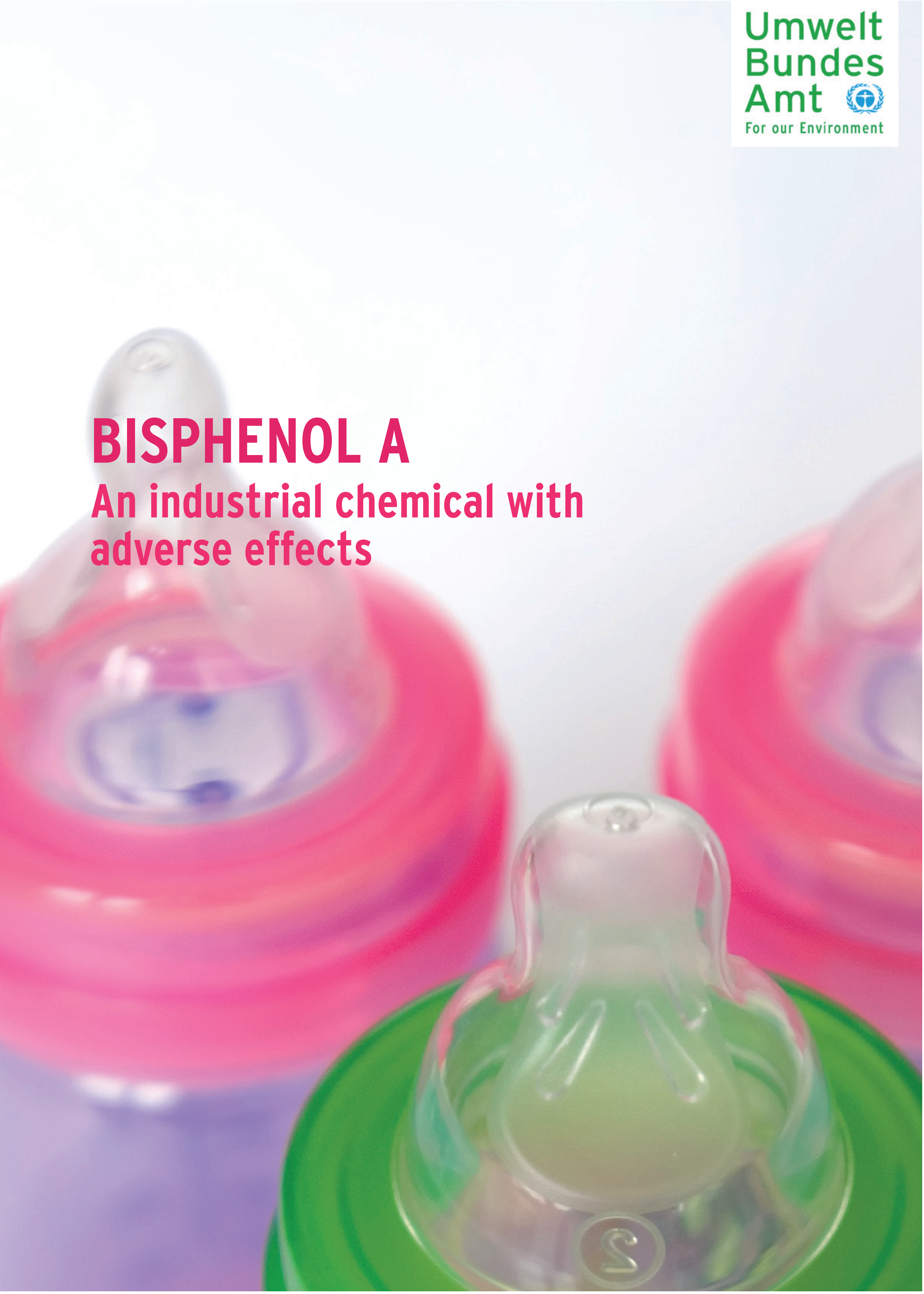
BISPHENOL A

An industrial chemical with adverse effects



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Content

Introduction

Bisphenol A was one of the first synthetic substances of which it was known that it can have a similar effect to that of the female sex hormone oestrogen. The British biochemists Edward Charles Dodds and Wilfrid Lawson [1; 2] searched in 1936 for chemicals that were able to replace natural oestrogen in medical therapy. This female hormone was extremely expensive, since it had to be synthesized from the urine of pregnant mares. In similar animal experiments carried out today with rats, whose ovaries have been removed, scientists have identified bisphenol A as a substance with weak oestrogenic activity. Nevertheless, bisphenol A did not pursue a career in pharmacy, since the same researchers soon identified much more potent synthetic oestrogens, including, above all, diethylstilbestrol (DES) [3], which was used and misused as a drug in the following decades [4].

No longer needed as a drug, bisphenol A found an alternative career as industrial chemical, and it is nowadays found in many everyday products. The hoped for pharmacological blessing turned out, however, to be a problem, since bisphenol A affects our hormone system. How dangerous bisphenol A can be for human health is presently the subject of dispute. While some scientists raise the alarm, others play down the issue. Is there something to the reports, how dangerous is bisphenol A, in which concentrations are humans and the environment subject to exposure, and how does the German Federal Environment Agency (Umweltbundesamt – UBA) assess the risk?

With this background paper, the Federal Environment Agency (hereafter: also UBA) would like to describes what sort of a substance bisphenol A is, for what purpose it is used, how it takes effect, and how the UBA and others assess the risk to humans and the environment. In many cases this report draws on data from the Council Regulation (EEC) No. 793/93 on existing substances and the Existing Substance Programme (ESP) derived from it. Within the scope of this programme Member States assessed the risk to humans and the environment from substances used in large quantities. In 2003, the European Commission published an initial risk assessment for bisphenol A [5], as agreed among the Member States. In 2008, the United Kingdom – the rapporteur Member State – supplemented and updated the report with new information [6]. The original assessment from 2003 and the addendum from 2008 have recently been merged into one document [7]. Reference to EU risk assessment in the following text concerns data collected in the merged reports.

