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Human Exposure to Butylbenzyl Phthalate
A Source-Effect Chain Approach

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Abstract

The human exposure to Butylbenzyl phthalate (BBP) is estimated using a source-effect chain approach. Exposure is both indirect (via the environment) and direct (via consumer products and at the working place of a vinyl manufacturer). Exposure via the environment is estimated with use of the EUSES model and consumer exposure is estimated with the use of the CONSEXPO model. Integrated uptake is calculated by adding inhalatory, dermal and oral uptake and combining environmental and residential exposure. Risk assessment is made on base of integrated uptake and the temporary TDI. This TDI is based on effects of BBP on rodent livers. In addition, BBP may have effects on embryofetal development and the male reproductive system. On base of the temporary TDI, effects from BBP are unlikely to occur.

Summary

Butylbenzyl phthalate (BBP) is a plasticizer and mainly applied in vinyl products. Some adhesives, paintings and lacquers contain BBP and it is found in a minority of cosmetics. The central question in this study is: What is the human exposure to BBP, and can human risks of BBP exposure be estimated with a source-effect chain approach ?

In order to answer the question, indirect human exposure in The Netherlands is estimated with the European Union system for the Evaluation of Substances (EUSES). Emission is estimated on base of emission fractions during production, distribution, processing and private use of the substance and amount of BBP in these life stages. Emission types differ according to spatial scale: on a local scale point emissions are estimated for processing plants of vinyl and paint, and diffuse emissions are used for The Netherlands and the rest of Europe (respectively at a regional and continental scale). Following environmental transport through the spatial scales and degradation, environmental concentrations are predicted. The predicted average concentration of BBP in surface water is $2.9 \cdot 10^{-6}$ mg/l and corresponds to measurements in surface water by RIWA. Comparison of predicted concentrations in food with measurements from Great Britain indicates that regional BBP levels in food underestimate the actual level of BBP in food. On base of the EUSES diet for adults, oral uptake of BBP via food is calculated to be $4.5 \cdot 10^{-4}$ mg/kg·day. BBP intake via infant formulae is $1.5 \cdot 10^{-4}$ mg/kg·day. The averaged BBP concentration in air is $4.5 \cdot 10^{-6}$ mg/m^3, resulting in an estimated inhalatory uptake via the environment of $7.8 \cdot 10^{-7}$ mg/kg·day for adults and $2.2 \cdot 10^{-6}$ mg/kg·day for babies.

Exposure at the working place of a vinyl manufacturer is estimated with the EASE model for worker exposure. The predicted exposure level of BBP in air surpasses measured concentrations in a Swedish vinyl manufacturer tenfold. On base of the Swedish concentrations, average inhalatory uptake is $7.0 \cdot 10^{-3}$ mg/kg·day and worst case uptake $2.0 \cdot 10^{-2}$ mg/kg·day.

Residential exposure is estimated for emission of BBP released by vinyl flooring, wall paper, hair spray, adhesives and paints. Indoor air concentration of BBP from vinyl products is estimated on base of emission rate, area of vinyl products, room size and ventilation rate. Average and worst case inhalatory exposure are estimated with the CONSEXPO model for consumer exposure for a bedroom, kitchen and living room with vinyl flooring. In addition, the bedroom has vinyl wallpaper. Assuming people spend all day in rooms with vinyl products, average (and worst case), an inhalatory exposure of $7.7 \cdot 10^{-5}$ ($1.2 \cdot 10^{-4}$) mg/kg·day for adults and $3.4 \cdot 10^{-4}$ ($5.5 \cdot 10^{-4}$) mg/kg·day for babies is calculated. Dermal and inhalatory BBP exposure as a result of use of hairspray, adhesives and paints containing BBP is also estimated. Estimating the frequency of use and duration of exposure and assuming a person

uses all consumer products, an average uptake of $5.1 \cdot 10^{-3}$ mg/kg·day is calculated (worst case: $6.9 \cdot 10^{-3}$ mg/kg·day).

Integrated uptake is calculated by adding inhalatory, dermal and oral uptake and combining environmental and residential exposure. This results in an average (and worst case) total uptake of $1.1 \cdot 10^{-3}$ ($7.5 \cdot 10^{-3}$) mg/kg·day for adults and $4.9 \cdot 10^{-4}$ ($7.0 \cdot 10^{-4}$) mg/kg·day for babies.

Concern exists that BBP may be responsible for a range of human reproductive problems. At this moment there is no toxicological evidence to conclude whether effects of BBP on the reproductive system are the most sensitive effect of BBP on humans. In this study, risk assessment is made on base of the temporary TDI (0.1 mg/kg·day) and integrated uptake, by calculating Margins of Safety (MOS). All MOS are considerably larger than 1 and effects are unlikely to occur as a result from BBP exposure via the environment and consumer products, or at the working place of a vinyl manufacturer.

Samenvatting

Butylbenzyl ftalaat (BBP) is een weekmaker en wordt veelvuldig toegepast in vinyl produkten. Enkele lijmen, verven en lakken bevatten ook BBP en het is aangetroffen in een klein aantal cosmetica produkten. De probleemstelling van dit onderzoek is: Wat is de humane blootstelling aan BBP en is het humane risico van BBP te schatten met een bron-effekt ketenbenadering ?

Om deze vraag te beantwoorden is de indirekte humane blootstelling in Nederland geschat met behulp van het European System for the Evaluation of Substances (EUSES). Emissie is geschat op basis van emissiefracties tijdens de produktie, distributie, verwerking en privé gebruik van de stof en hoeveelheid BBP in deze levensfases. Emissietypes verschillen per ruimtelijke schaal: op de lokale schaal zijn punt emissies geschat voor de produktie van vinyl en verf. Diffuse emissies zijn berekend voor Nederland en de rest van Europa (respectievelijk op regionale en continentale schaal). Milieuconcentraties zijn voorspeld na afbraak en na transport van BBP door het milieu en de ruimtelijke schalen. De voorspelde gemiddelde concentratie van BBP in oppervlakte water is $2.9 \cdot 10^{-6}$ mg/l en komt overeen met RIWA metingen in het oppervlakte water. Uit vergelijking van voorspelde concentraties in voedsel met metingen uit Groot- Brittanië, blijkt dat de voorspelde regionale BBP-concentratie in voedsel de werkelijke concentratie onderschat. Op basis van het standaard dieet voor volwassenen in EUSES is berekend dat de orale opname van BBP via voedsel $4.5 \cdot 10^{-4}$ mg/kg·dag is. BBP inname via babyvoeding is $1.5 \cdot 10^{-6}$ mg/kg·dag. De gemiddelde BBP concentratie in lucht $4.5 \cdot 10^{-6}$ mg/m^3, waaruit een inhalatoire opname van $7.8 \cdot 10^{-7}$ mg/kg·dag voor volwassenen en $2.2 \cdot 10^{-6}$ mg/kg·dag voor baby's volgt.

Blootstelling op de werkplek van een vinyl producerend bedrijf is geschat met het EASE model voor arbeidsblootstelling. De voorspelde blootstellingsconcentratie aan BBP in de lucht is een tienvoudige overschatting van gemeten concentraties in een zweeds vinyl producerend bedrijf. Op basis van de zweedse metingen is de gemiddelde inhalatoire opname ($7.0 \cdot 10^{-3}$ mg/kg·dag) en de worst case opname ($2.0 \cdot 10^{-2}$ mg/kg·dag) berekend.

Blootstelling in en om huis is geschat voor emissie uit vinyl vloerbedekking en behang, haarlak, lijmen en verven. De binnenlucht concentratie van BBP uit vinyl produkten is geschat op basis van emissiesnelheid, oppervlak van de vinyl produkten, kamergrootte en ventilatiesnelheid. De gemiddelde en worst case inhalatoire blootstelling is geschat met het CONSEXPO model voor consumentenblootstelling, voor een slaapkamer, keuken en woonkamer met vinyl vloerbedekking. De slaapkamer heeft ook vinyl behang. De gemiddelde (en worst case) inhalatoire blootstelling is $7.7 \cdot 10^{-5}$ ($1.2 \cdot 10^{-4}$) mg/kg·dag voor volwassenen en $3.4 \cdot 10^{-4}$ ($5.5 \cdot 10^{-4}$) mg/kg·dag voor baby's, aangenomen dat mensen de hele dag doorbrengen in kamers met vinyl produkten. Dermale en inhalatoire blootstelling door het gebruik van haarlak, lijmen en verven die BBP bevatten, is ook geschat. Op basis van de

frequentie van gebruik en de duur van de blootstelling en de aanname dat alle consumentenprodukten worden gebruikt, is een gemiddelde blootstelling van $5.1 \cdot 10^{-3}$ mg/kg·dag berekend (worst case: $6.9 \cdot 10^{-3}$ mg/kg·dag).

Gecombineerde opname is berekend door inhalatoire, dermale en orale opname bij elkaar op te tellen en blootstelling via het milieu te combineren met blootstelling in en om huis. Hieruit volgt een gemiddelde (en worst case) opname van $1.1 \cdot 10^{-3}$ ($7.5 \cdot 10^{-3}$) mg/kg·dag voor volwassenen en $4.9 \cdot 10^{-4}$ ($7.0 \cdot 10^{-4}$) mg/kg·dag voor baby's.

Er is gesuggereerd dat BBP verantwoordelijk zou zijn voor een reeks vruchtbaarheidsproblemen. Op dit moment is er geen toxicologisch bewijs waaruit geconcludeerd kan worden of effecten van BBP op het reproduktie-systeem het meest gevoelige effect van BBP op mensen is. De risicoschatting is gemaakt op basis van de tijdelijke TDI (0.1 mg/kg·dag) en gecombineerde opname, door Margins of Safety (MOS) te berekenen. Alle MOS zijn aanzienlijk groter dan 1 en het is niet te verwachten dat BBP effecten zal veroorzaken tengevolge van blootstelling via het milieu, consumentenproducten of op de werkplek van een vinyl producerend bedrijf.

Abbreviations

BAF	Bioaccumulation factor
BBP	Butylbenzyl Phthalate
bw	body weight
cAMP	cyclic adenosine monophosphate
DBP	Dibutyl phthalate
DEHP	Bis(2-ethylhexyl) phthalate
DIBP	Diisobutyl phthalate
DIDP	Diisodecyl phthalate
DINP	Diisononyl phthalate
EU	European Union
FSH	Follicle Stimulating Hormone
hr	hour
IGB	(Dutch) Inspectorate Health Protection *Inspectie Gezondheidsbescherming*
IMLO	department of RIZA
iter.	iterations
IV	Intravenous
K_{oc}	carbon-normalized partition coefficient
K_{ow}	octanol-water partition coefficient
LH	Luteinizing Hormone
LOAEL	Lowest Observed Adverse Effect Level
MAFF	Ministry of Agriculture, Fisheries and Food
MBeP	Monobenzyl Phthalate
MBuP	Monobutyl Phthalate
MEHP	Mono(2-ethylhexyl) phthalate
MOS	Margin of Safety
MSDS	Material Safety Data Sheet
NAEL	No Adverse Effect Level
NOAEL	No Observed Adverse Effect Level
PEC	Predicted Environmental Concentration
PTEAM	Particle Total Exposure Assessment Methodology
RACB	Reproductive Assessment by Continuous Breeding
RIZA	(Dutch) Institute for Inland Water Management and Waste Water Treatment *Rijksinstituut voor Integraal Zoetwaterbeheer en Afvalwaterbehandeling*
TDI	Tolerable Daily Intake
TDS	Total Diet Study
TGD	Technical Guidance Document
UK	United Kingdom
VCP	(Dutch) Food Consumption Survey *Voedselconsumptiepeiling*
VOC	Volatile Organic Chemicals
ww	wet weight

1. Introduction

Phthalates are plasticizers which are generally used in the production of flexible plastic products, predominantly polyvinyl chloride (PVC). Phthalates are added to give the material its flexible properties. Over 30 different phthalates are produced world wide on a large scale and the plasticized PVC in which they are applicated is used in a wide range applications such as medical tubing and blood bags, flooring and wall-covering, clothing and toys. A minority of the amount of phthalates is also used in rubber products, paints, printing inks and some cosmetics. (ECPI, 1998). PVC contains up to 60% plasticizer (De Groot et al., 1987). Phthalates consist globally of an aromatic ring with two carbon side chains. As the length of the side chains increases, the water solubility decreases (Peereboom et al., 1991). Plasticizers are not chemically bound to PVC polymer, but rather float around the polymer (Greenpeace, 1997a). Phthalate emissions into the environment can occur in all life stages and because of their hydrophobicity, phthalates may accumulate in the environment (Peereboom et al., 1991).

Phthalates came in publicity because of public concern that phthalates are responsible for a range of human reproductive problems - including reduced sperm counts and infertility (Greenpeace, 1997b; ECPI, 1998). Humans may be exposed to phthalates via several pathways: directly via consumer products containing phthalates or indirectly via the environment by consuming food and breathing air. In order to estimate human risk as a result of phthalate exposure, the source-effect chain (figure 1) can be described.

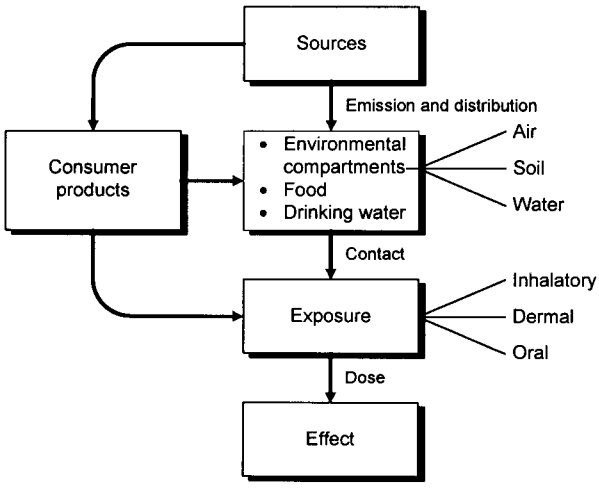

Figure 1 : Source-effect chain (Van Veen et al., in prep)

The route from sources to effect can be represented by the components sources, environmental fate and effect (figure 1). Consumer products have a particular spot in the chain, because they are transported to the site of use where emission occurs, possibly causing exposure and emission into the environment. Environmental concentrations are linked to exposure by contact, and substance levels in food and drinking water are linked to exposure by intake (Van Veen et al., in prep.). Health risks of chemicals are determined by exposure and an effect dose (Sexton et al., 1993).

Despite phthalates are commonly found in the environment, the extent of human exposure has only been studied for diethylhexyl phthalate (WHO, 1992) and dibutylphthalate (VROM et al., in prep.). For butylbenzyl phthalate (BBP), no such study exists.

In order to estimate health risks as a result from human exposure to BBP, the source-effect chain will be described, regarding emission, exposure and possible health effects of BBP. Environmental concentrations of BBP will be estimated on base of data reported in literature and with use of a risk assessment tool (EUSES). Indirect environmental exposure and direct exposure as a result of use of consumer products with BBP, or as a result of working at a site where BBP is processed, will be assessed. Some potential effects of BBP on development and the reproductive system will be discussed and uptake via various routes will be compared with a toxicological limit value in order to estimate human risks. The emphasis of this study lies on the exposure assessment.
The central question this study should answer is formulated as:

What is the human exposure to butylbenzyl phthalate (BBP), and can human risks of BBP be estimated with a source-effect chain approach ?

2. Base characteristics of BBP

Most applied phthalates are enumerated in table 1, outlining the relative use of BBP in comparison to other phthalates (Harris et al., 1997). Phthalates that are often mixed with other plasticizers are: DIDP, DINP, DBP and BBP (De Groot et al., 1987).

Table 1: Some phthalates in order of amount consumed (Harris et al., 1997)

Phthalate name	Abbreviation	European consumption (tonnes/annum)
Bis(2-ethylhexyl) phthalate	DEHP	400,000-500,000
Diisononyl phthalate	DINP	100,000-200,000
Diisodecyl phthalate	DIDP	100,000-200,000
Butylbenzyl phthalate	**BBP**	**20,000-50,000**
Dibutyl phthalate	DBP	20,000-40,000
Diisobutyl phthalate	DIBP	20,000-40,000

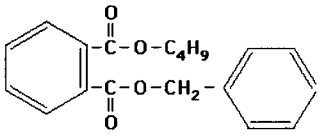

Figure 2: Structure formula of butylbenzyl phthalate

BBP is widely used as a plasticizer for polyvinyl and cellulosic resins, primarily in polyvinyl chloride (PVC). Some industrial synonyms are "Santicizer® 160" and "Palatinol BB". Pure BBP is a clear, colorless and viscous liquid (Solutia, 1997; NTP, 1991). The structure formula is shown in figure 2 and physico chemical properties are summarized in table 2. Water solubility, volatility and the octanol water coefficient will be described in detail.

Table 2: Physico chemical properties of butylbenzyl phthalate

Physical property	Value	Reference
CAS No.	85-68-7	Staples et al., 1997
Formula	$C_{19}H_{20}O_4$	
Molecular Weight [g/mol]	312	
Melting point [°C]	-35	
Boiling point [°C]	377	Peijnenburg et al., 1991
Water solubility [mg/l]	2.7	Staples et al., 1997
Vapor pressure [Pa]	$6.65 \cdot 10^{-4}$	
log K_{ow}	4.59	

Water solubility

Water solubility influences biodegradation and bioaccumulation potential of a chemical, as well as it aquatic toxicity. Water solubility also is a determining factor controlling environmental distribution. Measurement of water solubility for hydrophobic compounds (<1 mg/l) can be confounded by a variety of experiment problems. First, inability to separate colloidal emulsions of undissolved chemical from aqueous phase may cause difficulties in determining water solubility (Yalkowsky et al., 1992). Another source of error of particular concern for phthalate esters is artificial contamination from laboratory plastics. Such problems can lead to experimental artifacts that yield measured values that overestimate true

water solubility. However, measurement of low molecular weight phthalates, like BBP, are generally in good agreement and are believed to be reliable (Staples et al., 1997).

Volatility

Vapor pressure plays a role in the fate of fugitive emissions and other releases of phthalate esters to atmosphere. Vapor pressure is typically determined by direct pressure measurement at elevated temperatures. Such data may be extrapolated to estimate vapor pressure at ambient temperatures. Techniques of direct pressure measurement are limited by sensitivity of the pressure measuring device for poorly volatile substances. Phthalates have very low volatility because of low vapor pressure. Measured values obtained in different studies can vary from $1.21 \cdot 10^{-2}$ Pa (Russom et al., 1991) to $1.16 \cdot 10^{-4}$ Pa (Sears et al., 192).

Octanol-Water Coefficient

The equilibrium distribution of an organic chemical between water and octanol (K_{ow}) predicts the tendency of a chemical partition to water, animal lipids, sediment, and soil organic matter. Results of K_{ow}-measurement can be confounded by traces of water soluble impurities or chemical transformations. In general, phthalates are hydrophobic and K_{ow} values obtained in different studies are fairly consistent for lower weight phthalates, like BBP (Staples et al., 1997).

3. Indirect exposure via environment

Indirect exposure via the environment is assessed on base of reported data in literature and with the EUSES model. Paragraph 3.1 describes the model and paragraph 3.2 discusses the releases of BBP into the environment. Environmental distribution processes are described in paragraph 3.3 and finally environmental concentrations of BBP in water, food and air are discussed.

3.1 EUSES - The model

3.1.1 History and development

In the European Union (EU), Environmental policy started in 1973 with adoption of the first five year European Community Environmental Action. Since then, the principle of prevention and risk reduction have been firmly established in many regulations of the European Commission (EC) and with it the concepts of risk assessment and risk management of substances. Technical Guidance Documents (TGDs) have been developed to support regulations with respect to the risk assessment. It is against this background that the European Union System for the Evaluation of Substances (EUSES) has been developed (Vermeire et al., 1997). In The Netherlands, a risk assessment system was developed for new and existing substances and agricultural and non-agricultural pesticides by integrating existing risk assessment tools (USES 1.0). USES 1.0 was already in line with TGDs for new and existing substances and also appeared to be useful as a risk assessment tool outside The Netherlands. Out of USES, EUSES was developed for quantitative assessment of the risks posed by new and existing substances to man and environment in the European Union. Risk to man pertain to consumers, workers and humans exposed through the environment. EUSES is used in the screening of the assessment. A refined assessment can be made by replacement of default values, estimated parameter values or intermediate results by more accurately estimated values or by measured data (Vermeire et al., 1997).

