SECTION-1: Identification of the substance / mixture and the company / undertaking

Catalogue Number	CS-O-50015
Product Name	Octabromodiphenyl ether
CAS No.	32536-52-0
Category	Building Blocks
Synonyms	Plasafety EBR 8,Tardex 80
Brand	Clearsynth Labs Ltd.
Identified uses	Laboratory Chemicals
Uses advised against	Not available
Company	Clearsynth Labs Ltd. Mumbai, India
Emergency Phone #	+91-22-245045900
REACH No.	Not available

SECTION 2: Hazards identification

Disclaimer: This is sample MSDS. Please email **sales@clearsynth.com** for more details.

2.1 Classification of the substance or mixture-Regulation (EC) No 1272/2008:

Not available

2.2 Label Elements

Signal Word: Warning



Hazard Statement(s)

Code	Statement
H360	Not available
H372	Not available
H373	Not available
H413	Not available

Precautionary Statement(s)

Code	Statement
P203	Not available
P260	Not available
P264	Wash hands thoroughly after handling.
P270	Not available
P273	Not available
P280	Wear protective gloves/protective clothing/eye protection/face protection.
P318	Not available
P319	Get medical help if you feel unwell.
P405	Store locked up.
P501	Dispose of contents/container in accordance with local/regional/national/international regulatio

SECTION 3: Composition / information on ingredients

3.1 Substance

Component : Octabromodiphenyl ether
CAS Number : 32536-52-0
Molecular Formula : C12H2Br8O
Molecular Weight : 2.76
Parent Chemical : -
Synonyms : Plasafety EBR 8,Tardex 80
Concentration : Not available

SECTION 4: First aid measures

Not available

SECTION 5: Firefighting measures

Not available

SECTION 6: Accidental release measures

Not available

SECTION-7: Handling and storage

Not available

SECTION 8: Exposure controls / personal protection

Not available

SECTION 9: Physical and chemical properties

9.1 Information on basic physical and chemical properties

Test	Result
Appearance	No data available
IR spectrum	No data available
pH	No data available
Solubility	No data available

Property	Value
a) Physical State	No data available
b) Color	No data available
c) Odor	No data available
d) pH	No data available
e) Vapour Pressure	No data available
f) Viscosity	No data available
g) Initial Boiling Point and boiling range	No data available
h) Melting Point / Freezing Point	No data available
i) Auto Ignition Temperature	No data available
j) Flash Point	No data available
k) Explosion Limit, Lower	No data available
l) Explosion Limit, Upper	No data available
m) Decomposition Temperature	No data available
n) Loss on Drying	No data available
o) Relative Density	No data available

Property	Value
p) Solubility (in DMSO)	No data available
q) Oxidizing Properties	No data available

SECTION 10: Stability and reactivity

Not available

SECTION 11: Toxicological information

11.1 Information on toxicological effects
- Acute toxicity: Animal data show an absorption of Octabromodiphenyl ether (OBDPE) by oral or inhalation route with an accumulation of the parent compound or its metabolites in the liver and also in the adipose tissue and the lung following inhalation administration. The extent of absorption and elimination cannot be assessed from the data available. No information on the metabolism of OBDPE is available. Following oral administration, OBDPE is an inducer of xenobiotic metabolism. There are no measured data on OBDPE dermal absorption. However based on OBDPE physicochemical properties and analogy with PCBs, a dermal absorption of 4.5% may be estimated. Evidence from humans indicates that OBDPE, HxBDPE, HpBDPE and NonaBDPE which are components of commercial OBDPE can be absorbed into the body and distributed into the blood. Distribution to the adipose tissue was evidenced at least for OBDPE and HxBDPE. There are no data available on the rate of elimination or on bioaccumulation of OBDPE from human adipose tissue neither for PeBDPO but given the high lipophilicity of these compounds and the adipose tissue accumulation observed in rats following oral or inhalation routes, it can be assumed that in humans OBDPE might bioaccumulate in these tissues as well. Following pregnancy HxBDPE and others PBDPEs such as TeBDPE and PeBDPEs are excreted in the breast milk. Unfortunately, such measurements were not carried out on OBDPE. However, based on the high lipophilicity of OBDPE, its potential to bioaccumulate in adipose tissues and the breast milk measured data with HxBDPE (one component of commercial OBDPE), excretion of OBDPE in the breast milk may be anticipated OBDPE has a low acute toxicity in animals. Acute oral toxicity data indicate a rat LD50 greater than 28,000 mg/kg. No deaths, no weight changes or necropsy lesions were reported up to 5,000 mg/kg. At 10,000 mg/kg and 28,000 mg/kg, no deaths were observed but no more information on these studies are available. A dermal LD50 greater than 2,000 mg/kg has been demonstrated in rabbits using DBDPE applied neat under occlusive wraps for 24 hours. No deaths were observed up to 2,000 mg/kg. Local and general signs of toxicity were not reported and necropsies were not performed in this dermal toxicity study. An inhalation LC50 greater than 60 mg/l has been demonstrated in rats exposed with OBDPE during one hour. No deaths and no clinical signs of toxicity were observed up to 60 mg/l. OBDPE is not a dermal or an ocular irritant. There is no indication of skin sensitization in animals. The only information concerning the effects of repeated oral and inhalation exposure to OBDPE comes from studies in rats involving administration of commercial OBDPE. These studies consistently indicate that the liver is the key target organ within 4 and 13 weeks of repeated oral dosing and within 14 days and 90 days of inhalation exposure. The changes in thyroid status are apparent within 4 and 13 weeks of repeated oral dosing from 1,000 ppm and within 13 weeks of repeated inhalation dosing from 16 mg/m3 (analytical concentration). The LOAEL is considered to be 100 ppm . 7.2 mg/kg/day in the 90 day dietary study based on the liver changes (increase of liver weight and granular cytoplasmic changes) observed from 100 ppm . 7.2 mg/kg/day. The NOAEC for systemic toxicity is considered to be 1.1 mg/cu m in the 90 day rat study by inhalation route based on the liver and thyroid status changes observed at the concentration just above: 16 mg/cu m . Alterations in thyroid homeostasis were reported with organochlorine compounds for many species, including humans and a thyroid hormone like affinity for the serum transport protein transthyretin was shown for hydroxylated

PCBs as well as for PBDPE congeners such as DiBDPE and TeBDPE. To our knowledge, no studies on transthyretin-T4 competition have been carried out on OBDPE neither on DBDPE. Following inhalation exposure, local toxicity was demonstrated with hyperplasia/hypertrophy of the goblet cells within 2 weeks of exposure and with chronic active lung inflammation and alveolar histiocytosis within 13 weeks of exposure. It is obvious that the observed effect at 1.1 mg/cu m is minimal and reveals only a trend to a chronic inflammation however this value has been taken to set up the LOAEC for local toxicity. Regarding mutagenicity no in vivo data are available. However based on the available in vitro data, OBDPE is considered as non-genotoxic in vitro and no concern for mutagenicity is assumed. No chronic or carcinogenicity studies in animals are available. No specific fertility study is available. A recent rat inhalation sub-chronic study, well conducted and specifically designed to investigate reproductive organs, did not demonstrate adverse effects on male reproductive organs. Therefore no concern is assumed for male fertility. Regarding female reproductive organs, absence of corpora lutea was shown in this study in 3/10 females at 202 mg/m3 versus 0/10 in the control group. Since the absence of corpora lutea is considered to be an unusual finding in rats at 20 weeks of age, the 30% incidence in this group was considered treatment-related and therefore a NOAEC for female fertility of 16 mg/m3 was considered. Developmental effects are observed in rats in two studies (decrease of fetal body weight from 10 mg/kg/day, increase of post-implantation loss with late resorptions, increase in dead or resorbed conceptuses per litter at 25 mg/kg/day (33.2% versus 4.3%); decrease in the average number of live fetuses per litter (8.9 versus 14.6) and fetal malformation/variation and delayed skeletal ossification at 25 mg/kg/day. Those developmental effects do not seem to be related to maternal toxicity. However, these developmental effects are not confirmed in a third assay in rats conducted with a test article containing a lower percentage of the OBDPE component. In rabbits, the substance produces only slight foetotoxicity from 5 mg/kg/day (slight decrease of the fetal body weight and increase in delayed ossification). The lowest identified NOAEL is considered i.e. 2 mg/kg/day from the rabbit study. Since some of these results are indicative of developmental effects which are most likely unrelated to maternal toxicity, OBDPE is considered as a developmental toxicant. With regard to neurotoxicity, recently behavioural disturbances have been reported when mice (10 day old) were exposed to a single oral dose of hexabromo-diphenyl ether (0.45, 0.9 and 9 mg/kg bw). Those effects are observed at 2, 4 but also 6 months of age. Nicotinic receptors were also affected in adult mouse in the previous conditions of exposure. The study has certain limitations compared with regulatory guidelines and thus uncertainty as regards interpretation of the results remains. Moreover only an abstract of this study is available with very few details. Therefore, no firm conclusion can be drawn from these data. Like other halogenated aromatic hydrocarbons, polybrominated diphenyl ethers bind to the cellular aryl hydrocarbon receptor (AhR), which regulates the synthesis of a variety of proteins. Activation of the AhR induces a number of enzymes, including cytochrome P-450-dependent monooxygenases of the CYP1A and CYP2B families, UDP-glucuronosyltransferase, and ethoxyresorufin-o-deethylase. PBDEs are also believed to disrupt the production, transport, and disposition of thyroid hormones. One mechanism of this involves metabolites ot PDBEs competing with thyroxine to bind to transthyretin, decreasing serum thyroid hormone levels. This change in thyroid hormone levels has been linked to both thyroid toxicity and neurobehavioral alterations. Certain PDBEs and their metabolites are also endocrine disruptors and may act as agonists at the estrogen receptors or antagonists at the androgen and progesterone receptors. (L628, A262)

