CLARITY-BPA: BPA SAFETY CONFIRMED IN LARGEST EVER STUDY

Bisphenol A (BPA) is safe for consumers – that is the overall outcome of the core "CLARITY-BPA" study, the largest-ever scientific investigation on the basic chemical building block used to produce the high-performance materials polycarbonates and epoxy resins.

CLARITY – **C**onsortium **L**inking **A**cademic and **R**egulatory **I**nsights on BPA **T**oxicit**y** – is a large-scale US study program on BPA. It has been conducted by a consortium of US government scientists[1] and several specialized academic research groups, and is fully funded by US government institutes.

BPA is already one of the best researched industrial chemicals. Many comprehensive guideline studies respecting Good Laboratory Practices (GLP) are available, as well as an enormous amount of exploratory studies which are often not GLP-compliant. Some of these question the safety of BPA for human health.

CLARITY-BPA now merges elements of proven guideline compliant study protocols with the exploratory approach of academia to generate new scientific insight into hotly debated areas of potential concern, such as alleged adverse hormonal effects of BPA or the so-called low-dose hypothesis.
CLARITY-BPA has two components:

- chronic (lifetime) guideline compliant toxicity study conducted by FDA scientists (core study), and
- 14 grants to academics using in their studies samples from the chronic study to test their hypotheses (grantee studies)

"Our initial review supports our determination that currently authorized uses of BPA continue to be safe for consumers."

Dr. Steven Ostroff, Deputy Commissioner for Foods and Veterinary Medicine, US Food and Drug Administration (FDA)

INDEPENDENT, TRANSPARENT, UNPRECEDENTED

- **Capstone of 10 years multi million $ US government research program**
- **Fully authority funded**
- **Focus on debated endpoints**
- **Involvement of academic researchers**
- **Coded samples to avoid research bias**
- **High statistical power**
- **All raw data publically available**
- **Scientific review process with public hearing**

More info: https://ntp.niehs.nih.gov/whatwestudy/topics/bpa/index.html

The core chronic study specifically investigated the areas in which there is continuous debate about the interpretation of available data. With respect to low dose exposure in particular, it found

- **no biologically relevant health effects from low dose exposure to BPA**
- **no evidence of non-monotonic dose-responses, often referred to as "low dose effects"**
- **no evidence of endocrine disruption**
- **no evidence of effects from developmental exposure to BPA later in life**

Re-Assessment of BPA in Europe

EFSA has started a re-evaluation of the safety of BPA for food contact applications in 2017. The re-evaluation process assesses the newly generated scientific information since 2013. The results of the CLARITY-BPA core study and of the grantee studies will form an important piece of the re-evaluation process.

What happened?

September 2018:
- core chronic study final report[2]
- raw data release of academic grantee studies

October 2019:
publication of the core chronic study in scientific journal "Food and Chemical Toxicology" https://doi.org/10.1016/j.fct.2019.110728

What comes next?

2020
final integrated CLARITY-BPA report expected

2020/21:
EFSA re-assessment on BPA expected

[1] from National Toxicology Program (NTP), National Institute of Environmental Health Sciences (NIEHS), FDA's National Center for Toxicological Research (NCTR)

[2] NTP CLARITY-BPA core study report: https://ntp.niehs.nih.gov/results/pubs/rr/reports/abstracts/rr09/index.html

Documentation of peer review meeting available on-line: https://ntp.niehs.nih.gov/about/org/sep/rrprp/past/index.html

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PlasticsEurope
Association of Plastics Manufacturers
Polycarbonate/Bisphenol A Group