3.1.2 System dimensions

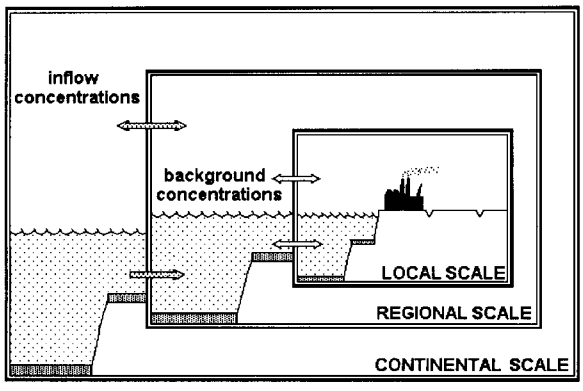

Figure 3: Relationship between continental, regional and local scale exposure assessments (EC, 1996).

For risk assessment within EUSES, a distinction can be made in different spatial scales (figure 3). The *continental scale* is in EUSES defined as the sum of all EU Member States, and serves as background for the regional system. The *regional scale* assesses risks to man and environment due to all releases in a larger region assuming standard environmental characteristics. The regional model calculates steady state concentrations

in environmental compartments, taking into account release of the chemical followed by distribution (Vermeire et al., 1997; EC, 1996). On the *local scale,* substances released from point sources are assessed for a predefined local environment. This is not an actual, but a hypothetical site with predefined environmental characteristics, embedded within the regional scale. The local scale receives the background concentration from the regional scale. The regional scale receives inflowing air and water from the continental scale (EC, 1996). Standard characteristics (like area, amount of surface water and soil composition) of the region are in harmony with environmental characteristics of The Netherlands. In this exposure assessment, the regional scale is regarded as The Netherlands. On the *personal scale* (not shown in figure 3) individual consumers or workers are considered (Vermeire et al., 1997). The exposure scenario is a generic one; exposure from specific behavior of children or other subpopulations is not taken in account.

3.1.3 Structure of assessment

The main structure of EUSES is presented in figure 4. The basic input data required for EUSES are physico-chemical properties as described in Table 2, chapter 2. Releases are estimated by EUSES with use of emission factors and relevant substance amount per use category and life stage. Based on the known properties, uses and functions of a substance, emission factors for various life cycle stages are selected from a database or derived from literature. The distribution module contains models necessary to estimate distribution of a substance in the environment at the appropriate scale. End-points are predicted concentrations in the environmental compartments (PEC). Based on PECs, human exposure levels are calculated in the exposure module. A distinction is made for exposure through the environment and exposure at the workplace. Effects assessment has the goal to derive no effect levels for relevant time scales. In the risk characterization module, results of the exposure assessment are compared with outcomes of the effects assessment (EC, 1996).

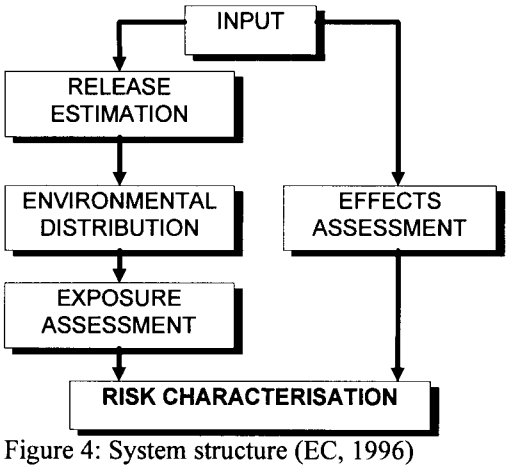

Figure 4: System structure (EC, 1996)

3.2 Release Estimation

3.2.1 Life cycle of substances

The release of plasticizers, including BBP, into the environment may occur during production, distribution, and incorporation into PVC. In addition, because plasticizers in flexible PVC are not chemically bound to the polymer, they may be lost from finished articles during use or after final disposal (Cadogan et al., 1993). These stages form the life cycle of a substance as shown in figure 5. A combination of life stages is characterized by a "use

patterns", defined by industrial use and use category of the substance. EUSES calculates environmental emission by multiplying the amount of BBP in every life stage and use pattern with release fractions. Therefore, only use patterns with a considerable amount of BBP are relevant for emission estimation. The majority of BBP is applicated in vinyl products and paint related products like lacquer, sealant and adhesives. This will be discussed in paragraph 3.2.3. These two types of products will be regarded in EUSES.

In Technical Guidance Documents, the life stage between production and processing is referred to as "formulation". In this stage, chemicals are combined in a process of blending and mixing to obtain a product or a preparation. Blending of phthalates with PVC resin can be interpreted as "formulation", however, this process is always combined with immediate application and shaping of the produced (soft) PVC. Therefore, blending of phthalates and PVC and application are regarded as one life cycle step; processing. The "processing" stage of paint conform TGDs is regarded as industrial use of paint (Van der Poel, 1997). In this risk assessment, processing of paint is the stage in which paint and paint related products, are produced. The opportunity to estimate emissions during "formulation" is used to estimate emission during distribution of pure BBP.

3.2.2 Life stage and emission

Emission fractions vary throughout life stages and are calculated on base of figures given in reports. If specific data for BBP are lacking, emission factors are derived from data of phthalates in general. In the absence of such data, default emission fractions within EUSES are not overruled. Available data are described below and release fractions are summed up in table 3. Within EUSES, only one emission fraction for releases into air, waste water, surface water and industrial soil can be distinguished per life stage and use.

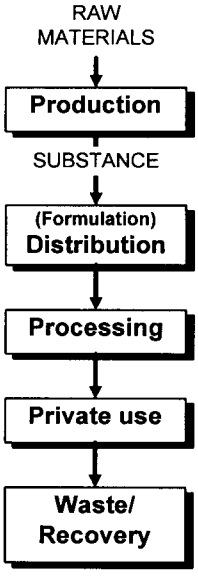

Figure 5: Life cycle of substances (EC, 1996)

Production

Production is the stage in which the substance is manufactured (EC, 1996). Phthalates are produced in closed systems by esterification of phthalic anhydride with alcohol (Cadogan et al., 1993). Emissions during production are negligible because of the low vapor pressure and low solubility of phthalates. Production takes place at temperatures ranging from 150-200°C and often at reduced pressure. In addition these processes are controlled (Peijnenburg et al., 1991). Cadogan et al. (1993) estimates total emission of plasticizers during production to be 0.025 %, of which 90% is to the water compartment. Releases during production of DBP are estimated to be 0.001% to air and 0.3% to water (VROM et al., in prep.). Emission during production of BBP is assumed to be the same as for production of DBP.

Emissions during production of BBP in EUSES are calculated using the total amount of BBP produced, regardless of the applications (EC, 1996). Therefore, emissions during production are considered for the major application only.

Emission during distribution

Most phthalates consumed in western Europe are distributed via road tanks. Environmental emission may result from tank cleaning. Cleaning is a relatively small operation because plasticizers do not adhere strongly to tanker walls due to their low viscosities. Wash water of modern washing facilities is passed through separators to remove residual plasticizer and is incinerated. One tank load roughly contains 20 tonnes phthalates and it is estimated that, as a result of cleaning and spillages, every load looses a maximum of 1 kg into the environment (Cadogan et al., 1993).

Within Europe, approximately 13% of all consumed plasticizers are transported by ship. Product losses because of residues on tank walls, in lines and pumps, are estimated to be close to 0.3%. Residues are removed by cleaning with water and at most 10% is emitted to the environment (Cadogan et al., 1993). Since polluted cleaning water of ships is treated in the harbor (VROM, 1991) emissions are likely to be into waste water.

The emission factor of BBP to waste water is calculated as a weighed average of emissions as a result road transport ($^{1}/_{20,000}$) and transport by ship (0.003 x 0.1), assuming that conveyance by ship and road are the only means of transport.

Processing

The term "processing" is used for a sequence of steps from blending of raw materials (PVC resin, plasticizers and other additives) to final shaping of PVC products. During the processing stage of calendered vinyl products, plasticizers are exposed for several minutes to temperatures between 150 and 160°C (Cadogan et al., 1993). Emission to air during processing of vinyl products is low because of use of filters. The emission of BBP to air was measured during vinyl wall paper production (Van de Wiel et al., 1987). These measurements indicate an emission factor to air of 0.014% of the amount of processed BBP. Emission into environment during production of calendered flooring is 0.03% of plasticizer consumption (Cadogan et al., 1993). Emission factor of BBP to air for vinyl products in this life stage, is the average of the emission factor of Van de Wiel et al. (1987) and Cadogan et al., (1993). Emission to (waste) water is negligible (Van de Poel et al., 1989).

During production of paint, total loss of plasticizer is estimated, by a manufacturer of paint, lacquers and glue, to be 2% of which 20% is released to water (Peijnenburg et al., 1991). To which compartment the bulk of plasticizer losses are released is unknown. Therefore, the releases of BBP in this life stage are based on the default emission table within EUSES for production of paints (Van der Poel, 1997).

Private use

This stage considers the use and application of substances in formulations, such as vinyl products and paint, on scale of households and consumers (EC, 1996).

Little data are available for indoor losses of plasticizers. In Cadogan et al. (1993) an average emission rate for plasticizers in PVC products of $2.4 \cdot 10^{-4}$ $\mu g \cdot sec^{-1} \cdot m^{-2}$ is given. Our study (paragraph 5.2) shows that this rate is probably too high; use of the Cadogan emission rate leads to over estimation of emission to air of vinyl products. The emission factor for emission to air during private use of vinyl flooring is calculated on base of the emission rate of Cadogan et al., the total area of vinyl floor covering in The Netherlands and the amount of BBP in flooring. In The Netherlands, $7.5 \cdot 10^{6}$ m^2 vinyl floor covering is sold every year (De Groot et al., 1992). The average use duration is eight years (Potting et al., 1993) resulting in total area of vinyl flooring of $60 \cdot 10^{6}$ m^2 (i.e. life duration times sale per year). Emission is calculated by multiplying this flooring area with the emission rate, revealing an emission factor to air of $3.6 \cdot 10^{-4}$, when emission (0.45 tonnes/year) is divided by the amount of BBP in vinyl flooring, i.e. 1275 tonnes/year (figure 6).

Plasticizer may leach from flooring during cleaning with soapy water. The emission factor for loss to waste water is estimated to be 0.005%, based on specific research in Denmark (Tukker et al., 1996). The emission factor of vinyl wall covering during private use is assumed to be equal to that of vinyl flooring emission.

For paint products, data were lacking to make such estimation. Therefore, default release fractions during private use of paint are used (Van der Poel et al., 1997).

Waste

The last stage of the life cycle is when chemicals end up in waste water and waste materials. Waste water is increasingly treated in sewage treatment plants. In most cases, waste materials are incinerated, while no combustion waste streams are landfilled at special sites (Van der Poel., 1997).

Emission of BBP caused by combustion of waste are not expected to be high. Modern incineration techniques result in complete combustion of all phthalates to carbon dioxide and water (Peijnenburg et al., 1991). Incinerations in The Netherlands have combustion gas-cleaning-installations (Bremmer et al., 1993). Therefore, we expect zero emission of BBP to air.

BBP containing products can be added to a landfill. After dumping in landfills, plasticizer may slowly leach from the product (Cadogan et al., 1993). Since measurements are taken to reduce emission from landfills in The Netherlands, emission of pollution from landfills into water is generally low (VROM, 1995). Therefore, emission of BBP to the environment is assumed to be negligible.

Since emission of BBP in the last life stage is assumed to be zero, this life stage does not add to environmental concentrations and is excluded from assessment.

Table 3: Emission fractions

Fraction of tonnage emitted into:	Life stage					
	Production	**Distribution**	**Processing**		**Private Use**	
			Vinyl	Paint	Vinyl	Paint
Air	$1.0 \cdot 10^{-5}$	0	$2.2 \cdot 10^{-4}$	$2.5 \cdot 10^{-3}$	$3.6 \cdot 10^{-4}$	0
Waste water	$3.0 \cdot 10^{-3}$	$8.25 \cdot 10^{-5}$	0	0.02	$5.0 \cdot 10^{-5}$	$5.0 \cdot 10^{-3}$
Surface water	0	0	0	0	0	0
Industrial soil	0	0	0	0	0	$5.0 \cdot 10^{-3}$
Reference	VROM et al., in prep.	Cadogan et al., 1993 + assumptions	Cadogan et al., 1993 + Van de Poel et al., 1989 + Van de Wiel et al., 1987 +assumptions	Van der Poel, 1997	Cadogan et al., 1993 +Tukker et al., 1996 + CONSEXPO output + assumptions	Van der Poel, 1997

3.2.3 Amount of BBP

Since emissions in all life stages can contribute to environmental presence of BBP, it must be clear how much BBP is present in each relevant life stage.

Europe has only three producers of BBP and it is not produced in The Netherlands (Van der Poel et al., 1988). Pure BBP is imported (1000-10000 tonnes/year). Most imported BBP (91%) is processed in vinyl products like flooring and wall covering, and some BBP ends up in adhesives, sealants and paints. Destination of a minority of imported BBP is unknown since it is (mainly) used for trade. Most of the applied BBP is exported in vinyl products (Van der Poel et al., 1988).

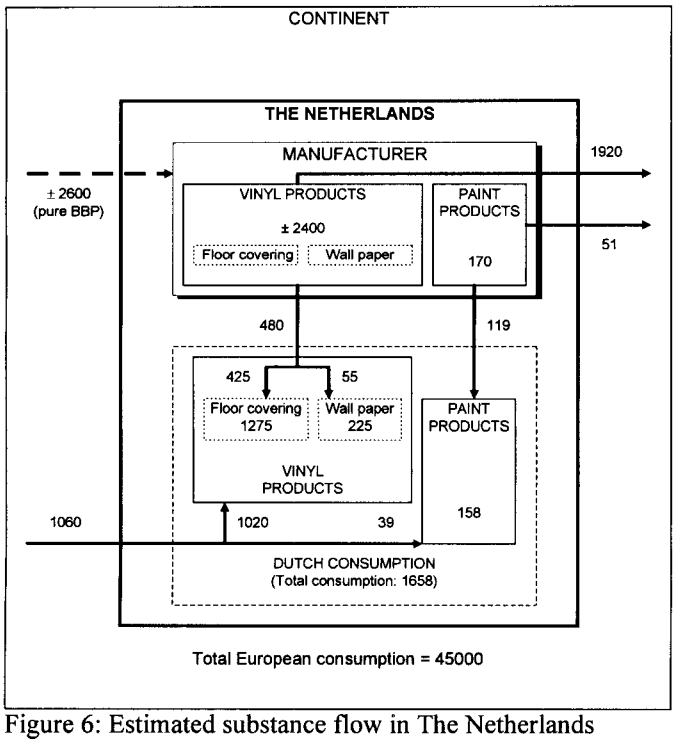

Figure 6: Estimated substance flow in The Netherlands (BBP in tonnes/year)

Using estimations and assumptions about Dutch consumption and import of vinyl flooring and vinyl wallpaper and the amount of BBP in these products, the amount of BBP in every relevant life stage for vinyl products can be calculated. Relating the amount of BBP in paint-related products to Dutch production, consumption and export of paint, amount of BBP in these types of products are estimated (appendix I). Results of these calculations are summarized in figure 6.

3.2.4 Relevant amount per scale

Continental and regional

Not every life stage of consumed products, is relevant for The Netherlands. For instance; BBP is not produced in The Netherlands and therefore emissions during this life stage take place outside the region. With import and export of products containing BBP, emissions during private use and waste treatment move with the products (figure 7).

Based on relevant life stages, three "use patterns" for each product are selected. First use pattern is for exported products, second use pattern for products produced and consumed within the same scale, and the last use pattern is for imported products. The amount of BBP in every use pattern at continental or regional scale (tables 4a, 4b) is derived from figure 7 and summarized in table 3. For example, the amount of BBP in use pattern 1 for vinyl products is at regional scale 1920 tonnes and at continental scale 1020 tonnes.

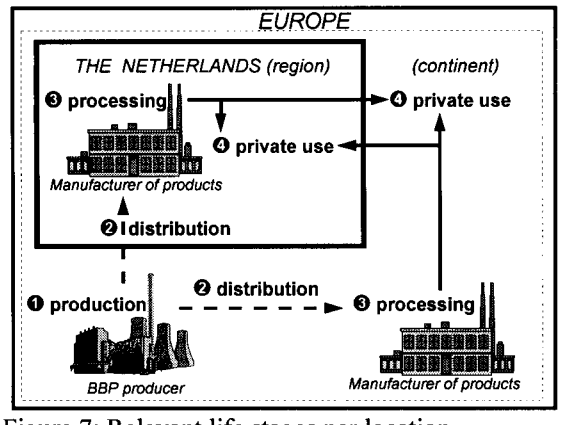

Figure 7: Relevant life stages per location

Local

In general, emissions of BBP in The Netherlands are diffuse, and the most suitable scale to describe these emissions, is the regional scale. However, local emissions can occur near paint factories or vinyl processing plants. In EUSES, size of the main local source is determined by a fraction of the regional tonnage of a use pattern (tables 4a, 4b).

There are about 90 paint and lacquer manufacturers in The Netherlands (Eijssen, 1992). We assume that one of the bigger companies produces 20% of Dutch manufactured "BBP-paint". Accordingly a local assessment is made for a fictive paint factory, producing 20% of the amount of Dutch paint, sealant and adhesive. The fraction of the local source of emissions during formulation of paint, is calculated as fraction of the regional amount in use pattern 5: $^{0.20 \times 170}/_{119} \approx 0.286$.

There are 2 manufacturers of vinyl floor covering in The Netherlands, of which one produces 90% of all produced flooring (Potting et al., 1993). A local assessment is made for the emission of BBP during production of vinyl, with the local source being the biggest vinyl flooring manufacturer of The Netherlands. Since the amount of processed BBP in vinyl (0.90 x ±2400) is comparable to the amount of BBP in use pattern 1, the fraction of the main local source of BBP emission during processing is calculated to be 1(figure 6).

Table 4a: EUSES Use Patterns for Vinyl products

Use Pattern[1]		Life stage	Continent [tonnes/year]	Region [tonnes/year]	Fraction of local source	Total EU[2] [tonnes/year]	
1	(Export)	distribution + processing	1020	1920	1[3] (processing)	2940	(0.0653)[4]
2	("produced +consumed")	(production) + distribution + processing + private use	37280 (39200-1920)[2]	480	0	37760	(0.8391)[4]
3	(Import)	private use	1920	1020	0	2940	(0.0653)[4]

(1) Combination of life stages with a certain Use category (i.e. "softeners" in case of BBP) and Industry category, (i.e. for vinyl products "Polymers Industry"), leads to Use Patterns
(2) Total tonnage BBP (in vinyl products) in EU is 40700 tonnes/year,
Continental tonnage of BBP in vinyl: 39200 tonnes/year
(3) Amount of BBP in all exported vinyl products is comparable to the amount of BBP in vinyl flooring produced by the biggest manufacturer in The Netherlands.
(4) Fraction of tonnage for application

Table 4b: EUSES Use Patterns for Paint related products

Use Pattern[1]		Life stage	Continent [tonnes/year]	Region [tonnes/year]	Fraction of local source	Total EU[2] [tonnes/year]	
4	(Export)	distribution + processing	39	51	0	90	(0.002)[4]
5	("produced +consumed")	distribution + processing + private use	4080 (4130-51)[2]	119	0.286[3] (processing)	4200	(0.0933)[4]
6	(Import)	private use	51	39	0	90	(0.002)[4]

(1) Combination of life stages with a certain Use category (i.e. "softeners" in case of BBP) and Industry category, (i.e. for paint related products "Paints, lacquers and varnishes Industry), leads to Use Patterns
(2) Total tonnage BBP (in paint related products) in EU is 4300 tonnes/year,
Continental tonnage of BBP in paint related products: 4130 tonnes/year
(3) Fraction of the main local source (paint manufacturer) is calculated for "Use pattern 5",
i.e. (0.20 x 170 tonnes) / 119 (tonnage in region) = 0.286
(4) Fraction of tonnage for application

3.3 Environmental distribution

Environmental concentrations of chemicals are mediated by transport and transformation processes (3.3.1). EUSES models the fate of chemicals at different scales as described in paragraph 3.3.2. The fate of a chemical at regional and continental scale differs from the fate at local scales in the sense that more time is available for transport and transformation processes. Outcomes of predicted environmental concentrations are compared with measured concentrations in paragraph 3.4.