- Skin corrosion/irritation: No data available.
- Serious eye damage/eye irritation: Animal data show an absorption of Octabromodiphenyl ether (OBDPE) by oral or inhalation route with an accumulation of the parent compound or its metabolites in the liver and also in the adipose tissue and the lung following inhalation administration. The extent of absorption and elimination cannot be assessed from the data available. No information on the metabolism of OBDPE is available. Following oral administration, OBDPE is an inducer of xenobiotic metabolism. There are no measured data on OBDPE dermal absorption. However based on OBDPE physicochemical properties and analogy with PCBs, a dermal absorption of 4.5% may be estimated. Evidence from humans indicates that OBDPE, HxBDPE, HpBDPE and NonaBDPE which are components of commercial OBDPE can be absorbed into the body and distributed into the blood. Distribution to

the adipose tissue was evidenced at least for OBDPE and HxBDPE. There are no data available on the rate of elimination or on bioaccumulation of OBDPE from human adipose tissue neither for PeBDPO but given the high lipophilicity of these compounds and the adipose tissue accumulation observed in rats following oral or inhalation routes, it can be assumed that in humans OBDPE might bioaccumulate in these tissues as well. Following pregnancy HxBDPE and others PBDPEs such as TeBDPE and PeBDPEs are excreted in the breast milk. Unfortunately, such measurements were not carried out on OBDPE. However, based on the high lipophilicity of OBDPE, its potential to bioaccumulate in adipose tissues and the breast milk measured data with HxBDPE (one component of commercial OBDPE), excretion of OBDPE in the breast milk may be anticipated OBDPE has a low acute toxicity in animals. Acute oral toxicity data indicate a rat LD50 greater than 28,000 mg/kg. No deaths, no weight changes or necropsy lesions were reported up to 5,000 mg/kg. At 10,000 mg/kg and 28,000 mg/kg, no deaths were observed but no more information on these studies are available. A dermal LD50 greater than 2,000 mg/kg has been demonstrated in rabbits using DBDPE applied neat under occlusive wraps for 24 hours. No deaths were observed up to 2,000 mg/kg. Local and general signs of toxicity were not reported and necropsies were not performed in this dermal toxicity study. An inhalation LC50 greater than 60 mg/l has been demonstrated in rats exposed with OBDPE during one hour. No deaths and no clinical signs of toxicity were observed up to 60 mg/l. OBDPE is not a dermal or an ocular irritant. There is no indication of skin sensitization in animals. The only information concerning the effects of repeated oral and inhalation exposure to OBDPE comes from studies in rats involving administration of commercial OBDPE. These studies consistently indicate that the liver is the key target organ within 4 and 13 weeks of repeated oral dosing and within 14 days and 90 days of inhalation exposure. The changes in thyroid status are apparent within 4 and 13 weeks of repeated oral dosing from 1,000 ppm and within 13 weeks of repeated inhalation dosing from 16 mg/m3 (analytical concentration). The LOAEL is considered to be 100 ppm . 7.2 mg/kg/day in the 90 day dietary study based on the liver changes (increase of liver weight and granular cytoplasmic changes) observed from 100 ppm . 7.2 mg/kg/day. The NOAEC for systemic toxicity is considered to be 1.1 mg/cu m in the 90 day rat study by inhalation route based on the liver and thyroid status changes observed at the concentration just above: 16 mg/cu m . Alterations in thyroid homeostasis were reported with organochlorine compounds for many species, including humans and a thyroid hormone like affinity for the serum transport protein transthyretin was shown for hydroxylated PCBs as well as for PBDPE congeners such as DiBDPE and TeBDPE. To our knowledge, no studies on transthyretin-T4 competition have been carried out on OBDPE neither on DBDPE. Following inhalation exposure, local toxicity was demonstrated with hyperplasia/hypertrophy of the goblet cells within 2 weeks of exposure and with chronic active lung inflammation and alveolar histiocytosis within 13 weeks of exposure. It is obvious that the observed effect at 1.1 mg/cu m is minimal and reveals only a trend to a chronic inflammation however this value has been taken to set up the LOAEC for local toxicity. Regarding mutagenicity no in vivo data are available. However based on the available in vitro data, OBDPE is considered as non-genotoxic in vitro and no concern for mutagenicity is assumed. No chronic or carcinogenicity studies in animals are available. No specific fertility study is available. A recent rat inhalation sub-chronic study, well conducted and specifically designed to investigate reproductive organs, did not demonstrate adverse effects on male reproductive organs. Therefore no concern is assumed for male fertility. Regarding female reproductive organs, absence of corpora lutea was shown in this study in 3/10 females at 202 mg/m3 versus 0/10 in the control group. Since the absence of corpora lutea is considered to be an unusual finding in rats at 20 weeks of age, the 30% incidence in this group was considered treatment-related and therefore a NOAEC for female fertility of 16 mg/m3 was considered. Developmental effects are observed in rats in two studies (decrease of fetal body weight from 10 mg/kg/day, increase of post-implantation loss with late resorptions, increase in dead or resorbed conceptuses per litter at 25 mg/kg/day (33.2% versus 4.3%); decrease in the average number of live fetuses per litter (8.9 versus 14.6) and fetal malformation/variation and delayed skeletal ossification at 25 mg/kg/day. Those developmental effects do not seem to be related to maternal toxicity. However, these developmental effects are not confirmed in a third assay in rats conducted with a test article containing a lower percentage of the OBDPE component. In rabbits, the substance produces only slight foetotoxicity