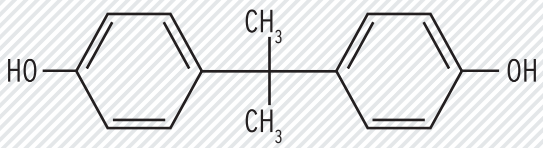
How and where does bisphenol A occur?

Bisphenol A is found in many everyday products: in CDs and DVDs, in cash register receipts made of thermal paper and in plastic bowls. But what is bisphenol A, for what purpose is it used and in what quantities? Box 1 explains its chemistry, production and subsequent processing.

Products containing bisphenol A

The substance is found in many technical appliances and household products that are made of very stable plastics, so-called polycarbonates.
Polycarbonates are produced from bisphenol A and have great stability, toughness, stiffness and hardness, as a result of which they are shatter-resistant. In addition, they are characterized by good electrical insulation properties and enhanced weather and radiation resistance. Mobile telephones and motorcycle helmets, for example, are made of polycarbonates. Furthermore, polycarbonates are employed in many areas as constructional materials; for example, for transparent roof coverings, computer housings and water boilers. Medical equipment (for example, dialysis equipment) and food containers (for example, baby bottles) are also manufactured with polycarbonates. Finally, polycarbonates are characterized by a further property: though they are inflammable, they cease to burn after removal from an ignition source [10].

BOX 1 Explanation of the chemistry of bisphenol A



Chemical name: 2,2-Bis-(4-hydroxyphenyl)propane or 4,4'-Isopropylidendiphenol
Molecular formula: $C_{15}H_{16}O_2$
CAS-Nr.: 80-05-7

Production process:
Produced through condensation of two parts of phenol and one part of acetone.

Commercial supplies of bisphenol A contain up to 16 different contaminants with a phenol structure. In the light of total production in the EU of about 1.15 million tonnes per year, this amounts to about 10,000 tonnes of contaminants.

Subsequent processing:
As intermediate: polymerization to polycarbonate plastic and epoxy resins. In this process bisphenol A is chemically converted into a polymer (plastic or epoxy resin) and at the same time firmly bonded in the polymer matrix.
As chemical: application as stabilizing agent and colour development component. In this application, bisphenol A is employed in its unchanged form, in which it is also present in the product.

BOX 2 Selection of products that are frequently manufactured with polycarbonate plastics or epoxy resins and can therefore contain bisphenol A [8; 9; 11]

Polycarbonate plastics	• Safety glass (glassy polymers) • Parts for plugs and switches • Housings of electrical/electronic devices and equipment (for example, mobile telephones, water boilers, coffee machines and computers) • Optical storage media, such as CDs, DVDs and Blu-ray discs™ • Car parts (transparent plastic parts), such as reflectors • Bottles and containers for food and drinks • Spectacle glasses • Microwave-proof crockery, plastic cutlery and cooking utensils • Motorcycle helmets and shields • Medical equipment
Epoxy resins	• Floorings • Varnishes (for example, as coatings for household appliances and equipment) • Beverage cans and food cans (as inner coating) • Printed circuit boards in electronic products • Composite materials (e.g. for tennis rackets and surfboards) • Adhesives • Inner coatings for decontamination of drinking water containers and wastewater tanks and pipes [12].

Epoxy resins are also produced from bisphenol A. Epoxy resins are fluid. With the addition of hardeners they react into hard, indissoluble and chemical-resistant plastics. They are predominantly used in the form of resin adhesives, coating resins and casting resins for surface coatings, including the inner coatings of metal packaging (such as beverage and food cans) [9; 11].
In the production of polycarbonates and epoxy resins bisphenol A is chemically converted in such a way that long chains and nets – so-called polymers – are formed from the individual molecules. Polymerized bisphenol A is chemically bonded, but can be released under certain conditions (See Chapter: „How does bisphenol A enter the human body?"). Occasionally, all of the bisphenol A is not chemically converted in production processes. Products made of these materials can therefore contain unbonded bisphenol A residues. The content is, however, small; it lies in the case of polycarbonates in the ppm range (that is, parts per million), which means that the bisphenol A content accounts for just a few millionths of the product) [9].

Besides conversion to polymer polycarbonate or epoxy resin bisphenol A is also used as an additive; for example, for coating thermal paper, in the production and processing of PVC (polyvinylchloride) plastics as well as in brake fluids.

Thermal papers are special papers, with which the direct transfer of heat during printing leads to a chemical reaction and, as a result, to blackening of the paper [13]. Bisphenol A serves here as developer substance alongside the actual dye. It is worldwide the most common colour development component in thermal paper [9].

In PVC plastics, bisphenol A serves the purpose of inter alia retarding the ageing of soft PVC (for instance, in high-temperature cables and tyres). It is also employed as a stabilizer in brake fluids, thereby enhancing both useful life and durability [5].

In the application of bisphenol A as an additive the substance is not chemically bonded. It is therefore more easily released from products such as thermal paper or PVC products [9]. Bisphenol A is contained in these products, however, in comparatively small quantities. The share of bisphenol A in thermal paper, for example, is 1 % [6; 9]. In soft PVC, such as cables, bisphenol A can account for 0.5 % of the employed plasticizer [9],[14]; the actual concentration in the product is accordingly in most cases less than 0.1 %.