3.3.1 Transport and transformation

Transport

Distribution of a substance is described by transport. Measured data on this process for the various compartments are not available. However, environmental fate can be calculated on base of partition coefficients. These in turn, can be extrapolated from substance properties (EC, 1996). In order to overrule default partition coefficients within EUSES, partition coefficients of BBP, like "Henry Laws constant" and water-solid partitioning are derived from literature. Values of overruled parameters are summarized in table 5.

Atmospheric transport of phthalates, including BBP, on particulate matter and subsequent "wash out" in rain, is a significant environmental transport route (Cadogan et al., 1993). Sorption of phthalate esters to soil, sediment or suspended solids, is partially governed by hydrophobicity of a chemical. Because of their lipophilicity, phthalates partition onto organic-rich particulate matter in water. This particulate matter settles to sediment which contains approximately three orders of magnitude higher levels of phthalate than the overlying water. The lipophilic nature of phthalates implies that it is unlikely that phthalates will be mobile in organic rich soil (Cadogan et al., 1993).

Table 5: Parameters determining environmental distribution

Parameter	Value	Reference
Henry's Constant [$Pa \cdot m^3 \cdot mol^{-1}$]	$7.71 \cdot 10^{-2}$	Staples et al., 1997
K_{oc} [L/kg] (soil/sediment)	$17 \cdot 10^3$ $9 \cdot 10^3$	Russel et al., 1986 Gledhill et al., 1980
K_{oc} [L/kg] (suspended solids)	$1 \cdot 10^5$	Furtmann, 1993
Washout Ratio [W]	$3.1 \cdot 10^4$	Staples et al., 1997

Transformation

Changes of concentration and chemical form of the substance with time, i.e. transformation, includes both biotic and abiotic processes. Since measured data on environmental degradation processes are not usually available, they must be extrapolated from standard laboratory tests (EC, 1996). The degradation rate is expressed as half-life of BBP (table 6). Half-lives are derived from reported laboratory test results. For studies in which 100% degradation is reported, half-lives are estimated by dividing the test duration by three (Staples at al., 1997). If degradation was about 50%, half-live was estimated to be the test duration.

In general, risk assessment focuses on the parent compound (EC, 1996), and distribution and environmental risk assessment of metabolites is not taken in account.

Abiotic Degradation

Phthalate esters, including BBP, are susceptible to hydrolysis, however at slow rates. The products of hydrolyses are an acid and an alcohol. Hydrolysis is unlikely to be an important fate process for phthalates under typical environmental conditions (Staples et al., 1997). Gledhill et al. (1980) estimated the hydrolysis half-life to be > 100 days for BBP.

Aqueous photolysis occurs through absorption of UV light from sunlight in the region of 290-400 nm. However photo-oxidation of phthalates in surface water does not appear to be an important transformation process (Staples et al., 1997). Few studies on phthalate photolysis are available and aqueous photolysis half-time was unanimous estimated to be >100 days (Gledhill et al., 1980; Wolfe et al., 1980).

In contrast to the minor role of photo-degradation in natural waters, these reactions appear to be much more important in the atmospheric fate of phthalates. Reaction with hydroxyl radicals is generally the most important photo-degradation process for organic chemical pollutants in the atmosphere (Staples et al., 1997). Half-lives for BBP due to atmospheric photo-oxidation is estimated to be between 0.5 and 5 days (Atkinson 1988).

Biodegradation

Biodegradation is a critical process affecting environmental fate of phthalate esters. Several generalizations can be made for biodegradation of phthalates. Research suggests that the metabolic pathway of phthalates for microbial mechanisms begins with ester hydrolysis under both anaerobic and aerobic circumstances. Phthalate esters may be used by aerobic and anaerobic microbes as a source of carbon and energy. The extent of biodegradation occurring over biodegradation tests suggest that phthalate esters are not expected to be highly persistent in most environments. Primary degradation in water, sediment and soil compartments are expected to be controlled by biodegradation rather than abiotic loss mechanisms. Longer half-lives are likely under anaerobic conditions and in cold, nutrient poor environments (Staples et al., 1997).

Biodegradation half-lives are estimated for surface water, sediment and sewage treatment plants (table 6).

Table 6: Environmental degradation half-lives

Degradation Process		Estimated half-life [days]	Estimation based on values reported in:
Abiotic degradation	Aqueous Hydrolysis	**150**	Gledhill et al., 1980
	Aqueous Photolysis	**150**	Gledhill et al., 1980
	Atmospheric Photo-oxidation	**3.0**	Atkinson, 1988
Biodegradation	Surface water	**2.3**	Saeger et al., 1973; Saeger et al., 1976; Ritsema et al., 1989; Furtmann, 1993 (appendix II, table IIa)
	Aerated sediment	**2.3**	Gledhill, 1980; Adams et al., 1989 (appendix II. table IIb)
	Sewage Treatment Plant	**2**	Saeger et al., 1976; Patterson et al., 1981; Tabak et al., 1981; Furtmann, 1993 (appendix II, table IIc)
	Soil	**23**	Staples et al., 1997

3.3.2 Distribution in EUSES

Local distribution

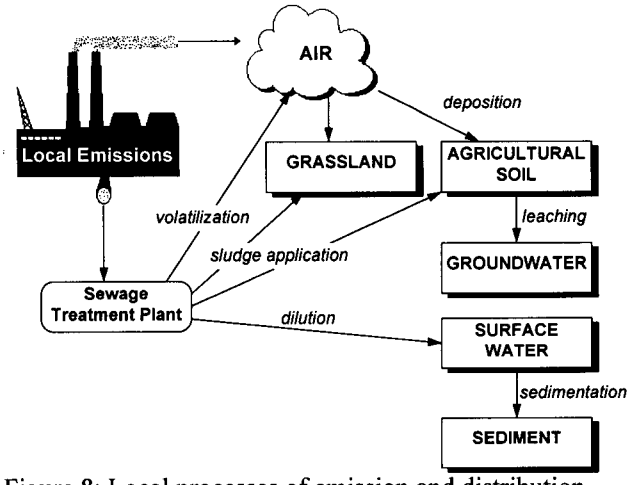

Figure 8: Local processes of emission and distribution (EC, 1996)

Local processes of emission and distribution are schematically represented in figure 8. Concentrations at local spatial scale are almost entirely controlled by mixing, i.e. dilution in background concentrations. Models predicting local concentrations therefore disregard other removal processes. Dedicated modeling approaches are used to calculate concentrations in air, surface water and soil at the local scale. EUSES uses OPS as described by Van Jaarsveld (1990) as air distribution model (EC, 1996). Local air levels are calculated as an average concentration 100 meters from the source. Average deposition (wet and dry) is calculated for a circle around the source with a radius of 1000m. Deposition is used as input for soil. In EUSES, it is assumed that waste water will pass through a sewage treatment plant before being discharged into the environment. Concentration in surface water is calculated after complete mixing of the effluent outfall, using a standard dilution factor and accounting for adsorption to suspended matter. Concentration in soil is calculated for agricultural area, dressed with sludge from a sewage treatment plant and receiving continuos airborne deposition from a nearby point source. The concentration in groundwater is calculated below this agricultural area, using concentration in the pore water of agricultural soil as indicator (EC, 1996).

Regional distribution

At longer distances from point sources, i.e. when mixing has progressed, or when emissions are diffuse, inter-media transport and degradation become more important. A multimedia model, 'Simple Box', models the fate of chemicals on different spatial scales using steady state conditions. It takes into account that emissions at the regional scale increase concentrations at larger spatial scales and that continental scales contribute to increased concentrations at the regional scale (EC, 1996).

Processes on regional scale are schematically represented in figure 9. The *air compartment* is considered to be 'open' in the sense that air flows to and from larger spatial scales. These airflows, import and export chemicals. The *water compartment* contains chemical in dissolved state and associated with particulate matter, where sediment particles act as carriers of chemicals. The water compartments of regional and continental scales are modeled as 'open'. Residence times of water in the various water systems (i.e. sewage treatment plant,

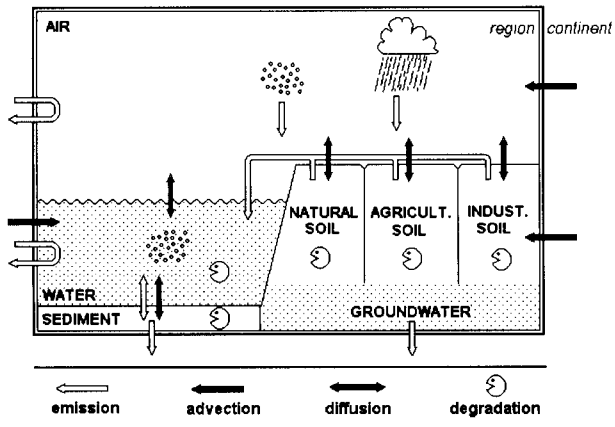

Figure 9: Schematic representation of the model for calculating regional PEC (EC, 1996)

surface water, rainfall etc.) are determined by volume and flow through the system. The *sediment compartment* consists of a solid phase and a pore-water phase. Only the top few centimeters of sediment with continuously refreshment by new deposited material, are modeled. There are three soil compartments in the model, reflecting typical differences in characteristics (mixing depth, porosity, etc.) and use. *Soil compartments* are: 'natural' soil receiving input from atmospheric deposition, 'agricultural' soil, which receives sludge from sewage treatment plants in addition to atmospheric deposition and 'industrial' soil, which receives direct emissions. EUSES accounts for direct diffuse emissions to air, water and industrial soil, and indirect emissions with effluent and sludge from sewage treatment plants to water and agricultural soil (EC, 1996).

Indirect exposure of humans via the environment may occur by consumption of food, drinking of water, inhalation of air and ingestion of soil. Exposure via soil ingestion and dermal contact is not addressed because these represent significant exposure routes for specific situations of soil pollution only, and are therefore not taken in account. Assessment of indirect exposure via the environment starts with assessing the concentration in intake media, following assessment of intake rates of each medium (using a standard consumption pattern and combining these two assessments). EUSES contains simple methods for prediction of indirect exposure and serves primarily for screening purposes. The concentration in food is estimated from concentration in water, soil and air and bioconcentration or bioaccumulation behavior (EC, 1996).

3.4 Environmental concentrations

This paragraph discusses predicted concentrations in relevant media for human exposure. The steady state concentrations computed by the EUSES model should be interpreted as spatially and temporally averaged concentrations of the chemical in the environment, and should be regarded as an approximation (Cowan et al., 1995). Predicted environmental levels of BBP are compared with BBP levels measured in surface water and food in order to verify whether predicted concentrations are realistic. For other environmental compartments, no relevant measured data are available.

3.4.1 BBP in water

BBP levels in surface water, waste water and drinking water are estimated with EUSES and shown in table 7.

In the past, BBP is detected in water of Meuse and Rhine, in contradiction to the Westerscheldt and Yssel (Peijnenburg et al., 1991). Nowadays RIZA measures BBP regularly in surface water and waste water in The Netherlands. Data were obtained by RIZA, IMLO and derived from a data set with measured samples during a period of the end of 1995 till the end of 1997. BBP is detected in 8 out of 107 surface water samples (RIZA, 1998). More detailed information of measured concentrations can be find on appendix III.

Since BBP is only detected in rivers Meuse and Rhine at the borders of The Netherlands, measured surface water concentrations can be compared with predicted surface water in the region and continent as well, to check if predicted values match with reality. Predicted concentrations are spatially and temporally averaged and are compared with the average of measurements. Calculating the average concentration of BBP in surface water depends very much on the assumption made for samples below the detection limit of BBP. The detection limit could not be traced (Kienhuis, 1998) and is assumed to be the same as the reported detection limit for BBP in surface water in Peijnenburg et al. (1991): 0.01µg/l. Assuming concentrations of samples below the detection limit are between $^1/_{100}$ - $^1/_2$ of the assumed detection limit, average of "measured" BBP concentrations is between $2.7 \cdot 10^{-6}$ mg/l and $7.1 \cdot 10^{-6}$ mg/l. Comparing measured concentrations with predicted concentrations in surface water (table 7), can be concluded that these figures are not in contradiction; i.e. the predicted concentration of BBP in surface water has the same order of magnitude than the average of "measured" BBP concentrations.

RIZA (1998) also measures BBP in waste water, defined as water in the neighborhood of local pollution areas and drains, with possibility of high concentrations. BBP levels varied from 0.06 mg/l up to 42 mg/l. Predicted concentrations in untreated waste water (EUSES) cannot compared directly with measured concentrations in waste water since sampling locations are unknown.

Table 7: "Measured" concentrations and predicted concentrations of BBP in water

Water type	Average of "measured" concentrations [mg/l]	Predicted concentration (EUSES) [mg/l]	
Surface water	$2.7 \cdot 10^{-6}$ - $7.1 \cdot 10^{-6}$	Continental	$1.7 \cdot 10^{-6}$
		Regional	$2.9 \cdot 10^{-6}$
Waste water	0.06 - 42	Untreated waste water (vinyl)	0
		Untreated waste water (paint)	1.13
Drinking water	?	Regional	$5.8 \cdot 10^{-7}$

3.4.2 BBP in food

Since BBP and other phthalates are not measured in Dutch food, British measurements are discussed. Predicted levels of BBP in food (EUSES) are compared to these data. Uncertainties in measured concentrations are discussed in order to estimate levels of BBP in Dutch food.

Predicted levels of BBP in food

Plant products are consumed by humans and cattle. Contamination of plants may therefore have a significant influence on human exposure. In EUSES, a distinction is made between tuberous plants and leaf crops. The exposure from plants includes uptake from soil as well as uptake from air. Lipophilic substances are known to accumulate in meat and can be subsequently transferred to milk. Cattle can be exposed to substances in grass, via adhering soil, drinking water and through inhalation of air. Bioaccumulation factors (BAF) can be defined as steady state concentration in meat and milk, divided by the daily intake of a chemical. Travis and Arms (1988) calculated BAFs for meat and milk of cows by log-linear regression on experimental data for a number of chemicals. However, uncertainties in the estimated BAFs are considerable (EC, 1996). Table 8 shows regional and local predicted BBP levels in food in The Netherlands.

Table 8: Predicted BBP levels in food (mg/kg wet weight)

Food group	Regional	Local (Vinyl manufacturer)	Local (Paint manufacturer)
fish	$3.2 \cdot 10^{-4}$	$3.2 \cdot 10^{-4}$	(5.4)
leaf crops	$4.1 \cdot 10^{-4}$	1.3	0.27
root crops	$9.5 \cdot 10^{-5}$	$5.4 \cdot 10^{-4}$	0.93
meat	$2.7 \cdot 10^{-5}$	0.087	0.018
milk	$8.5 \cdot 10^{-6}$	0.028	$5.7 \cdot 10^{-3}$

Measured phthalates in food and infant formulae

The British Food Safety Directorate of the Ministry of Agriculture, Fisheries and Food (MAFF), has carried out a survey of the levels of total and individual phthalates in samples of food of the 1993 Total diet study (TDS). Total diet studies are carried out continuously and food samples are purchased from different locations throughout UK (MAFF, 1993). Total phthalates were determined by converting all phthalates into dimethyl phthalate, and measured in retail food samples of Norwich (pilot study) and in TDS 1993 samples. Results indicated that concentrations of phthalates in food of different locations may vary considerably; dietary intakes of phthalates on base of retail samples of Norwich (one location) are considerably below intake estimates on base of concentrations found in the TDS samples (MAFF, 1996a).

Total phthalates measurement in TDS 1993 samples are the mean of duplicate determinations in 10 samples in each food group (except for milk; 2 samples were analyzed). Average of

differences between duplicate determinations, expressed as a percentage of the corresponding mean, was below 10 percent for most commodities but was higher (around 35 percent) for milk and carcass meat (MAFF, 1996a). The detection limit for total phthalates in milk was 0.34 mg/kg for analysis of TDS 1993 samples. Given the 35 percent variance in milk samples, and average concentration being 0.5 mg/kg, concentration of phthalates in one of the two samples was about the detection limit. This may introduce uncertainty whether the analysis method was sensitive enough.

MAFF also measured phthalates in infant formulae. The average intake of total phthalates via infant formulae is 0.13 mg/kg·day for new born babies, falling to 0.10 mg/kg·day at six months (MAFF, 1996b). The Dutch inspectorate for health protection (IGB) has investigated phthalate concentrations in infant formula available in The Netherlands. For soya dominated, and milk protein dominated formulae, phthalate intake for babies till 4 months appeared to be independent of body weight and was equal to 0.0075 mg/kg·day (Heisterkamp et al., 1997). Comparing this intake with the one calculated by the MAFF (1996b), is concluded that Dutch intake of BBP by babies is lower (average about 15 times).

Measured BBP in food and infant formulae

BBP concentration in food was measured in two TDS 1993 samples of carcass meat, poultry, eggs and milk. Concentrations of BBP varied from 0.002 mg/kg in milk up to 0.09 mg/kg in carcass meat and eggs. Considering the total phthalates variance measured in the TDS samples, it is doubtful whether two samples are a representative mean of BBP concentration in UK food.

MAFF also measured BBP in infant formulae. BBP was measured in 59 individual samples of 15 different brands of infant formulae, purchased from retail outlets in five towns across United Kingdom. Average concentration of BBP in infant formulae is 0.10 mg BBP/kg. Measurements are fairly consistent: the highest BBP concentration measured, varies about a factor 6 with the lowest BBP level in infant formulae. Following comparison of concentrations of BBP found in infant formulae (MAFF, 1996b) and food (MAFF, 1996a), is concluded that BBP concentrations are in the same order of magnitude.

In The Netherlands, BBP was estimated to be 2% of the total amount of phthalates, resulting in a BBP intake of 0.15 µg/kg·day on base of Dutch phthalate measurement in infant formulae (Heisterkamp et al., 1997).

Estimation of the Dutch food situation

Use of phthalates in plastic food packaging is limited. Phthalates are no longer used in cling film and most other food contact plastic materials. Research results indicate that phthalates are present in food from general contamination rather than specific sources such as food

packaging (MAFF, 1996a). Therefore, measured BBP concentrations in food are compared with outcomes of EUSES (table 9).

Table 9: Comparing predicted BBP in food (EUSES) with measured data [mg/kg wet weight]

	Regional	Local (Vinyl manufacturer)	Local (Paint manufacturer)	MAFF, 1996a
meat [mg/kg ww]	$2.8 \cdot 10^{-5}$	0.087	0.0182	0.09
milk [mg/kg ww]	$8.5 \cdot 10^{-6}$	0.0275	$5.74 \cdot 10^{-3}$	$2.0 \cdot 10^{-3}$

If measured values of BBP in food are representative for the average concentration of BBP in food, measured values should be in coherence with predicted concentrations of BBP in food in the region (assuming United Kingdom and The Netherlands do not differ that much). However, predicted concentrations of BBP in (regional) meat and milk are considerably lower (about 1000 times) than measured by the MAFF (1996a). BBP levels in meat and milk in the close surrounding of a local source, as predicted by EUSES, are in the same order of magnitude as determined by the MAFF (table 9). These results suggest that concentrations of BBP in meat and milk, measured by MAFF, are a result of samples taken in the neighborhood of a local source (vinyl flooring or paint manufacturer). However, design of Total Diet Studies makes such coincidence doubtful. In addition, comparison of measured concentrations found in British infant formulae (which are in the same order of magnitude as phthalate concentrations in food), can be seen that Dutch samples of infant formulae contain only about 15 times less phthalate, not about 1000 times. Since phthalate levels in infant formulae are not expected to be determined by local pollution, difference between Dutch and British infant formulae cannot be explained by contamination by a local source.

Predicted BBP levels in food are outcomes of a long chain of estimations and calculations and uncertainty at any step of the assessment may influence BBP food concentrations. According to Jager (1998) model input, as described in paragraphs 3.2 and 3.3, does not contain exceptional parameter values and input meets requirements of the EUSES model. Since regional concentrations and measured concentrations are not at all in coherence, it is doubtful if EUSES is an appropriate tool for regional estimation of dietary exposure.