from 5 mg/kg/day (slight decrease of the fetal body weight and increase in delayed ossification). The lowest identified NOAEL is considered i.e. 2 mg/kg/day from the rabbit study. Since some of these results are indicative of developmental effects which are most likely unrelated to maternal toxicity, OBDPE is considered as a developmental toxicant. With regard to neurotoxicity, recently behavioural disturbances have been reported when mice (10 day old) were exposed to a single oral dose of hexabromo-diphenyl ether (0.45, 0.9 and 9 mg/kg bw). Those effects are observed at 2, 4 but also 6 months of age. Nicotinic receptors were also affected in adult mouse in the previous conditions of exposure. The study has certain limitations compared with regulatory guidelines and thus uncertainty as regards interpretation of the results remains. Moreover only an abstract of this study is available with very few details. Therefore, no firm conclusion can be drawn from these data. /LABORATORY ANIMALS: Acute Exposure/ Single applications of 100 mg commercial octabromodiphenyl ether (OBDE) were made into the conjunctival sac of the eye of 3 male and 3 female New Zealand white rabbits. Examinations were made at 24, 48, and 72 hr, and 7 days. A slight discharge was noted from the eyes of 2 rabbits at 24 hr and a slight redness was noted in the eye of one rabbit at 48 hr. No ocular irritation or corneal damage.
- Respiratory or skin sensitization: Animal data show an absorption of Octabromodiphenyl ether (OBDPE) by oral or inhalation route with an accumulation of the parent compound or its metabolites in the liver and also in the adipose tissue and the lung following inhalation administration. The extent of absorption and elimination cannot be assessed from the data available. No information on the metabolism of OBDPE is available. Following oral administration, OBDPE is an inducer of xenobiotic metabolism. There are no measured data on OBDPE dermal absorption. However based on OBDPE physicochemical properties and analogy with PCBs, a dermal absorption of 4.5% may be estimated. Evidence from humans indicates that OBDPE, HxBDPE, HpBDPE and NonaBDPE which are components of commercial OBDPE can be absorbed into the body and distributed into the blood. Distribution to the adipose tissue was evidenced at least for OBDPE and HxBDPE. There are no data available on the rate of elimination or on bioaccumulation of OBDPE from human adipose tissue neither for PeBDPO but given the high lipophilicity of these compounds and the adipose tissue accumulation observed in rats following oral or inhalation routes, it can be assumed that in humans OBDPE might bioaccumulate in these tissues as well. Following pregnancy HxBDPE and others PBDPEs such as TeBDPE and PeBDPEs are excreted in the breast milk. Unfortunately, such measurements were not carried out on OBDPE. However, based on the high lipophilicity of OBDPE, its potential to bioaccumulate in adipose tissues and the breast milk measured data with HxBDPE (one component of commercial OBDPE), excretion of OBDPE in the breast milk may be anticipated OBDPE has a low acute toxicity in animals. Acute oral toxicity data indicate a rat LD50 greater than 28,000 mg/kg. No deaths, no weight changes or necropsy lesions were reported up to 5,000 mg/kg. At 10,000 mg/kg and 28,000 mg/kg, no deaths were observed but no more information on these studies are available. A dermal LD50 greater than 2,000 mg/kg has been demonstrated in rabbits using DBDPE applied neat under occlusive wraps for 24 hours. No deaths were observed up to 2,000 mg/kg. Local and general signs of toxicity were not reported and necropsies were not performed in this dermal toxicity study. An inhalation LC50 greater than 60 mg/l has been demonstrated in rats exposed with OBDPE during one hour. No deaths and no clinical signs of toxicity were observed up to 60 mg/l. OBDPE is not a dermal or an ocular irritant. There is no indication of skin sensitization in animals. The only information concerning the effects of repeated oral and inhalation exposure to OBDPE comes from studies in rats involving administration of commercial OBDPE. These studies consistently indicate that the liver is the key target organ within 4 and 13 weeks of repeated oral dosing and within 14 days and 90 days of inhalation exposure. The changes in thyroid status are apparent within 4 and 13 weeks of repeated oral dosing from 1,000 ppm and within 13 weeks of repeated inhalation dosing from 16 mg/m3 (analytical concentration). The LOAEL is considered to be 100 ppm . 7.2 mg/kg/day in the 90 day dietary study based on the liver changes (increase of liver weight and granular cytoplasmic changes) observed from 100 ppm . 7.2 mg/kg/day. The NOAEC for systemic toxicity is considered to be 1.1 mg/cu m in the 90 day rat study by inhalation route based on the liver and thyroid status changes observed at the concentration just above: 16 mg/cu m . Alterations in thyroid homeostasis were reported with organochlorine

compounds for many species, including humans and a thyroid hormone like affinity for the serum transport protein transthyretin was shown for hydroxylated PCBs as well as for PBDPE congeners such as DiBDPE and TeBDPE. To our knowledge, no studies on transthyretin-T4 competition have been carried out on OBDPE neither on DBDPE. Following inhalation exposure, local toxicity was demonstrated with hyperplasia/hypertrophy of the goblet cells within 2 weeks of exposure and with chronic active lung inflammation and alveolar histiocytosis within 13 weeks of exposure. It is obvious that the observed effect at 1.1 mg/cu m is minimal and reveals only a trend to a chronic inflammation however this value has been taken to set up the LOAEC for local toxicity. Regarding mutagenicity no in vivo data are available. However based on the available in vitro data, OBDPE is considered as non-genotoxic in vitro and no concern for mutagenicity is assumed. No chronic or carcinogenicity studies in animals are available. No specific fertility study is available. A recent rat inhalation sub-chronic study, well conducted and specifically designed to investigate reproductive organs, did not demonstrate adverse effects on male reproductive organs. Therefore no concern is assumed for male fertility. Regarding female reproductive organs, absence of corpora lutea was shown in this study in 3/10 females at 202 mg/m3 versus 0/10 in the control group. Since the absence of corpora lutea is considered to be an unusual finding in rats at 20 weeks of age, the 30% incidence in this group was considered treatment-related and therefore a NOAEC for female fertility of 16 mg/m3 was considered. Developmental effects are observed in rats in two studies (decrease of fetal body weight from 10 mg/kg/day, increase of post-implantation loss with late resorptions, increase in dead or resorbed conceptuses per litter at 25 mg/kg/day (33.2% versus 4.3%); decrease in the average number of live fetuses per litter (8.9 versus 14.6) and fetal malformation/variation and delayed skeletal ossification at 25 mg/kg/day. Those developmental effects do not seem to be related to maternal toxicity. However, these developmental effects are not confirmed in a third assay in rats conducted with a test article containing a lower percentage of the OBDPE component. In rabbits, the substance produces only slight foetotoxicity from 5 mg/kg/day (slight decrease of the fetal body weight and increase in delayed ossification). The lowest identified NOAEL is considered i.e. 2 mg/kg/day from the rabbit study. Since some of these results are indicative of developmental effects which are most likely unrelated to maternal toxicity, OBDPE is considered as a developmental toxicant. With regard to neurotoxicity, recently behavioural disturbances have been reported when mice (10 day old) were exposed to a single oral dose of hexabromo-diphenyl ether (0.45, 0.9 and 9 mg/kg bw). Those effects are observed at 2, 4 but also 6 months of age. Nicotinic receptors were also affected in adult mouse in the previous conditions of exposure. The study has certain limitations compared with regulatory guidelines and thus uncertainty as regards interpretation of the results remains. Moreover only an abstract of this study is available with very few details. Therefore, no firm conclusion can be drawn from these data.
- Germ cell mutagenicity: Animal data show an absorption of Octabromodiphenyl ether (OBDPE) by oral or inhalation route with an accumulation of the parent compound or its metabolites in the liver and also in the adipose tissue and the lung following inhalation administration. The extent of absorption and elimination cannot be assessed from the data available. No information on the metabolism of OBDPE is available. Following oral administration, OBDPE is an inducer of xenobiotic metabolism. There are no measured data on OBDPE dermal absorption. However based on OBDPE physicochemical properties and analogy with PCBs, a dermal absorption of 4.5% may be estimated. Evidence from humans indicates that OBDPE, HxBDPE, HpBDPE and NonaBDPE which are components of commercial OBDPE can be absorbed into the body and distributed into the blood. Distribution to the adipose tissue was evidenced at least for OBDPE and HxBDPE. There are no data available on the rate of elimination or on bioaccumulation of OBDPE from human adipose tissue neither for PeBDPO but given the high lipophilicity of these compounds and the adipose tissue accumulation observed in rats following oral or inhalation routes, it can be assumed that in humans OBDPE might bioaccumulate in these tissues as well. Following pregnancy HxBDPE and others PBDPEs such as TeBDPE and PeBDPEs are excreted in the breast milk. Unfortunately, such measurements were not carried out on OBDPE. However, based on the high lipophilicity of OBDPE, its potential to bioaccumulate in adipose tissues and the breast milk measured data with HxBDPE (one component of commercial OBDPE), excretion of OBDPE in the breast milk may be anticipated OBDPE has a low