A further special application is in dentistry. Here, fillings and sealing materials (similar to epoxy resin, and known as dental composites) are produced from substances such as bisphenol A glycidyl methacrylate (bis-GMA) and bisphenol A -dimethacrylate (bis-DMA), which are based on bisphenol A. Bisphenol A itself is not used [9; 15]; it can, however, be released during or after dental treatment [16].

Bisphenol A is also a starting material for tetrabromobisphenol A (TBBPA), which is employed as a flame retardant [5]. In the environment, TBBPA can reconvert to bisphenol A (reductive halogenization) [5], [17].

BOX 3 Selection of products in whose manufacture bisphenol A can be employed	
Other applications	• Thermal paper (e.g. fax paper, cash register receipts) [6; 9; 13] • Electrical and electronic products (treatment of envelopment materials or electronic components with TBBPA as flame retardant) [6; 9] • Brake fluid [5] • Rubber and PVC products, such as high-temperature cable (as a stabilizer) [6; 9] • Dental fillings and sealing materials, braces, prostheses (as starting material for composites) [15]

Box 3 displays a selection of products, in the manufacture of which bisphenol A can be employed as an additive, or that are possibly furnished with TBBPA as a flame retardant.

Environmental and consumer protection associations have also detected bisphenol A or bisphenol A derivatives in aluminium bottles, beverage cans (beer cans) with plastic inner coatings [18; 19], swimming aids, garden hoses and nail varnish [20].

Quantities produced and applied

In 2006, the chemicals industry produced worldwide 3.8 million tonnes of bisphenol A [21]. This corresponds to almost 100,000 40-tonne HGVs, the largest that are permitted on our roads. Lined one behind the other, the line of HGVs would be around 1,900 kilometres long, somewhat longer than the distance from Rome to Hamburg. In 2005/2006 almost one-third of world production (1.15 million tonnes) was accounted for by the then 15 Member States of the European Union (EU); Germany accounting for around 70% of European production (840,000 tonnes of bisphenol A [22]). By comparison, other chemicals that are also produced and consumed in large quantities in the EU are phthalates and flame retardants. Annual production of phthalates amounts to around 1 million tonnes, of which more than 90% are used as plasticizers in the production of soft PVC [23]. Consumption of flame retardants in the EU amounted in the year 2006 to 465.500 tonnes [24].

Figure 1 shows application of bisphenol A in the EU (reference period: 2005/2006 [6]). The largest share is further processed in Europe to polycarbonates and epoxy resins (865,000 and 192,000 thousand tonnes per year, respectively, a total of 1.06 million tonnes per year). All other applications total about 23,000 tonnes per year. In comparison to major applications this is only a small share, but regarded in absolute terms it is still a lot, namely 600 40-tonne HGVs. It includes thermal paper coating (about 1,900 tonnes per year and PVC (polyvinylchloride) processing (a total of 1,800 tonnes per year). Usage for the production of phenoplast casting resins, unsaturated polyesters, brake fluids, tyres and other applications [6] amount to 19,700 tonnes per year. 65,000 tonnes per year are exported from the EU.

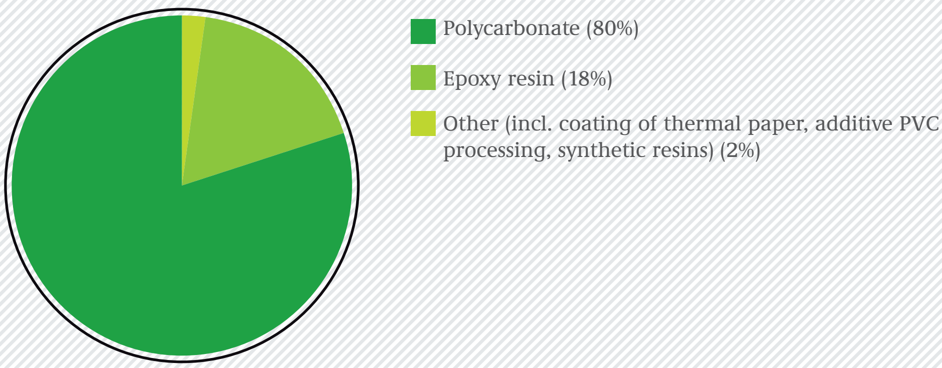
Outside the EU, bisphenol A serves as starting material for the production of tetrabromobisphenol A (TBBPA). Approximately 6,500 tonnes of this substance are imported each year into the EU, and tens of thousands of tonnes enter the EU [25] each year in products treated with flame retardants. Since TBBPA can be converted in the environment into bisphenol A, this substance has to be taken into account in the assessment as a possible source of bisphenol A [6].

How does bisphenol A enter the human body?

According to present knowledge, we take in bisphenol A primarily by way of food [6]. And how does the substance get into food?

Bisphenol A can be found in cans, namely in their inner coating. From there the substance can get into food. This happens by means of the chemical process of hydrolysis, by which bisphenol A is released through chemical reaction with water from the bonded (polymer) form [26]. How much of the substance is freed heavily depends on the can-material production pro-

Figure 1 Application of bisphenol A (annual production quantity in 2005/2006 in the EU: 1.15 million tonnes. Database: [6])



cess. In food from cans with a coated inner surface, chemical measurements have shown bisphenol A concentrations of between 5 and 38 µg/kg (micrograms per kilogram) of can content. In canned meat even higher concentrations have occasionally occurred [27].

Tests with polycarbonate containers have also shown that bisphenol A can be released, for instance, through hot water [28]. Detergent residues encourage the release of bisphenol A, the quantity depending on temperature, heating duration and water hardness [29], as well as on the detergents used [30]. In this case, bisphenol A is probably not detached from the plastic; the plastic decomposes in the course of time and sets bisphenol A free [28; 31].