Measured concentrations are uncertain because of lack of knowledge of respresentativity for average concentrations. The pilot study reveals other samples but TDS 1993 sample can contain less phthalate. In addition there is uncertainty whether Dutch food contains comparable amounts of BBP in United Kingdom food. Comparing concentrations measured in infant formulae in both countries, Dutch samples seem to contain considerably less phthalates (about 15 times). From these observations, the assumption is derived that Dutch food contains less phthalate than food in the United Kingdom. Therefore, average concentration of BBP in food in The Netherlands is assumed to be between the predicted regional concentration and the highest local BBP concentration. BBP levels in Dutch food are

calculated as geometrical average of predicted local and regional concentrations (table 8). An exception is made for fish; in contradiction to the other food groups, BBP concentration in fish is not directly influenced by air concentration and the predicted regional level assumed to be representative for Dutch fish. Table 10 shows estimated BBP level in Dutch food. Calculated average for meat is about 60 times lower than measured by the MAFF (1996a) and for milk about 10 times. Regarding all uncertainties, calculated "average" concentration of BBP in these food groups is assumed to be reasonable for the Dutch situation.

Table 10: Estimated concentrations of BBP in Dutch food [mg/kg wet weight]

Food group	BBP level
Fish	$3.2 \cdot 10^{-4}$
Leaf crops	$2.3 \cdot 10^{-2}$
Root crops	$9.4 \cdot 10^{-3}$
Meat	$1.5 \cdot 10^{-3}$
Milk	$2.2 \cdot 10^{-4}$

3.4.3 BBP in air

EUSES calculates regional and local air concentrations as a year average. Calculated concentrations in meat and milk heavily depend on air concentrations, since cattle graze grass, that is contaminated by deposition from air (EC, 1996). Since calculated regional food concentrations appear to be underestimated, the same counts for air concentrations. The geometrical average air concentration may be a better estimation for Dutch air concentrations (calculating such air average leads directly to geometrical averaged food concentrations). Average air concentration in The Netherlands is calculated out of the highest local air concentration ($3.2 \cdot 10^{-4}$ mg/m^3) and the regional concentration ($6.3 \cdot 10^{-8}$ mg/m^3) and is $4.5 \cdot 10^{-6}$ mg/m^3. No measured data of BBP in air in The Netherlands are available to compare with predicted air concentration.

4. Worker exposure

4.1 Ease - The model

Substances in the workplace may entry the body by inhalation, by passing through the skin, or by ingestion. Exposure by inhalation is defined as the concentration of substance in the breathing zone and is usually expressed as an average concentration over a reference period. EUSES provides a general purpose predictive model for exposure assessment in the workplace, called EASE (Estimation and Assessment of Substance Exposure). EASE was specifically developed for the purpose of modeling inhalation and dermal workplace exposure across a wide range of circumstances. Based on evaluations, the model often yield results which are numerically higher than those in apparently analogous situations in workplaces (EC, 1996). BBP exposure is estimated for workers in a PVC-processing plant. Since BBP is not directly handled, dermal exposure is not relevant.

4.2 Inhalatory exposure

Based on process temperature for calendering (thin) PVC film, 180°C (Cadogan et al., 1993), and vapor pressure at 25°C, EASE calculates vapor pressure at process temperature. Exposure is calculated for a situation where BBP is not directly handled and included onto a matrix at a working place with local exhaust ventilation. EASE calculates inhalatory exposure to be 0.13 - 0.65 mg/l.

Exposure to phthalates was measured at a Swedish PVC-processing plant. Their PVC contained mainly DIDP, DEHP and BBP as plasticizers. The plasticized PVC was treated to a maximum of 180°C. Phthalates in air were measured by personal sampling with a detection limit for phthalates in air of 0.01 mg/m^3. On base of phthalate exposure, workers were divided in three equally sized groups, "low", "medium" and "high" exposed. The mean exposure concentration in these three groups was calculated at 0.1, 0.2 and 0.7 mg phthalates/ m^3 air. BBP was included in PVC at the lowest level and was detected in air at concentrations less than 10% of sum phthalates (Nielsen et al., 1985). The upper limit of BBP in air can be calculated as 0.01-0.07 mg/m^3. The risk assessment is based on this exposure level.

5. Residential exposure

Exposure to BBP in consumer products is estimated with use of the CONSEXPO model. First, the CONSEXPO model is introduced. Second, exposure to BBP from vinyl products is estimated. Finally, exposure to BBP is estimated for use of hair spray, adhesive or paint containing BBP. The exposure estimations are made for some scenarios which are reasonable to exist in real world, not for every possible situation.

5.1 CONSEXPO - The model

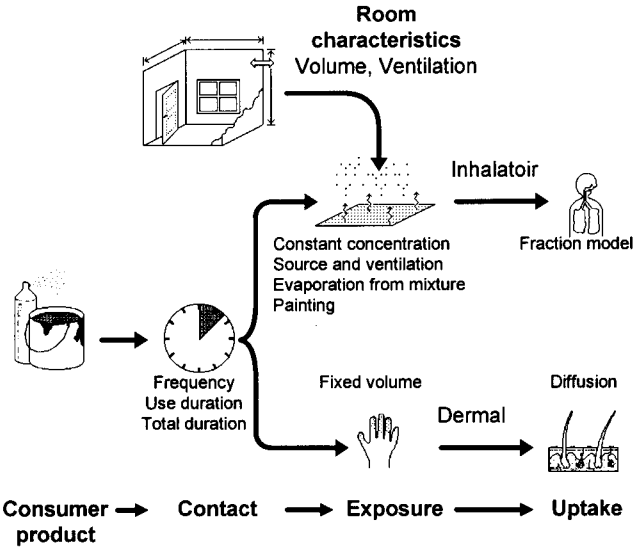

Figure 10: Schematically overview of (applied components) of CONSEXPO

Three components are important with respect to the (internal) exposure of a compound: contact, exposure and uptake (figure 10). *Contact* defines how long and how often the product is contacted. *Exposure* is defined as the concentration of BBP in air or in the product border on the body. Concentration in air depends among others on room characteristics. *Uptake* represents translation from external to internal concentrations. Several models are available to describe these components (Van Veen, 1996).

5.1.1 Inhalatory exposure

Inhalatory exposure can be calculated with the models constant concentration, source and ventilation, evaporation from mixture and painting (see figure 10). These models vary from simple to complex and require their own input parameters. All models include an "user" and a "non user" version, accounting for users being exposed closer to the source. The difference between user and non user for inhalatory exposure is basically the volume of air. The user experiences an imaginary volume of 5 m^3 air, in order to model source approminity. The total room volume is relevant for the non user (Van Veen, 1997).

Indoor air concentration depends in large terms on ventilation rate. The ventilation rate is determined by a lot of factors, like open or closed doors and windows, season, climate and weather conditions, isolation, natural or mechanical ventilation and old or new housing. Bremmer et al. (in prep) estimated default values for ventilation rates, mainly on base of Dutch data (Van der Wal, 1991; Bloemen, 1992; Bloemen, 1993; Lebret, 1990).

Indoor air concentration also depends on room size. The content and area of separate rooms in The Netherlands is registered in the "qualitative housing registration" (VROM, 1997). These data were used to estimate default values for Dutch rooms. The defaults represent 75th percentile in order to represent the upper tail (Bremmer et al., in prep.).

5.1.2 Dermal exposure and uptake

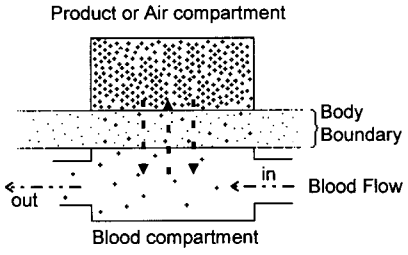

Figure 11: Schematic presentation of dermal uptake as described by the diffusion model (Van Veen, 1997)

Dermal exposure is described with the "fixed volume" scenario. Uptake in the diffusion model (figure 11) is defined by the area of dermal contact, skin permeability and concentration of the compound in the product (Van Veen, 1997).

A number of factors are known to affect percutaneous absorption of xenobiotics. These include dose, surface area of the site of application and skin conditions. The physicochemical properties of the compound applied are also important determinants of absorption (Elsisi et al., 1989).

Skin permeability is a rate parameter which defines how fast the skin is passed and can be estimated by empirical formulas which use the K_{ow} and the molecular weight to predict permeability. Six of these formulas have been implemented in CONSEXPO (Van Veen, 1997). Skin permeabilities for BBP estimated with these formulas range from $9.83 \cdot 10^{-4}$ - $2.14 \cdot 10^{-2}$ cm/min.

Percutaneous absorption of phthalates is also subject of *in vivo* and *in vitro* research. Skin permeability for BBP is not directly reported in literature, however observations of *in vitro* skin permeability for DEHP range from $1.8 \cdot 10^{-9}$ to $3.8 \cdot 10^{-7}$ cm/min (Scott et al., 1987; Barber et al., 1992). Calculated skin permeabilities for DEHP on base of the emperical formulas in CONSEXPO range from $1.41 \cdot 10^{-3}$-$9.25 \cdot 10^{-1}$ cm/min, indicating that calculated skin permeability may considerably overestimate skin permeability for phthalates.

In order to estimate skin permeability for BBP, doses and absorption of percutaneous absorption experiments for BBP and DEHP (Scott et al., 1987; Elsisi et al., 1989; Barber et al., 1992; Ng et al., 1992), are modeled in CONSEXPO by fitting the skin permeability. DEHP skin permeability is derived to see if this method to predict permeability is reliable. Fitted skin permeabilities of DEHP ($5.5 \cdot 10^{-9}$- $2.0 \cdot 10^{-8}$ cm/min) are fairly consistent and within the range of reported skin permeabilities. Therefore, fitted skin permeability for BBP, $3.2 \cdot 10^{-7}$ cm/min, on base of *in* vivo test results (Elsisi et al., 1989) and CONSEXPO, is assumed to be a reasonable estimate.

5.1.3 Uncertainty or variability?

Parameters may be represented as point values or distributions. Such distributions represent variability or uncertainty. In this exposure assessment, a parameter distribution was only used if literature referred to parameter variation. Whether parameter range can be interpreted as variability or uncertainty is indicated in appendix IV-VII by underlines. Some parameters, given as point values, represent a best guess on limited data. Instead of introducing an unknown parameter distribution, these "best guess" parameters are given in point values in order to keep the exposure estimation clear and understandable.

With use of the Monte-Carlo procedure in CONSEXPO, the value of any percentile of a distribution can be estimated. In order to get a stabile output of the distribution, a minimum number of iterations must be made. The amount of results above the desired percentile must be reasonably large (between 5 and 50). For example, in order to report a 95th percentile, 100 - 1000 iterations must be made, and for a 99th percentile, 500-5000 iterations are required (Huber, 1998). The worst case estimates in this exposure assessment represent the 95th percentile on base of 500 iterations.

5.2 Vinyl products

BBP is applied in vinyl floor covering as a plasticizer in PVC. According to a small manufacturer of vinyl floor covering, BN International in Huizen, BBP is applied in the top coating of the flooring (BN International, 1998). Inhalatory exposure is a result of volatilization of BBP out of the vinyl flooring. The volatilization rate will be very slow because BBP has a low volatility and it is locked in a matrix of PVC. Despite of the low emission of BBP out of vinyl, inhalatory exposure can be an important route because contact can be frequent and life time long.

5.2.1 Inhalatory exposure

The emission of BBP of vinyl flooring can potentially be estimated following different scenarios. These will be discussed below. The most suitable scenario is selected to estimate indoor concentration of BBP from vinyl products.

Ideal model

In an experiment of Clausen et al. (1993) it was indicated that emission of volatile compounds of vinyl floor-covering may be limited by diffusion. A relative stable concentration gradient profile will establish in the matrix, after a short initial period. The emission rate depends on the thickness of the source and the flux inside the matrix. VOCs in the vinyl floor-covering are distributed in three layers; two dense layers and a fluffy backing. Diffusion in the foam layer is probably much faster than in the more compact layers. Thus, the diffusion in the wear layer becomes the limiting step and a concentration gradient will develop in this layer (Clausen et al., 1993). A simplified model was developed for emission controlled by internal diffusion in the source, applying a diffusion coefficient which depends

on the concentration in the source. The outcomes of an experiment revealed that this model described the emission curves of the test substances, phenol and cyclohexanone, satisfactory (Clausen et al., 1993).

The model seems to be appropriate to estimate BBP emission out of vinyl products. However, because of lack of data to estimate the parameters for BBP, this model cannot be used. Emission of BBP out of vinyl products must be estimated with alternative models like "evaporation from mixture" and "source and ventilation".

Evaporation from mixture

Evaporation from mixture is an exposure model in CONSEXPO and can be used for any liquid mixture of chemicals from which a compound evaporates (Van Veen, 1997). For vinyl floor covering, BBP will be the chemical of interest and PVC (polymer chains) the other chemical. Vinyl floor covering consists of soft PVC with ± 50% plasticizer. The amount of BBP is considered to be 20% (see appendix I, point 4). The model calculates partial vapor pressure of BBP in PVC by using Raoults Law. Partial vapor pressure depends on the average molecular weight of the matrix (Van Veen, 1997). This model is worst case, assuming vinyl floor covering to be well mixed, with the PVC matrix having an average molecular weight of 400 g/mol.

Emission rate Cadogan

The Environ Corporation has developed a model which attempts to quantify indoor plasticizer losses. The model is based on three different approaches, two of which are theoretical and one semi-experimental. The model is a general one for all plasticizers and PVC products and predicts emission rates at 25 °C in the range 1.8 - $3.0 \cdot 10^{-4}$ $\mu g \cdot sec^{-1} \cdot m^{-2}$ (Cadogan et al., 1993). BBP emission can be calculated with this emission rate and the surface area of vinyl products. The range of the emission rate is considered to be an uniform distribution and as such implemented in CONSEXPO, using the source and ventilation model.

Measurement air samples

In California, indoor air concentrations of phthalates were measured by the PTEAM. The investigators measured both particle-phase and vapor-phase phthalates inside 125 homes. Outdoor sampling was conducted at approximately one-half of the homes. At day, indoor concentration of BBP was 62 ng/m^3 versus 51 ng/m^3 at night. Outdoor, BBP was not detectable. This indicates that the predominant sources of phthalates are indoor (Sheldon et al., 1994). Measured indoor air concentrations of BBP are used as a frame of reference to compare model outcomes.

Comparing models

Because vinyl floor covering is the major application of BBP, the assumption is made that vinyl flooring is the main indoor source of BBP in air. Outcomes of the "evaporation from mixture" and "source and ventilation" models are compared with measured concentration in California (Sheldon et al., 1994) to see which model estimates indoor air concentration best. Ventilation rate and room volume are unknown for rooms where air samples were taken. For comparison, average circumstances were selected by modeling a room with a ventilation rate close to the default ventilation rate of a complete residence, i.e. average bedroom with closed windows. Outcomes of the scenarios are summed up in table 11. For details, see appendix IV, table IVa.

Table 11: Outcomes of scenarios estimating BBP air concentration from vinyl products

CONSEXPO scenario: **Air concentration:**	**Evaporation from mixture**	**Source and ventilation**(1)	**Measured concentration**(2)
Mean BBP concentration [$mg \cdot m^{-3}$]	$1.7 \cdot 10^{-2}$	$3.5 \cdot 10^{-4}$	$5.7 \cdot 10^{-5}$
Reasonable worst case concentration [$mg \cdot m^{-3}$] (95th percentile, 500 iter.)	not applicable	$4.2 \cdot 10^{-4}$	$6.1 \cdot 10^{-5}$

(1) Based on Cadogan et al. (1993) (2) Based on Sheldon et al. (1994)

Comparing estimated BBP concentrations with measured concentrations can be seen that both models over-estimate BBP concentrations in air. Estimated air concentration with "source and ventilation" is about 6 times above measured. Evaporation from mixture predicts a 300 fold higher concentration, being unreasonable worst case. Therefore, "source and ventilation" is assumed to be the best model to predict BBP concentration in rooms with vinyl products.

On base of the Cadogan et al. (1993) emission rate, the source and ventilation model estimated the indoor concentration of BBP in a bedroom, kitchen and living with vinyl floor covering. In addition, bedroom walls are assumed to be covered with vinyl wallpaper. Rooms are ventilated with ambient air with outdoor concentration assuming to be equal to averaged air concentration as calculated by EUSES. Table 12 shows mean and worst case indoor air concentrations with parameter settings as described in table IVb, appendix IV.

Table 12: Indoor air concentration of BBP (source: vinyl products)

Air concentration	**Bedroom**	**Kitchen**	**Living room**
Mean concentration [$mg \cdot m^{-3}$]	$8.8 \cdot 10^{-4}$	$9.1 \cdot 10^{-5}$	$3.2 \cdot 10^{-4}$
Reasonable worst case concentration [$mg \cdot m^{-3}$] (95th percentile, 500 iter.)	$1.42 \cdot 10^{-3}$	$1.1 \cdot 10^{-4}$	$4.7 \cdot 10^{-4}$

5.2.2 Dermal exposure

Dermal exposure can result from walking on bare feet on vinyl floor covering. The exposure and uptake in this situation is hard to estimate since it is depending on migration of BBP in vinyl floor covering (see ideal model) and there is no usable estimation method available. It may be possible to estimate the exposure and uptake by assuming "fluid" vinyl flooring and a diffusion model, but such an estimation is far from realistic.

Dermal exposure can also occur when vinyl flooring is cleaned with hot water and bare hands. The manufacturer of BBP in America has performed a water extraction test; pieces of film with BBP were placed in water and put in an oven at 50°C for 24 hr. The weight loss was measured (Chemical Fabrics & Film Association, 1993). After 24 hr, 0.06, 0.07 and 0.08% of weight was lost of films containing 30%, 40% and 50% BBP respectively (Solutia, 1997) It is reasonable to assume the weight loss was due to a loss of BBP. It was impossible to extrapolate these data in order to model exposure during cleaning of vinyl flooring and therefore exposure analyses could not be performed.

5.3 Hair spray, Adhesives and Paints

Exposure and uptake depend, among others, on frequency of product use and, duration of contact. Both are determined by life style. The uptake of BBP, as a result of use of hair spray, adhesive and paint, is calculated per event. Uptake after inhalatory exposure is assumed to be worst case; i.e. 100% (see paragraph 7.4). Actual uptake also depends on frequency of use and is calculated in chapter 6.

5.3.1 Hair spray

BBP in hair spray

BBP is applied in cosmetics as plasticizer in hair spray (Nikitas, 1988) According to data supplied to the Food and Drug Administration (FDA), 2 (out of 261) aerosol fixative hair sprays contain BBP at a concentration of <1.0%. Data supplied to the FDA in 1984 indicated that BBP was applied in 4 aerosol hair spray formulations, with one formulation containing BBP at a concentration of 0.1 - 1.0%, and the remaining three formulations containing BBP at a concentration of 0.1 % (Skinner, 1992). (Van Baar, 1986 and Nater et al., 1985) report that airosol hair spray contains in general 0 - 0.1% plasticizer. For CONSEXPO the assumption is made that hair spray contains 0.1% BBP.

Inhalatory and dermal exposure

Weegels (1997) investigated the usage of hair styling products in The Netherlands. The study showed that about half of 20 subjects used hair spray. The amount of hair spray used per instance was 4.3 grams average (σ = 3.7). The mean duration of spraying was 11 seconds (σ = 6) and duration of contact with the nebula was 23 seconds (σ = 11) The average distance

between the nozzle of the spray to the nose/mouth was 25 cm. Because of this small distance it is assumed that during use spray distributes over a volume of 1 m^3 air.

Using the "source and ventilation" model, inhalatory exposure to BBP during use of hair spray is calculated. Generation of spray is assumed to be constant during spraying (11 seconds). Inhalation rate of the user is based on the inhalation rate of a 70 kg person in light exercise, i.e. 13.3 $m^3 \cdot d^{-1}$ (Freijer et al., 1997).

Dermal contact is calculated on base of the assumption that 90% of the total amount of hair spray settles in hair and 15% of this amount will have skin contact. The area of exposed skin is set to 10% of the total area of the head (Vermeire et al., 1993). Duration of dermal contact is assumed to be 24 hr., i.e., hair spray will be applied in the morning and washed out the following day. The skin permeability for BBP is estimated to be $3.2 \cdot 10^{-7}$ cm/min (paragraph 5.1.2).

The exposure and uptake is only calculated for a user of hair spray. One could say that spray will spread in the air and can also be relevant for non-users. However, spray consists of droplets and will probably descent on the user and therefore not become a source of exposure for the non-user.

Average and "worst case" uptake as a result of hair spray use is summarized in table 13. More details on parameter settings and the form of exposure and uptake distributions can be find on appendix V.