acute toxicity in animals. Acute oral toxicity data indicate a rat LD50 greater than 28,000 mg/kg. No deaths, no weight changes or necropsy lesions were reported up to 5,000 mg/kg. At 10,000 mg/kg and 28,000 mg/kg, no deaths were observed but no more information on these studies are available. A dermal LD50 greater than 2,000 mg/kg has been demonstrated in rabbits using DBDPE applied neat under occlusive wraps for 24 hours. No deaths were observed up to 2,000 mg/kg. Local and general signs of toxicity were not reported and necropsies were not performed in this dermal toxicity study. An inhalation LC50 greater than 60 mg/l has been demonstrated in rats exposed with OBDPE during one hour. No deaths and no clinical signs of toxicity were observed up to 60 mg/l. OBDPE is not a dermal or an ocular irritant. There is no indication of skin sensitization in animals. The only information concerning the effects of repeated oral and inhalation exposure to OBDPE comes from studies in rats involving administration of commercial OBDPE. These studies consistently indicate that the liver is the key target organ within 4 and 13 weeks of repeated oral dosing and within 14 days and 90 days of inhalation exposure. The changes in thyroid status are apparent within 4 and 13 weeks of repeated oral dosing from 1,000 ppm and within 13 weeks of repeated inhalation dosing from 16 mg/m3 (analytical concentration). The LOAEL is considered to be 100 ppm . 7.2 mg/kg/day in the 90 day dietary study based on the liver changes (increase of liver weight and granular cytoplasmic changes) observed from 100 ppm . 7.2 mg/kg/day. The NOAEC for systemic toxicity is considered to be 1.1 mg/cu m in the 90 day rat study by inhalation route based on the liver and thyroid status changes observed at the concentration just above: 16 mg/cu m . Alterations in thyroid homeostasis were reported with organochlorine compounds for many species, including humans and a thyroid hormone like affinity for the serum transport protein transthyretin was shown for hydroxylated PCBs as well as for PBDPE congeners such as DiBDPE and TeBDPE. To our knowledge, no studies on transthyretin-T4 competition have been carried out on OBDPE neither on DBDPE. Following inhalation exposure, local toxicity was demonstrated with hyperplasia/hypertrophy of the goblet cells within 2 weeks of exposure and with chronic active lung inflammation and alveolar histiocytosis within 13 weeks of exposure. It is obvious that the observed effect at 1.1 mg/cu m is minimal and reveals only a trend to a chronic inflammation however this value has been taken to set up the LOAEC for local toxicity. Regarding mutagenicity no in vivo data are available. However based on the available in vitro data, OBDPE is considered as non-genotoxic in vitro and no concern for mutagenicity is assumed. No chronic or carcinogenicity studies in animals are available. No specific fertility study is available. A recent rat inhalation sub-chronic study, well conducted and specifically designed to investigate reproductive organs, did not demonstrate adverse effects on male reproductive organs. Therefore no concern is assumed for male fertility. Regarding female reproductive organs, absence of corpora lutea was shown in this study in 3/10 females at 202 mg/m3 versus 0/10 in the control group. Since the absence of corpora lutea is considered to be an unusual finding in rats at 20 weeks of age, the 30% incidence in this group was considered treatment-related and therefore a NOAEC for female fertility of 16 mg/m3 was considered. Developmental effects are observed in rats in two studies (decrease of fetal body weight from 10 mg/kg/day, increase of post-implantation loss with late resorptions, increase in dead or resorbed conceptuses per litter at 25 mg/kg/day (33.2% versus 4.3%); decrease in the average number of live fetuses per litter (8.9 versus 14.6) and fetal malformation/variation and delayed skeletal ossification at 25 mg/kg/day. Those developmental effects do not seem to be related to maternal toxicity. However, these developmental effects are not confirmed in a third assay in rats conducted with a test article containing a lower percentage of the OBDPE component. In rabbits, the substance produces only slight foetotoxicity from 5 mg/kg/day (slight decrease of the fetal body weight and increase in delayed ossification). The lowest identified NOAEL is considered i.e. 2 mg/kg/day from the rabbit study. Since some of these results are indicative of developmental effects which are most likely unrelated to maternal toxicity, OBDPE is considered as a developmental toxicant. With regard to neurotoxicity, recently behavioural disturbances have been reported when mice (10 day old) were exposed to a single oral dose of hexabromo-diphenyl ether (0.45, 0.9 and 9 mg/kg bw). Those effects are observed at 2, 4 but also 6 months of age. Nicotinic receptors were also affected in adult mouse in the previous conditions of exposure. The study has certain limitations compared with regulatory guidelines and thus uncertainty as regards interpretation of the results remains. Moreover only an abstract of this study is available with very few

details. Therefore, no firm conclusion can be drawn from these data. /GENOTOXICITY/ OctaBDE did not increase the frequency of chromosomal aberration assays in human peripheral blood lymphocytes in vitro, when compared with the negative controls at doses up to 1000 ug/mL. In these chromosomal aberration assays, octaBDE was tested at concentrations that induced cytotoxicity in the presence or absence of Aroclor-1254 induced rat liver metabolic activation.
- Carcinogenicity: Animal data show an absorption of Octabromodiphenyl ether (OBDPE) by oral or inhalation route with an accumulation of the parent compound or its metabolites in the liver and also in the adipose tissue and the lung following inhalation administration. The extent of absorption and elimination cannot be assessed from the data available. No information on the metabolism of OBDPE is available. Following oral administration, OBDPE is an inducer of xenobiotic metabolism. There are no measured data on OBDPE dermal absorption. However based on OBDPE physicochemical properties and analogy with PCBs, a dermal absorption of 4.5% may be estimated. Evidence from humans indicates that OBDPE, HxBDPE, HpBDPE and NonaBDPE which are components of commercial OBDPE can be absorbed into the body and distributed into the blood. Distribution to the adipose tissue was evidenced at least for OBDPE and HxBDPE. There are no data available on the rate of elimination or on bioaccumulation of OBDPE from human adipose tissue neither for PeBDPO but given the high lipophilicity of these compounds and the adipose tissue accumulation observed in rats following oral or inhalation routes, it can be assumed that in humans OBDPE might bioaccumulate in these tissues as well. Following pregnancy HxBDPE and others PBDPEs such as TeBDPE and PeBDPEs are excreted in the breast milk. Unfortunately, such measurements were not carried out on OBDPE. However, based on the high lipophilicity of OBDPE, its potential to bioaccumulate in adipose tissues and the breast milk measured data with HxBDPE (one component of commercial OBDPE), excretion of OBDPE in the breast milk may be anticipated OBDPE has a low acute toxicity in animals. Acute oral toxicity data indicate a rat LD50 greater than 28,000 mg/kg. No deaths, no weight changes or necropsy lesions were reported up to 5,000 mg/kg. At 10,000 mg/kg and 28,000 mg/kg, no deaths were observed but no more information on these studies are available. A dermal LD50 greater than 2,000 mg/kg has been demonstrated in rabbits using DBDPE applied neat under occlusive wraps for 24 hours. No deaths were observed up to 2,000 mg/kg. Local and general signs of toxicity were not reported and necropsies were not performed in this dermal toxicity study. An inhalation LC50 greater than 60 mg/l has been demonstrated in rats exposed with OBDPE during one hour. No deaths and no clinical signs of toxicity were observed up to 60 mg/l. OBDPE is not a dermal or an ocular irritant. There is no indication of skin sensitization in animals. The only information concerning the effects of repeated oral and inhalation exposure to OBDPE comes from studies in rats involving administration of commercial OBDPE. These studies consistently indicate that the liver is the key target organ within 4 and 13 weeks of repeated oral dosing and within 14 days and 90 days of inhalation exposure. The changes in thyroid status are apparent within 4 and 13 weeks of repeated oral dosing from 1,000 ppm and within 13 weeks of repeated inhalation dosing from 16 mg/m3 (analytical concentration). The LOAEL is considered to be 100 ppm . 7.2 mg/kg/day in the 90 day dietary study based on the liver changes (increase of liver weight and granular cytoplasmic changes) observed from 100 ppm . 7.2 mg/kg/day. The NOAEC for systemic toxicity is considered to be 1.1 mg/cu m in the 90 day rat study by inhalation route based on the liver and thyroid status changes observed at the concentration just above: 16 mg/cu m . Alterations in thyroid homeostasis were reported with organochlorine compounds for many species, including humans and a thyroid hormone like affinity for the serum transport protein transthyretin was shown for hydroxylated PCBs as well as for PBDPE congeners such as DiBDPE and TeBDPE. To our knowledge, no studies on transthyretin-T4 competition have been carried out on OBDPE neither on DBDPE. Following inhalation exposure, local toxicity was demonstrated with hyperplasia/hypertrophy of the goblet cells within 2 weeks of exposure and with chronic active lung inflammation and alveolar histiocytosis within 13 weeks of exposure. It is obvious that the observed effect at 1.1 mg/cu m is minimal and reveals only a trend to a chronic inflammation however this value has been taken to set up the LOAEC for local toxicity. Regarding mutagenicity no in vivo data are available. However based on the available in vitro data, OBDPE is considered as non-genotoxic in vitro and no concern for mutagenicity

is assumed. No chronic or carcinogenicity studies in animals are available. No specific fertility study is available. A recent rat inhalation sub-chronic study, well conducted and specifically designed to investigate reproductive organs, did not demonstrate adverse effects on male reproductive organs. Therefore no concern is assumed for male fertility. Regarding female reproductive organs, absence of corpora lutea was shown in this study in 3/10 females at 202 mg/m3 versus 0/10 in the control group. Since the absence of corpora lutea is considered to be an unusual finding in rats at 20 weeks of age, the 30% incidence in this group was considered treatment-related and therefore a NOAEC for female fertility of 16 mg/m3 was considered. Developmental effects are observed in rats in two studies (decrease of fetal body weight from 10 mg/kg/day, increase of post-implantation loss with late resorptions, increase in dead or resorbed conceptuses per litter at 25 mg/kg/day (33.2% versus 4.3%); decrease in the average number of live fetuses per litter (8.9 versus 14.6) and fetal malformation/variation and delayed skeletal ossification at 25 mg/kg/day. Those developmental effects do not seem to be related to maternal toxicity. However, these developmental effects are not confirmed in a third assay in rats conducted with a test article containing a lower percentage of the OBDPE component. In rabbits, the substance produces only slight foetotoxicity from 5 mg/kg/day (slight decrease of the fetal body weight and increase in delayed ossification). The lowest identified NOAEL is considered i.e. 2 mg/kg/day from the rabbit study. Since some of these results are indicative of developmental effects which are most likely unrelated to maternal toxicity, OBDPE is considered as a developmental toxicant. With regard to neurotoxicity, recently behavioural disturbances have been reported when mice (10 day old) were exposed to a single oral dose of hexabromo-diphenyl ether (0.45, 0.9 and 9 mg/kg bw). Those effects are observed at 2, 4 but also 6 months of age. Nicotinic receptors were also affected in adult mouse in the previous conditions of exposure. The study has certain limitations compared with regulatory guidelines and thus uncertainty as regards interpretation of the results remains. Moreover only an abstract of this study is available with very few details. Therefore, no firm conclusion can be drawn from these data.