People who receive intensive medical care are much more exposed to the chemical than the general population. High exposure was particularly found during dialysis treatment and in newborn intensive care units [32; 33]. Increased concentrations of bisphenol A in the human body have also been measured at workplaces in the production and processing of bisphenol A [6].

Bisphenol A virtually does not occur in drinking water. Its concentrations in Germany's surface waters are already rather low, with annual means of 0.5 µg/L and maxima of 5 µg/L (see section: "Concentrations in the environment"), and this is further reduced in the course of drinking water abstraction and treatment. This is confirmed by a study which found only one-thousandth of these concentrations in bank-filtered water from the Danube and in drink-ing water from Lake Constance (0.0003 – 0.002 µg/L) [34].

Nearly the same is true for the release into drinking water of BPA from tech-nical storage systems and devices for the distribution of drinking water that are coated with epoxy resin for corrosion protection. These coatings mainly consist of BPA that is polymerised and therefore strongly bound. Results from studies carried out by the Federal Environment Agency and elsewhere show that when properly and professionally applied, the coating - after the system is first put into service - causes no release of BPA into drinking water or at most a release as low as to result in concentrations well below 1 µg/L.

BPA concentrations above 30 µg/L were occasionally measured only where excessive heating (> 70°C) occurred in coated hot-water pipes. In one case, concentrations of up to 280 µg/l were reached. This was a hot-water pipe system which had not been properly and professionally installed and oper-ated and in which bisphenol A could accumulate in a circulation system. Such problems can be avoided through the selection of suitable materials (the UBA publishes a list of tested and therefore suitable materials [12]) and by commissioning qualified pipe installers. Under these conditions, even pipe materials coated with expoxy resin constitute no relevant source of human exposure to bisphenol A.

Besides pure bisphenol A, phenolic contaminants in technical grade bisphenol A could also contribute to the effect (see Box 1). They are structurally similar and therefore presumably have an oestrogenic effect. In total, they amount to 10,000 tonnes per year in the EU. Since toxicological analyses are mostly carried out with the pure chemical, the risk they represent for human health cannot be reliably assessed.

Conclusion: Since materials containing polycarbonates are in widespread use and bisphenol A is variedly employed, practically every person comes into contact with the substance. Different studies assess the median daily intake of adults and children at between 0.03 and 0.07 micrograms per kilogram body weight and day (µg/kg bw/day) [35], [36]. For bottle-fed infants the value is 0.8 µg/kg bw/day [35]. Scientists have identified the highest daily intake by children as 7 µg/kg bw/day [36] (median implies that half of the investigated samples were below the stated values).

Available data on human exposure indicates that as yet not all sources of exposure have been identified, and that besides oral intake there are probably other intake pathways [22].

How does bisphenol A enter the environment?

As a rule, bisphenol A enters the environment by way of wastewater, primarily through discharge into water bodies. A large proportion comes from businesses that produce and process bisphenol A. At the top of the list are manufacturers of polycarbonates and epoxy resins [6]. Furthermore, companies that produce and recycle thermal paper or process PVC plastics discharge bisphenol A into the environment [6].

With the wastewater flow bisphenol A is then fed either into the wastewater treatment plants of the companies or into municipal sewage treatment plants.

Insofar as wastewater plants are supplied with sufficient oxygen (aerobic conditions), microorganisms can easily degrade bisphenol A in water. This is confirmed by different laboratory tests, according to which the substance degrades almost completely within 2 – 17 days [5; 6; 37]. If too little oxygen is available (anaerobic conditions), however, the bisphenol A content reduces either not at all or extremely slowly [38; 39]. Practical experience also confirms that wastewater treatment plants eliminate bisphenol A with varied success. An investigation at different wastewater treatment plants in Germany produced degradation rates of between 61 and 98 per cent [37]. Studies from Canada show, too, that degradation in wastewater treatment plants can vary greatly. They established an average degradation rate of 68 % [40]. Degradation rates depend on the method of wastewater treatment and the performance of the treatment plant. Should purified wastewater still contain bisphenol A, the substance is discharged from wastewater plants into water bodies. Here it is further degraded under aerobic conditions. Varied evidence of bisphenol A in sediments shows, however, that the chemical is still not completely degraded and that residues remain in water bodies.

Contamination of municipal sewage plants can be explained with the example of recycled paper: waste paper that is used for the manufacture of recycled paper also contains, despite thorough sorting processes, thermal paper. This, in turn, contains bisphenol A. The proportion of thermal paper in processed paper is on average just about 0.1%, but, depending on the end product, it can fluctuate greatly [6]. One possible end product is recycled toilet paper. With wastewater it enters municipal sewage plants and brings with it bisphenol A, which, in the case of insufficient degradation, then enters into water bodies. The relevance of this mass flow is still unclear.

Bisphenol A residues can also remain in sludge that is produced in paper recycling. If this sludge is used for farmland fertilization, as is common in certain European countries, bisphenol A enters into the soil. In Germany and Austria this sludge is burnt. Sewage sludge from municipal sewage plants, which is also used in Germany as a fertilizer, might also contain bisphenol A. The Federal Environment Agency, however, has no measurements concerning this at its disposal.

Furthermore, bisphenol A can enter the environment through the use of products made of PVC (for example, external cables). The EU Risk Assessment Report on bisphenol A makes certain assumptions in this respect [5]. The quantity that is discharged into the environment cannot, however, be reliably estimated.

Concentrations in the environment

Evidence for the presence of bisphenol A in water bodies and river sediments has been provided since the 1970s (inter alia [41-43]). Scientific publications as well as government monitoring programmes have confirmed the widespread occurrence of bisphenol A in water bodies in recent years.

