Factsheet on Bisphenol A (BPA)

What is BPA?
Bisphenol A (BPA) is an industrial chemical used to make one type of polycarbonate plastic and certain types of epoxy resins. These plastics are found in many products, such as refillable beverage containers, protective linings in food cans, compact disks, plastic dinnerware, impact resistant safety equipment and epoxy resins. Source: CDC

How can a person be exposed to BPA?
General population exposure (99%) is by eating food or drinking beverages that contain trace amounts of BPA.

What research has been conducted on BPA?
Thousands of studies have examined the impact of BPA to determine its effects in laboratory animals. Researchers have performed these studies using both oral and injected doses of BPA. It is important to distinguish between these two methods of administration as research has shown that the toxicity of BPA differs greatly depending on whether the chemical is administered orally or injected. Different things happen to the chemical depending on how it makes its way into and through the body.

For example, when BPA is administered to laboratory animals orally, the chemical first passes through the gastrointestinal (GI) tract to the liver where it is conjugated (combined) with glucuronic acid, rendering it pharmacologically inactive and converting it to a very water soluble compound that is readily excreted in the urine. Therefore, when administered orally, BPA generally leaves the body without significant circulation in the blood stream.

On the other hand, when BPA is administered to laboratory animals by injection it enters the blood stream directly, does not pass directly through the GI tract or the liver, is not rendered pharmacologically inactive, and can circulate in the blood stream for a significant period of time before reaching the liver to be conjugated and excreted.

Because 99% of the general population's exposure to BPA is through oral ingestion of food or beverages, as opposed to being injected, studies involving the oral route of administration are a more appropriate indicator of BPA's toxicity.

What is NSF International and what role has NSF played in regard to BPA?
NSF International is an independent, not-for-profit public health organization that works with public health officials, regulators, academia, scientists, industry and consumer groups to develop national standards to protect the public heath in the areas of food, water and indoor air safety. NSF International also tests and certifies products to make sure they meet these standards. NSF is a World Health Organization Collaborating Centre for Food and Water Safety and Indoor Environment.

Included among the public health standards that NSF International helped develop are NSF/ANSI Standards 60 and 61, which set limits for any material/product coming into contact with drinking water.

NSF/ANSI Standard 60: Drinking Water Treatment Chemicals is the nationally-recognized health effects standard for chemicals used to treat drinking water.

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NSF/ANSI Standard 61: Drinking Water System Components is the nationally-recognized health effects standard for all devices, components and materials that come in contact with drinking water.

These standards were approved by the American National Standards Institute (ANSI) and are now the national standards for drinking water. ANSI coordinates the development of standards in the U.S. and is the U.S. member of the International Organization for Standardization (ISO). Many states require that manufacturers who make products that come into contact with food or water be tested to verify that their products meet these standards. The manufacturers must pay the costs associated with testing and certification. NSF is an ANSI-accredited, third-party that evaluates chemicals and products for toxicological safety and verifies that they meet the NSF/ANSI Standards.

NSF takes its public health mission very seriously. Our standards, methods and procedures are very rigorous and products that do not meet the standards are not certified. (ANSI and other accrediting bodies conduct thorough audits of NSF and our laboratories to ensure proper procedures are followed.)

In 1988, the U.S. Environmental Protection Agency (EPA) replaced its own drinking water additives program with NSF/ANSI Standards 60 and 61, which set public health standards for all chemicals used to treat water and products coming into contact with drinking water (including, but not limited to, faucets, meters, pipe, valves and tank liners).

It is because of the Drinking Water Additives program that NSF International tests for BPA in any component that may contact drinking water, and one of the many types of materials that NSF International evaluates is polycarbonates.

As part of the evaluation process, NSF International utilizes EPA- or FDA- established maximum allowable levels (MAL) to verify consumers are not being exposed to levels of a chemical that exceed regulated levels.

In cases where there are no existing federal levels, NSF International may develop criteria for product evaluations. Since there are no federal drinking water Health Advisory or Maximum Contaminant Level (MCL) values for BPA, NSF conducted the BPA risk assessment to develop drinking water standards for use in the certification and testing program.

NSF International asked Dr. Calvin Willhite, an internationally-known toxicologist with expertise in reproductive and developmental toxicology, to review the scientific literature on BPA along with two NSF toxicologists. NSF International follows National Academy of Science and EPA protocols in their Human Health Risk Assessment program.