- Reproductive toxicity: Animal data show an absorption of Octabromodiphenyl ether (OBDPE) by oral or inhalation route with an accumulation of the parent compound or its metabolites in the liver and also in the adipose tissue and the lung following inhalation administration. The extent of absorption and elimination cannot be assessed from the data available. No information on the metabolism of OBDPE is available. Following oral administration, OBDPE is an inducer of xenobiotic metabolism. There are no measured data on OBDPE dermal absorption. However based on OBDPE physicochemical properties and analogy with PCBs, a dermal absorption of 4.5% may be estimated. Evidence from humans indicates that OBDPE, HxBDPE, HpBDPE and NonaBDPE which are components of commercial OBDPE can be absorbed into the body and distributed into the blood. Distribution to the adipose tissue was evidenced at least for OBDPE and HxBDPE. There are no data available on the rate of elimination or on bioaccumulation of OBDPE from human adipose tissue neither for PeBDPO but given the high lipophilicity of these compounds and the adipose tissue accumulation observed in rats following oral or inhalation routes, it can be assumed that in humans OBDPE might bioaccumulate in these tissues as well. Following pregnancy HxBDPE and others PBDPEs such as TeBDPE and PeBDPEs are excreted in the breast milk. Unfortunately, such measurements were not carried out on OBDPE. However, based on the high lipophilicity of OBDPE, its potential to bioaccumulate in adipose tissues and the breast milk measured data with HxBDPE (one component of commercial OBDPE), excretion of OBDPE in the breast milk may be anticipated OBDPE has a low acute toxicity in animals. Acute oral toxicity data indicate a rat LD50 greater than 28,000 mg/kg. No deaths, no weight changes or necropsy lesions were reported up to 5,000 mg/kg. At 10,000 mg/kg and 28,000 mg/kg, no deaths were observed but no more information on these studies are available. A dermal LD50 greater than 2,000 mg/kg has been demonstrated in rabbits using DBDPE applied neat under occlusive wraps for 24 hours. No deaths were observed up to 2,000 mg/kg. Local and general signs of toxicity were not reported and necropsies were not performed in this dermal toxicity study. An inhalation LC50 greater than 60 mg/l has been demonstrated in rats exposed with OBDPE during one hour. No deaths and no clinical signs of toxicity were observed up to 60 mg/l. OBDPE is not a dermal or an ocular irritant. There is no indication of skin sensitization in animals. The only information concerning the effects of repeated oral

and inhalation exposure to OBDPE comes from studies in rats involving administration of commercial OBDPE. These studies consistently indicate that the liver is the key target organ within 4 and 13 weeks of repeated oral dosing and within 14 days and 90 days of inhalation exposure. The changes in thyroid status are apparent within 4 and 13 weeks of repeated oral dosing from 1,000 ppm and within 13 weeks of repeated inhalation dosing from 16 mg/m3 (analytical concentration). The LOAEL is considered to be 100 ppm . 7.2 mg/kg/day in the 90 day dietary study based on the liver changes (increase of liver weight and granular cytoplasmic changes) observed from 100 ppm . 7.2 mg/kg/day. The NOAEC for systemic toxicity is considered to be 1.1 mg/cu m in the 90 day rat study by inhalation route based on the liver and thyroid status changes observed at the concentration just above: 16 mg/cu m . Alterations in thyroid homeostasis were reported with organochlorine compounds for many species, including humans and a thyroid hormone like affinity for the serum transport protein transthyretin was shown for hydroxylated PCBs as well as for PBDPE congeners such as DiBDPE and TeBDPE. To our knowledge, no studies on transthyretin-T4 competition have been carried out on OBDPE neither on DBDPE. Following inhalation exposure, local toxicity was demonstrated with hyperplasia/hypertrophy of the goblet cells within 2 weeks of exposure and with chronic active lung inflammation and alveolar histiocytosis within 13 weeks of exposure. It is obvious that the observed effect at 1.1 mg/cu m is minimal and reveals only a trend to a chronic inflammation however this value has been taken to set up the LOAEC for local toxicity. Regarding mutagenicity no in vivo data are available. However based on the available in vitro data, OBDPE is considered as non-genotoxic in vitro and no concern for mutagenicity is assumed. No chronic or carcinogenicity studies in animals are available. No specific fertility study is available. A recent rat inhalation sub-chronic study, well conducted and specifically designed to investigate reproductive organs, did not demonstrate adverse effects on male reproductive organs. Therefore no concern is assumed for male fertility. Regarding female reproductive organs, absence of corpora lutea was shown in this study in 3/10 females at 202 mg/m3 versus 0/10 in the control group. Since the absence of corpora lutea is considered to be an unusual finding in rats at 20 weeks of age, the 30% incidence in this group was considered treatment-related and therefore a NOAEC for female fertility of 16 mg/m3 was considered. Developmental effects are observed in rats in two studies (decrease of fetal body weight from 10 mg/kg/day, increase of post-implantation loss with late resorptions, increase in dead or resorbed conceptuses per litter at 25 mg/kg/day (33.2% versus 4.3%); decrease in the average number of live fetuses per litter (8.9 versus 14.6) and fetal malformation/variation and delayed skeletal ossification at 25 mg/kg/day. Those developmental effects do not seem to be related to maternal toxicity. However, these developmental effects are not confirmed in a third assay in rats conducted with a test article containing a lower percentage of the OBDPE component. In rabbits, the substance produces only slight foetotoxicity from 5 mg/kg/day (slight decrease of the fetal body weight and increase in delayed ossification). The lowest identified NOAEL is considered i.e. 2 mg/kg/day from the rabbit study. Since some of these results are indicative of developmental effects which are most likely unrelated to maternal toxicity, OBDPE is considered as a developmental toxicant. With regard to neurotoxicity, recently behavioural disturbances have been reported when mice (10 day old) were exposed to a single oral dose of hexabromo-diphenyl ether (0.45, 0.9 and 9 mg/kg bw). Those effects are observed at 2, 4 but also 6 months of age. Nicotinic receptors were also affected in adult mouse in the previous conditions of exposure. The study has certain limitations compared with regulatory guidelines and thus uncertainty as regards interpretation of the results remains. Moreover only an abstract of this study is available with very few details. Therefore, no firm conclusion can be drawn from these data. /EPIDEMIOLOGY STUDIES/ ... /The/ goal /of this study/ was to examine whether high breast milk PBDE levels in reproductive-age females lead to interference with menstruation characteristics. ... 15 PBDE congeners /were analyzed/ in 46 breast milk samples. Fifteen PBDE congeners (BDE-15 /4,4'-dibromodiphenyl ether/, 28 /4,4'-dibromodiphenyl ether/, 47 /2,2',4,4'-tetrabromodiphenyl ether/, 49 /2,2',4,5'-tetrabromodiphenyl ether/, 99 /2,2',4,4',5-pentabromodiphenyl ether//, 100 /2,2',4,4',6-pentabromodiphenyl ether/, 153 /2,2',4,4',5,5'-hexabromodiphenyl ether/, 154 /2,2',4,4',5,6'-hexabromodiphenyl ether/, 183 /2,2',3,4,4',5',6-heptabromodiphenyl ether/, 196 /2,2',3,3',4,4',5,6'-octabromodiphenyl ether/, 197 /2,2',3,3',4,4',6,6'-octabromodiphenyl ether/, 203 /2,2',3,4,4',5,5',6-octabromodiphenyl ether/, 207

