Press Kit

Presentation of reports on the health effects and uses of bisphenol A

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Press Release

Bisphenol A: ANSES issues a call for contributions on substitute products to reduce exposure of the most susceptible populations

As part of its assessment of the risks associated with bisphenol A, ANSES is today publishing two reports: one on the health effects of bisphenol A and the other on its uses. This work highlights health effects that have been proven in animals and suspected in humans, even at low levels of exposure. These effects may also depend greatly on individuals being exposed during different phases of their development, which means that it may be possible to identify categories of people who are particularly vulnerable to bisphenol A. This work is one step in a continuing risk assessment process. The Agency considers, however, that it now has enough scientific evidence to be able to identify that the priority should be to prevent exposure of the most susceptible populations, such as infants, young children, and pregnant and breastfeeding women. This objective entails reducing exposure to bisphenol A, mainly by replacing it in the food contact materials that are the main source of exposure of these populations. In this context, the Agency is submitting the findings of its work for consultation and is issuing a call for contributions in order to collect, by the end of November 2011, any relevant scientific data concerning, in particular, the available substitutes and their safety and effectiveness.

ANSES's work falls within the scope of solicited requests from the authorities, dating from 2009 and 2010, on endocrine disruptors, including bisphenol A. The first stage of this expert appraisal consisted in identifying the various uses of bisphenol A while at the same time characterising all of its health effects. The reports published today are the tangible results of this first phase.
Based on an analysis of all the available scientific literature, the ANSES expert group found that there were proven effects in animals (effects on reproduction, effects on the mammary gland, effects on metabolism, the brain and behaviour) and other suspected effects in humans (effects on reproduction, the metabolism of sugars and fats, and cardiovascular diseases). These effects were demonstrated at doses that were significantly lower than the reference doses used for regulatory purposes, especially during certain periods of life characterised by susceptibility to the effects of bisphenol A (pregnancy, pre- and post-natal periods).

Concerning uses of the substance, ANSES notes that a very wide range of industry sectors have reported that they use bisphenol A. The manufacturing of polycarbonate plastic accounts for a large proportion of the applications, whereas another important share comes from the synthesis of epoxy resins, which are often used in food contact materials.

The Agency is continuing to assess human dietary and environmental exposure and to characterise the health risks of bisphenol A and the risks associated with other potential endocrine disruptors. On account of the complexity and scope of the questions raised, this expert

appraisal work is a long-term undertaking. Nevertheless, ANSES considers that it now has enough scientific evidence to confirm that the primary objective should be to reduce exposure of the most susceptible populations to bisphenol A. This objective requires that alternative substances or technologies whose safety has been demonstrated, be substituted for bisphenol A in items intended for these vulnerable populations (food contact materials, toys, childcare items, etc.).

In this context and in parallel with its ongoing investigations, the Agency has issued a call for contributions to first get feedback on the content and consequences of its work and secondly, to collect any scientific data, especially concerning the available substitutes, as well as data on their safety and effectiveness. This call for contributions runs until 30 November 2011, and the information it yields will be made public and analysed in detail by the Agency when drafting its recommendations, to be published in early 2012.

At the same time, the Agency has reiterated its 2010 recommendation, intended as a preventive measure, to provide the public with clear information in the form of systematic labelling of household utensils in contact with food and containing bisphenol A, that may lead to exposure.

Finally, the Agency will also communicate the results of this initial work on the health effects of bisphenol A to the relevant European authorities (EFSA, ECHA, etc.), to enable them to examine the relevance of a review of the reference doses used for regulatory purposes.

Contents:

ANSES and bisphenol A: a review of previous work

The Agency has been working on the issue of BPA since 2008. It has thus conducted several different assessments which led in 2010, to the publishing of three opinions together with **recommendations**:

- reduce exposure to BPA, especially for the most susceptible populations (children, pregnant women),
- improve consumer information through the systematic labelling of household utensils and containers in contact with food and containing BPA, in order to prevent their use for the excessive heating of food,
- encourage manufacturers to develop substitutes for BPA, products whose safety has been demonstrated for use with food.

Work in progress

Since then, ANSES has continued to investigate this substance and **is now working on a wide-ranging solicited request investigating fifty potential endocrine disruptors** (bisphenols, phthalates, parabens, perfluorinated compounds, brominated compounds, alkylphenols, etc.) and a second request specific to BPA.

