A REVISED AQUATIC HAZARD ASSESSMENT OF BISPHENOL A: EVIDENCE THAT CURRENT RISK MODELS MAY NOT BE SUFFICIENTLY PROTECTIVE

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We will Discuss;

1. Conducted and updated an aquatic hazard assessment for BPA using the weight of evidence approach, using ecologically relevant endpoints such as survival, growth and development, and reproductive success.

2. Derived a PNEC

3. Compared the environmental concentrations of BPA found in the aquatic environment to the PNEC.

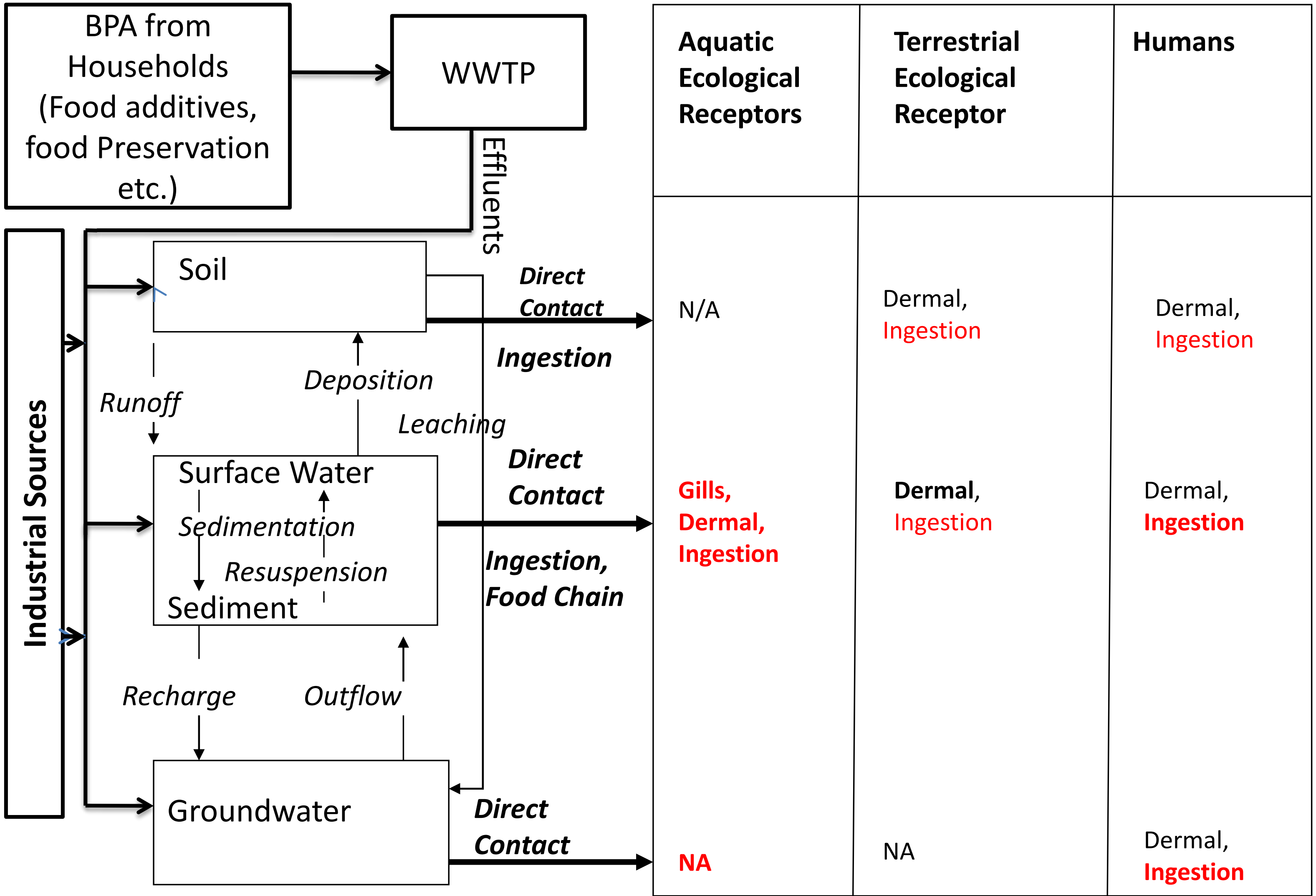

Figure 1. BPA Exposure Pathways

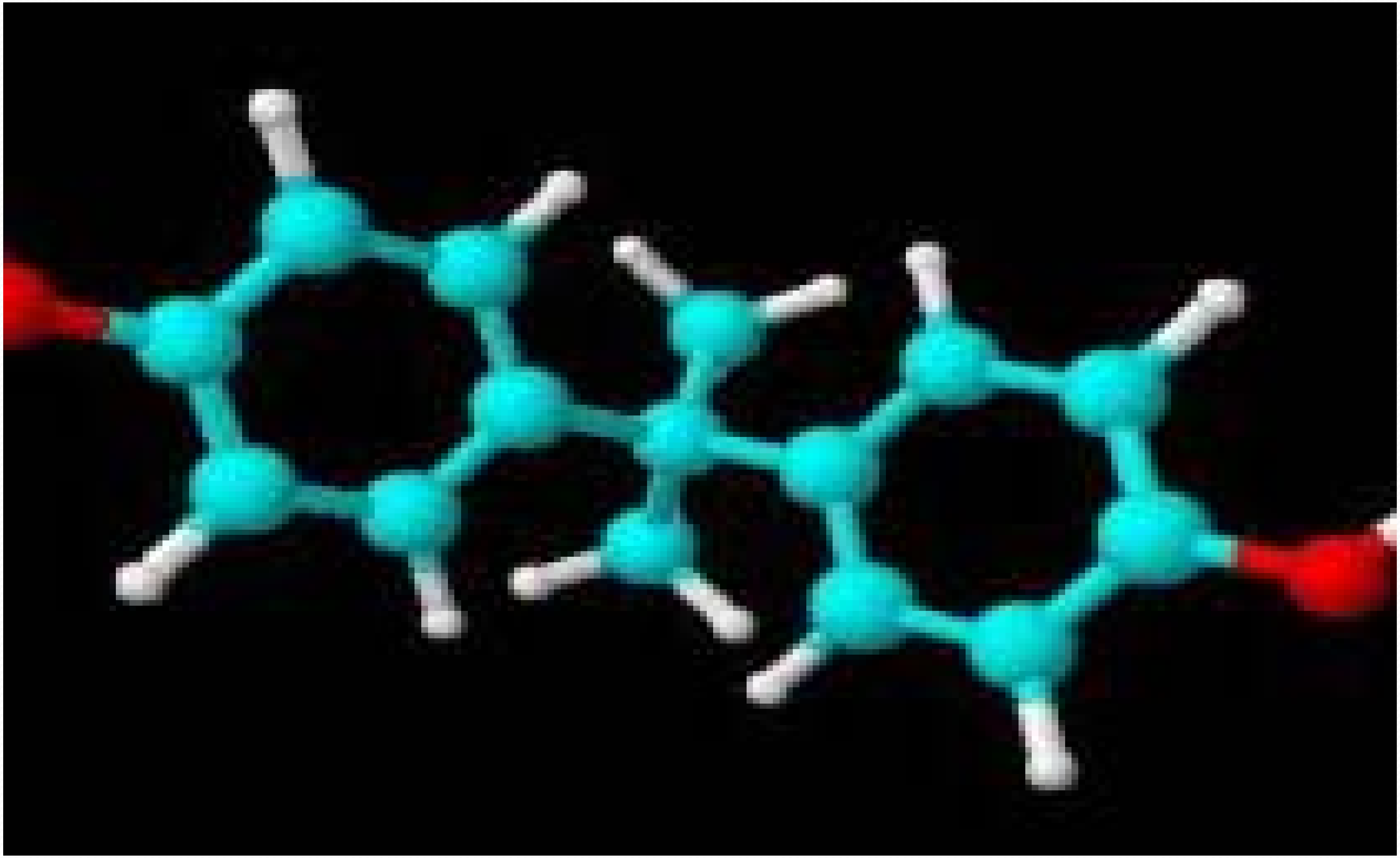

Figure 2. Molecular Structure of BPA (http://images.google.com)

Uses

Polycarbonate

- Compact disks,
- window panes and roofing,
- headlight and taillight covers, reflectors,
- telephones and distributor equipment,
- lamp sockets, relay parts,
- components for electronic calculators, fluorescent tube sockets, current meters,
- polycarbonate bottles and containers (including milk bottle for baby and water bottle)

Epoxy Resin

- water-borne epoxy coatings with high-solids and powder,
- protective coatings for food and drink cans, adhesives, automobile body primers,
- specialty products such as fiber-reinforced composites, electrical laminates,
- castings, toolings, and adhesives

Environmental Hazard Assessment

Environmental Hazard Assessment of chemicals consists of;

- Identification of the effects that a chemical may have on organisms in the environment.
- Effects are expressed in terms of the acute and chronic toxicity of a chemical on the exposed organisms.
- Effects are generally given as either the lethal concentration (LC) or as the effective concentration (EC)
- *hazard profile or toxicity profile.*

The Weight of Evidence (WOE) Approach

- Multiple measurement endpoints are related to an assessment endpoint to evaluate whether significant risk of harm is posed to the environment.