/2,2',3,3',4,4',5,6,6'-nonabromodiphenyl ether/, 208 /2,2',3,3',4,5,5',6,6'-nonabromodiphenyl ether/, and 209 /decabromodiphenyl ether/) were analyzed using a gas chromatograph equipped with a high resolution mass spectrometer. The mean sum of PBDEs (SigmaPBDEs) in breast milk was 3.42 ng/g lipid. Women's age at menarche was not correlated with breast milk PBDE levels. Increased BDE-208 and 209 levels were significantly associated with the prolonged length of average and the longest menstrual cycle independent of age, pre-pregnant BMI, and parity. Higher concentrations of SigmaPBDEs and the higher brominated PBDEs from BDE-183 to 209, except 197, were significantly linked to women whose menstruation periods were still coming irregularly at the sampling time. Age-adjusted odds ratios (ORs) of BDE-153, 183, 207, 208, and SigmaPBDEs were significantly higher in women with length of average menstrual cycle >32 days, compared to the control. Women whose menstruation periods still came irregularly when they were 18 years old had higher age-adjusted ORs of BDE-207, 208, 209, and SigmaPBDEs than those whose periods came regularly at the same age. Although SigmaPBDEs and certain higher brominated PBDEs appear to have potential to prolong length of average menstrual cycle and delay the age when menstruation periods begin coming regularly, these findings are not conclusive...
- STOT-single exposure: Animal data show an absorption of Octabromodiphenyl ether (OBDPE) by oral or inhalation route with an accumulation of the parent compound or its metabolites in the liver and also in the adipose tissue and the lung following inhalation administration. The extent of absorption and elimination cannot be assessed from the data available. No information on the metabolism of OBDPE is available. Following oral administration, OBDPE is an inducer of xenobiotic metabolism. There are no measured data on OBDPE dermal absorption. However based on OBDPE physicochemical properties and analogy with PCBs, a dermal absorption of 4.5% may be estimated. Evidence from humans indicates that OBDPE, HxBDPE, HpBDPE and NonaBDPE which are components of commercial OBDPE can be absorbed into the body and distributed into the blood. Distribution to the adipose tissue was evidenced at least for OBDPE and HxBDPE. There are no data available on the rate of elimination or on bioaccumulation of OBDPE from human adipose tissue neither for PeBDPO but given the high lipophilicity of these compounds and the adipose tissue accumulation observed in rats following oral or inhalation routes, it can be assumed that in humans OBDPE might bioaccumulate in these tissues as well. Following pregnancy HxBDPE and others PBDPEs such as TeBDPE and PeBDPEs are excreted in the breast milk. Unfortunately, such measurements were not carried out on OBDPE. However, based on the high lipophilicity of OBDPE, its potential to bioaccumulate in adipose tissues and the breast milk measured data with HxBDPE (one component of commercial OBDPE), excretion of OBDPE in the breast milk may be anticipated OBDPE has a low acute toxicity in animals. Acute oral toxicity data indicate a rat LD50 greater than 28,000 mg/kg. No deaths, no weight changes or necropsy lesions were reported up to 5,000 mg/kg. At 10,000 mg/kg and 28,000 mg/kg, no deaths were observed but no more information on these studies are available. A dermal LD50 greater than 2,000 mg/kg has been demonstrated in rabbits using DBDPE applied neat under occlusive wraps for 24 hours. No deaths were observed up to 2,000 mg/kg. Local and general signs of toxicity were not reported and necropsies were not performed in this dermal toxicity study. An inhalation LC50 greater than 60 mg/l has been demonstrated in rats exposed with OBDPE during one hour. No deaths and no clinical signs of toxicity were observed up to 60 mg/l. OBDPE is not a dermal or an ocular irritant. There is no indication of skin sensitization in animals. The only information concerning the effects of repeated oral and inhalation exposure to OBDPE comes from studies in rats involving administration of commercial OBDPE. These studies consistently indicate that the liver is the key target organ within 4 and 13 weeks of repeated oral dosing and within 14 days and 90 days of inhalation exposure. The changes in thyroid status are apparent within 4 and 13 weeks of repeated oral dosing from 1,000 ppm and within 13 weeks of repeated inhalation dosing from 16 mg/m3 (analytical concentration). The LOAEL is considered to be 100 ppm . 7.2 mg/kg/day in the 90 day dietary study based on the liver changes (increase of liver weight and granular cytoplasmic changes) observed from 100 ppm . 7.2 mg/kg/day. The NOAEC for systemic toxicity is considered to be 1.1 mg/cu m in the 90 day rat study by inhalation route based on the liver and thyroid status changes observed at the concentration just above: 16 mg/cu m . Alterations in thyroid homeostasis were reported with organochlorine compounds for many species, including

humans and a thyroid hormone like affinity for the serum transport protein transthyretin was shown for hydroxylated PCBs as well as for PBDPE congeners such as DiBDPE and TeBDPE. To our knowledge, no studies on transthyretin-T4 competition have been carried out on OBDPE neither on DBDPE. Following inhalation exposure, local toxicity was demonstrated with hyperplasia/hypertrophy of the goblet cells within 2 weeks of exposure and with chronic active lung inflammation and alveolar histiocytosis within 13 weeks of exposure. It is obvious that the observed effect at 1.1 mg/cu m is minimal and reveals only a trend to a chronic inflammation however this value has been taken to set up the LOAEC for local toxicity. Regarding mutagenicity no in vivo data are available. However based on the available in vitro data, OBDPE is considered as non-genotoxic in vitro and no concern for mutagenicity is assumed. No chronic or carcinogenicity studies in animals are available. No specific fertility study is available. A recent rat inhalation sub-chronic study, well conducted and specifically designed to investigate reproductive organs, did not demonstrate adverse effects on male reproductive organs. Therefore no concern is assumed for male fertility. Regarding female reproductive organs, absence of corpora lutea was shown in this study in 3/10 females at 202 mg/m3 versus 0/10 in the control group. Since the absence of corpora lutea is considered to be an unusual finding in rats at 20 weeks of age, the 30% incidence in this group was considered treatment-related and therefore a NOAEC for female fertility of 16 mg/m3 was considered. Developmental effects are observed in rats in two studies (decrease of fetal body weight from 10 mg/kg/day, increase of post-implantation loss with late resorptions, increase in dead or resorbed conceptuses per litter at 25 mg/kg/day (33.2% versus 4.3%); decrease in the average number of live fetuses per litter (8.9 versus 14.6) and fetal malformation/variation and delayed skeletal ossification at 25 mg/kg/day. Those developmental effects do not seem to be related to maternal toxicity. However, these developmental effects are not confirmed in a third assay in rats conducted with a test article containing a lower percentage of the OBDPE component. In rabbits, the substance produces only slight foetotoxicity from 5 mg/kg/day (slight decrease of the fetal body weight and increase in delayed ossification). The lowest identified NOAEL is considered i.e. 2 mg/kg/day from the rabbit study. Since some of these results are indicative of developmental effects which are most likely unrelated to maternal toxicity, OBDPE is considered as a developmental toxicant. With regard to neurotoxicity, recently behavioural disturbances have been reported when mice (10 day old) were exposed to a single oral dose of hexabromo-diphenyl ether (0.45, 0.9 and 9 mg/kg bw). Those effects are observed at 2, 4 but also 6 months of age. Nicotinic receptors were also affected in adult mouse in the previous conditions of exposure. The study has certain limitations compared with regulatory guidelines and thus uncertainty as regards interpretation of the results remains. Moreover only an abstract of this study is available with very few details. Therefore, no firm conclusion can be drawn from these data.

- STOT-repeated exposure: Animal data show an absorption of Octabromodiphenyl ether (OBDPE) by oral or inhalation route with an accumulation of the parent compound or its metabolites in the liver and also in the adipose tissue and the lung following inhalation administration. The extent of absorption and elimination cannot be assessed from the data available. No information on the metabolism of OBDPE is available. Following oral administration, OBDPE is an inducer of xenobiotic metabolism. There are no measured data on OBDPE dermal absorption. However based on OBDPE physicochemical properties and analogy with PCBs, a dermal absorption of 4.5% may be estimated. Evidence from humans indicates that OBDPE, HxBDPE, HpBDPE and NonaBDPE which are components of commercial OBDPE can be absorbed into the body and distributed into the blood. Distribution to the adipose tissue was evidenced at least for OBDPE and HxBDPE. There are no data available on the rate of elimination or on bioaccumulation of OBDPE from human adipose tissue neither for PeBDPO but given the high lipophilicity of these compounds and the adipose tissue accumulation observed in rats following oral or inhalation routes, it can be assumed that in humans OBDPE might bioaccumulate in these tissues as well. Following pregnancy HxBDPE and others PBDPEs such as TeBDPE and PeBDPEs are excreted in the breast milk. Unfortunately, such measurements were not carried out on OBDPE. However, based on the high lipophilicity of OBDPE, its potential to bioaccumulate in adipose tissues and the breast milk measured data with HxBDPE (one component of commercial OBDPE), excretion of OBDPE in the breast milk may be anticipated OBDPE has a low