The EU Risk Assessment Report consolidates numerous scientific publications concerning the occurrence of bisphenol A in European waters during the years 1997 to 2005 [6]. It took into account several hundred measuring stations in 13 countries. Bisphenol A was detected in half of the measurements (detection limits, depending on method, between 0.1 and 0.00004 μg/l). The highest concentration, 43 μg/l, was measured in a Norwegian water body that is located close to an industrial centre. From the data, the EU Risk Assessment Report calculated an average water concentration of 0.01 μg per litre (median: 50th percentile). Statistically, in 5 % of all European waters concentrations of more than 0.35 μg/l are to be expected (statistical 95th percentile). Sediment concentration is on average (median) 6 μg/kg sediment (related to wet weight). 5% of all sediments contain, from a statistical point of view, more than 98 μg bisphenol A per kilogram sediment.

A government monitoring programme concerned with substance concentrations in selected rivers from 2002 to 2007, in accordance with the EU Water Framework Directive [44], confirmed these results: On average, 0.05 μg/l bisphenol A (median) was found in the waters under investigation. Merely in five of 1,230 samples was no bisphenol A found. In the investigated German flowing waters the highest concentration was 5.2 μg/l, on yearly average a maximum of 0.49 μg/l (2007, yearly average value of the measuring station with the highest values). The federal states carried out the required measurements in the period from 2006 to 2008.

These measurements substantiate the occurrence of bisphenol A in the environment. Since single data collections are involved, and no time series, the measurements do not allow an assessment of the concentration-time course. Assignment to individual sources is also difficult. For the EU Risk Assessment Report [5; 6] expected water and sediment concentrations were therefore calculated on the basis of data on degradation and distribution in the environment. The values thus calculated are 0.03 μg/l on average and 1.47 μg/l at most in water. Measured environmental concentrations are therefore, in part, above the calculated values. As far as sediment is concerned, the EU Risk Assessment Report calculated 0.52 μg bisphenol A per kilogram sediment on average and 24 μg/kg sediment at most.

What is the effect of bisphenol A on humans and the environment?

Mechanisms of hormone action

The mechanisms of hormone action induced by bisphenol A is in the focus of public attention (for example: [20; 45; 46]). Substances interfere with the hormonal system can – if they enter the body in a sufficient concentration – change the hormone system, disrupt embryonal development and impair reproduction [47]. In science, such substances are named environmental hormones or endocrine disrupters [48]. In the same way as natural hormones, many of these substances attach to „docking sites“ (receptors) for natural sex hormones and activate or hinder these receptors. As a result they influence processes that are normally triggered by natural hormones (for example, sexual development). Fish, for example, can feminize when they ingest substances that activate the receptor of the natural female sex hormone oestrogen.

In the case of bisphenol A, investigations show that it strengthens the effect of female sex hormones and weakens male sex and thyroid hormones [49; 50]. In certain test systems, in particular with non-genomic effects that are imparted by way of the membrane oestrogen receptor, bisphenol A has an effect that is almost just as strong as that of the natural female sex hormone [67,68] [51].

With humans, the oestrogen-type effect is triggered only by a free, non-metabolized substance. Though bisphenol A is rapidly metabolized – in part, already in the intestine – to bisphenol A glucuronide and bisphenol A sulphate, in human tissues such as testicles and the placenta the active form of bisphenol A can be released [52]. Almost all studies that investigate human blood have found relevant concentrations of non-metabolized bisphenol A [53].

The mechanisms of hormone action induced by bisphenol A also cause damage in animals (for example fish and birds). This is confirmed in numerous studies, which have been condensed in a report of the American Environmental Protection Agency (EPA) [54]. They show that in different animal species bisphenol A attaches to the receptor for female sex hormones (oestrogenic receptor), activates it and triggers effects that are to be expected with such an effect mechanism (for example, malformation of the reproductive organs). The results of a number of studies are summarized in Box 4. In comparison to the highly-potent natural sex hormone oestradiol, however, concentrations 100 to 10,000 times higher would be necessary to trigger the same effect.

The effects observed with insects, snails and crustaceans (for example, effect on egg production or the timing of hatching) indicate that bisphenol A has an adverse effect on the hormone-controlled reproductive system (see Box 4). The hormonal systems of these organisms, however, are as yet insufficiently researched to enable unequivocal statements on the mechanisms of action.

Can bisphenol A affect our health?

The European Food Safety Authority (EFSA) is of the opinion that bisphenol A does not represent a risk to human health. This assessment is based on studies with rodents that are regarded as highly relevant. Their result: Harmful effects relevant to the assessment below an intake of 5 milligrams per kilogram body weight per day cannot be established. According to EFSA, the daily human intake remains well below the tolerable daily intake of 50 μg per kilogram body weight derived from studies with rodents. On the other hand, numerous authors report of the effect of much lower doses of bisphenol A on reproductive health parameters and development [55]. Due to varied criticism of the studies, however, low-dose effects on individual organs and fertility were not taken into account by European authorities for the assessment. The Federal Government commented on this in detail during the last legislative period [55a].

These investigations do, however, point to possible effects of bisphenol A (for example, certain changes in behaviour), which are not recorded in studies that conform to standardized test procedures.
More than 100 investigations with rats and mice indicate that low concentrations of bisphenol A affect behaviour, learning ability and certain brain structures, in particular in the offspring of exposed animals. Prostate enlargement, reduced sperm concentrations and early puberty were also observed in laboratory animals [26; 55]. These studies support the hypothesis that bisphenol A could affect sex-specific brain and organ development in humans.