- Strengths and weaknesses of different measurement methods when determining whether the results show that a stressor has caused, or could cause, a harmful environmental effect.

Weight-of-evidence is reflected in three characteristics of measurement endpoints:

1. The weight assigned to each measurement endpoint;
2. The magnitude of response observed in the measurement endpoint; and
3. The concurrence among outcomes of multiple measurement endpoints.

EFFECTS ASSESSMENT

Survival — Acute and Chronic

- Survive both short- and long-term exposures to BPA.

Growth and Development

- Grow and develop normally

Reproductive Success

- Species that make up those communities and ecosystems must successfully reproduce.

Hazard Assessment

- NOEC and LOECs for ecologically relevant endpoints were used to evaluate the survival , growth and development, and reproductive success of aquatic organisms following exposure to BPA.
- Chronic endpoints were derived from studies deemed acceptable i.e., classified as "valid" or "use with care".
- Acute and chronic toxicity data from laboratory studies with BPA can be used to support an ecological risk assessment for aquatic environment.

NOEC-No Observe Effect Concentration; LOEC-Lowest Observed Effect Concentration

Methodology

1. Critically reviewed available literature up to 2008 on BPA aquatic toxicity.

2. Conducted and updated an aquatic hazard assessment for BPA using a weight-of-evidence approach using the ecologically relevant endpoints of survival, growth and development, and reproductive success.

3. Derived a refined PNEC

4. Compared derived PNEC to the concentration range found in the aquatic environment and determine protectiveness for aquatic organisms.

Specific criteria for quality and usefulness of a study included:

1. Thorough description of the experimental design, including exposure regime and replication;
2. Analytical confirmation of test concentrations;
3. Description of ecologically relevant endpoints and all supplemental secondary biochemical and morphological information collected;
4. Use of test procedures that are based, at least generally, on internationally accepted procedures and practices. Newly developed test procedures must be able to be repeated, and meet all other required criteria.

Specific Criteria (Contd.)

5. Clear linkage of reported findings with the exact experimental design

6. Sufficient reporting of results, including system performance, toxicity results, and statistical methods employed to ascertain how the data support the conclusions that are drawn.

Assessment Criteria;

Valid- 4-6 of 6

Acceptable for Use- 1-3 of 6
(Use with care)

Not Valid- Insufficient information to allow proper evaluation

Once study results were obtained and tabulated

- First, use NOEC and LOEC to generate a scatter plot in Stata for each endpoint vs. BPA concentration (µg/L).
- Second, derive a Predicted No Effect Concentration (PNEC) using the Hazardous Concentration for 5% of the Specie (HC_5) Approach
- Third, compared the derived PNEC with concentrations of BPA found in the aquatic environment to determine the sufficiency of protection for aquatic species.

The PNEC is an ecotoxicological measure for multiple species systems. It can be defined as the concentration below which a specified percentage of species in an ecosystem are expected to be protected.

Van der Hoeven's HC_5 Approach;

- Developed by a group of scientists in the Netherlands
- It assumes that it is not possible to protect 100% or organisms but one should aim to protect 95% of species
- The level of chemical that affects 5% of specie is known as HC_5
- Makes no assumption about the distribution of the data

Specifically,

- The HC_5 value is the level or concentration of BPA in the aquatic system at which 95% of the species are theoretically unaffected. It is based on endpoints of survival, growth and reproduction.

Some Problems with the HC_5 Approach;

- Small sample size (small number of experiments on which it is based)
- Overestimation of toxicity values (lab) leading to too low a HC_5 value

Results

- 61 studies which represented twenty four (24) different species were reviewed and included in this analysi
- 13 of these studies were deemed not valid and were not included in the analysis.
- A total of 94 LOEC and NOEC values were obtained from the studies deemed acceptable ("valid" or "use with care") for use, and included in the analysis.