A comprehensive study of endocrine disruptors

In 2009, the French Ministry of Health issued a request to various organisations (AFSSAPS, AFSSA, AFSSET, INSERM, InVS, INPES) asking them to investigate, in their respective spheres of competence, the issue of endocrine disruptors. INSERM was commissioned to undertake a collective expert assessment on the effects of substances known as "endocrine disruptors" on the reproductive system by collating and analysing all of the available scientific literature.

On the basis of the substances identified by INSERM as being of concern due to their reproductive toxicity and/or endocrine disruptor action, the Agency was requested to:

- rank the substances to be studied in order of priority,
- identify products and items containing substances toxic to reproduction or likely to be so (including endocrine disruptors),
- analyse and, if possible, quantify the routes of exposure of the general population to these substances. A specific analysis should be conducted of vulnerable populations and people exposed to these substances at work, through the use of products intended for the general public,
- conduct an assessment of the risks and benefits (expected health benefits of some products).

One of the objectives of this work is ultimately to identify possible substitutes for the products or substances for which a health risk has been determined, while ensuring that the potential alternatives have undergone a **risk assessment** prior to their authorisation for use.

The first phase conducted at the Agency involved screening uses to identify the chemicals to be studied in order of priority. This initial analysis led to the drawing-up of a list of 12 substances considered to be a priority. The Agency was responsible for identifying the uses to which **these substances are put,** by drawing on existing databases and industry surveys to ensure it had useful feedback from the field.

The substances which had been identified as priorities **are now being evaluated for their toxicity, along with quantifying of exposure and assessing of the risks involved.** This major project will lead to a series of risk assessment reports, each for a specific substance. It will last for several years, beginning in 2011 with bisphenol A. In 2012, reports addressing the other substances will gradually be published.
The overall work will involve international cooperation (notably with our counterparts in Germany and North America), in order to **develop new risk assessment methodologies** that are recognised internationally.

- **Bisphenol A, a textbook case**

As part of this project, ANSES has just published **two reports** on the **uses of BPA** and its **health effects**.
This work draws on the expert assessments already conducted by other national institutes, such as INSERM, and more generally on all the scientific publications and international studies on this major issue. These two reports conclude the first phase of the bisphenol A project conducted by the Agency.

ANSES will now be studying the feasibility and relevance of conducting a **health risk assessment** that takes into account all routes of exposure and uses (excluding health products). To this end, ANSES's experts have made a series of recommendations concerning methodological perspectives and research to be undertaken to facilitate risk assessment. Work is already underway to **characterise exposure** to bisphenol A via different media. Assaying of this substance in foods (samples from the Total Diet Study or specific foods such as jars of baby food, etc.), in water (bottled water and the public water supply), in the home environment (indoor air, dust, etc.), till receipts, etc. is being done or will be initiated by ANSES.

Specifically with regard to dietary exposure, a number of opinions and results of research studies on bisphenol A are expected at the international level (in particular from the FDA). The Agency is monitoring the issue closely in an effort to keep abreast of the latest scientific knowledge and regulations.
Finally, it should also be noted that ANSES is simultaneously **collecting information for a dossier on bisphenol A for its classification in the context of the European REACh Regulation** with a view to possibly restricting its use.

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French agency for food, environmental and occupational health & safety

List of works published by the Agency on bisphenol A

- 24/10/08: AFSSA Opinion regarding bisphenol A in polycarbonate baby bottles likely to be heated in microwave ovens
- 21/11/08: AFSSA Opinion regarding the exposure assessment of bisphenol A in water intended for human consumption and possible resulting health risks
- 07/07/09: Memo regarding the publication by Stahlhut *et al* (2009) on urinary elimination of bisphenol A in humans
- 29/01/10: AFSSA Opinion on the critical analysis of the results of a study of the toxicity of bisphenol A on the development of the nervous system together with other recently-published data on its toxic effects
- 02/03/10 AFSSA Opinion regarding clarification of the AFSSA Opinion on bisphenol A issued on 29 January 2010
- 31/05/10: Annex to AFSSA's Opinion dated 29 January 2010 on the critical analysis of the results of a developmental neurotoxicity study of bisphenol A together with other recently-published data on its toxic effects
- 07/06/2010: AFSSA Opinion regarding exposure to bisphenol A in the French population and maximum levels of bisphenol A in foods

Bisphenol A, what is it used for?

Bisphenol A (or BPA) is a synthetic chemical that has been used for over 50 years, **mainly for the manufacture of polycarbonate plastic and epoxy resins.**

It is also used in various resins (polyester, polysulfone and polyacrylate resins), plays a role in the synthesis of or as an additive in flame retardants, and is a developer in thermal papers.