www.bisphenol-a-europe.org

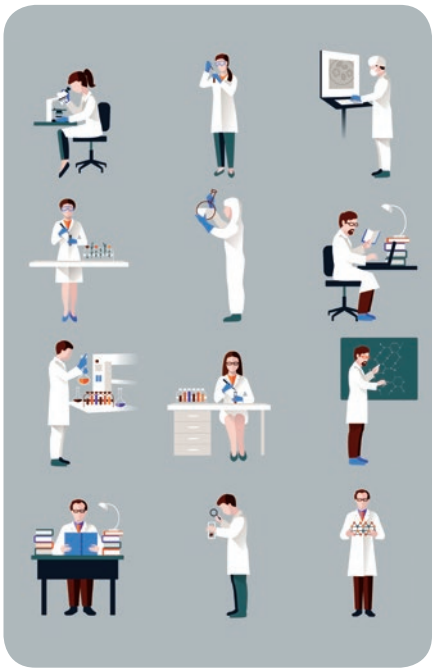
CLARITY-BPA:
UNPRECEDENTED REGIME, SCOPE AND MAGNITUDE

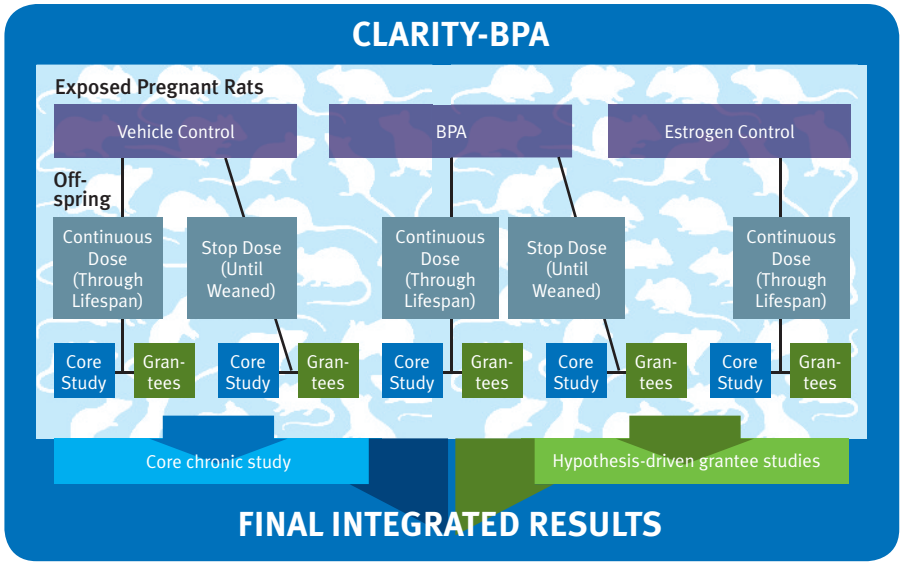
CLARITY-BPA is the capstone study program completing a long-term research effort of the US government to determine the safety of BPA for human health. The goal of the US goverment was to evaluate certain health parameters, which have been reported to be adversely impacted by BPA exposure in hypothesis-driven studies. To ensure utmost reliability, all scientists worked on samples treated in exactly the same way, and the core chronic study was conducted according to GLP principles.

Study essentials

Three groups of pregnant rats (vehicle control group[1], BPA-exposed, estrogen-exposed) were used in the study. In the BPA-group the mother animals and their offspring were exposed to different doses of BPA, either on a continuous dose throughout their whole lifespan, or by "stop-dose", i.e. until weaning. Various target tissues were examined, for example from the brain, heart, kidneys, liver, mammary gland, ovaries, prostate, testis, thymus, thyroid, uterus, and many more.

- The Continuous Dose exposure during pregnancy through offspring's whole lifespan is directly relevant for human exposure and safety assessment
- The Stop Dose exposure during pregnancy through offspring weaning investigates whether developmental exposure shows adverse effects later in life
- 5 dose levels (2.5 to 25,000 micrograms/kg bodyweight/day) covering a wide span from low doses close to actual human exposure, to doses about 250,000 times higher, focused on examining whether effects at low doses and/or non-monotonic dose-responses[2] could be seen
- The estrogen control (two different doses of ethinylestradiol) served to validate the sensitivity of animals so the animals' response to a classic estrogen could be compared with response to BPA





Academic research – more publications to come

Fourteen academic researchers, including several of those who in the past published results claiming to see various effects of BPA, received animals or tissue samples from the CLARITY chronic study to conduct hypothesis-driven studies.

To minimise potential bias, an elaborate procedure of coding and "blinding" was applied to the test samples. Only after test animals and/or tissue samples had been evaluated and the raw data were uploaded to the NTP database, the respective treatment scheme of the samples was decoded to then enable scientific analysis and interpretation. The testing phase of the grantee studies was completed end of 2014.

To date, findings from 10 out of 14 grantee studies have been released. The raw data from all grantee studies are publicly available since September 2018.

Overall, the core chronic study found that BPA is safe at typical consumer exposure levels.

The results from the core chronic study indicate that BPA has very little potential to cause health effects even when people are exposed to it throughout their lives. The study's Principal Investigator Dr Barry Delclos stated in a webinar in which the study results were discussed in detail that "BPA did not elicit clear, biologically plausible, adverse effects …" at levels even remotely close to typical, very low consumer exposure levels.

[1] vehicle control group = animals exposed only to the solvent used in the study, not containing any test substance (such as BPA).

[2] Typical dose-response curves are monotonic, meaning a greater response is observed as the dose increases ("The dose makes the poison"). Non-monotonic dose response (NMDR) curves change direction as the exposure dose increases i.e. creating unusual curves, such as "U" or "inverted U" shapes.

More information on BPA:

Jasmin Bird
Polycarbonate/Bisphenol-A Group PlasticsEurope
Email: jasmin.bird.consultant@plasticseurope.org

PlasticsEurope
Association of Plastics Manufacturers
Polycarbonate/Bisphenol A Group
www.bisphenol-a-europe.org