acute toxicity in animals. Acute oral toxicity data indicate a rat LD50 greater than 28,000 mg/kg. No deaths, no weight changes or necropsy lesions were reported up to 5,000 mg/kg. At 10,000 mg/kg and 28,000 mg/kg, no deaths were observed but no more information on these studies are available. A dermal LD50 greater than 2,000 mg/kg has been demonstrated in rabbits using DBDPE applied neat under occlusive wraps for 24 hours. No deaths were observed up to 2,000 mg/kg. Local and general signs of toxicity were not reported and necropsies were not performed in this dermal toxicity study. An inhalation LC50 greater than 60 mg/l has been demonstrated in rats exposed with OBDPE during one hour. No deaths and no clinical signs of toxicity were observed up to 60 mg/l. OBDPE is not a dermal or an ocular irritant. There is no indication of skin sensitization in animals. The only information concerning the effects of repeated oral and inhalation exposure to OBDPE comes from studies in rats involving administration of commercial OBDPE. These studies consistently indicate that the liver is the key target organ within 4 and 13 weeks of repeated oral dosing and within 14 days and 90 days of inhalation exposure. The changes in thyroid status are apparent within 4 and 13 weeks of repeated oral dosing from 1,000 ppm and within 13 weeks of repeated inhalation dosing from 16 mg/m3 (analytical concentration). The LOAEL is considered to be 100 ppm . 7.2 mg/kg/day in the 90 day dietary study based on the liver changes (increase of liver weight and granular cytoplasmic changes) observed from 100 ppm . 7.2 mg/kg/day. The NOAEC for systemic toxicity is considered to be 1.1 mg/cu m in the 90 day rat study by inhalation route based on the liver and thyroid status changes observed at the concentration just above: 16 mg/cu m . Alterations in thyroid homeostasis were reported with organochlorine compounds for many species, including humans and a thyroid hormone like affinity for the serum transport protein transthyretin was shown for hydroxylated PCBs as well as for PBDPE congeners such as DiBDPE and TeBDPE. To our knowledge, no studies on transthyretin-T4 competition have been carried out on OBDPE neither on DBDPE. Following inhalation exposure, local toxicity was demonstrated with hyperplasia/hypertrophy of the goblet cells within 2 weeks of exposure and with chronic active lung inflammation and alveolar histiocytosis within 13 weeks of exposure. It is obvious that the observed effect at 1.1 mg/cu m is minimal and reveals only a trend to a chronic inflammation however this value has been taken to set up the LOAEC for local toxicity. Regarding mutagenicity no in vivo data are available. However based on the available in vitro data, OBDPE is considered as non-genotoxic in vitro and no concern for mutagenicity is assumed. No chronic or carcinogenicity studies in animals are available. No specific fertility study is available. A recent rat inhalation sub-chronic study, well conducted and specifically designed to investigate reproductive organs, did not demonstrate adverse effects on male reproductive organs. Therefore no concern is assumed for male fertility. Regarding female reproductive organs, absence of corpora lutea was shown in this study in 3/10 females at 202 mg/m3 versus 0/10 in the control group. Since the absence of corpora lutea is considered to be an unusual finding in rats at 20 weeks of age, the 30% incidence in this group was considered treatment-related and therefore a NOAEC for female fertility of 16 mg/m3 was considered. Developmental effects are observed in rats in two studies (decrease of fetal body weight from 10 mg/kg/day, increase of post-implantation loss with late resorptions, increase in dead or resorbed conceptuses per litter at 25 mg/kg/day (33.2% versus 4.3%); decrease in the average number of live fetuses per litter (8.9 versus 14.6) and fetal malformation/variation and delayed skeletal ossification at 25 mg/kg/day. Those developmental effects do not seem to be related to maternal toxicity. However, these developmental effects are not confirmed in a third assay in rats conducted with a test article containing a lower percentage of the OBDPE component. In rabbits, the substance produces only slight foetotoxicity from 5 mg/kg/day (slight decrease of the fetal body weight and increase in delayed ossification). The lowest identified NOAEL is considered i.e. 2 mg/kg/day from the rabbit study. Since some of these results are indicative of developmental effects which are most likely unrelated to maternal toxicity, OBDPE is considered as a developmental toxicant. With regard to neurotoxicity, recently behavioural disturbances have been reported when mice (10 day old) were exposed to a single oral dose of hexabromo-diphenyl ether (0.45, 0.9 and 9 mg/kg bw). Those effects are observed at 2, 4 but also 6 months of age. Nicotinic receptors were also affected in adult mouse in the previous conditions of exposure. The study has certain limitations compared with regulatory guidelines and thus uncertainty as regards interpretation of the results remains. Moreover only an abstract of this study is available with very few

details. Therefore, no firm conclusion can be drawn from these data.
- Aspiration hazard: No data available.

Likely routes of exposure
- Animal data show an absorption of Octabromodiphenyl ether (OBDPE) by oral or inhalation route with an accumulation of the parent compound or its metabolites in the liver and also in the adipose tissue and the lung following inhalation administration. The extent of absorption and elimination cannot be assessed from the data available. No information on the metabolism of OBDPE is available. Following oral administration, OBDPE is an inducer of xenobiotic metabolism. There are no measured data on OBDPE dermal absorption. However based on OBDPE physicochemical properties and analogy with PCBs, a dermal absorption of 4.5% may be estimated. Evidence from humans indicates that OBDPE, HxBDPE, HpBDPE and NonaBDPE which are components of commercial OBDPE can be absorbed into the body and distributed into the blood. Distribution to the adipose tissue was evidenced at least for OBDPE and HxBDPE. There are no data available on the rate of elimination or on bioaccumulation of OBDPE from human adipose tissue neither for PeBDPO but given the high lipophilicity of these compounds and the adipose tissue accumulation observed in rats following oral or inhalation routes, it can be assumed that in humans OBDPE might bioaccumulate in these tissues as well. Following pregnancy HxBDPE and others PBDPEs such as TeBDPE and PeBDPEs are excreted in the breast milk. Unfortunately, such measurements were not carried out on OBDPE. However, based on the high lipophilicity of OBDPE, its potential to bioaccumulate in adipose tissues and the breast milk measured data with HxBDPE (one component of commercial OBDPE), excretion of OBDPE in the breast milk may be anticipated OBDPE has a low acute toxicity in animals. Acute oral toxicity data indicate a rat LD50 greater than 28,000 mg/kg. No deaths, no weight changes or necropsy lesions were reported up to 5,000 mg/kg. At 10,000 mg/kg and 28,000 mg/kg, no deaths were observed but no more information on these studies are available. A dermal LD50 greater than 2,000 mg/kg has been demonstrated in rabbits using DBDPE applied neat under occlusive wraps for 24 hours. No deaths were observed up to 2,000 mg/kg. Local and general signs of toxicity were not reported and necropsies were not performed in this dermal toxicity study. An inhalation LC50 greater than 60 mg/l has been demonstrated in rats exposed with OBDPE during one hour. No deaths and no clinical signs of toxicity were observed up to 60 mg/l. OBDPE is not a dermal or an ocular irritant. There is no indication of skin sensitization in animals. The only information concerning the effects of repeated oral and inhalation exposure to OBDPE comes from studies in rats involving administration of commercial OBDPE. These studies consistently indicate that the liver is the key target organ within 4 and 13 weeks of repeated oral dosing and within 14 days and 90 days of inhalation exposure. The changes in thyroid status are apparent within 4 and 13 weeks of repeated oral dosing from 1,000 ppm and within 13 weeks of repeated inhalation dosing from 16 mg/m3 (analytical concentration). The LOAEL is considered to be 100 ppm . 7.2 mg/kg/day in the 90 day dietary study based on the liver changes (increase of liver weight and granular cytoplasmic changes) observed from 100 ppm . 7.2 mg/kg/day. The NOAEC for systemic toxicity is considered to be 1.1 mg/cu m in the 90 day rat study by inhalation route based on the liver and thyroid status changes observed at the concentration just above: 16 mg/cu m . Alterations in thyroid homeostasis were reported with organochlorine compounds for many species, including humans and a thyroid hormone like affinity for the serum transport protein transthyretin was shown for hydroxylated PCBs as well as for PBDPE congeners such as DiBDPE and TeBDPE. To our knowledge, no studies on transthyretin-T4 competition have been carried out on OBDPE neither on DBDPE. Following inhalation exposure, local toxicity was demonstrated with hyperplasia/hypertrophy of the goblet cells within 2 weeks of exposure and with chronic active lung inflammation and alveolar histiocytosis within 13 weeks of exposure. It is obvious that the observed effect at 1.1 mg/cu m is minimal and reveals only a trend to a chronic inflammation however this value has been taken to set up the LOAEC for local toxicity. Regarding mutagenicity no in vivo data are available. However based on the available in vitro data, OBDPE is considered as non-genotoxic in vitro and no concern for mutagenicity is assumed. No chronic or carcinogenicity studies in animals are available. No specific fertility study is available. A recent rat inhalation sub-chronic study, well conducted and specifically designed to investigate reproductive organs,