With no other chemical is the quality of studies the

BOX 4 Summary of the results of different studies on the mechanisms of hormone action induced by bisphenol A of bisphenol A (modified in accordance with [54])

Organism group	Effect mechanism	Observed effects in the organism
Frogs	Activation of the oestrogen receptor, effects on thyroid hormones	Feminization, malformation
Birds	Attachment to the oestrogen receptor	Malformation of reproductive organs
Fish	Activation of the oestrogen receptor	Malformation of reproductive organs, decline in sperm quality, retardation of sperm maturity, shifting of the gender ratio
Snails	Not clearly known	Increased egg production, malformation of the reproductive organs of females and males
Crustaceans	Not clearly known	Increased egg production
Insects	Not clearly known	Retarded hatching

subject of such controversial debate as in the case of bisphenol A. Not only investigations that establish health effects of low doses in test animals, but also studies that find no adverse effects are contested. One example is the discussion concerning the latest study from Ryan et al. [56-58]

Bisphenol A leads in isolated cases to sensitization in humans, which indicates an allergenic potential. Different studies have recently described how links exist between exposure to bisphenol A and development disorders and illnesses. For example, men who work in factories that process bisphenol A increasingly suffer from erectile and ejaculation problems as well as from libido disorder. This is all the more striking since the content of bisphenol A in the blood of the men in question was on average just 5% of the level that is regarded by the European Food Safety Authority as harmless. At the same time, the bisphenol A content in the blood of the workers was more or less in the range that was found in a number of German children and adolescents [28]. On the other hand, no reproductive disorders were es-tablished in woman that have occupational contact to bisphenol A [59].

The daughters of women who were subject to higher exposure to bisphenol A during pregnancy display at two years of age a more aggressive behaviour than their contemporaries [60].

Those sections of the American general population that are subject to greater exposure to bisphenol A suffer more frequently from diabetes and respiratory illnesses [61; 62]. Similarly, higher concentrations of bisphenol A have been found in the bodies of women suffering from endometriosis (endometrial excrescences) [63]. It is unclear, however, whether increased bisphenol A values are the cause or the consequence of these illnesses.

What are the effects of bisphenol A on aquatic and soil organisms?

Scientists have thoroughly investigated how different aquatic and soil organisms react to bisphenol A. The results of their studies are summarized in the EU Risk Assessment Report on bisphenol A [5; 6] and displayed in Box 5.

The results of these investigations are not easy to assess. They show unequivocally that bisphenol A impairs the sexual development and reproduction of different animal species. It is unclear, however, at which concentrations these effects occur. Isolated tests provide indications that the development and reproduction of frogs, snails and fish are impaired even by very low concentrations of bisphenol A. Since these tests have methodical failings, the EU Risk Assessment Report did not include their findings. The tests imply, however, that the effect of bisphenol A on aquatic and soil organisms is possibly underestimated in the current EU Risk Assessment Report on bisphenol A.

The findings in the EU Risk Assessment Report on bisphenol A, as well as unconsidered, unverified effects are displayed in Box 5.

Assessment of risks for humans

The assessment of possible health risks from bisphenol A have been the subject of controversial debate for years. The EU Risk Assessment Report on bisphenol A, in accordance with the EU Existing Substances Programme (ESP), comes to the conclusion – as does the European Food Safety Authority – that there is no cause for concern on the part of European consumers that a health hazard exists when products containing bisphenol A are properly used [6], [64]. The Federal Institute for Risk Assessment (BfR), which is responsible for food safety and consumer protection in Germany, shares this view.

Individual European countries do not, however, rule out health risks from the chemical. Against the backdrop of uncertainties in the EU Risk Assessment Report, these countries stress the necessity to introduce further precautionary legal measures. Due to the effects on reproduction Norway intends to restrict the content of bisphenol A in consumer products to 0.0025% by weight [65]. In March 2010 Denmark enacted a temporary ban on products that can release bisphenol A and have contact to food for children [66]. This concerns food packaging, children‘s beakers and children‘s bottles.

In France, in March 2010, the Senate unanimously passed a bill that prohibits drink bottles manufactured on the basis of bisphenol A. Before enactment, the bill requires the assent of the National Assembly, the second chamber of the French parliament [67].

In its report published in 2008, the US Food and Drug Administration (FDA) took the view that there were no health risks [68]. It has, however, recently revised its opinion. Due to concern that even in small doses bisphenol A could damage health, the FDA is taking reasonable steps to reduce human exposure. It intends, in particular, to reduce the bisphenol A content in children‘s food and bottles [69]. The assessment of the US National Toxicology Program [70] also expressed „some concern“ regarding adverse effects on the brain and behaviour, as well as on the prostate glands of foetuses, infants and children. It expressed „minimal „concern“ over other health effects in these sections of the population [70].

Individual EU Member States, Canada and several states in the USA regard measures as necessary. In several cities and states in the USA, bans on baby bottles that release bisphenol A are in force or the subject of legislative procedures (inter alia Chicago, Minnesota, Michigan,

BOX 5 Effects on aquatic organisms [5; 6]
The concentrations are listed, at which no effects were observed (no observed effect concen-tration, NOEC) in the test, as well further indications that were not taken into account in the EU Risk Assessment Report for bisphenol A.

Organism group	NOEC
Fish	16 – 3.640 µg/l Indications that sperm quality is already reduced at 1.75 µg/l
Frogs	60.4 µg/l Indications from one test that the gender ratio might already be shifted at 2.3 µg/l
Insects and crustaceans	100 – 3,146 µg/l
Snails	EC10* = 2.1 µg/l Indications that effects on reproduction already occur with considerably lower concentrations (factor 10 - 1000) * EC10 can serve as a substitute for NOEC, and describes the concentration at which effects are shown in 10% of animals
Algae and aquatic plants	1,360 and 7,800 µg/l
Further species (cnidarians and sponges)	42 and 1,600 µg/l
Soil organisms (earthworms, springtails, plants)	20 to more than 100 mg/kg soil

California, Connecticut and Washington). Canada has banned baby bottles containing bisphenol A [71]. The Canadian Government explained its ban with the precautionary principle, and announced further research projects to close existing knowledge gaps.

