Bisphenol A –contested science, divergent safety evaluations

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The first known endocrine disruptor: early warnings

1934: Dodds & Lawson

Searching for synthetic chemicals that could replace expensive natural estrogen in pharmacologycal applications

1936: Diethystilbestrol (DES)

A growing problem

2006: 3.8 million tonnes worldwide

1.15 million consumed in the EU

Polycarbonate

Epoxy resins

Thermal papers

Recycled papers

Commercial BPA contains 16 impurities

Leaching from plastic

Recycling code 7

Dental sealants

Food containers

EU: 3 mg/kg limit in Food

Nightmare for analytical chemist: labware

Identifying the risk was an accident, nor the result of a regulatory process

1991: Wingspread Racine/Endocrine Disruptors

1993: BPA leaching from polycarbonate flasks

David Felmand (Stanford Univ)

1996: Our Stolen future

It was basically an accident; we were not looking for it. We study receptors for steroid hormones like estrogen, and wondered if they had originally evolved in yeast. Although that turned out not to be the case, we were looking for both receptors and hormones when we found what looked like an estrogenic molecule in the yeast tissue culture medium we grew the yeast in. However, the medium had been sterilized by autoclaving (a process that involves very high heat and pressure) in "autoclavable" polycarbonate flasks.

We identified the estrogenic molecule as BPA using mass spectrometry, and discovered it was present even in samples of pure water that had been autoclaved in the flasks. At that point we realized that we had identified a molecule that was leaching out of the plastic that, because of its estrogenic hormonelike properties, had the potential to be important and perhaps even dangerous to people who were eating or drinking out of containers made of this type of plastic, polycarbonate. Since polycarbonate has so many uses as a clear and strong plastic, it is ubiquitous in packaging food and beverages, and epoxy resin is used in lining metal cans.

Bisphenol beyond Paracelsus

All things are poison and nothing is poison, only dose permits something not to be poisonous.

BPA like natural hormones frequenttly produces dose-response curves that are non-linear. These doe-response curves resemble an upside-down U

Maybe the results of two or more effects with different dose-response characteristics

This kind of curve is much more than a curiosity, it challenge Paracelsus paradigma

The time makes the poison

Not only the chemical characteristics and the internal dose are important but also the exact timing of stimulus

The time of exposure is not necessarily the time when the effects can be detected (spermatogenesis, ovarian ciclycity breast cancer…)

Concern or not concern: that is the question

The complexity of the exposure assessment, the toxicologycal profile of BPA and the probably the high economic importance of this substance may have contributed to the fact that risk assessment for this substance differ more markedly that for any other chemical

BPA Reviews and Risk assessment

- EFSA and EU risk assessment
- EU Risk assessment Report (RAR)
- The NTP of the USA
- Environment Canada and Health Canada
- The Chapel Hill Consensus Statement
- The US Food and Drug Administration
- European Food Safety Authority 201
- The German Federal Environment Agency
- The French Agency for Food ANSES

BPA Reviews and Risk assessment

Regulatory Agencies have used Good Laboratory Practice (GLP) guideline studies as the only source of data on the toxicity of BPA

EFSA has systematically dismissed low dose studies on BPA because:

- Only one or two doses tested
- Low number of animals
- Inadequate processing of data
- Result not consistent with other studies.

BPA in Human Bodies

Little controversy about the external exposure of humans to BPA

Estimates of daily intake

Biomonitoring

Discrepancies: Only free-BPA is important

Pharmacokinetics

Spheres of Influence

The question arises whether BPA-producing industries had previously influenced the assessment processes

Some examples:

The Weinberg Group

EFSA

Lessons to be learned

Best Science and transparency
Precaution
Towards more independent Science