



Polycarbonate Safety in Medical Applications: Bisphenol A & Recent Findings

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BPA History and Applications: *A Brief Overview*

- Bisphenol A (BPA) is used primarily to manufacture clear, shatter-resistant polycarbonate plastic and durable epoxy resins
 - Polycarbonate: Medical device components, reusable food/beverage containers, sports safety equipment, electronic equipment and automotive components, and much more
 - Epoxy resins: Protective coatings in food/beverage cans, structural steel coatings, adhesives and laminates
 - Only trace levels of BPA remain in finished products
- BPA is one of the most thoroughly tested chemicals in commerce today and has a 50-year safety track record
 - Rich scientific database available to assess safety



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Polycarbonate in Medical Devices

Polycarbonate – a high performance material that meets a range of requirements for medical devices

- Material requirements
 - Optical clarity and colorability
 - Impact resistance
 - Dimensional stability
 - High flow and enhanced release
 - Flame retardant options available
- Healthcare requirements
 - Sterilization
 - Chemical resistance
 - Biocompatibility
 - Food contact compliant
 - Good manufacturing practices



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What the Science Tells Us about BPA Safety

- Numerous expert panels and government agencies worldwide have extensively reviewed available data on the safety of BPA
 - Reviews focused on food-contact applications, but underlying science is applicable to medical devices
- The consensus of major government agencies around the world is that BPA is safe as used in its current applications

“Is BPA safe?”

Yes. Based on FDA’s ongoing safety review of scientific evidence, the available information continues to support the safety of BPA for the currently approved uses in food containers and packaging.”

“This assessment is based on review by FDA scientists of hundreds of studies including the latest findings from new studies initiated by the agency.” (FDA, 2013)



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Extensive Ongoing Activity in Europe *EFSA - Food-Contact*

- Most recent review from European Food Safety Authority (EFSA)
 - Draft Opinion issued January 2014
 - Complete re-evaluation; includes non-food contact exposure
 - Very conservative approach to establish a Tolerable Daily Intake
 - “EFSA says the health risk for all population groups is low – including for fetuses, infants, young children and adults.” (EFSA statement, January 2014)
- EFSA currently evaluating extensive public comments
 - Aim to finalize opinion by end of 2014



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● ● ● Extensive Ongoing Activity in Europe *SCENIHR - Medical Devices*

- Draft Opinion from Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) issued January 2014
- Evaluation of health effects and safe intake level builds on EFSA's draft opinion
- Exposure scenarios estimated for a wide range of medical applications
 - External, dental, implants, hemodialysis, surgical, intensive care
 - Short to long contact times
- Estimated exposures generally very low, often in range of consumer exposure
 - Available exposure data is very limited
 - Estimates based on “conservative assumptions and extrapolations”
 - Exposure estimates should be “viewed and used with some caution”



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Extensive Ongoing Activity in Europe *SCENIHR - Medical Devices*

- Margin of safety exists even for worst case exposure
 - Some risk of adverse effects noted for limited exposure scenarios
 - Better exposure data needed to fully understand risk potential
- Importantly, SCENIHR states:

“[T]he benefit of medical devices has also to be considered”
- SCENIHR expressed caution regarding replacement of BPA:

“The possibility to replace BPA in these products should be considered against their efficiency in the treatment, as well as the toxicological profile of alternatives”
- Final report expected in 2014



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Metabolism and Pharmacokinetics

- Pharmacokinetics describes processes by which a substance is absorbed, distributed, metabolized and eliminated
 - Sets limits on potential for toxicity
- Human studies with BPA confirm:
 - Efficient conversion to inactive metabolite after oral exposure
 - No free BPA detected in blood after high dietary exposure
 - Metabolite rapidly eliminated in urine; half-life of a few hours
- Non-human primate and rodent studies corroborate human data
 - Efficient metabolism occurs at all ages: adults, pregnant animals, neonates and the fetus
 - BPA also efficiently metabolized and eliminated after IV exposure; does not accumulate in body

Efficient Metabolism Predicts Low Toxicity



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Toxicity

- Controversy around endocrine-mediated effects at “low doses”
 - Reproductive/developmental, neurobehavioral, cancer, etc.
- Multiple multi-generation reproduction/development studies found no low-dose effects
 - Sponsored by industry and government
 - Consistent results from studies on multiple strains of rats and mice
- No low-dose effects found in FDA’s recent large-scale subchronic study
- Neurobehavioral effects not found in FDA and EPA studies
- No clear evidence of carcinogenicity in 2-year studies on rodents
- Current safe intake limits of 25-50 micrograms BPA/kg bodyweight

Extensive Test Data Confirm Low Toxicity



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Human Exposure

- Urine biomonitoring provides best direct measure of human exposure to BPA
 - Short half-life in body; entirely excreted in urine as metabolite
- Population scale urine biomonitoring studies (US and Canada) show median daily intake < 50 nanograms BPA/kg bodyweight
 - Typical human exposure ~300-1,000 fold below safe intake limits
- Low exposure corroborated by low levels of BPA available in polycarbonate products
 - Numerous studies show very low BPA migration from polycarbonate consumer products
 - Low migration expected from polycarbonate medical devices, but few published studies available to confirm

Human Exposure Extremely Low



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What's Next?

- New/updated regulatory agency reviews on the way
 - Further updates from FDA likely as additional research is published
 - Draft reports from EFSA and SCENIHR to be finalized in 2014
- More significant government lab research will further reduce uncertainty
 - FDA chronic toxicity study now underway
 - NTP human pharmacokinetic studies (oral and dermal exposures) underway
 - FDA medical device exposure studies underway

For more information on BPA, please go to <http://www.FactsAboutBPA.org> and http://www.science20.com/profile/steve_hentges



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