Assessment of risks to the environment

The updated EU Risk Assessment Report on bisphenol A of 2008 [6] comes to the conclusion that calculated concentrations in the environment are well below the levels at which effects on soils and aquatic organisms are to be expected. The risk is held to be tolerable; no measures have to be taken to reduce concentrations (so-called „risk reduction measures“) in the environment [6].

The Risk Assessment reveals, however, some uncertainties. The United Kingdom summarized them at the conclusion of work in the Existing Substances Programme [72]:

- Further information is necessary, in order to clarify whether bisphenol A has an effect on aquatic organisms at lower concentrations than previously assumed. (see Box 5).
- Concentrations measured in the environment provide indications that the values calculated for the Risk Assessment underestimate the exposure of water bodies (see chapter: „Concentrations in the environment).

Japan also comes to the data-based conclusion that bisphenol A represents no risk to the environment, and that no regulatory measures are necessary [73]. Norway and Canada, however, reached different conclusions. Due to the mechanisms of hormone action and high toxicity for aquatic organisms, both countries plan measures – on the basis of national legislation – to reduce the discharge of bisphenol A into the environment [40; 65].

What happens next?

The EU Chemicals Regulation REACH (Registration, Evaluation and Authorisation of Chemicals) [74] imposes an obligation on manufacturers and importers of chemicals. It requires that companies that manufacturer or import bisphenol A assess the risks for humans and the environment of all intended uses of bisphenol A. By the end of 2010 they must document their assessment in a chemical safety report and, at the same time, look into the indications of underestimation of risk raised by the United Kingdom. It is the duty of companies to describe the conditions under which bisphenol A can be safely used over its entire life cycle. Where necessary, they have a duty to apply and recommend risk reduction measures.

The chemical safety report together with other information enable the authorities to decide whether they regard additional measures for the protection of humans and the environ-ment to be necessary. Differences between REACH and the Regulation on Existing Substances , as well as the duties of companies and authorities, are displayed in Box 6. A harmonised position exists on further action on the part of the Federal Government [55a; 74a].

Federal Environment Agency evaluation of risks to human health

The overall picture provided by available studies on the effects of and exposure to bisphenol A reveals indications of possible risks to human health. There are presently still distinct gaps in knowledge and uncertainties with regard to certain aspects of risk assessment. In the view of the Federal Environment Agency it is therefore justified to consider precautionary measures to reduce the exposure of those sections of the population that on account of their sensitivity and exposure are primarily at risk.

The workshop on the assessment of bisphenol A, which was organized by the Federal Environment Agency in March 2009, recommended that all available data be drawn on by the authorities for the assessment of the substance. The numerous studies that have been published in renowned journals provide a consistent picture. Their findings should be properly considered in addition to the few investigations that have been carried out in accordance with the principles of good laboratory practice [22].

In these studies, the intake of bisphenol A is considerably below the quantity that the European Food Safety Authority assesses to be a risk to health; these quantities are nevertheless able to cause serious adverse effects in animals.

Although gaps in knowledge exist with regard to risk assessment and level of exposure, from our scientific point of view there are sufficient grounds for concern. The Federal Environment Agency is therefore in favour of precautionary action and restrictions on the use of certain products that contain bisphenol A. This applies, in particular, to products that come into contact with food. For these products there are additional regulatory options beyond chemicals law (REACH).
As far as regulatory options are concerned, a distinction has to be made between food packaging materials and products, such as baby bottles, which come into direct contact with food, and other articles that inevitably come into contact with the mucous membranes of the mouth, such as dummies.
Legal specifications for both groups of products mainly result from European legislation. National measures may only be introduced when permitted by European law.

European regulations on food packaging and storage products are by and large final. There is therefore little legislative leeway for German legislators. Efforts towards lowering upper limits on the presence of bisphenol A in food packaging and storage containers made of plastic, such as bottles, have therefore to be initially undertaken at the European level.

If the EU cannot reach agreement on a common approach, Member States still have the opportunity to take provisional measures regarding food packaging and storage products. That could be the case if Member States come to the conclusion, on the basis of new information or through the reevaluation of existing information, that human health could be endangered. New information and knowledge concerning bisphenol A must therefore be examined, to establish whether this requirement is met. Separate national regulations can only endure if the European Commission adopts the national assessment.

BOX 6 Duties of authorities and companies (comparison of the Regulation on Existing Substances and REACH)

Council Regulation (EEC) No. 793/93 on existing substances (repealed on 01.06.2008)

Companies	Authorities
Submit available information and comment on assessments of authorities	Assess the risk to humans and the environment of selected substances that are produced in large quantities (including bisphenol A) and decide, where appropriate, on necessary measures to reduce risks.

REACH Regulation (EEC) No. 1907/2006 (since 01.06.2007)

Companies	Authorities
Assess the risk to humans and the environment under their own responsibility, determine possibly necessary measures for the reduction of risk, apply such measures and pass on relevant information to downstream users. The objective is to guarantee safe use throughout the entire life cycle of a substance.	Reevaluation of selected risk assessments. Decide whether risk reduction measures are necessary that go beyond those applied by companies. Possible measures are restrictions on individual uses or authorization. A restriction can be effected if a substance poses an unacceptable risk to human health or the environment. For authorization, the authorities must identify the substance community wide in accordance with certain criteria as a substance of very high concern (SVHC).