Table 13: Uptake of BBP in hair spray per (use) event [mg/kg bw]

Route of exposure:	Inhalatory	Dermal
Average uptake per event	$5.4 \cdot 10^{-4}$	$7.6 \cdot 10^{-4}$
Worst case uptake per event (95th percentile, 500 iter.)	$2.6 \cdot 10^{-3}$	$5.9 \cdot 10^{-3}$

5.3.2 Adhesives

BBP in adhesive, putty and sealing

In the product register of Sweden is recorded that 19 tonnes BBP are manufactured in adhesives and 9 tonnes in putty and sealings (KEMI, 1996). This implies that at least several brands of adhesives contain BBP. In the Material Safety Data Sheet of "DAP Weldwood Hobby & Craft Glue" BBP is recorded as one of the top five components of the product (DAP, 1997). It is estimated that glue contains 10% BBP, in line with concentrations of other phthalates generally found in adhesives and sealings (Sigma, 1996; AKZO, 1997).

Inhalatory and dermal exposure

The scenario used to estimate the exposure to BBP as a consequence of the use of adhesive containing BBP, is also relevant for putty and seals. Inhalatory exposure is estimated with "evaporation from mixture". The release area (1 m^2) can be interpreted as the area of application of adhesive or seal. The room volume is set to 10 m^3 , i.e., the volume of a shed, where the consumer might uses the adhesive. The total contact duration is 2 hr, and the actual use duration 1 hr. Dermal exposure is calculated with "diffusion" exposure model, assuming 250 μg adhesive is spilled on the fingers (2.5 cm^2).

Outcomes of the uptake assessment reveal that inhalatory uptake is $2.9 \cdot 10^{-5}$ mg/kg·bw and dermal uptake $2.8 \cdot 10^{-4}$ mg/kg· bw per event. Details on parameter setting can be found in appendix VI.

5.3.3 Paint

BBP in paint

According to the product register of Sweden, imported coatings in Sweden contain 21 tonnes of BBP (KEMI, 1996). An American manufacturer of BBP claims an excellent performance of Butylbenzyl Phthalate (Stanticizer® 160) in a wide range of coatings like nitrocellulose lacquers, PVAcetate and acrylic coatings and polyurethane-based coatings (Solutia, 1997). Sigma (1996) and AKZO (1997) do not report BBP as an ingredient of paint and lacquers. However, other phthalates (mainly di octyl phthalate and di butyl phthalate) are applied in several Dutch paintings and lacquers. In general these products contain between 1% and 5% phthalates (AKZO, 1997; Sigma, 1996). Two Material Safety Data Sheets (MSDS) report BBP as an ingredient of paint. One concerns a spray paint (Metalist™ SBR-2000) and the other is an acrylic floor finish (Metalist™ 20 Floor Finish). The spray paint contains 0.68% BBP and the floor lacquer 0.83% (National Laboratories, 1998a,b). The dermal and inhalatory exposure and uptake of BBP as a result of the use of the spray paint and the floor finish is calculated.

Inhalatory and dermal exposure

Bremmer et al. (in prep.) composed default parameters for exposure to compounds in paint. During the use of spray paint the nozzle of the spray and the object (bounce back effect) are close to nose and mouth (about 20-50 cm), thus the relevant volume of air around the user is set to 1m^2. Generation rate of BBP is based on the generation of spray paint; i.e. 25 g/min (Weegels, 1997) and the amount of spray paint available for inhalatory exposure; i.e. 0.5% (Bremmer et al., in prep.). Once the spray is in the air, it will take some time before all aerosols are settled down. Therefore, the total contact time with spray aerosol is set to be equal to the duration time (15 minutes). Dermal exposure to spray paint is assessed for a spillage of 1.5 grams of paint on 10% of the area of hands and head (Bremmer et al. in prep.). Dermal contact with paint is assumed to be one hour.

For exposure to BBP in floor finish is assumed the floor of an average living room in The Netherlands is painted. Parameters for the painting scenario are based on the default parameter set for painting of large areas with high solid paint, containing BBP, adapted for the area of floor in a living room.

Calculated uptakes are presented in table 14. For details on parameter settings, see appendix VII.

Table 14: Uptake of BBP per use event of paint [mg/kg bw]

	Inhalatory		Dermal	
	Spray paint	**Floor finish**	**Spray paint**	**Floor finish**
Average uptake per event	$6.4 \cdot 10^{-3}$	$4.8 \cdot 10^{-5}$	$1.7 \cdot 10^{-4}$	$2.8 \cdot 10^{-4}$
Worst case uptake per event (95th percentile, 500 iter.)	not applicable	$5.1 \cdot 10^{-5}$	not applicable	not applicable

Post application exposure

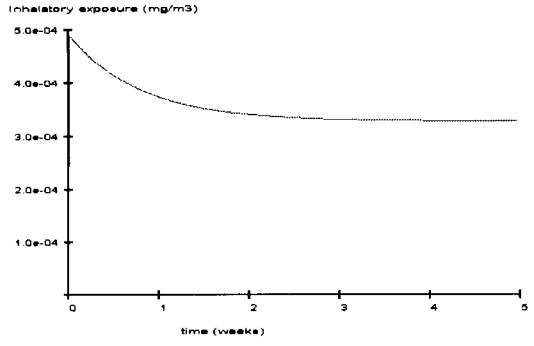

Figure 12: Indoor BBP concentration (post application) from floor finish

As a result of emission of BBP out of applicated paint, floor finish may give post application exposure. After a few weeks, indoor concentration becomes constant at $3.4 \cdot 10^{-4}$ mg/m^3 (figure 12). Since the painting model does not take into account that paint is drying, the outcomes of the model must be interpreted as worst case. The extent of inhalatory post application exposure from a painted floor is equal to exposure in the living room from vinyl flooring: $3.2 \cdot 10^{-4}$ - $4.7 \cdot 10^{-4}$ mg/m^3 (table 12). Therefore, residential inhalatory BBP exposure is estimated on base of emission out of vinyl products.

6. Uptake scenario

Exposure is defined in many ways. The *potential* exposure is defined as the concentration of a chemical in a medium, like water or air. If a person is at a certain moment at a certain site, that person will contact the concentration present at that moment at that site. Contact defines where and when a potential exposure is actually experienced by a person, and therefore transforms the potential exposure to an *actual* exposure (Van Veen, 1996). This chapter describes uptake of BBP via the environment, at the working place and residential uptake. For worst case risk assessment, inhalatory and oral uptake are assumed to be 100% of the intake. Dermal uptake is determined by skin permeability. Combined uptake via all routes will be discussed in the risk assessment (chapter 9).

6.1 Uptake via the environment

Inhalatory

Exposure to background levels is based on the outdoor BBP concentration: $4.5 \cdot 10^{-6}$ mg/m^3 (paragraph 3.4.3.) and the simplification that indoor air concentration is equal to the outdoor level in absence of indoor BBP sources. Uptake is calculated from BBP concentration and inhalation rate. Inhalatory uptake for adults summarized in table 15. To compare inhalatory uptake of BBP from background levels to residential uptake as a result from vinyl products, duration of assumed activity level identical for both. For babies uptake of BBP is calculated in a similar way, being $2.3 \cdot 10^{-6}$ mg/kg·day. Their inhalation rate is $2 \cdot 10^{-2}$ m^3/kg·hr (Freijer et al., 1997).

Table 15: Inhalatory uptake (outdoor/ indoor no BBP sources)

BBP concentration [mg/m^3] (1)	$4.5 \cdot 10^{-6}$		
	Adult		Baby
Activity (2)	sleeping	resting	-
Inhalation rate [m^3/kg·hr] (3)	$5.8 \cdot 10^{-3}$	$7.9 \cdot 10^{-3}$	$2 \cdot 10^{-2}$
Time [hr] (2)	8	16	24
Inhaled BBP [mg/kg·day]	$2.1 \cdot 10^{-7}$	$5.7 \cdot 10^{-7}$	$2.2 \cdot 10^{-6}$
Total amount [mg/kg·day]	**$7.8 \cdot 10^{-7}$**		**$2.2 \cdot 10^{-6}$**

(1) See paragraph 3.4.3 (2) Best guess (3) Freijer et al., 1997

Oral

Diet composition shows an appreciable amount of variation among individuals. As a consequence, intake of BBP will vary greatly. To account for the fact that intake rates vary among countries, EUSES defines a standard consumption pattern with for each food group the highest 'country-average' consumption rate of EU member states. This leads to a worst case diet (EC, 1996). Oral intake of BBP via food (table 16) is calculated on base of the food concentrations in table 10 (paragraph 3.4.2) and the standard diet of EUSES.

Table 16: BBP levels in diet and dietary intake of BBP for adults and babies

Food group	BBP concentration [mg/kg·wet weight]	Intake by Adults [mg/kg·day]	Intake by Babies [mg/kg·day]
drinking water (1)	$5.8 \cdot 10^{-7}$ mg/l	$1.7 \cdot 10^{-8}$	$5.8 \cdot 10^{-7}$
fish (2)	$3.2 \cdot 10^{-4}$	$5.3 \cdot 10^{-7}$	
leaf crops (2)	$2.3 \cdot 10^{-2}$	$3.9 \cdot 10^{-4}$	
root crops (2)	$9.4 \cdot 10^{-3}$	$5.1 \cdot 10^{-5}$	
meat (2)	$1.5 \cdot 10^{-3}$	$6.5 \cdot 10^{-6}$	Infant formulae:
milk (2)	$2.2 \cdot 10^{-4}$	$1.8 \cdot 10^{-6}$	$1.5 \cdot 10^{-4}$
Total	-	**$4.5 \cdot 10^{-4}$**	**$1.5 \cdot 10^{-4}$**

(1) See table 7 (2) See table 10

The Dutch inspectorate for health protection (IGB) has performed research on phthalate intake of babies in The Netherlands. Based on phthalates in infant formulae and baby diets, intake was calculated. Intake of total phthalates appeared to be practically independent on body weight for babies till 4 months, and was equal to 7.5 µg/kg·day. On base of MAFF measurements, Heisterkamp estimated the fraction of BBP to be 2 % of total phthalates. This results in an estimation of BBP intake by babies of 0.15 µg/kg·day (Heisterkamp et al., 1997). The intake of BBP in drinking water is estimated to be $5.8 \cdot 10^{-7}$ mg/day for babies on base of 1 liter water intake per day.

6.2 Uptake at the working place

The exposure assessment revealed a BBP concentration in a vinyl processing plant of 0.01-0.07 mg/m^3 (paragraph 4.2). Assuming a worker has an inhalation rate of $2.2 \cdot 10^{-2}$ m^3/kg·hr (light exercise) and spends 8 hours at the working place, the average uptake is $7.0 \cdot 10^{-3}$ mg/kg·day. Worst case inhalatory uptake is $1.2 \cdot 10^{-2}$ mg/kg·day, when 8 hours are spend in the upper concentration.

6.3 Residential uptake

6.3.1 Vinyl products

Assuming BBP air concentration in rooms with vinyl products has reached an equilibrium, year average indoor air concentrations can be considered representative. In this situation, BBP air concentration is also constant over the time.

Making a worst case exposure scenario, people are assumed to spend al their time indoor, in rooms with vinyl products (table 17a). Average and worst case indoor concentrations are used to calculate inhalatory uptake. Adults are assumed to spend 2 hours in the kitchen, 8 hours in the bedroom and 14 hours in the living room.

Table 17a: Indoor inhalatory uptake for an adult, source: vinyl products

	Bedroom	Kitchen	Living room
BBP concentration [mg/m^3] (1)	$8.8\cdot10^{-4}$ $(1.4\cdot10^{-3})^*$	$9.5\cdot10^{-5}$ $(1.1\cdot10^{-4})^*$	$3.2\cdot10^{-4}$ $(4.7\cdot10^{-4})^*$
Activity (2)	sleeping	resting	resting
Inhalation rate [m^3/kg·hr] (3)	$5.8\cdot10^{-3}$	$7.9\cdot10^{-3}$	$7.9\cdot10^{-3}$
Time [hr] (1)	8	2	14
Uptake [mg/kg·day]	$4.1\cdot10^{-5}$ $(6.5\cdot10^{-5})^*$	$1.4\cdot10^{-6}$ $(1.7\cdot10^{-6})^*$	$3.5\cdot10^{-5}$ $(5.2\cdot10^{-5})^*$
Total uptake [mg/kg·day]	**$7.7\cdot10^{-5}$ $(1.2\cdot10^{-4})^*$**		

(1) See table 12 (2) Best guess (3) Freijer et al., 1997 * worst case, 95th percentile, 500 iterations

Babies are assumed to spend most of the time in the bedroom (18 hours) and some time in the living room and kitchen (table 17b). This scenario leads to a reasonable worst case uptake scenario; most time is spend in a room with the highest BBP concentration.

Table 17b: Inhalatory uptake for babies, source: vinyl products

	Bedroom	Kitchen	Living room
BBP concentration [mg/m^3] (1)	$8.8\cdot10^{-4}$ $(1.4\cdot10^{-3})^*$	$9.5\cdot10^{-5}$ $(1.1\cdot10^{-4})^*$	$3.2\cdot10^{-4}$ $(4.7\cdot10^{-4})^*$
Inhalation rate [m^3/kg·hr] (2)	$2\cdot10^{-2}$		
Time [hr] (*)	18	1	5
Uptake [mg/kg·day]	$3.1\cdot10^{-4}$ $(5.0\cdot10^{-4})^*$	$1.8\cdot10^{-6}$ $(2.2\cdot10^{-6})^*$	$3.2\cdot10^{-5}$ $(4.7\cdot10^{-5})^*$
Total uptake [mg/kg·day]	**$3.4\cdot10^{-4}$ $(5.5\cdot10^{-4})^*$**		

(1) See table 12 (2) Best guess (3) Freijer et al., 1997 * worst case, 95th percentile, 500 iterations

6.3.2 Hair spray, adhesives and paints

Inhalatory and dermal uptake of BBP is averaged over a year and calculated exclusively for adults, since babies are not expected to use hair spray or other consumer products.

Inhalatory

All modeled consumer products cause inhalatory exposure. Using consumer products, BBP air concentration rises temporarily and varies in time, depending on frequency of use and use duration. The average frequency of hair styling with hair spray is 0.76 per day ($\sigma = 0.68$) with a maximum of three times per day (Weegels, 1997). Frequency of use of paint products is based on the Bremmer et al. (in prep.) defaults. Inhalatory uptake is reported in table 18.

Table 18: Averaged inhalatory uptake of BBP, source: consumer products

Consumer product	Inhalatory uptake per event [mg/kg] (1)	Frequency of use	Averaged uptake [mg/kg·day]
Hair spray	$5.4\cdot10^{-4}$ $(2.6\cdot10^{-3})^*$	0.76 / day $\sigma = 0.68$ (2)	$4.1\cdot10^{-4}$ $(5.3\cdot10^{-3})^*$
Adhesive	$2.9\cdot10^{-5}$	6/year (3)	$4.8\cdot10^{-7}$
Spray paint	$6.4\cdot10^{-3}$	2/year (4)	$3.5\cdot10^{-5}$
Floor finish	$4.8\cdot10^{-5}$ $(5.1\cdot10^{-5})^*$	0.5/year (4)	$6.6\cdot10^{-8}$ $(7.0\cdot10^{-8})^*$
Total uptake			**$4.5\cdot10^{-4}$ $(5.3\cdot10^{-3})^*$**

(1) paragraph 4.3 (2) Weegels et al., 1997 (3) Best guess (4) Bremmer et al., in prep. * worst case, 95th percentile, 500 iter.

Dermal

Dermal uptake of BBP is calculated on base of the use-frequency as reported for inhalatory uptake (see table 18). Total dermal uptake is calculated for a consumer who uses all BBP containing products and is presented in table 19.

Table 19: Averaged dermal uptake of BBP, source: consumer products

Consumer product	Dermal uptake per event [mg/kg] (1)	Frequency of use	Averaged uptake [mg/kg·day]
Hair spray	$7.6 \cdot 10^{-4}$ $(5.9 \cdot 10^{-3})^*$	0.76 / day $\sigma = 0.68$(2)	$5.8 \cdot 10^{-4}$ $(1.6 \cdot 10^{-3})^*$
Adhesive	$2.8 \cdot 10^{-4}$	6/year(3)	$4.6 \cdot 10^{-6}$
Spray paint	$1.7 \cdot 10^{-4}$	2/year (4)	$9.3 \cdot 10^{-7}$
Floor finish	$2.8 \cdot 10^{-4}$	0.5/year(4)	$3.8 \cdot 10^{-7}$
Total uptake			**$5.9 \cdot 10^{-4}$ $(1.6 \cdot 10^{-3})^*$**

(1) paragraph 4.3 (2) Weegels et al., 1997 (3) Best guess (4) Bremmer et al., in prep. * worst case, 95th percentile, 500 iter.

7. Kinetics and metabolism

In this chapter the bioaccumulation potential of BBP is estimated on base of half-lives. The exposure route may influence the kinetics of BBP. Metabolism and excretion after oral, intravenous and dermal exposure are compared to discuss route to route extrapolation.

7.1 Oral

Phthalate diesters are metabolized in the gastro-intestinal tract to a monoester and alcohol by a variety of esterases in the gut (intestinal microflora, pancreatic lipases, gut esterase). The monoester can be metabolized by ω - and ω-1 oxidation to a number of hydroxylated products. Monoester and products can also be conjugated with glucuronic acid prior to excretion (Foster et al., 1997).

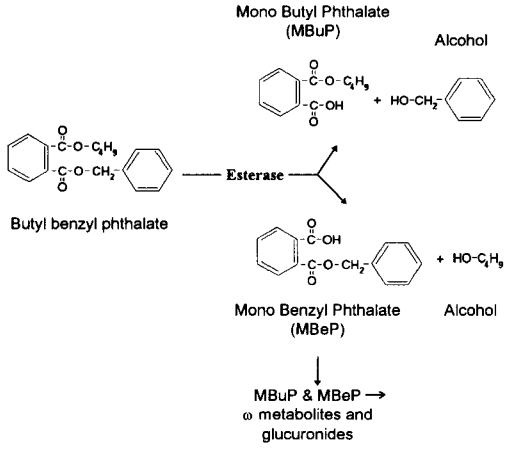

Figure 13: Metabolism of BBP (Eigenberg et al., 1986; Foster et al., 1997)

After oral administration of BBP to rats, rapid excretion was found at all doses (2 - 2000 mg/kg bw). About 80% of the dose was excreted in 24 hours and over 92% was excreted by 4 days. Most BBP metabolites were excreted in urine (75%), and 20% in feces. Major urinary metabolites of BBP are monophthalate and monophthalate-glucuronide. Although BBP is an asymmetric diester with potential of forming equal amounts of monobutyl (MBuP) or monobenzyl (MBeP) phthalate, larger quantities of MBuP are formed for unknown reasons (Eigenberg et al., 1986).

7.2 Intravenous

Following intravenous administration of BBP to rats (20 mg/kg·bw), it was rapidly distributed to tissues and eliminated. Monophthalate was rapidly formed and distributed to tissues. Peak blood levels of monophthalates were observed after 5 minutes of dosing and decayed in a biexponential manner. Tissue and blood concentrations of BBP and its metabolites are shown in figure 14a. Half-life times of BBP and its metabolites in fat and testis were 1.2 hours and 2.1 hours respectively (Eigenberg et al., 1986). On base of the K_{ow} from BBP is expected that BBP potentially accumulates in the fat compartment. However, from the observed short half-lives of BBP in fatty tissue is concluded that BBP will not accumulate. Following intravenous or oral administration of BBP, major route of elimination is excretion of metabolites into bile. In bile, large quantities of MBuP-glucuronide and MBeP-glucuronide, unidentified metabolites, and trace amounts of free MBuP and MBeP can be found. No parent compound appeared in bile. The majority of the dose is eliminated in urine and over 90% is excreted after 24 hours (figure 14b) (Eigenberg et al., 1986).