In 2006, global production of bisphenol A came to approximately 3.8 million tonnes, two thirds of which was used for the **manufacture of polycarbonate** and one third for **resins**.

Facts/Key figures on BPA production

- In 2006, annual production of BPA was estimated at 3.8 million tonnes worldwide
- At European level, production was 1.6 million tonnes in 2005
- Between 2003 and 2006, consumption of BPA grew by around 10% annually, mainly due to the strong demand for polycarbonate
- No production of BPA has been recorded in France

Who uses bisphenol A and for what purposes?

The purpose of the industry survey conducted by ANSES as part of its investigation was to pinpoint more systematically the sectors and ultimately the consumer products and items concerned.

The survey identified nearly sixty sectors that potentially use bisphenol A in France, either from the literature study or the questionnaire sent to French manufacturers identified as possible users of this substance. They cover a wide range of activities from construction to aerospace, and include manufacturing of food containers and packaging, and coatings for metal containers.

This work also resulted in a non-exhaustive list being drawn up of the uses, items and preparations likely to contain bisphenol A (see Annex 1). A great number of objects and preparations have been identified: cables, sealants, adhesives, food grade containers and other containers, headlamp inserts, sporting goods, aviation parts, brake fluids, heat transfer fluids, electrical installation equipment, domestic appliances, medical devices and equipment, printing inks, etc.

The oral route of exposure is predominant. For vulnerable populations (pregnant women, nursing mothers and children), it is especially linked to use of products such as containers and coatings intended for food contact, toys and childcare items.

The issue of substitution

Although not exhaustive, ANSES's research has shown that a wide variety of industries and materials use BPA, and that consequently a wide range of consumer products and items were likely to contain it. It also shows that, owing to the current discussion about the effects of bisphenol A on health and the environment, researchers are attempting to find

alternatives. However, the initial review of the literature undertaken by the Agency shows that substitutes are always very specific depending on the substance, material, use or industrial process in question.

The Agency is continuing to look for alternatives, first in order to draw up a detailed list for each identified use and to get feedback from users about the success or failure of the substitute implemented (including international investigations), and secondly to ascertain their safety. Specifically in this regard, the Agency is issuing a call for contributions from the scientific community and stakeholders in order to gather any scientific data on the substitutes available, according to the different uses, and data on their safety and effectiveness. This information will be used by the Agency in its subsequent work.

Endocrine disruptors

In recent decades, epidemiological studies have shown a rise in various diseases affecting the reproductive organs as well as impaired fertility. In addition, over the last few years some scientists and stakeholders have expressed great concern about the health impact of potential endocrine disruptors found in the environment or in consumer products, and particularly bisphenol A. However, the precise role played by these substances, their modes of action, and their possible responsibility for the increase in diseases of the reproductive system and other systems, is still widely disputed and has been the subject of numerous international studies.

What are endocrine disruptors?

Endocrine disruptors are generally defined as chemical substances of natural or artificial origin, which may interfere with the functioning of the endocrine glands, the organs responsible for the secretion of hormones.

This may occur in different ways:

- The endocrine disruptor can mimic the action of a natural hormone, thereby causing the response due to this hormone
- The substance can prevent a hormone from binding to its receptor and thereby prevent transmission of the hormonal signal
- Finally, the substance can disrupt the production or regulation of hormones and their receptors.

Where do endocrine disruptors come from?

Endocrine disruptors may be of natural origin (hormones and phytoestrogens) or be due to human activities (crop treatment products, drugs, products from the chemical industry, etc.). They can therefore occur naturally or as a result of contamination in different media (water, food, consumer products or goods, etc.).

Ultimately, by disrupting the endocrine system, these substances can affect various processes such as the production, use and storage of energy and more generally regulation of the metabolism and development. Some of these substances may also have other toxic effects, including reprotoxic effects, and may impair fertility or affect foetal development.

What are the characteristics of these substances?

Many effects attributed to endocrine disruptors have been observed from experimental studies in animals and cannot easily be transposed to suspected effects in humans. In addition, in the current state of knowledge, **it is difficult to link the observed effects to currently known toxic mechanisms of action.** It therefore would appear that the effects of endocrine disruptors do not involve "traditional" mechanisms of toxicity (dysfunctions or cell death), but are linked to signalling and body regulation phenomena.

