 at the lower exposure concentration (0.1 mg/l of parent).

For the other potential degradation product **pentaerythritol** (CAS 115-77-5), an experimental BCF range of 0.3-2.1 has been derived in an OECD 305 test (MITI as cited in OECD, 1998).

4.3.3 Other supporting information[2]

No data available.

4.3.4 Summary and discussion of bioaccumulation

No reliable experimental data on bioaccumulation are available. In order to re-evaluate the available OECD 305 –test result, water solubility should be determined experimentally. The very high logKow (19.6), the high molecular mass (1178 g/mol) and the long maximun diameter (17.9 Å)

[2]For example, measured concentrations in biota

indicate, that the bioconcentration of the substance is likely to be low. For both potential degradation products, experimental data indicate low bioaccumulation potential.

5 HUMAN HEALTH HAZARD ASSESSMENT

In a repeated dose toxicity test with rats, a 3 months exposure at oral doses of 2,000, 10,000 and 50,000 ppm resulted a NOAEL of 2500 mg/kg bw (Ciba Additive GmbH as cited in European Commission, 2000). In a repeated dose toxicity study with dogs, A NOAEL of 322.4 mg/kg bw was derived from 3 moths oral exposure using 1,000 and 10,000 ppm doses. In a two generation reproduction toxicity study with rats over 20 months, parental and offspring NOAELs were determined to be 10,000 ppm, which was also the highest exposure level (oral exposure) (Ciba Additive GmbH as cited in European Commission, 2000). Another reproduction toxicity test (with mice) showed no teratogenic effects up to the highest oral dose level (1000 mg/kg/d). In 10-day developmental toxicity tests with mice and rats, NOAELs of 1000 mg/kg bw (the highest exposure level) were determined.

In a study on gastrointestinal absorption, two albino rats (male and female) were preconditioned with unlabeled Irganox 1010 at 2% dietary level for six weeks. The amount of feed consumed by the rats and the exposure concentration were not reported. On the first test day, after a 24-hours fast (water permitted), the rats were intubated with radioactive Irganox 1010. The test material was suspended in corn oil and administered directly into the stomachs of the rats. The dose received by the male was 24.909 µc and 24.759 µc by the female of an Irganox preparation with a concentration of 27.16 µc/g. (IBT, 1966a).

Figure 5.1 shows the total radioactivity recovery from the rats. Around 84% of the total radioactivity was recovered in the male rat (recovery in the female rat higher), whereas the main part was gained in faeces (80%). From expired air 1.3%, 0.2% from urine and from blood only 0.003% were recovered.

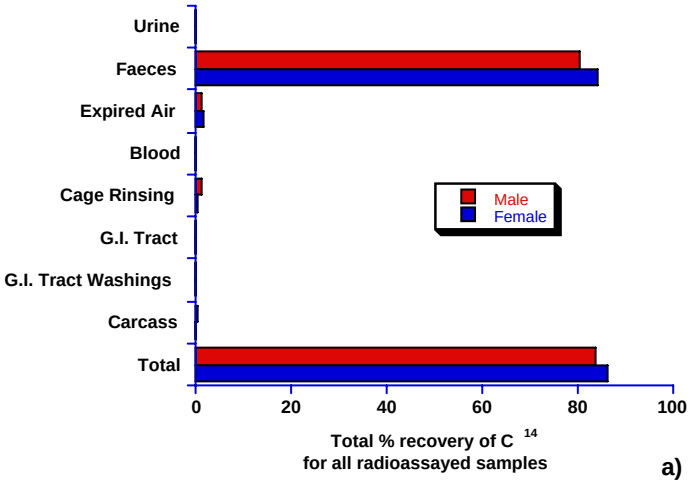

Figure 5.1 Total recovery from all radioassayed samples (based on IBT, 1966a).

A rapid elimination of the substance could be observed. The male rat eliminated around 38% of the substance in the first 24 hours (Figure 5.2a) and 77% by 72 hours (Figure 5.2b).

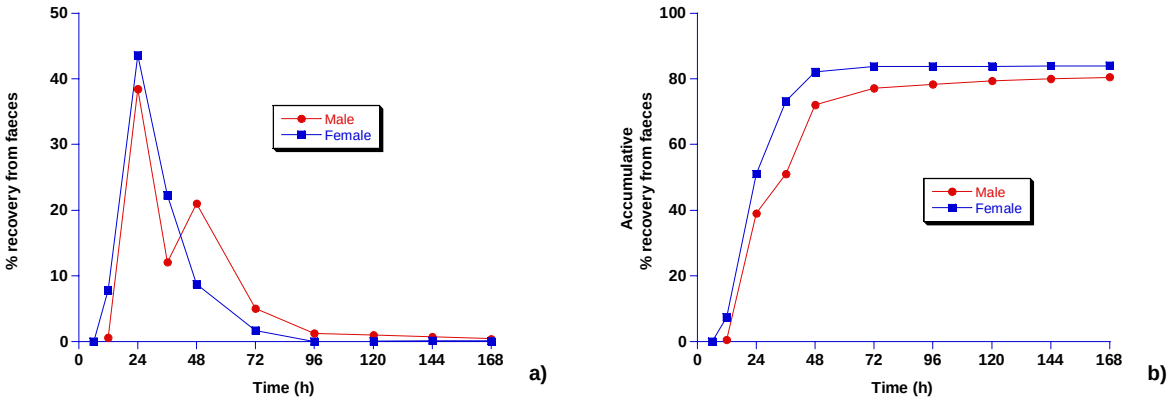

Figure 5.2 (a) Radioactivity recovery from faeces vs time and (b) accumulative radioactivity recovery from faeces vs time (based on IBT, 1966a).