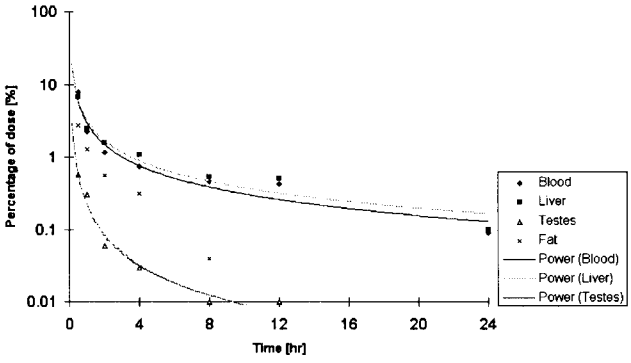

Figure 14a: Percent of BBP (and metabolites) in tissue after IV dosing (after 12 hours, BBP was undetectable in fat) (Eigenberg et al., 1986)

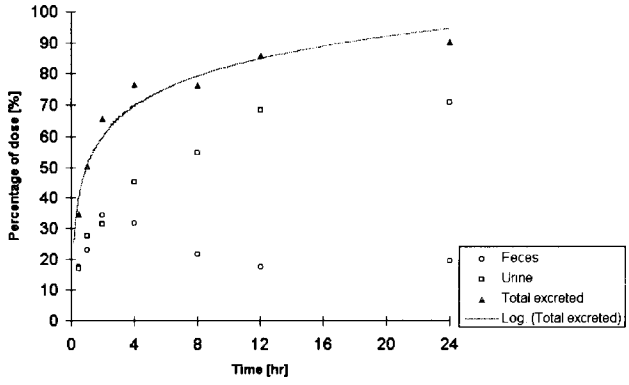

Figure 14b: Percent of BBP (and metabolites) in excreta after IV dosing (Eigenberg et al., 1986)

7.3 Dermal

No data about dermal metabolism are available for BBP. However, dermal metabolism of DEHP was measured in an *in vitro* experiment. There was a dose related increase in metabolism but the total of metabolites (MEHP) was less than 1% of the applied dose (Ng et al., 1992). Therefore, dermal metabolism is considered negligible for BBP.

7.4 Route to route

To justify the use of dose-effect relations from oral studies for risk characterization after dermal or inhalatory exposure, differences in metabolism and uptake must be taken in account.

Metabolism of phthalates in skin is negligible and BBP is assumed not to be metabolized in lungs (before BBP reaches blood). Therefore, kinetics and metabolism of BBP following inhalatory and dermal uptake, can be compared with kinetics and metabolism as seen after intravenous dosing of BBP. Metabolites of BBP are expected to play an important role in toxicity (chapter 8), and addition of inhalatory, dermal and oral uptake of BBP seems to be justified.

8. Effects

The emphasis of this study is on the exposure assessment and a full toxicological effect assessment is no part of it. First the temporary TDI will be discussed to describe the accepted standard in of BBP toxicology. Because of public concern of endocrine disruption by phthalates and postulated effects on the reproductive system, including reduced sperm count and infertility (Greenpeace, 1997b; ECPI, 1998), effects of BBP on the male reproductive system and on fetus and embryo during pregnancy are discussed. The estrogenic potency of BBP is discussed in the last paragraph.

8.1 Tolerable Daily Intake

BBP possesses a low degree of acute toxicity. BBP does not irritate the skin since no primary irritation or sensitization reactions were observed in 200 human volunteers after 15 daily applications of a subsequent challenge with BBP. Following oral or inhalatory administration of BBP to rodents, peroxisome proliferation appeared to be the most sensitive effect (Hammond et al., 1987)

The "Tolerable Daily Intake" (TDI) represents a toxicological threshold; if exposure is below the TDI; no adverse effects are expected. In an ideal situation, the TDI for BBP is based on the most sensitive effect, relevant for humans. The temporary TDI for BBP is 100 μg/kg·body weight·day (Peijnenburg et al., 1991; MAFF, 1996a,b). This TDI is based on the most sensitive effect of phthalates in rats; peroxisome proliferation in liver. In extrapolating this toxicological endpoint to humans, it should be noted that humans are far less sensitive for this effect than rats, or are even insensitive (VROM et al., in prep.; ECETOC, 1992). However, the derivation of the TDI implies a safety factor of 10 in the extrapolation, assuming humans are more sensitive than rats.

8.2 Testicular toxicity (adult rats)

8.2.1 Observed effects

In order to evaluate potential effects of BBP on the male reproductive system, a 14 day dietary study was conducted in adult male F344 (Agarwal et al., 1985). Exposure to BBP produced a dose dependent gonadotoxic effect in males. The reduction of testicular weight and evidence of seminiferous tubular atrophy were similar to effects reported for other phthalate mono- and diesters. In addition, BBP reduced accessory sex organ weights (e.g. epididymis, seminal vesicles and prostate) and aspecific toxic effects occur in all male gonadal tissues. Serum testosterone was reduced and plasma LH and plasma FSH levels were elevated in a dose dependent manner. Morphological changes include atrophic seminiferous tubules, relative absence of spermatids in lumen and large numbers of immature sperm. Degenerative effects to Leydig cells were not observed and could therefore not explain the reduced plasma testosterone levels. The no-observed-effect-dose in this study was 1.25%

BBP at dietary level (Agarwal et al., 1985). Foster et al., 1980, Sjöberg et al., 1986 and Dostal et al., 1988 report age susceptibility for testicular toxicity produced by phthalates. In all instances in which phthalate induced testicular toxicity have been studied in rodents of different ages, there is an increased ability to produce testicular lesions in young, pubertal rats compared with the corresponding adults (Foster, 1997).

8.2.2 Mechanisms of testicular toxicity in (adult) male rats

Mechanisms of testicular damage are mainly investigated for DEHP and DBP (Fukuoka et al., 1989l; Fukuoka et al., 1990; Zhou et al., 1990; Fukuoka et al., 1993). Sertoli cells play a key role in most hypothesized mechanisms for testicular toxicity. Sertoli cells are crucial during the whole process of spermatogenesis, since they 'nurse' the germ cells during their maturation (Orth et al., 1988). There is general agreement that metabolites of phthalates play a central role in testicular toxicity (Zhou et al., 1990; Foster et al., 1980; Sjöberg et al., 1986) A key factor is the presence of metals which are known to be essential to maintain Sertoli-germ cell interaction. A decrease of metal ion levels in testis after exposure to phthalates may cause the observed loss of germ cells (Foster et al., 1982; Fukuoka et al., 1993; Oishi et al., 1980a,b; Zhou et al., 1990; Zhou et al., 1993). The sloughing of germ cells is also characterized by decreases in activities of energy supplying enzymes, possibly leading to a shortage for germ cells (Fukuoka et al., 1990; Fukuoka et al., 1993; Zhou et al., 1990). Phthalates may induce testicular toxicity by inhibiting FSH to stimulate Sertoli cell function , probably by decreasing intracellular levels of cAMP (Creasy et al., 1987; Grasso et al., 1991; Heindel et al., 1989; Heindel et al., 1992; Foster et al., 1997). Because of feedback systems, changes in hormonal actions of FSH may have effect on other hormonal processes (see figure 15). The Fas system, responsible for the balance between germ cell proliferation and apoptosis, may be involved in increased germ cell dead after exposure to phthalates (see figure 16). Phthalates may increase expression of the Fas gene, leading to increased apoptosis of germ cells (Roberts et al, 1997; Lee et al., 1997).

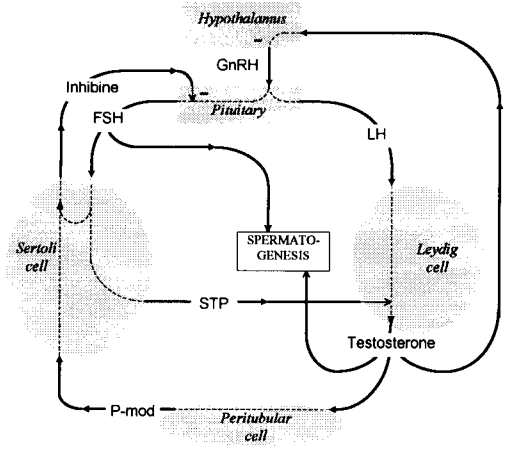

Figure 15: Main processes of endocrine regulation of testicular function ('-' = negative feedback, otherwise positive) (Norris et al., 1997)

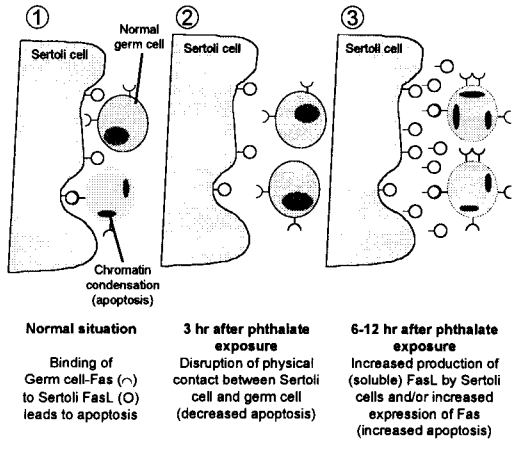

Figure 16: Hypothesized mono phthalate-induced mechanism of alterations in Fas-mediated germ cell apoptosis in testis (Roberts et al., 1997)

8.2.3 Critical window and NOAEL

Testicular toxicity is observed in studies with adult male rats. These effects can occur throughout adulthood, although young pubertal rats seem to be more sensitive for testicular toxicity. The sensitive window for effects to take place may be characterized by the period where Sertoli cells are present. Oral 14 day studies showed rat strain-dependent sensitivity for reduced testicular weight and histlogical changes after BBP exposure. NOAELs were 160, 480 and 625 mg/kg·day for Sprague Dawley, Wistar and F344 rats respectively (Piersma et al., 1995).

8.3 Developmental toxicity

8.3.1 Observed effects

The effects of BBP on prenatal development in rats were studied by Ema et al. (1990). Pregnant rats were exposed to BBP in diet from day 0 of pregnancy till day 20. On day 20, the pregnant rats were killed and fetuses were analyzed for weight, number and sex ratio. In the 375 mg/kg·day dosing group, signs of maternal toxicity and incidental embryofetal effects were observed. Maternal toxicity appeared to be significant in the 654 mg/kg·day dosing group, and embryofetal effects were only significant in the highest dose group (974 mg/kg·day) (Ema et al., 1990)

8.3.2 Role of metabolites in developmental toxicity

Ema et al., (1995) compared developmental toxicity of BBP and DBP and showed that BBP and DBP produced a similar toxicity pattern. Ema et al. (1995) suggest that the susceptibility to teratogenicity of BBP and DBP depends on the developmental stage at time of administration. Fetal malformations found with BBP were similar in types to those observed with DBP (Ema et al., 1995). The spectrum of observed malformations after exposure to MBuP and MBeP were similar to those observed with BBP and DBP (Ema et al., 1996a,b). The similarity in phase specificity of teratogenicity and in types of fetal malformations by BBP, MBuP, MBeP and DBP suggest that they may act by the same mechanism. It appears that MBuP and MBeP and/or their further metabolites may be the responsible agent, at least in part, for developmental toxicity of BBP (Ema et al., 1996b)

8.3.3 Maternal toxicity

In several studies, BBP or its metabolites caused maternal toxicity, as evidenced by significant decreases in maternal weight and food. It is generally agreed that it is difficult to establish whether the developmental toxicity is selective to embryos or is attributable to an indirect effect of pertubated homeostasis in dams (Ema et al., 1996a). Previous research has suggested that maternal toxicity may be regarded as an etiological factor for some fetal effects and embryo-fetal mortality (Khera, 1985). In contrast, maternal toxicity, as defined by maternal lethality and decrease in maternal weight gain, is not always associated with the same adverse developmental effects (Kavlock et al., 1985). Thus, the relation between maternal toxicity and adverse developmental effects still remains a critical issue in the developmental toxicity studies (Ema et al., 1996a).

8.3.4 Critical window and NOAEL

The critical window for developmental toxicity of BBP is the period of pregnancy. However, within this period rat embryos seem to be less sensitive to BBP during days 10-12 of pregnancy compared to day 7-9 or 13-15 of pregnancy (Ema et al., 1995; Ema et al., 1996a,b). After daily exposure to BBP during pregnancy, findings of Ema et al. (1990) indicate that the NOAEL for maternal toxicity is lower then for embryofetal toxicity; i.e. 375 and 654 mg/kg·day respectively (Ema et al., 1990).

8.4 Reproductive development

8.4.1 Mechanism(s) of changes in (reproductive) development

Exposure to endocrine disrupters during development may be of particular concern because many feedback functions of the endocrine system are not operational during this period. Permanent changes in endocrine function may be induced at levels of exposure to a toxicant that has no effect in the adult animal (Crisp et al., 1998).

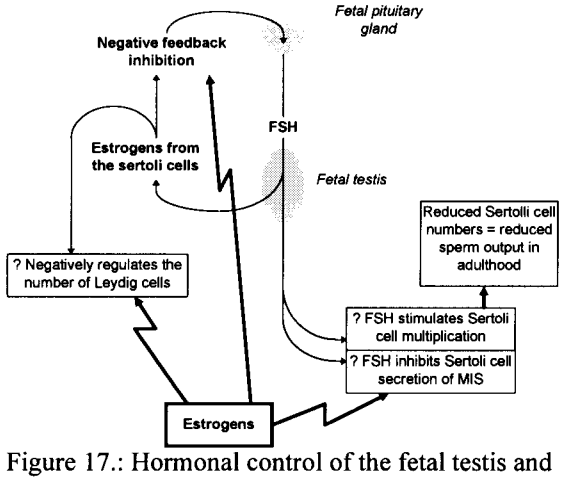

Figure 17.: Hormonal control of the fetal testis and possible pathways via which estrogens could cause impaired development (Sharpe et al., 1993)

Sperm production in adulthood is limited by two factors, the efficiency (and normality) of the process of spermatogenesis and the number of Sertoli cells. The number of Sertoli cells puts a 'ceiling' on the maximum attainable sperm output, because each Sertoli cell can only nurse a finite number of germ cells through development into spermatozoa. Since germ cells constitute the bulk of the testis, ultimate testicular size is determined by the number of Sertoli cells (Orth et al., 1988). Sertoli cell numbers (and thus testicular size) can be changes in endocrine levels prior to (rat) postnatal day 15. Suppression of the blood levels of FSH in the critical period before day 15 inhibits Sertoli cell multiplication. If Sertoli cell duplication is inhibited transiently, it results in adulthood in parallel reductions of testicular weight and sperm output. Since administration of FSH increases Sertoli cell mitoses, FSH is an important factor involved in regulating Sertoli cell multiplication. (Sharpe, 1993; Sharpe et al., 1994).

8.4.2 Observed effects

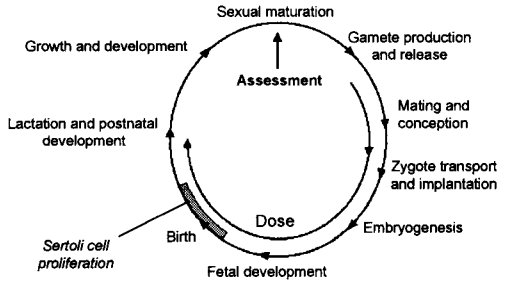

Figure 18: Sharpe protocol (Foster 1997; Sharpe et al., 1995)

In order to evaluate whether fetal and neonatal exposure to BBP has any effect on testicular size and spermatogenesis in adult life, a study was undertaken by Sharpe et al. (1995). Adult female rats were exposed to BBP in drinking-water (1 mg/l) two weeks before mating, throughout mating and gestation, during weaning up until day 22 after giving birth (figure 18). Exposure of the male offspring to the test chemicals was indirect, via the placenta or milk, and partly direct via drinking water. After 90 to 95 postnatal days, the male rats were killed and a number of endpoints were analyzed. Exposure to BBP resulted in a fairly consistent reduction in testis size and weight in adult rats. Testicular morphology was indistinguishable from control animals and no obvious abnormalities were evident in the cross-sectional analysis of the seminiferous tubules. Daily sperm production was significantly reduced. The decreased testicular size and daily sperm production, is not attributed to any obvious overt toxicity, judged by body weight and kidney weight. A possible explanation of these reductions is that the BBP reduced Sertoli cell divisions in the developing testes (Sharpe et al., 1995).

BBP failed to affect the sexual development of pups in a similar experiment of Ashby et al. (1997) and the results of Sharpe et al. (1995) could not be reproduced.

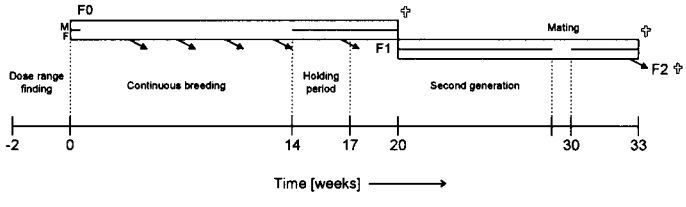

Figure 19: Continuous breeding protocol for control, low, middle and high dose groups. The small horizontal line dividing each bar, indicates separate housing of males and females. The bar indicates (continuous) exposure to the test chemical. ✞, animals are killed. (Wine et al., 1997; Chapin et al., 1997).

Since developmental toxicity of DBP is similar to BBP (Ema et al., 1995), both phthalates may induce similar reproductive toxicity. Wine et al. (1997) examined reproductive toxicity of DBP in a continuous breeding protocol (figure 19).

In the litters produced by the F1 adults, decreased live pup weights were observed in all dose groups. Both the total spermatid head per testis (a measure of testicular output) and the spermatid head per gram testis (a measure of spermatogenic efficiency) were decreased in high dosed males. Severe structural defects, including small and malformed prepuces and/or penises, underdeveloped or defective epididymis, and degenerate seminiferous tubules, were observed in the 0.5% and 1.0% dose group. Because the F1 rats were exposed during gestation and nursing, and were dosed during maturation until through mating, it is not possible to identify

which period of development is most sensitive to the effects of DBP or its metabolites. However, the male reproductive defects suggest that the period of organogenesis in the prenatal and perinatal periods, is the most critical time. In conclusion, the results from the RACB study indicate that the developmental and reproductive toxicities are more prominent in animals exposed during development and maturation than in animals exposed as adults only (Wine et al., 1997).

8.4.3 Critical window and NOAEL

According to Sharpe and Skakkebaek (1993) the critical window for effects on the reproductive system is the period when the fetal testis and particularly the testicular Sertoli cell, are undergoing differentiation and replication.

In order to extrapolate developmental toxicity findings in rats to possible effects on humans; timing of Sertoli cell development is compared (table 20). In humans, differentiation of the reproductive system starts in the sixth week after conception and the first period of Sertoli cell development ends about 3 months after birth. This may give a critical window of 10.5 months (see table 20). If only Sertoli cell development determines the critical window, two critical windows must be distinguished. The first critical window is around birth, over a period of ± 4 months, and the second critical window during puberty.

Table 20: Timing of developmental events after conception

	Rat [days]	Human [weeks]
Differentiation of reproductive system	14 /15 - ? (1)	6 - 20 (2)
Sertoli cell differentiation (2)	± 19 - postnatal ± 15	28/40 - 12 weeks after birth + during puberty (3)

(1) Welsh, 1995) (2) Sharpe, 1993 (3) Cortes et al., 1987

In the experiment of Wine et al. (1997) rats were exposed during a lifetime. Some of the observed structural deficits indicate that Sertoli cells are not the only targets of phthalates; i.e. the whole reproductive system may be sensitive during development. The critical window may be characterized by differentiation of the reproductive system, including complete development of Sertoli cells.

The assessments of Ashby et al. (1997) and Sharpe et al. (1995) are based on only one, and the same exposure dose and their findings are not in harmony. A NOAEL for reproductive developmental effects cannot be derived from these studies. In the study of Wine et al. (1997) live pup weights (F1) were significantly decreased in the absence of change in maternal weight at 385 mg/kg·day. In all dose groups, life F2 pup weights were decreased. The lowest dose given to females was 0.1% in diet, resulting in 80 mg/kg·day. Applying a factor 10 for extrapolation of the LOAEL to a NAEL, this would result in 8 mg DBP/kg·day

8.5 Estrogen activity

8.5.1 Observations

Butylbenzyl phthalate has been *in vitro* screened for estrogenic activity using a recombinant yeast screen. BBP showed the highest estrogenic activity of the phthalates tested, followed by DBP and DIBP. BBP was about 1-3 million fold less potent than estradiol (Harris et al., 1997; Soto et al., 1995) making it considerably less potent than other environmental estrogens such as bisphenol A and DDT. Most of the active phthalates were unable to produce a maximum response in the yeast screen. BBP reached a plateau at approximately 50 - 90% of the maximum response with estradiol (Harris et al., 1997; Soto et al., 1995) and is therefore acting *in vitro* as a (partially) agonist. Monobutyl phthalate and monobenzyl phthalate, the metabolites of BBP, were inactive in the assay, suggesting that only the parent compound has *in vitro* estrogenic activity (Harris et al., 1997).