Furthermore, while the toxic effects of these substances at high doses have been clearly established by animal studies or the monitoring of populations exposed at work, **the question of their very long-term effects on human health at low doses still remains.**

The work conducted also shows that susceptibility to endocrine disruptors may vary according to specific periods in life. Thus, **certain groups** (pregnant women, infants, young children) **have increased susceptibility** to these substances and the period of exposure (window) to these substances must therefore be taken into account when analysing their effects.
Finally, various compounds suspected of being endocrine disruptors are found in the environment as trace elements. An individual is thus exposed via **multiple routes** (ingestion, inhalation, skin contact, etc.) and several media (water, food, consumer products or items, etc.) to very low doses of **several compounds** whose effects may vary and may also be the same as those of other causes.
Understanding the effects of endocrine disruptors therefore requires an overall view which places humans in their environment, but also takes into account the individual's exposure to a mixture of substances, as well as their interactions within the body over the long term.

Faced with this complexity, knowledge of the effects of endocrine disruptors at the doses found in the environment is at present hindered by current toxicology and risk assessment methodologies. The challenge is therefore to develop new ones, suited to the specificities of these compounds.

Mobilisation of the scientific community
At present, there are no **regulatory criteria** for identifying an endocrine disruptor. Various European authorities (EFSA[1], ECHA[2], European Commission) are working in conjunction with the authorities of the Member States to try to identify relevant criteria for classifying these substances.

At the international level, the OECD[3] has for several years been focusing on the **development of protocols for toxicological and ecotoxicological tests** to detect effects related to endocrine disruptors and thus identify the substances responsible. Similarly, the Agency is involved in ongoing discussions on the strategy of using these different tests to better understand the effects associated with these chemicals. In the United States, **the Tox 21 research programme** was undertaken on the basis of a report by the National Academy of Sciences[4]. Its objective is to identify the key toxicity pathways activated by a few thousand compounds and to ultimately be able to reason in terms of activated toxicity pathways (around twenty) instead of chemical compounds taken in isolation (more than 100,000 substances in existence).

[1] European Food Safety Authority
[2] European Chemicals Agency
[3] Organisation for Economic Cooperation and Development
[4] *Toxicity testing in the twenty-first century: a vision and a strategy,* http://www.nap.edu/catalog/11970.html

ANSES, a new player in health and safety

The French Agency for Food, Environmental and Occupational Health & Safety was created on 1 July 2010 through the merger of two French health agencies: AFSSA (the French Food Safety Agency) and AFSSET (the French Agency for Environmental and Occupational Health Safety). By incorporating their respective missions, ANSES now provides a cross-functional perspective on health issues and can identify, overall, the risks to which people are exposed through their lifestyles and consumption patterns, or the characteristics of their environment, including in the workplace.

Protecting human, animal and plant health

In terms of human health, ANSES covers three fields: food, the environment and the workplace. Its mission is also to assess risks to animal and plant health. On the basis of its scientific reports, it draws up opinions and recommendations for the authorities.

Ensuring food safety and quality

The Agency assesses health and nutritional risks throughout the agri-food sector. It evaluates the nutritional properties of substances in food and feed, as well as the concomitant benefits. It monitors eating habits and trends, and identifies those groups of people who are most at risk. Lastly, it assesses the health quality of water intended for consumption.

Assessing health risks related to the environment

Health and the environment are closely related. ANSES assesses the impact of the environment on human health, so as to better identify health risks related to pollution of the human environment (air, water, soil). It covers several topics: cancer and the environment, exposure to biological, chemical and physical agents, regulations on the use of hazardous chemicals, etc.

Assessing health risks in the workplace

At present, there is increasing concern about exposure to occupational diseases and deferred risks related to chemicals such as those found in nanomaterials or asbestos. ANSES is studying the mechanisms of exposure in the workplace and the health risks specific to different professions, through innovative evaluation methods and tools. Within the National Network for Monitoring and Prevention of Occupational Diseases (RNV3P), ANSES is actively furthering knowledge of hazards and exposure in the workplace, as well as the definition of vigilance strategies.

Annexes

Annex 1: Summary of items and preparations likely to contain BPA

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This table provides a summary of the items and preparations likely to contain BPA. It concerns polymers, resins and other compounds synthesised from bisphenol A.