It took NSF International more than a year to review and summarize the literature and derive an oral dose for BPA. The BPA risk assessment incorporated approximately 400 published papers on the toxicology of BPA and calculated an oral reference dose for BPA. NSF's human health risk assessment on BPA (the oral reference dose) was peer-reviewed by several members of NSF's Health Advisory Board, an independent, unpaid volunteer group of toxicologists who serve as an advisory board to provide NSF's own toxicologists with additional scientific advice and expertise. (Because Dr. Willhite also is a member of the NSF Health Advisory Board, he did not participate in the peer review of the risk assessment.)

Subsequently, Dr. Willhite and the two toxicologists who prepared the BPA risk assessment submitted to the Journal of Toxicology and Environmental Health, a publication that focuses on toxicological and environmental issues and publishes large reviews of this nature. The Journal article was peer-reviewed by five anonymous scientists selected by the Journal's editor, and the editor himself, prior to publication.

A copy of that article is available at the Journal of Toxicology and Environmental Health: http://www.informaworld.com/smpp/content~content=a789485048~db=all~order=page.

What is a risk assessment?
A risk assessment identifies key studies and critical toxicological effects for the chemical, selects appropriate uncertainty factors, and calculates an oral reference dose (RfD) following U.S. EPA guidelines. The RfD is the amount that could be taken orally without causing a risk to human health.

Why did NSF conduct this risk assessment on BPA?
NSF conducted its BPA risk assessment to develop drinking water standards for use in NSF's certification and testing program as there were no Federal drinking water Health Advisory or Maximum Contaminant Level (MCL) values for BPA at that time.

Who conducted the NSF risk assessment on BPA?
The BPA risk assessment was developed by:

- Calvin C. Willhite, Ph.D., NSF International Consultant
- Gwendolyn L. Ball, Ph.D., NSF Senior Toxicologist II
- Clifton J. McLellan, M.S., NSF Director of Toxicology

Dr. Calvin Willhite holds a Ph.D. in pharmacology from Dartmouth Medical School, a M.S. in toxicology from Utah State University, and has numerous professional and scientific affiliations, including the National Toxicology Program, National Academy of Sciences and U.S. EPA appointments to advisory boards. Dr. Willhite is a member of the Department of Health and Human Service's National Toxicology Program's Scientific Advisory Committee, and has served as an expert panelist for their Center for the Evaluation of Risk to Human Reproduction (CERHR). Dr. Willhite has editorial appointments with many leading toxicology publications: *Toxicology and Applied Pharmacological Toxicology*, *Toxicology Letters* and *Reproductive Toxicology.*

Dr. Willhite, who is a senior toxicologist for the State of California's Department of Toxic Substances Control (DTSC), was contracted by NSF to conduct the review with two other NSF toxicologists because of his expertise in reproductive and developmental toxicology.

It should also be noted that Willhite asked the DTSC Legal Office, to approve his work with NSF prior to beginning it, and the DTSC said there was no conflict of interest.

What were NSF's findings as a result of the risk assessment on BPA?
NSF International reviewed the scientific literature on BPA, following National Academy of Science and EPA protocols in their Human Health Risk Assessment program. The risk assessment incorporated approximately 400 published scientific papers and studies on the toxicology of BPA that had been published through the third quarter of 2007. It took NSF more than a year to review and summarize the scientific literature and derive an oral dose for BPA.

In order to understand the pharmacology of BPA, it is important that the concept of exposure be explained very clearly. With BPA, the ingested dose (called administered dose by toxicologists) is only the first step. The ingested BPA is metabolized in the intestinal cells then in the liver to the pharmacologically-inactive glucuronide conjugate. The conjugate is then excreted in the urine and 100 percent of the ingested BPA can be accounted for as the inactive metabolite. These factors are called the "absorbed" and "metabolized" doses, respectively.

Thus, the administered dose is not as important to the oral risk assessment for BPA as the absorbed and the metabolized doses since it is the ER agonist activities of free BPA that constitute the clearly established biochemical mode of action. However, when BPA is administered by injection, it enters the blood stream directly and because it does not pass

through the GI tract or the liver in the same way, glucuronide conjugation is precluded or reduced substantially.

To further clarify, thousands of studies have examined the impact of BPA to determine its effects in laboratory animals. Researchers have performed these studies using both oral and injected doses of BPA. It is important to distinguish between these two methods of administration as research has shown that the toxicity of BPA differs greatly depending on whether the chemical is administered orally or injected. Different things happen to the chemical depending on how it makes its way into and through the body. When BPA is administered to laboratory animals by injection it enters the blood stream directly, does not pass directly through the GI tract or the liver, is not rendered pharmacologically inactive, and can circulate in the blood stream for a significant period of time before reaching the liver to be conjugated and excreted.