The *in vivo* effects of xeno-estrogens are of interest in relation to their potential health risks on humans. Biological activity of estrogens is dependent on the complex *in vivo* pharmacokinetics associated with uptake, metabolism and excretion. There are almost no systematic, detailed studies of the nature and time course of the estrogenic effects *in vivo* in mammals of, *in vitro* estrogenic active, chemicals. As a first stage to assessing the *in vivo* estrogenic activity, a study was undertaken to establish the relative potency of such compounds in an acute *in vivo* mammalian assay (Milligan et al., 1998).

Vascular permeability in the uterus, an early specific estrogen-stimulated response was used as the basis for comparing relative estrogenic potencies of phthalates and other industrial compounds. In order to estimate the dose-response effects of xenobiotic estrogens on uterine vascular permeability, ovarieoctomized mice were injected with various doses of BBP and other *in vitro* estrogens. Non of the phthalates tested, produced significant effect on uterine vascular permeability at doses of 10^{-4} mol (Milligan et al., 1998).

The possibility that low doses of phthalates (i.e., below the level required to induce an estrogenic response) might act as anti-estrogens was investigated by examining the effect of a nonstimulatory dose of the compounds in combination with a stimulatory dose of estradiol. There was no evidence that any of the tested phthalates (dose 10^{-3} mol) produced any significant inhibitory effect on the estradiol-stimulated increase in vascular permeability.

The effect of low doses of phthalates given in combination was examined to determine whether there was any evidence of synergistic interactions in the induction of increases in uterine vascular permeability. There was no evidence of any positive or negative synergy between the phthalates (al at 10^{-3} mol) (Milligan et al., 1998).

8.5.2 Critical window and NOAEL

From these findings it appears that BBP has no estrogenic activity *in vivo* at the high doses tested. Doses were given by subcutaneous injection of 0.1 ml saline with an amount of the compound as described above. The highest dose of 10^{-3} mol BBP (Milligan et al., 1998) corresponds with 312 mg BBP. The average body weight of female rats is 225 grams (Ema et al., 1990). This results in a injected dose of 1.4 g/kg, acting as NOAEL. Since BBP does not seem to have estrogenic potency, a critical window for these type of effects is not relevant.

9. Risk Assessment

The quantitative risk characterization is carried out by calculating "Margins of Safety" (MOS). The MOS indicates the derivation between calculated dose and a toxicological limit value (EC, 1996). In this assessment, the temporary TDI (100 μg/kg·day) is used as limit value and the MOS is calculated by dividing the TDI through the dose.

In judging the acceptability of the MOS, the MOS should account for the uncertainties in the effect assessment and in the exposure assessment (EC, 1996). Exposure assessment is considered to be worst case. Uncertainties around the temporary TDI are accepted since no toxicological limit value can be derived from available findings of reproductive toxicity. Uncertainties as a result of extrapolation of effects are negotiated with safety factors and integrated in the TDI. Since MOS is based on the TDI, accounting for accepted uncertainties in effect assessment, a MOS > 1 is judged to be acceptable.

Uptake as described in chapter 6 is presented in table 21a for adults and in table 21 b for babies. As described in paragraph 7.4, inhalatory, oral and dermal uptake can be added to integrate uptake. Integrated uptake is calculated for the three sources of exposure (①); environmental, at the vinyl-processing working place or at home. This corresponds to classical risk characterization where risk is assessed for environmental, worker and consumer exposure separately (EC, 1996; VROM et al., in prep.). In addition uptake is integrated for combined exposure; via the environment and residential pathways (②). Such integrated uptake is assumed to be representative for uptake of BBP in "real life", where individuals are exposed both to environmental BBP as well as to BBP in vinyl products and consumer products.

Comparing uptake from various sources (environmental, vinyl products or consumer products) it can be concluded that uptake for these routes are in the same order of magnitude. Likewise, the contributions of the various routes of exposure (inhalatory, dermal and oral) are in the same order of magnitude. Therefore potential risks are not dominated by a specific source of BBP or a single route of exposure. Instead all routes and pathways appear to be relevant for risk assessment.

All calculated MOS for adults and babies are considerably larger than 1 (table 21a, 21b). It is concluded that adverse effects on base of the temporary TDI and as a result of integrated BBP uptake for the separate routes of exposure (①), as well as of combined environmental and residential uptake (②), are unlikely to occur.

Table 21a: Risk assessment for uptake of BBP [mg/kg·day] by adults

Route of exposure:	**Environmental exposure** Air [1]	Food [2]	**Residential exposure** Vinyl products [3]	Consumer products [4]	**Worker exposure** vinyl processing plant [5]
Inhalatory	$7.8 \cdot 10^{-7}$	-	$7.7 \cdot 10^{-5}$ ($1.2 \cdot 10^{-4}$)*	$4.5 \cdot 10^{-4}$ ($5.3 \cdot 10^{-3}$)*	$7.0 \cdot 10^{-3}$ ($1.2 \cdot 10^{-2}$)*
Dermal	-	-	-	$5.9 \cdot 10^{-4}$ ($1.6 \cdot 10^{-3}$)*	-
Oral	-	$4.5 \cdot 10^{-4}$	-	-	-
Integrated uptake ①	$4.5 \cdot 10^{-4}$		$1.0 \cdot 10^{-3}$ ($7.0 \cdot 10^{-3}$)*		$7.0 \cdot 10^{-3}$ ($1.2 \cdot 10^{-2}$)*
MOS	**270**		**96 (14)***		**14 (8)***
Integrated uptake ② (Environmental + Residential)	$1.1 \cdot 10^{-3}$ ($7.5 \cdot 10^{-3}$)*				
MOS	**90 (13)***				

(1) Table 15 (2) Table 16 (3) Table 17a (4) Table 18a,18b (5) paragraph 6.2 * Worst case

Table 21b: Risk assessment for year uptake of BBP [mg/kg·day] by babies

Route of exposure:	**Environmental exposure** Air [1]	Food [2]	**Residential exposure** Vinyl products [3]
Inhalatory	$2.2 \cdot 10^{-6}$	-	$3.4 \cdot 10^{-4}$ ($5.5 \cdot 10^{-4}$)*
Dermal	-	-	-
Oral	-	$1.5 \cdot 10^{-4}$	-
Integrated uptake ①	$1.5 \cdot 10^{-4}$		$3.4 \cdot 10^{-4}$ ($5.5 \cdot 10^{-4}$)*
MOS	**667**		**294 (181)***
Integrated uptake ② (Environmental + Residential)	$4.9 \cdot 10^{-4}$ ($7.0 \cdot 10^{-4}$)*		
MOS	**204 (143)***		

(1) Table 15 (2) Table 16 (3) Table 17b * Worst case

10. Discussion and Conclusions

Despite limited data, we succeeded to describe the route from sources of BBP to exposure, without significant loss of available information data along the route. In order to make the human risk assessment, the source-effect chain is taken as the leading principle. Emission of BBP during the life stages of vinyl and paint-like products is estimated and PECs, as a result of environmental distribution and degradation of BBP, are assessed with EUSES. Indirect exposure via the environment is combined with residential exposure from consumer products. Finally, the exposure level is compared with the temporary TDI and possible effects of BBP on the reproductive development are discussed. On base of the present insight in exposure and TDI, it can be concluded that it is unlikely that adverse effects will occur as a result of BBP-exposure.

Despite the full description of the source-effect chain, uncertainties remain. The first part of the discussion points out uncertainties and sensitivity. It is followed by notes about the character of the assessment and suggestions for refinement. Finally effects of BBP are discussed.

All input data should have their origin in the same (recent) year in order to make a risk assessment relevant for present exposures. For BBP, "up to date" information was lacking and past data are combined with recent data. For example, quantification of the amount of BBP in EUSES use patterns is based on data derived over a period of 10 years, i.e. from 1987 until 1997. Such an assessment requires that emission of BBP has been stable over a rather long period. However emission may change over time, for example as a result of lower emission factors due to better techniques or a decline in the use of a substance. If emission has changed over the last decade, our method to estimate emission is not reliable for outlooks to the future.

Because limited data substantiate the assessment, uncertainty in parameter estimates and evaluation of the results is introduced. Uncertainty in input can be caused by lack of knowledge, measurement errors or natural variability (Jager et al., 1997) and has consequences for outcomes of models. Another source of uncertainty which is difficult to quantify is the uncertainty caused by the simplifications in a model concept (Jager et al., 1997). For most parameters in the EUSES and CONSEXPO models, the extent of variability and uncertainty sensu stricto caused by ignorance is unknown. Therefore, the variability and uncertainty in model outcomes will not be expressed as range or distribution which would be required for uncertainty analysis. Exposure predicted with EUSES is already based on over 250 defaults and parameters, and we expect a full uncertainty analysis to be a study on its own.

The impact of uncertainty in input depends on the sensitivity of the model for the parameter. Sensitivity analysis of the models reveals the most sensitive parameters for model outcomes. We explored the EUSES model with respect to its sensitivity for important parameters in predicting regional concentrations in water, air and food (as indicated by Etienne, 1996 and Jager, 1998) by changing the parameter value in the BBP assessment and reporting its effect on model outcomes.
According to Etienne (1996), predictions of concentrations in water sensitively depend on the area of surface water, water depth, water flows and degradation half-lives in water. Model outcomes for BBP in water are sensitive for the area of surface water and the amount of BBP emitted into water: doubling the emission or halving the area of surface water, doubles the predicted concentration. For other parameters enumerated by Etienne (1996) smaller effects on model outcomes are observed.
Predicted concentrations in air depend sensitively on Henry's law constant, temperature, mixing height, wind speed and half-lives in air (Etienne, 1996). The predicted concentration of BBP in air is sensitive to the amount of BBP emitted and the mixing height; doubling their values results, respectively, in doubling and halving of predicted BBP concentration in air. The BBP concentration in air is less sensitive to changes in wind speed and half-lives. Changes of Henry's law constant and temperature have no effect on predicted concentrations of BBP in air.
Predicted concentrations in the regional model are expected to be most sensitive for degradation rates (Jager, 1998). For BBP, degradation parameters appeared not to be sensitive; decreasing all degradation rates with a factor 10, only doubles concentrations in meat and milk. Travis and Arms (1988) calculated bioaccumulation factors (BAFs) for meat and milk of cows by log-linear regression on experimental data for a number of chemicals. Uncertainties in the estimated BAFs remain considerable (EC, 1996). Estimation of BAFs for meat and milk depend heavily on K_{ow}, and are only valid for organic substances with log K_{ow} in range of 1.5 - 6.5 (EC, 1996). BBP meets these restrictions, but uncertainty in BAFs will propagate to predicted BBP levels in food. Model outcomes are sensitive to BAF values: increasing BAFs with a factor 2 doubles BBP levels in food.
The EUSES and CONSEXPO sensitivity for shared parameters (e.g. physical properties of BBP) may differ and a risk assessment, that depends on both models, may be sensitive for other parameters than the separate models. Because the EUSES and CONSEXPO outcomes depend on a host of parameters, extensive sensitivity analysis is a study on its own and not feasible for this study. However such a sensitivity analysis is one of the important issues to tackle in a future analysis.

Given uncertainty in model parameters, the question emerges whether predicted exposure is representative for measured exposure. The realism of predicted potential exposure can be checked by comparing predicted concentrations with measurements. Data sets concerning surface water and food were available for comparison. The utility of measured food data was limited, but we concluded that measurements and model outcomes were not in harmony. For

surface water, the model outcomes were not in contradiction with measurements, but exposure is less relevant for humans since contact with surface water is limited and as drinking water it is purified. The main data omission for exposure assessment are representative measurements in air and food in The Netherlands, since concentrations in these media are of direct importance for exposure.
Measured data to compare with predicted residential exposure are not available. In addition to uncertainty in parameter estimates, predicted exposure is uncertain because there is a possibility that not all relevant processes for exposure are included in this assessment. For example, measurement of BBP absorbed to dust and particulate matter (Øie et al., 1997) indicate that BBP in air may absorb to solid particles. Since this process is not taken in account in the calculation of indoor air exposure, the exposure concentration of BBP in indoor air may be lower. If this is a significant process, inhalation of dust should be taken in account. Because of all uncertainties, the residential exposure assessment should be interpreted as tentative and model outcomes have the characteristics of screening.

The models for exposure assessment differ considerably in level of detail. Indirect exposure via the environment is assessed with EUSES and direct (residential) exposure with CONSEXPO. EUSES has no possibility to implement uncertainty or variability and outcomes are point values based on conservative standard scenarios. The exposure assessment with CONSEXPO is more refined; its assessment is based on the most suitable exposure scenario and outcomes can be expressed as statistical distributions. The question is if both models can be combined in the assessment. The answer is positive since results from both models have the characteristics of screening because lack of measured data, and outcomes of both models are combined.

Environmental exposure is calculated on base of time and place averaged BBP concentrations without variability. Environmental concentrations will however vary over time with a seasonal or daily pattern. In addition spatial variation will occur near BBP sources, where local concentrations are expected to be higher in comparison with sites far from BBP sources. If BBP concentrations differ spatially, an air pollution exposure model, such as AirPEx (Freijer et al., 1997), may be used to estimate variability in inhalatory exposure over the Dutch population.

BBP levels in food may also vary in time and place. Spatially variability may be a result from presence of local sources. Variability over time can be caused by temporal changes in emission or distribution of a substance, and/or by seasonal changes in substance uptake by organisms in the food chain. A refined assessment can be made on base of measurements of BBP in different retail food products in The Netherlands, over a season. The present assessment is based on the standard dietary intake present in EUSES, neglecting that consumption varies over the population. If BBP is measured in a substantial number of food

items, data of the Dutch food consumption survey (VCP) can be used to outline variation of dietary uptake of BBP in the Dutch population.

Instead of the present worst case scenario assessment, a more realistic population risk characterization can be made by discerning risk groups with elevated exposure or/and raised sensitivity for effects. For example, population groups with elevated inhalatory exposure may be characterized with use of time-activity patterns, or information about variation in frequency and duration of contact and use of specific consumer products containing BBP. On base of knowledge of the critical window for effects, and the timing of exposure, sensitive groups in the population can be characterized. Such detailed population risk analysis may give policy makers more insight in population groups with potential risks and protective measures may be more effective.

In this risk assessment, limited attention is paid to the human effects of BBP. In principle, it is desirable to characterize risk on base of the most sensitive relevant effect for humans. The present study does not include firm toxicological evidence and whether effects of BBP on the reproductive system are the most sensitive relevant effect of BBP on humans, cannot be concluded. If the NOAEL is to be based on reproductive effects, it is important to note that sensitivity for reproductive effects of BBP may be gender dependent and may vary with age. Attention must be paid on exposure dynamics during the critical window. Knowledge of kinetics of BBP may outline the internal dose of BBP in target organs and can contribute toward the selection of an appropriate exposure unit for conventions. Thus the relevant exposure dose may be an outcome of exposure averaged over the critical window, and may be expressed in an amount per period in which the substance does not accumulate in target organs.

This risk assessment is based on exposure to BBP, not on exposure to its metabolites. Metabolites of BBP may be present in the environment as a result of (primary) degradation and exposure to metabolites may cause developmental effects (Ema et al., 1996a,b). In contradiction to the environment, consumer products are not expected to be a relevant source for metabolite exposure since presence of BBP-metabolites in consumer products is not reported in literature.
Metabolite exposure as a result of degradation in the environment cannot be integrated in the exposure assessment with EUSES. If metabolites exposure is included in a source-effect chain assessment, emission and distribution of metabolites must also be taken in account.

In conclusion, on base of the exposure assessment and the temporary TDI for BBP, it is unlikely that adverse effects will occur as a result from BBP exposure via the environment and consumer products or at the working place.
Toxicological research is making an effort to understand mechanisms of observed effects of phthalates. At this moment, insufficient findings of reproductive effects of BBP are available

to draw conclusions and derive a NOAEL. In our opinion, attention must be paid to increased sensitivity for effects of the next generation as observed by Wine et al. (1997) for DBP, since DBP and BBP have similar effects on development (Ema et al., 1995). On base of *in vivo* findings, there is no evidence for estrogenic activity of BBP. We believe that the period of development of the reproductive system, in particular Sertoli cells, is the sensitive period for effects as suggested by Sharpe et al. (1993). If toxicological observations confirm these suggestions, perinatal exposure and exposure during puberty might appear crucial in the risk assessment.

Apart from worker exposure, population groups with the highest exposure in The Netherlands are people in houses with many vinyl products, low ventilation rates and frequent use of consumer products with BBP. Although exposure via the environment, particularly via food, may contribute to potential risks, this route of exposure is hard to control and may be considered as background exposure. If in the future the NOAEL is established at a lower level due to new toxicological insight, it may be necessary to characterize groups at potential risk by investigating variability of contact with vinyl products and consumer products with BBP.

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APPENDIX I: BBP FLUX

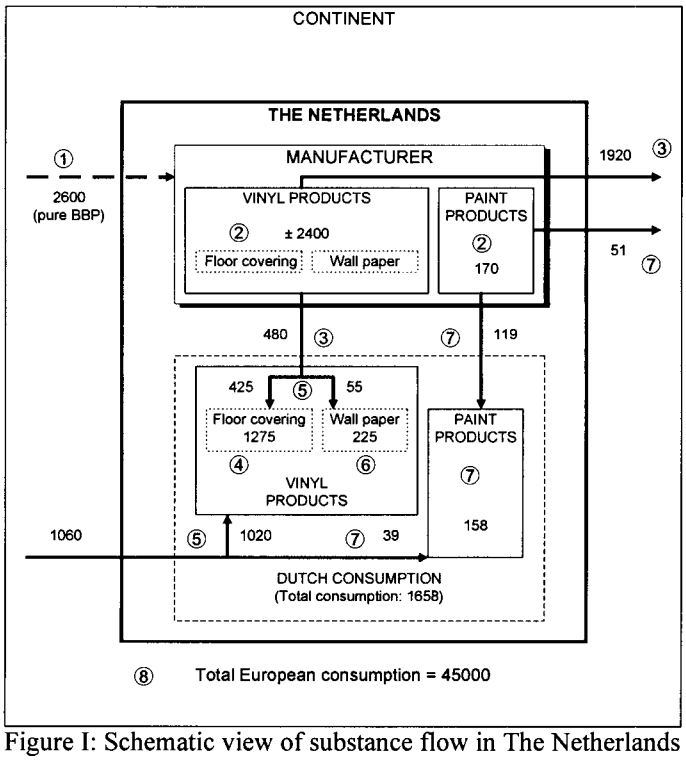

Figure I: Schematic view of substance flow in The Netherlands (BBP in tonnes/year)

1) Annual import of (pure) BBP is 1000-10000 tonnes/year(Van der Poel et al., 1988). A good estimate of the amount of imported BBP (as pure substance) would be 2600 tonnes/year (Van der Poel, 1998)

2) Of all imported (pure) BBP, over 91% is applicated in vinyl products (floor and wall covering) covering and over 6% in adhesives, sealants and paints. Application of less than 3% of the imported BBP is unknown since it is used for trade (Van der Poel et al., 1989). This results in about 2400 tonnes/year for vinyl products and 170 tonnes/year in adhesives, sealants and paints.

3) Only 20% of vinyl products produced in The Netherlands, is sold in The Netherlands (Van de Poel et al., 1989), resulting in 480 tonnes. A part of this amount is in vinyl flooring and a part in wall covering.

4) Total market for vinyl flooring per year is estimated with the calculation method of De Groot (1987) using the consumption in The Netherlands. Per year, $7.5 \cdot 10^6$ m^2 vinyl floor covering is sold in the Netherlands (De Groot et al., 1992). Average weight of vinyl flooring is 1.7 kg/m^2. Vinyl flooring contains about 50% PVC with 30% plasticizers (Potting et al., 1993). It is assumed that PVC in vinyl floor covering contains 20% BBP. The realism of this figure is confirmed by BN International (1998). Total amount BBP in vinyl flooring is: ($7.5 \cdot 10^6$ m^2/year x 1.7 kg/m^2 x 0.5 x 0.2 =) 1275 tonnes BBP/year.

5) Vinyl floorcovering in The Netherlands is for $^2/_3$ part imported. (Potting et al., 1993). Therefore, ($^1/_3$ x 1275) 425 m^2 vinyl floorcovering / year is Dutch. This implies Dutch wall paper (sold in The Netherlands) contains (480-425) 55 tonne BBP per year.