Use	Category of items or preparations likely to contain BPA
Polycarbonates used in the manufacture of optical media	Blank optical media (CDs, DVDs, etc.)
Polycarbonates used in the manufacture of optical equipment	Contact lenses; glasses made from all materials
	Prescription glasses, protective or other
Polycarbonates used in the manufacture of tableware	Crockery, other tableware and household and toiletry items, other than porcelain
Polycarbonates used in the manufacture of food containers	Food containers and packaging (plates, cups, flasks, etc.)
	Demijohns, bottles, flasks and similar plastic items
Polycarbonates and epoxy resins used in the manufacture of domestic appliances	Domestic appliances (Hair dryers, microwaves, kettles, etc.)
Polycarbonate, polyarylate resins, polysulfone resins, polyether imide resins used in the manufacture of medical equipment and dental products	Medical and dental instruments and supplies (blood oxygenators, respirators, dialysers, incubators, breathing apparatuses, disposable instruments, autoclaves, surgical lighting systems)
Polycarbonate, polysulfone resins, polyetherimide resins used in the manufacture of electrical equipment	Electrical installation equipment
Polycarbonate used in the manufacture of transparent films	Plastic plates, sheets, tapes and strips, not fitted with a support or similarly combined with other materials
Polycarbonate used in the manufacture of protective equipment	Safety helmets and other safety products
Polycarbonate, epoxy resins, vinyl ester resins, unsaturated polyester resins used in the manufacture of sporting goods	Sporting goods
Polycarbonate used in the construction of roofs of sports facilities	Sports or recreational facilities
Polycarbonate, epoxy resins, vinyl ester resins, unsaturated polyester resins, polyols, polysulfone resins, polyether imide resins used in the manufacture of automobile parts Bisphenol A used in the manufacture of brake fluid and tyres	Motor vehicles (tyres, safety glazing, light reflectors, headlamp inserts, bumpers, radiator and ventilation grilles, interior lighting systems, motorcycle windshields and helmets, car roof modules, etc.)

Use	Category of items or preparations likely to contain BPA
Polycarbonate, epoxy resins, modified polyamide, polysulfone resins, polyether imide resins used in electrical and electronic applications Tetrabromo Bisphenol A used in printed circuits	Computer, electronic and optical products
Epoxy resins, vinyl ester resins used in flooring (buildings)	Plastic flooring, in rolls or tiles
	Linoleum and hard flooring with non-plastic surfaces, resilient floor coverings such as vinyl, linoleum, etc.
Epoxy resins used in coatings for tins and cans	Food containers and packaging
Epoxy resins, vinyl ester resins used in surface coatings of metal containers	Metal tanks, reservoirs and containers
Epoxy resins used in coatings for tubes and pipes	Steel tubes, pipes, hollow profiles and related accessories
Epoxy resins used in the construction of metal panels	Sandwich panels in coated steel plate
Epoxy resins, vinyl ester resins, unsaturated polyester resins used in concrete or concrete structures	Concrete parts/structures for construction
	Systems/circuits for fluids
Epoxy resins, phenolic resins used in the manufacture of glues, adhesives, etc.	Glue/adhesive/sealant/related products
Epoxy resins used in the manufacture of mastic	Mastic
Production of epoxy resins	Resins
Epoxy resins, ethoxylated bisphenol A used in the production of inks	Printing and reproduction products

Use	Category of items or preparations likely to contain BPA
Phenolic resins, unsaturated polyester resins, polyols, ethoxylated bisphenol A used as binders, plasticisers, paint hardeners, lacquers and other fillers	Paint/varnish/enamel/stain and associated products
Epoxy resins, vinyl ester resins, unsaturated polyester resins, polysulfone resins, polyetherimide resins used in aeronautical construction	Aerospace constructions
Epoxy resins, vinyl ester resins, unsaturated polyester resins used in the manufacture of boats	Ships and floating structures
	Pleasure boats
Epoxy resins, phenolic resins used in the manufacture of wood panels	Veneer and wood panels
Epoxy resins used in the manufacture of tools	Tools
Epoxy resins, ethoxylated bisphenol A used in the manufacture of varnish	Varnish/lacquer for wood flooring
	Non-water-soluble varnish/lacquer for wood flooring
Epoxy resins used in the manufacture of glass fibre	Fibreglass
Vinyl ester resins used in fibre optic media	Optical fibre cables
Vinyl ester resins used in gas cylinders	Metal containers for compressed or liquefied gas
Phenolic resins used in insulation	Sealant and insulation products
Phenolic resins used in abrasives	Abrasive/polishing products
Phenolic resins used in friction materials	Friction linings for brakes, clutches and related products
Phenolic resins used in the paper industry Bisphenol A used in the manufacture of thermal paper	Paper and cardboard
Polyols used in the production of polyurethane	Polyurethane foam
Bisphenol A used in the manufacture of resin-based composite materials for restoration and sealing for dental use	Adjuvants for medical prostheses (cement, glue)
Bisphenol A used in the composition of lubricants	Lubricant
Bisphenol A used in the composition of heat transfer fluids	Heat transfer fluids