Another study of IBT (1966b) was carried out to investigate the metabolic fate of the substance. The animals in this study were not preconditioned with unlabeled Irganox 1010. On the first test day the rats, after a 16-hours fast (water permitted), were intubated with radioactive Irganox 1010. The test material was suspended in corn oil and administered directly into the stomachs of the rats. In this study the dose received by the rats is unknown. Only the radioactivity of the intubation solution has been provided (7.005 µc/ml). In the female rat the main total radioactivity recovered was from faeces (34%), from expired air, urine, blood, liver and kidneys 0% was recovered in both sexes. This study is considered not reliable due to the very low total recovery.

It is noted, that no full mass balance was calculated neither the fat of the rats was analyzed in both studies cited above.

6 ENVIRONMENTAL HAZARD ASSESSMENT

Data not reviewed for this report.

6.1 Aquatic compartment (including sediment)

6.1.1 Toxicity test results

6.1.1.1 Fish

Acute toxicity

Long-term toxicity

6.1.1.2 Aquatic invertebrates

Acute toxicity

Long-term toxicity

6.1.1.3 Algae and aquatic plants

6.1.2 Sediment organisms

6.1.3 Other aquatic organisms

6.2 Terrestrial compartment

No data available.

6.3 Atmospheric compartment

No data available.

7 PBT AND vPvB

7.1 PBT, vPvB assessment

Persistence: Pentaerythritol tetrakis(3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate) fulfils the P/vP criteria according to screening data. The substance may degrade with an unknown but probably very slow rate to benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydroxy- (“Metilox

acid"; CAS 20170-32-5) and pentaerythritol (CAS 115-77-5). Both degradation products fulfil the P/vP criteria based on screening data (ready biodegradation –test results are available).

Bioaccumulation: The substance does not meet the B criterion based on indicators of limited bioconcentration. No reliable experimental data on bioaccumulation are available on the substance in environmental species. The very high logKow (19.6) and the maximum cross diameter (19.5 Å) exceed the screening triggers for limited bioconcentration. The octanol solubility (13900 mg/l) is, however, rather high considering the molecular weight (1178 g/mol) of the substance. Taking into account that no effects were observed at the highest dose levels in two repeated dose studies, two developmental toxicity studies (including a two generation study) and in two teratogenity studies with laboratory mammals and considering also the very low uptake of the substance in rats in a metabolism study, it is concluded that the substance has a very limited ability to be bioconcentrated.

The potential primary degradation product metilox acid has a BCF of 532 or lower based on two old studies. Furthermore, metilox acid was not bioaccumulated in a toxicokinetic study with rats. It is considered, that there is enough evidence to conclude, that the substance does not fulfill the B criterion. For the second potential degradation product pentaerythritol an experimental BCF range of 0.3-2.1 has been derived in an OECD 305 test and hence the substance does not meet the B criterion.

Toxicity: No assessment of ecotoxicity was carried out.

Summary:. Pentaerythritol tetrakis(3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate) meets the P/vP criteria according to screening data, although it cannot be excluded, that the substance would degrade with an unknown (very slow) rate. B criterion is not met based on indicators of limited bioconcentration. No assessment of ecotoxicity was carried out.

The potential degradation products are benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydroxy- ("Metilox acid"; CAS 20170-32-5) and pentaerythritol (CAS 115-77-5). Both degradation products fulfill the P/vP criteria based on screening data, but they do not meet the B criterion.

It is concluded, that pentaerythritol tetrakis(3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate) is not considered as a PBT –substance

INFORMATION ON USE AND EXPOSURE

Not relevant as the substance is not identified as a PBT.

OTHER INFORMATION

The information and references used in this report were taken from the following source:

European Commission, 2000. IUCLID Dataset, Pentaerythritol tetrakis(3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate), CAS 6683-19-8, 19.2.2000.

Other sources:

CERI, 2003. Information provided on CERI bioconcentration tests to the ECB.

Ciba Regulatory Services, 2004. Presentation of the pentaerythritol tetrakis(3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate) properties to the Rapporteur ,September 2004.

Ciba-Geigy Ltd., 1981. Biodegradability of TK 10797 in the Modified Sturm Test, OECD-guideline no. 301 B, Ciba-Geigy Ltd., Ecotoxicology, Basle, Switzerland, Project No.: 884588, April 26, 1989. As cited in CiBa, 1999.

Gakushuin University,1988. Bioconcentration study with CG31-1017 in Carp. Gakushuin University, Japan. Report No. G4.9821.C94.CP, September 30, 1998. As cited in CiBa, 2006.

Gakushuin University, 1986. Bioconcentration study with 3-(3-tert.-butyl-4-hydroxy-5-methyl-phenyl)-propionic acid. Gakushuin University, Japan. December 3, 1986. As cited in CiBa, 2006.

IBT, 1966a. Gastrointestinal absorption of C14 Irganox 1010 in albio rats. IBT No. 4546. Industrial Bio-Test Laboratories, Inc.Report to Geigy Chemicals Corporation, 11.8.1966.

IBT, 1966b. Metabolic fate of C14 Irganox 1010 in albio rats. IBT No. 4095. Industrial Bio-Test Laboratories, Inc.Report to Geigy Chemicals Corporation, 15.3.1966.

OECD, 1998. Pentaerythritol (CAS 115-77-5), SIAR for the 8th SIAM, France, October 28-30, 1998. UNEP Publications.