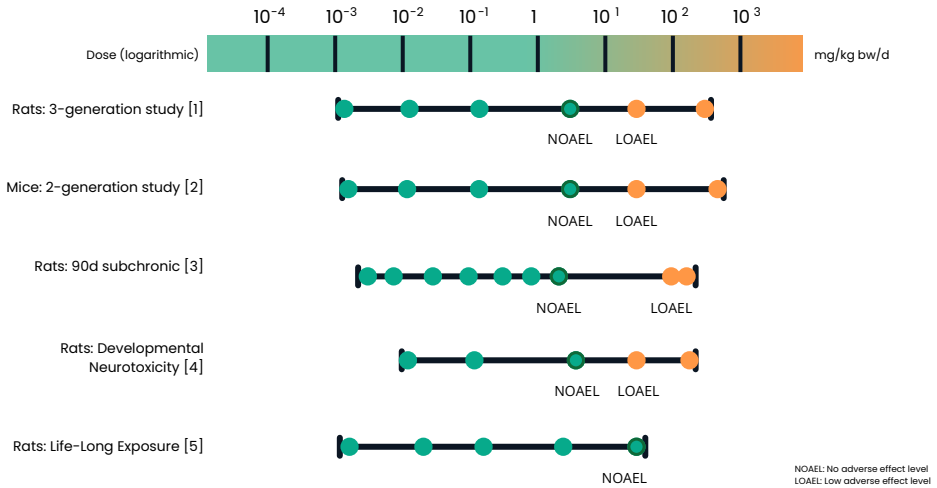
There is a threshold for Bisphenol A

- High-quality studies show that a clear threshold for BPA can be derived below which no adverse effects occur.
- BPA acts through receptor-mediated mechanisms, which have a threshold mode of action. There is no clear evidence of a non-monotonic dose-response (NMDR) relationship for the effects of BPA.

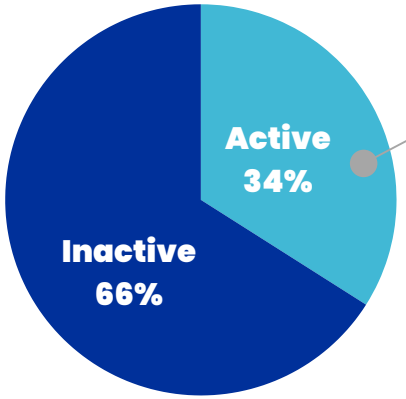
Together, the available data indicate that it is possible to identify a threshold for BPA toxicity.

A clear threshold for BPA in high-quality studies



High-quality studies conducted in rodents indicate a clear threshold for BPA toxicity above a no-observable-adverse-effect-level (NOAEL) range of 5-25 mg/kg bw/d BPA. [1,2,3,4,5] Reproductive and developmental effects, such as effects on fertility occur at high doses of BPA only and are accompanied by systemic toxicity. Below these thresholds no treatment related effects were observed. Developmental metabolic effects, neurotoxicity and immunotoxicity were not observed at any dose of BPA in these or other high-quality studies. [6,7,8,9,10,11,12]

BPA is active in 34% of ToxCast assays identified as having "receptor" or "receptor binding" as the assay target.



Receptor-mediated Assays with BPA Activity in ToxCast Database

- Androgen receptor in SRC non-receptor tyrosine kinases
- Constitutive androstane receptor
- Farnesoid X receptor and SRC non-receptor tyrosine kinases
- G protein-coupled receptor
- Glococorticoid receptor
- Glutamate receptor
- Mineralocorticoid receptor
- Peroxisome proliferator-activated receptor
- Pregnane X receptor
- Progesterone receptor
- Receptor tyrosine kinases
- Sigma non-opioid intracellular receptor
- Sodium channel receptor

The ToxCast project is a high-throughput chemical screening program by the US EPA developed to identify *in vitro* assays and responses that are relevant to *in vivo* toxicity. Data from EU EPA ToxCast indicate that BPA is an estrogen receptor agonist and is active in multiple receptor-mediated assays [13]; such ligand-receptor mechanisms are indicative of a threshold mode of action. The European Safety Authority (EFSA) found no clear indication of a NMDR relationship for BPA across multiple endpoints, indicating that BPA does not cause adverse effects at low doses that are not caused at higher doses. EFSA stated that the available data do not suggest that NMDR relationships are relevant for the risk assessment of BPA. [14]

Polycarbonate
Bisphenol A
Product Group of Plastics Europe

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