In contrast to measures concerning food packaging products and storage containers (for example, bottles), in the case of articles such as dummies national bans cannot be enacted; at the most, more stringent upper limits can be imposed.

Until the introduction of far-reaching legal regulations, the product responsibility of manufacturers is particularly important. The debate on the risks of bisphenol A had the effect in the USA that the five largest manufacturers of baby bottles voluntarily renounced the use of polycarbonates. We propose that in discussions with manufacturers the attempt be made to achieve the same level of protection for small children, initially on a voluntary basis in Germany. The chances are not bad, since some of the American companies are also the largest suppliers in Germany.

Federal Environment Agency evaluation of risks to the environment

In the view of the Federal Environment Agency, the EU Risk Assessment Report, in accordance with the Regulation on Existing Substances, describes the risks of bisphenol A to the environment [5; 6], as well as the uncertainties associated with the assessment in the estimation of environmental concentrations and adverse effects on the reproductive system of different animals [72], in a well-founded and balanced manner. Due to uncertainties, available information does not at present enable final assessment of the risks to the environment; it does indicate, however, that the risk to the environment is probably underestimated.

In accordance with REACH, the responsibility now lies with manufacturers and users of bisphenol A. Their chemical safety assessment must cover, by 2010, all current uses and therefore go beyond the previous assessment in accordance with the EU Existing Substances Programme. In their chemical safety assessment companies must take into consideration the high measured environmental concentrations described in the Chapter „How does bisphenol A enter the environment", and clear up the related uncertainties documented by the United Kingdom. The effects on snails and fish must also be reevaluated as soon as new data becomes available.

As soon as the registration dossier is available, the Federal Environment Agency will check company results. Particular attention will be paid to the assessment of exposure, and to new data on bisphenol A and aquatic organisms. The Federal Environment Agency will then decide whether, from a scientific point of view, additional legal measures in accordance with the REACH Regulation are necessary for risk reduction and, where appropriate, propose such measures. The Federal Environment Agency advises manufacturers, importers and users of bisphenol A to replace potentially problematic products with safer alternatives. The objective must be to reduce the discharge of bisphenol A into the environment as far as possible.

Summary

Bisphenol A is found in many everyday products. The largest portion of manufactured bisphenol A is converted into stable plastics (polycarbonate and epoxy resins). Under certain conditions, the chemical can be released from consumer products – from can coatings, for instance – and enter the human body by way of food or through the skin, from thermal paper for example. In the human body the substance can act like the female sex hormone oestrogen.

Bisphenol A also enters into the water cycle and thus the bodies of aquatic organisms. Measurements in recent years have confirmed the presence of bisphenol A in many water bodies. The substance originates mainly from the wastewater treatment plants of companies that produce and process bisphenol A.

Is there a risk to humans and the environment? Are legal measures therefore necessary for protection against bisphenol A?

Numerous studies have shown that bisphenol A disrupts the hormonal system of mammals and aquatic organisms. There are analyses that prove that even in low concentrations the chemical has a negative effect on sexuality, and that also establish a connection with the occurrence of diabetes and respiratory illnesses. Moreover, there are indications that bisphenol A can influence the development of mental abilities and behaviour, as well as encourage aggression and hinder learning. The scientific findings that are presently available are, however, not without inconsistencies. Many studies are the subject of controversial debate among scientists.

Studies have also established that with certain animal species (snails, for example) bisphenol A, even in very low concentrations, disrupts reproduction. The evaluation of these results is contested, however, since many of the tests have methodical failings.

In accordance with Council Regulation (EEC) No. 793/93 on existing substances, and within the scope of the EU Existing Substances Programme, Member States have assessed the risk of bisphenol A for humans and the environment. The result was that the majority of Member States concluded that with proper use of products containing bisphenol A there was no cause for concern about health risks. The European Food Safety Authority (EFSA) also came to the same conclusion. However, not all EU countries came to such an unequivocal conclusion. Denmark and France, for instance, have enacted further precautionary measures for certain products, while Canada has banned baby bottles containing bisphenol A on precautionary grounds. From the point of view of the German Federal Environment Agency (UBA) there are sufficient grounds for concern. Numerous studies present on the whole a consistent picture, so that despite uncertainties and gaps in knowledge concerning risk assessment and the level of exposure there is a need for action. The UBA is therefore in favour of precautionary action and restrictions on the use of certain products that contain bisphenol A.

The EU also regards the risk to the environment as tolerable. Calculated concentrations in the environment are noticeably below the level at which effects on soil and aquatic organisms are to be expected. At the same time, different studies provide evidence that the risk to aquatic and sediment organisms has possibly been previously underestimated.

Under the terms of the European Chemicals Regulation REACH, manufacturers and users of bisphenol A are obliged to exercise their own responsibility. They have to describe the conditions under which bisphenol can be safely used over its entire life. Where necessary, they have to apply risk reduction measures for this purpose.

On the basis of such information the Federal Environment Agency will re-evaluate the assessment of risk to the environment from bisphenol A. The Federal Environment Agency will then decide whether from a scientific point of view additional legal measures are necessary, which should be recommended to the EU for risk reduction in the environment. At the same time, possible product-related regulations for consumer products should be considered. As a basic principle, the Federal Environment Agency recommends that the content of bisphenol A in products be further restricted. In addition, the Agency advises manufacturers, importers and users of bisphenol to use alternative substances that pose less risk to human health and the environment in all areas of use that significantly contribute to exposure. This way, an important contribution can be made to product responsibility in the case of a substance for which precautionary protection of humans and the environment is advisable.

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