did not demonstrate adverse effects on male reproductive organs. Therefore no concern is assumed for male fertility. Regarding female reproductive organs, absence of corpora lutea was shown in this study in 3/10 females at 202 mg/m3 versus 0/10 in the control group. Since the absence of corpora lutea is considered to be an unusual finding in rats at 20 weeks of age, the 30% incidence in this group was considered treatment-related and therefore a NOAEC for female fertility of 16 mg/m3 was considered. Developmental effects are observed in rats in two studies (decrease of fetal body weight from 10 mg/kg/day, increase of post-implantation loss with late resorptions, increase in dead or resorbed conceptuses per litter at 25 mg/kg/day (33.2% versus 4.3%); decrease in the average number of live fetuses per litter (8.9 versus 14.6) and fetal malformation/variation and delayed skeletal ossification at 25 mg/kg/day. Those developmental effects do not seem to be related to maternal toxicity. However, these developmental effects are not confirmed in a third assay in rats conducted with a test article containing a lower percentage of the OBDPE component. In rabbits, the substance produces only slight foetotoxicity from 5 mg/kg/day (slight decrease of the fetal body weight and increase in delayed ossification). The lowest identified NOAEL is considered i.e. 2 mg/kg/day from the rabbit study. Since some of these results are indicative of developmental effects which are most likely unrelated to maternal toxicity, OBDPE is considered as a developmental toxicant. With regard to neurotoxicity, recently behavioural disturbances have been reported when mice (10 day old) were exposed to a single oral dose of hexabromo-diphenyl ether (0.45, 0.9 and 9 mg/kg bw). Those effects are observed at 2, 4 but also 6 months of age. Nicotinic receptors were also affected in adult mouse in the previous conditions of exposure. The study has certain limitations compared with regulatory guidelines and thus uncertainty as regards interpretation of the results remains. Moreover only an abstract of this study is available with very few details. Therefore, no firm conclusion can be drawn from these data.

Symptoms related to the physical, chemical and toxicological characteristics
- Animal data show an absorption of Octabromodiphenyl ether (OBDPE) by oral or inhalation route with an accumulation of the parent compound or its metabolites in the liver and also in the adipose tissue and the lung following inhalation administration. The extent of absorption and elimination cannot be assessed from the data available. No information on the metabolism of OBDPE is available. Following oral administration, OBDPE is an inducer of xenobiotic metabolism. There are no measured data on OBDPE dermal absorption. However based on OBDPE physicochemical properties and analogy with PCBs, a dermal absorption of 4.5% may be estimated. Evidence from humans indicates that OBDPE, HxBDPE, HpBDPE and NonaBDPE which are components of commercial OBDPE can be absorbed into the body and distributed into the blood. Distribution to the adipose tissue was evidenced at least for OBDPE and HxBDPE. There are no data available on the rate of elimination or on bioaccumulation of OBDPE from human adipose tissue neither for PeBDPO but given the high lipophilicity of these compounds and the adipose tissue accumulation observed in rats following oral or inhalation routes, it can be assumed that in humans OBDPE might bioaccumulate in these tissues as well. Following pregnancy HxBDPE and others PBDPEs such as TeBDPE and PeBDPEs are excreted in the breast milk. Unfortunately, such measurements were not carried out on OBDPE. However, based on the high lipophilicity of OBDPE, its potential to bioaccumulate in adipose tissues and the breast milk measured data with HxBDPE (one component of commercial OBDPE), excretion of OBDPE in the breast milk may be anticipated OBDPE has a low acute toxicity in animals. Acute oral toxicity data indicate a rat LD50 greater than 28,000 mg/kg. No deaths, no weight changes or necropsy lesions were reported up to 5,000 mg/kg. At 10,000 mg/kg and 28,000 mg/kg, no deaths were observed but no more information on these studies are available. A dermal LD50 greater than 2,000 mg/kg has been demonstrated in rabbits using DBDPE applied neat under occlusive wraps for 24 hours. No deaths were observed up to 2,000 mg/kg. Local and general signs of toxicity were not reported and necropsies were not performed in this dermal toxicity study. An inhalation LC50 greater than 60 mg/l has been demonstrated in rats exposed with OBDPE during one hour. No deaths and no clinical signs of toxicity were observed up to 60 mg/l. OBDPE is not a dermal or an ocular irritant. There is no indication of skin sensitization in animals. The only information concerning the effects of repeated oral and inhalation exposure to OBDPE comes from studies in rats involving administration of commercial OBDPE.

These studies consistently indicate that the liver is the key target organ within 4 and 13 weeks of repeated oral dosing and within 14 days and 90 days of inhalation exposure. The changes in thyroid status are apparent within 4 and 13 weeks of repeated oral dosing from 1,000 ppm and within 13 weeks of repeated inhalation dosing from 16 mg/m3 (analytical concentration). The LOAEL is considered to be 100 ppm . 7.2 mg/kg/day in the 90 day dietary study based on the liver changes (increase of liver weight and granular cytoplasmic changes) observed from 100 ppm . 7.2 mg/kg/day. The NOAEC for systemic toxicity is considered to be 1.1 mg/cu m in the 90 day rat study by inhalation route based on the liver and thyroid status changes observed at the concentration just above: 16 mg/cu m . Alterations in thyroid homeostasis were reported with organochlorine compounds for many species, including humans and a thyroid hormone like affinity for the serum transport protein transthyretin was shown for hydroxylated PCBs as well as for PBDPE congeners such as DiBDPE and TeBDPE. To our knowledge, no studies on transthyretin-T4 competition have been carried out on OBDPE neither on DBDPE. Following inhalation exposure, local toxicity was demonstrated with hyperplasia/hypertrophy of the goblet cells within 2 weeks of exposure and with chronic active lung inflammation and alveolar histiocytosis within 13 weeks of exposure. It is obvious that the observed effect at 1.1 mg/cu m is minimal and reveals only a trend to a chronic inflammation however this value has been taken to set up the LOAEC for local toxicity. Regarding mutagenicity no in vivo data are available. However based on the available in vitro data, OBDPE is considered as non-genotoxic in vitro and no concern for mutagenicity is assumed. No chronic or carcinogenicity studies in animals are available. No specific fertility study is available. A recent rat inhalation sub-chronic study, well conducted and specifically designed to investigate reproductive organs, did not demonstrate adverse effects on male reproductive organs. Therefore no concern is assumed for male fertility. Regarding female reproductive organs, absence of corpora lutea was shown in this study in 3/10 females at 202 mg/m3 versus 0/10 in the control group. Since the absence of corpora lutea is considered to be an unusual finding in rats at 20 weeks of age, the 30% incidence in this group was considered treatment-related and therefore a NOAEC for female fertility of 16 mg/m3 was considered. Developmental effects are observed in rats in two studies (decrease of fetal body weight from 10 mg/kg/day, increase of post-implantation loss with late resorptions, increase in dead or resorbed conceptuses per litter at 25 mg/kg/day (33.2% versus 4.3%); decrease in the average number of live fetuses per litter (8.9 versus 14.6) and fetal malformation/variation and delayed skeletal ossification at 25 mg/kg/day. Those developmental effects do not seem to be related to maternal toxicity. However, these developmental effects are not confirmed in a third assay in rats conducted with a test article containing a lower percentage of the OBDPE component. In rabbits, the substance produces only slight foetotoxicity from 5 mg/kg/day (slight decrease of the fetal body weight and increase in delayed ossification). The lowest identified NOAEL is considered i.e. 2 mg/kg/day from the rabbit study. Since some of these results are indicative of developmental effects which are most likely unrelated to maternal toxicity, OBDPE is considered as a developmental toxicant. With regard to neurotoxicity, recently behavioural disturbances have been reported when mice (10 day old) were exposed to a single oral dose of hexabromo-diphenyl ether (0.45, 0.9 and 9 mg/kg bw). Those effects are observed at 2, 4 but also 6 months of age. Nicotinic receptors were also affected in adult mouse in the previous conditions of exposure. The study has certain limitations compared with regulatory guidelines and thus uncertainty as regards interpretation of the results remains. Moreover only an abstract of this study is available with very few details. Therefore, no firm conclusion can be drawn from these data.

SECTION 12: Ecological information

Not available

SECTION 13: Disposal considerations

Not available

SECTION 14: Transport information

Not available

SECTION 15: Regulatory information

Not available

SECTION 16: Other information

Not available

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