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Because 99% of the general population's exposure to BPA is through oral ingestion of food or beverages, as opposed to being injected, studies involving the oral route of administration are a more appropriate indicator of BPA's toxicity.

Check out the KGO-TV San Francisco Segment explaining this in more detail.

What did NSF's risk assessment conclude?
From the risk assessment, NSF calculated an oral reference dose (RfD) for BPA. It's the number, which determines if there is a negative health effect. It is also the number, which is the basis to determine the pass/fail criteria for various products evaluated under NSF Standards 60 and 61. An oral reference dose can be converted to drinking water action levels, which is then used to calculate a drinking water standard used to evaluate products that come in contact with drinking water. A relative source contribution of 20% was used in deriving the action levels, so that drinking water exposure would not exceed 20% of the RfD, to allow for food and other non-water sources of oral exposure. (*There is a list of helpful definitions at the bottom of this fact sheet.)

The oral RfD of 0.02 mg/kg-day and drinking water level of 100 mcg/L derived using the Tyl (2002; 2008) multi-generation reproduction studies are protective of public health.

The oral RfD derived by NSF is similar to the IRIS (Integrated Risk Information System) (1988) oral RfD of 0.05 mg/kg-day that was based on reduced mean body weight in the rat lifetime chronic oral bioassay.

Source: Derivation of a Bisphenol A (BPA) Oral Reference Dose (RfD) and Drinking Water Equivalent Concentration. Presentation Dr. Gwendolyn Ball

A Simple Comparison: For example, the oral exposure to BPA in NSF's reference dose equals 100 parts per billion (or mcg/liter). (Or approximately 1 teaspoon in an average 16,000 gallon residential in ground swimming pool.)

What did the Journal of Toxicology and Environmental Health article conclude:
"There was no clear indication from the available data reviewed that the BPA doses normally consumed by humans pose an increase risk of immunologic or neurologic disease.
There was no evidence that BPA poses a genotoxic or carcinogenic risk."

Source: *Journal of Toxicology and Environmental Health Volume 11, pages 69 -146, February 2008.*

When was the Journal of Toxicology and Environmental Health Article published?
A peer-reviewed article on the risk assessment was published in the February 2008 issue of the Journal of Toxicology and Environmental Health. Dr. Willhite and the two NSF staff toxicologists who prepared the BPA risk assessment submitted an article on the risk assessment to the Journal of Toxicology and Environmental Health, a publication that focuses on toxicological and environmental issues and publishes large reviews of this nature. The assessment was peer-reviewed by a team of five anonymous scientists who were selected by the Journal, along with the Journal's editors. Dr. Willhite had no input into the peer-review process. Comments from these Journal reviewers were incorporated into the article, following that review. The article is available at:
http://www.informaworld.com/smpp/content~content=a789485048~db=all~order=page.

Who funded NSF's human health risk assessment on BPA?
NSF International, a not-for-profit public health and safety organization, fully funded the risk assessment on BPA. Neither Dr. Willhite nor NSF received any compensation whatsoever from any industry, trade association or any other organization to conduct the human health risk assessment on BPA. NSF International received no external funding for this risk assessment, including no funding or compensation in any form from any US or foreign government or agency, consumer or environmental advocacy group or industry or industry trade association.

How often are risk assessments reviewed?
Risk assessments are reviewed on a periodic basis. For chemicals with adopted criteria, a review occurs approximately every five years as new information is identified, which may alter the acceptance criteria.

Where can I learn more about BPA?
Check out this ABC segment

***Helpful Definitions:**
Reference Dose (RfD): An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a No-Observed-Adverse-Effect Level (NOAEL), a Lowest-Observed-Adverse-Effect Level (LOAEL) or a benchmark dose, with uncertainty factors generally applied to reflect limitations of the data used. It is generally used in EPA's noncancerous health assessments. Source: EPA
http://www.epa.gov/ncea/iris/help_gloss.htm#r

No-Observed-Adverse-Effect Level (NOAEL): The highest exposure level at which there are no biologically significant increases in the frequency or severity of adverse effect between the exposed population and its appropriate control; some effects may be produced at this level, but they are not considered adverse or precursors of adverse effects.
Source EPA: http://www.epa.gov/ncea/iris/help_gloss.htm#r

Lowest-Observed-Adverse-Effect Level (LOAEL): The lowest exposure level at which there are biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control group.
Source EPA: http://www.epa.gov/ncea/iris/help_gloss.htm#r