6) Total market for vinyl wall paper is $17 \cdot 10^6$ m^2 / year. Vinyl wallpaper contains 180-350 g soft PVC / m^2 , resulting in an average amount of 265 g/m^2 (De Groot, 1987). Soft PVC in vinyl wall paper contains 5% BBP (BN International, 1998). Out of these figures can be calculated that vinyl wallpaper in The Netherlands contains ($17 \cdot 10^6$ m^2 / year x 265 g/m^2 x 0.05=) 225 tonnes BBP/year.

7) About 170 tonnes BBP (over 6% of import) are applied in adhesives, paints and sealants, produced in The Netherlands (Van de Poel., 1989). Toe estimate export and the amount sold in The Netherlands, Dutch painting statistics are used (V.V.V.F., 1997). In 1996, 310 tonnes of paint were produced, of which 216 tonnes (≈ 70%) was sold in The Netherlands and 94 tonnes of paint exported (≈30%). Total consumption of paint in 1996 in The Netherlands was 287 tonnes, of which (287-216) 71 tonnes imported (≈ 25%) (V.V.V.F., 1997). The amount of BBP is assumed to be equivalent, resulting in Dutch consumption of BBP in paint 157 tonnes/year, import 39 tonnes and export 51 tonnes/BBP in paint, adhesives and sealants.

8) According to Harris et al. (1997), European consumption of BBP is 20,000-50,000 tonnes/year. A reasonable worst case of European consumption of BBP is 45,000 tonnes. Continental consumption is European consumption minus regional consumption. Continental application of BBP in diverse products is assumed to be proportional to the region.

De Groot (1987) estimates the amount of BBP in The Netherlands in 1986 to be 650 tonnes/year. According to De Groot (1998), this figure was realistic since industry agreed, after protest, with this estimation. Total amount of BBP in Dutch products; i.e. produced AND consumed is about 600 tonnes/year (480 + 119). Taking in account all uncertainties, these estimations seem to be in harmony.

APPENDIX II: BIOTIC DEGRADATION HALF-LIVES

Primary and secundary degradation

Tests assessing primary degradation are based on measuring dissapearance of parent phthalate by specific analytical method. In comparison, ultimate biodegradation, is assessed by measuring carbon dioxide evolution or oxygen uptake under aerobic conditions or methane evolution under anaerobic conditions. Primary degradation for lower molecular phthalates, like BBP, occured rapidly, typically exceeding 90% degradation within a week.

Aerobic primary biodegradation test results are generally in good agreement. Therefore, only test results from primary degradation are used, to estimate half life (in the same way as described by abiotic half life determination, paragraph 3.3.1).

Tabel IIa: Biodegradation in surface water

Test duration [days]	Degradation [%]	Half-live [days]	Reference
9	99	3	Saeger et al., 1976
7	100	2.3	Saeger et al., 1973
7	100	2.3	Ritsema et al., 1989
10	0		
7	100	2.3	Furtmann, 1993
5	100	1.7	
		2.3	**Best guess, used for EUSES**

Tabel IIb: Biodegradation in aerated sediment

Test duration [days]	Degradation [%]	Half-live [days]	Reference
7	95	2.5	Gledhill, 1980
2	47 - 60	2	Adams et al., 1989
		2.3	**Best guess, used for EUSES**

Tabel IIc: Biodegradation in a sewage treatment plant

Test type	Test duration [days]	Degradation [%]	Half-live [days]	Reference
Waste water, (aerobic)	7	100	2.3	Tabak et al., 1981
	7	>90	2.5	Patterson et al., 1981
	17	95	5.7	Furtmann, 1993
	7	100	2.3	
Activated Sludge (aerobic)	1	96	0.3	Saeger eta al., 1976
Overall			**2**	**Best guess, used for EUSES**

APPENDIX III: MEASURED BBP IN WATER

Table IIIa: BBP concentration in surface water in The Netherlands (RIZA, 1998)

Sampling Location	Year	Amount of BBP [µg/l]	Amount of samples above detection limit of BBP	Amount of samples below detection limit of BBP
River Rhine (Lobith)	1995	-	-	1
	1996	0.036	1	15
	1997	0.031 0.03	2	11
River Meuse (Eysden)	1995	-	-	-
	1996	0.014 0.023	2	16
	1997	0.046 0.033 0.064	3	14
Elsewhere	1995	-	-	6
	1996	-	-	18
	1997	-	-	26
Total	(1995+1996+1997)	$(2.7 \cdot 10^{-3} - 7.1 \cdot 10^{-3})^*$	8	107

* Average of "measured" concentrations, assuming concentrations of samples below the detection limit are between $^1/_{100}$ - $^1/_2$ of the assumed detection limit (0.01µg/l)

Table IIIb: BBP concentration in waste water at different locations in The Netherlands (RIZA, 1998)

Year	Amount of BBP [mg/l]	Amount of samples above detection limit of BBP	Amount of samples below detection limit of BBP
1996	0.095	1	>67
1997	0.0674 3.22 42.75 0.614	4	>40

APPENDIX IV: VINYL PRODUCTS

Tabel IVa: Comparing exposure models for vinyl flooring (Scenario:

Model/scenario:		**Evaporation from mixture**	**Source and ventilation**	**Constant concentration**
Room (average bedroom with closed windows)	Temperature [°C]	25 (D)	not applicable	not applicable
	Ventilation rate [$m^3 \cdot hr^{-1}$]	22 (1)	22 (1)	
	Room Volume [m^3]	22(1)	22(1)	1(4)
Emission parameters	Release area [m^2]	8.8 (1)	not applicable	not applicable
	Weight fraction [%]	20 (*,2)		
	Mean molweight matrix [g/mol]	400 (*)		
	Generation rate [$mg \cdot s^{-1}$]	not applicable	$\underline{1.58 \cdot 10^{-6}}$ - $\underline{2.63 \cdot 10^{-6}}$ (3, Ud)	not applicable
	Amount released [mg]	not applicable	not applicable	$\underline{5.1 \cdot 10^{-5}}$ - $\underline{6.2 \cdot 10^{-5}}$ (4, Ud)
Concentration in air	Mean concentration [$mg \cdot m^{-3}$]	$1.7 \cdot 10^{-2}$	$3.5 \cdot 10^{-4}$	$5.7 \cdot 10^{-5}$
	Reasonable worst case concentration [$mg \cdot m^{-3}$] (95th percentile, 500 iter.)	not applicable	$4.2 \cdot 10^{-4}$	$6.1 \cdot 10^{-5}$

References:
(1) Bremmer et al, in prep.
(2) BN International, 1997
(3) Cadogan et al., 1993
(4) Sheldon et al., 1994

Table IVb: Indoor air concentrations BBP (source: vinyl products)

Room/scenario:		**Bedroom**	**Kitchen**	**Living room**
Room	Ventilation rate [$m^3 \cdot hr^{-1}$]	$\underline{22 - 55}$ (1, Ud)	60 (1, Ud)	$\underline{40.6 - 87}$ (1, Ud)
	Room Volume [m^3]	22(1)	15(1)	58(1)
Emission parameters *(Source and ventilation)*	(Release area) [m^2]	9(1) (flooring) 30(1) (wall paper)	6(*,1)	23(*,1)
	Generation rate [$mg \cdot s^{-1}$]	$\underline{7.02 \cdot 10^{-6}}$ - $\underline{1.17 \cdot 10^{-5}}$ (2, Ud)	$\underline{1.08 \cdot 10^{-6}}$ - $\underline{1.8 \cdot 10^{-6}}$ (2, Ud)	$\underline{4.14 \cdot 10^{-6}}$ - $\underline{6.9 \cdot 10^{-6}}$ (2, Ud)
Concentration in air	Mean event concentration [$mg \cdot m^{-3}$]	$8.8 \cdot 10^{-4}$	$9.1 \cdot 10^{-5}$	$3.2 \cdot 10^{-4}$
	Reasonable worst case concentration [$mg \cdot m^{-3}$] (95th percentile, 500 iter.)	$1.42 \cdot 10^{-3}$	$1.1 \cdot 10^{-4}$	$4.7 \cdot 10^{-4}$

References:
(1) Bremmer et al, in prep.
(2) Cadogan et al., 1993

APPENDIX V: HAIR SPRAY

Table Va: Inhalatory exposure to hair spray

Parameters			Dimension
Contact	Duration of spraying	median 11 C.V. 0.55 (2, Ld)	[sec]
	Duration of contact with spray	median 27 C.V. 0.48 (2, Ld)	[sec]
Emission parameters *(Source and ventilation)*	Generation rate of BBP	median 0.37 C.V. 0.85 (*, 1, 2, Ld)	[mg/sec]
	Volume around user	1 (*,1)	[m^3]
	Ventilation rate	3 (1)	[hr^{-1}]
	Ambient BBP concentration	$4.5 \cdot 10^{-6}$ (3)	[mg/m^3]
Concentration in air	Mean event concentration	3.2	[mg/m^3]
	Reasonable worst case concentration (95th percentile, 500 iterations)	11.6	[mg/m^3]
Inhalatory uptake	Inhalation rate	20 (1)	[m^3/day]
	Average uptake per event	$5.4 \cdot 10^{-4}$	[mg/kg]
	Worst case uptake per event (95th percentile, 500 iterations)	$2.6 \cdot 10^{-3}$	[mg/kg]

References:
(1) Bremmer et al, in prep.
(2) Weegels et al., 1997
(3) Paragraph 3.4.3

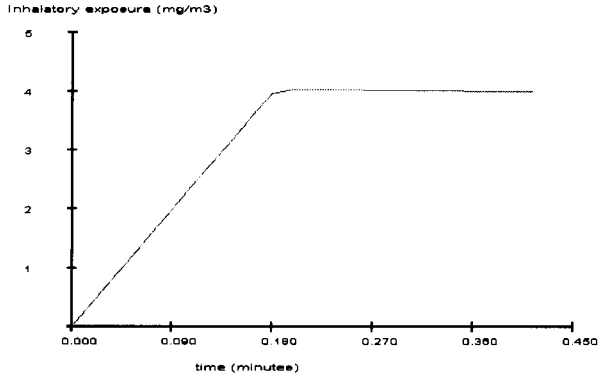

Figure Va: Inhalatory exposure of BBP in hair spray

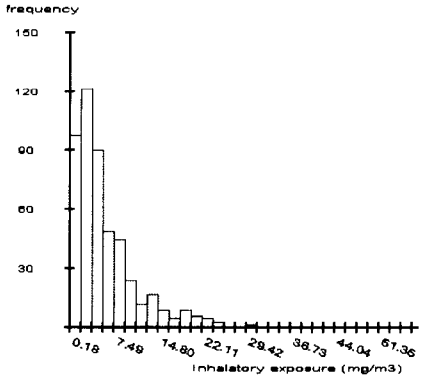

Figure Vb: Distribution of inhalatory exposure

Table Vb: Dermal exposure and uptake of BBP in hair spray per event

Parameters			Dimension
Contact	Contact of hair spray with skin	24 (*)	[hr]
Dermal exposure *(Fixed volume)*	Amount of hair spray on skin	0.14 - 0.18 - 0.42 - 0.49 - 0.49 - 0.55 - 0.69 - 1.1 - 1.2 - 1.4 - 1.4 (1)	[grams]
	Product volume	amount x 1 (*, 1)	[cm^3]
	Weight fraction of BBP	0.1 (*, 2, 3,4)	[%]
Diffusion	Skin contact area	118 (*, 5)	[cm^2]
	Blood volume (under contact area)	11.8 (5, 6)	[cm^3]
	Blood flow (under contact area)	15.2 (5, 6)	[cm^3/min]
	Skin permeability	$3.2 \cdot 10^{-7}$ (7)	[cm/min]
Dermal uptake	Average uptake per event	$7.57 \cdot 10^{-4}$	[mg/kg]
	Worst case uptake per event (95th percentile, 500 iterations)	$5.90 \cdot 10^{-3}$	[mg/kg]

References:
(1) Weegels et al., 1997
(2) Skinner, 1992
(3) Van Baar, 1986
(4) Nater et al., 1985
(5) Vermeire et al., 1993
(6) Van Veen (1997)
(7) Paragraph 5.1.2

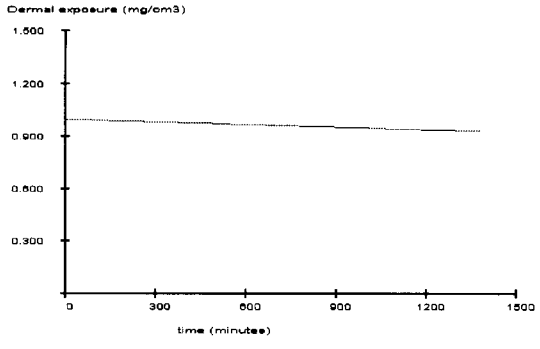

Figure Vc: Dermal exposure of BBP in hair spray

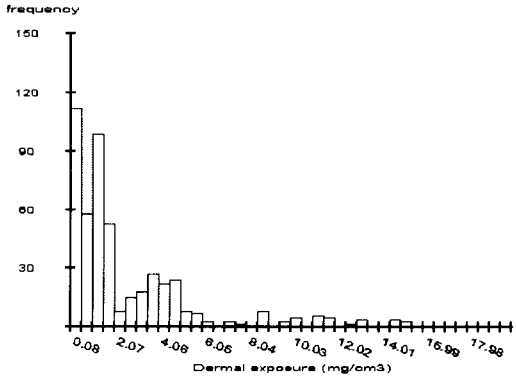

Figure Vd: Distribution of dermal exposure concentration

APPENDIX VI: ADHESIVE

Table VIa: Inhalatory exposure to BBP in adhesive, putty or sealant per use event

Parameters			Dimension
Contact	Duration of adhesive-use	$1^{(*)}$	[hr]
	Total duration	$2^{(*)}$	[hr]
Room	Temperature	$25^{(D)}$	[°C]
	Ventilation rate	$30^{(1)}$	[$m^3 \cdot hr^{-1}$]
	Ambient BBP concentration	$4.5 \cdot 10^{-6}$ (4)	[mg/m^3]
	Room Volume	$10^{(1)}$	[m^3]
Emission parameters *(Evaporation from mixture)*	Release area	$0.5^{(*)}$	[m^2]
	Weight fraction	$10^{(*, 2, 3)}$	[%]
	Mean molweight matrix	$300^{(*)}$	[mg/m^3] [g/mol]
Concentration in air	Mean event concentration	$1.21 \cdot 10^{-3}$	[mg/m^3]
Inhalatory uptake	Inhalation rate	20	[m^3/day]
	Average uptake per event	$2.9 \cdot 10^{-5}$	[mg/kg]

References:
(1) Bremmer et al, in prep.
(2) Sigma, 1996
(3) Akzo, 1997
(4) Paragraph 3.4.3

Table VIb: Dermal exposure to BBP in adhesive, putty or sealant

Parameters			Dimension
Contact	Contact of adhesive with skin	$1^{(*)}$	[hr]
Dermal exposure *(Fixed volume)*	Amount of adhesive on skin	$1^{(*)}$	[grams]
	Product volume	$1^{(*)}$	[cm^3]
	Weight fraction of BBP	$10^{(1, 2)}$	[%]
Diffusion	Skin contact area	$10^{(*)}$	[cm^2]
	Blood volume (under contact area)	$1^{(*, 3)}$	[cm^3]
	Blood flow (under contact area)	$1.29^{(*, 3)}$	[cm^3/min]
	Skin permeability	$3.2 \cdot 10^{-7}$ (4)	[cm/min]
Dermal uptake	Average uptake per event	$2.8 \cdot 10^{-4}$	[mg/kg]

References:
(1) Sigma, 1996
(2) Akzo, 1997
(3) Van Veen, 1997
(4) Paragraph 5.1.2

APPENDIX VII: SPRAY PAINT

Table VIIa: Inhalatory exposure to BBP in spray paint

Parameters			Dimension
Contact	Duration of spraying	4 (*,1,2)	[min]
	Total duration of contact	15 (*,1)	[min]
Emission parameters *(Source and ventilation)*	Generation rate of BBP	0.85 (*,1,2, 3)	[mg/min]
	Volume around user	1 (2)	[m^3]
	Ventilation rate	3 (2)	[hr^{-1}]
	Ambient BBP concentration	$4.5 \cdot 10^{-6}$ (4)	[mg/m^3]
Concentration in air	mean event concentration	2.2	[mg/m^3]
Inhalatory uptake	Inhalation rate	20 (2)	[m^3/day]
	Average uptake per event	$6.4 \cdot 10^{-3}$	[mg/kg]

References:
(1) Weegels et al., 1997
(2) Bremmer et al, in prep.
(3) National Laboratories, 1998a
(4) Paragraph 3.4.3
(*,1, 2) The amount of spray paint and the area of painting is estimated to be half the area and amount of the defaults for small painting jobs like widow frames (2), i.e. 1m^2 and 100 gr. Generation rate of spray paint is 25 g/min(1), containing 0.68% BBP(3). 0.5% is available for inhalatory exposure(1), resulting in 0.005 x 0.0068 x 25 g/min = 0.85 mg BBP/min

Table VIIb: Dermal exposure to BBP in adhesive, putty or sealant

Parameters			Dimension
Contact	Contact of spray paint with skin	60 (*)	[hr]
Dermal exposure *(Fixed volume)*	Amount of spray paint on skin	1.5 (1)	[grams]
	Product volume	2 (1)	[cm^3]
	Weight fraction of BBP	0.68 (2)	[%]
Diffusion	Skin contact area	120 (1)	[cm^2]
	Blood volume (under contact area)	12 (1)	[cm^3]
	Blood flow (under contact area)	15.48 (1)	[cm^3/min]
	Skin permeability	$3.2 \cdot 10^{-7}$ (3)	[cm/min]
Dermal uptake	Average uptake per event	$1.7 \cdot 10^{-4}$	[mg/kg]

References:
(1) Bremmer et al., in prep.
(2) National Laboratories, 1998b
(3) Paragraph 5.1.2

APPENDIX VIII: FLOOR FINISH

Table VIIIa: Inhalatory exposure to BBP in floorpaint

Parameters			Dimension
Contact	Duration of painting	300 (1)	[min]
	Total duration	500 (1)	[min]
Room	Temperature	25 (D)	[°C]
	Ventilation rate	40.6 - 87 (1, Ud)	[$m^3 \cdot hr^{-1}$]
	Ambient BBP concentration	$4.5 \cdot 10^{-6}$ (3)	[mg/m^3]
	Room Volume	58 (1)	[m^3]
Emission parameters *(Painting)*	Release area	23 (*, 1)	[m^2]
	Paint amount	23000 (*, 1)	[g]
	Density paint	1.27 (1)	[g/cm^3]
	Molecular weight matrix	275 (1)	[g/mol]
	Weightfraction of BBP	0.83 (2)	[%]
	Fraction paint layer 1	$1.0 \cdot 10^{-4}$ (1)	[-]
	Layer exchange rate	$1.0 \cdot 10^{-4}$ (1)	[-]
Concentration in air	Mean event concentration	$4.8 \cdot 10^{-4}$	[mg/m^3]
	Reasonable worst case concentration (95th percentile, 500 iterations)	$5.2 \cdot 10^{-4}$	[mg/m^3]
Inhalatory uptake	Inhalation rate	20 (1)	[m^3/day]
	Average uptake per event	$4.8 \cdot 10^{-5}$	[mg/kg]
	Worst case uptake per event (95th percentile, 500 iterations)	$5.1 \cdot 10^{-5}$	[mg/kg]

References:
(1) Bremmer et al., in prep.
(2) National Laboratorium, 1998b
(3) Paragraph 3.4.3

Table VIIIb: Dermal exposure to BBP in floorfinish

Parameters			Dimension
Contact	Contact of paint with skin	300 (*,1)	[min]
Dermal exposure *(Fixed volume)*	Amount of paint on skin	0.3 (1)	[grams]
	Product volume	0.24 (1)	[cm^3]
	Weight fraction of BBP	0.83 (2)	[%]
Diffusion	Skin contact area	20 (1)	[cm^2]
	Blood volume (under contact area)	2 (1)	[cm^3]
	Blood flow (under contact area)	2.58 (1)	[cm^3/min]
	Skin permeability	$3.2 \cdot 10^{-7}$ (3)	[cm/min]
Dermal uptake	Average uptake per event	$2.8 \cdot 10^{-4}$	[mg/kg]

References:
(1) Bremmer et al, in prep.
(2) National Laboratorium, 1998b
(3) Paragraph 5.1.2