- BPA sensitivities ranged from 0.002µg/L (growth NOEC) to 12500µg/L (reproduction LOEC)

- A cluster of BPA sensitivities (NOEC and LOEC) was observed from 0.0483µg/L to 12500µg/L, Figure 3.

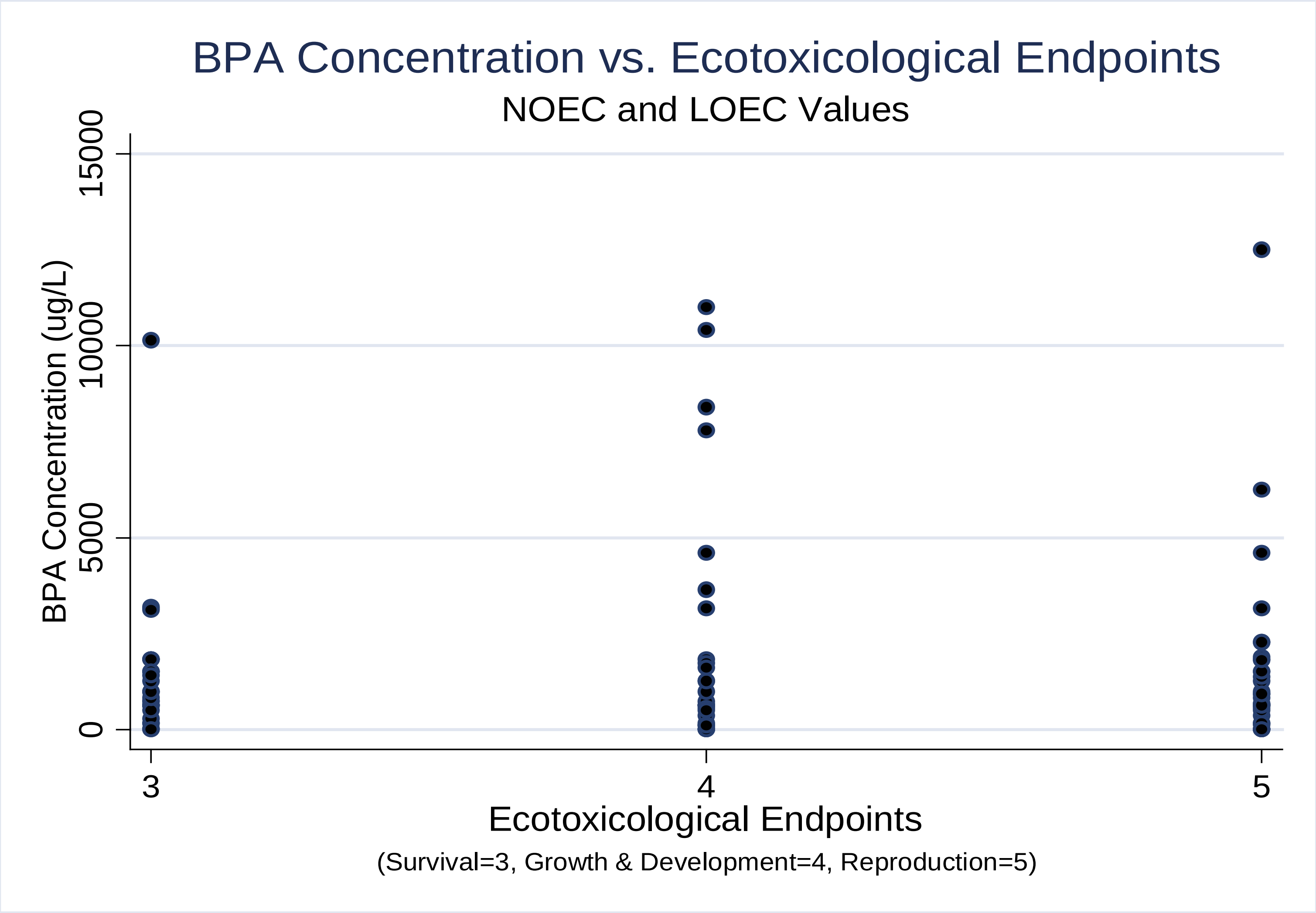

Figure 3. BPA Concentrations versus Ecotoxicological Endpoints

- The NOEC for BPA for all endpoints ranged from 0.002 to 10400µg/L (Figure 4).

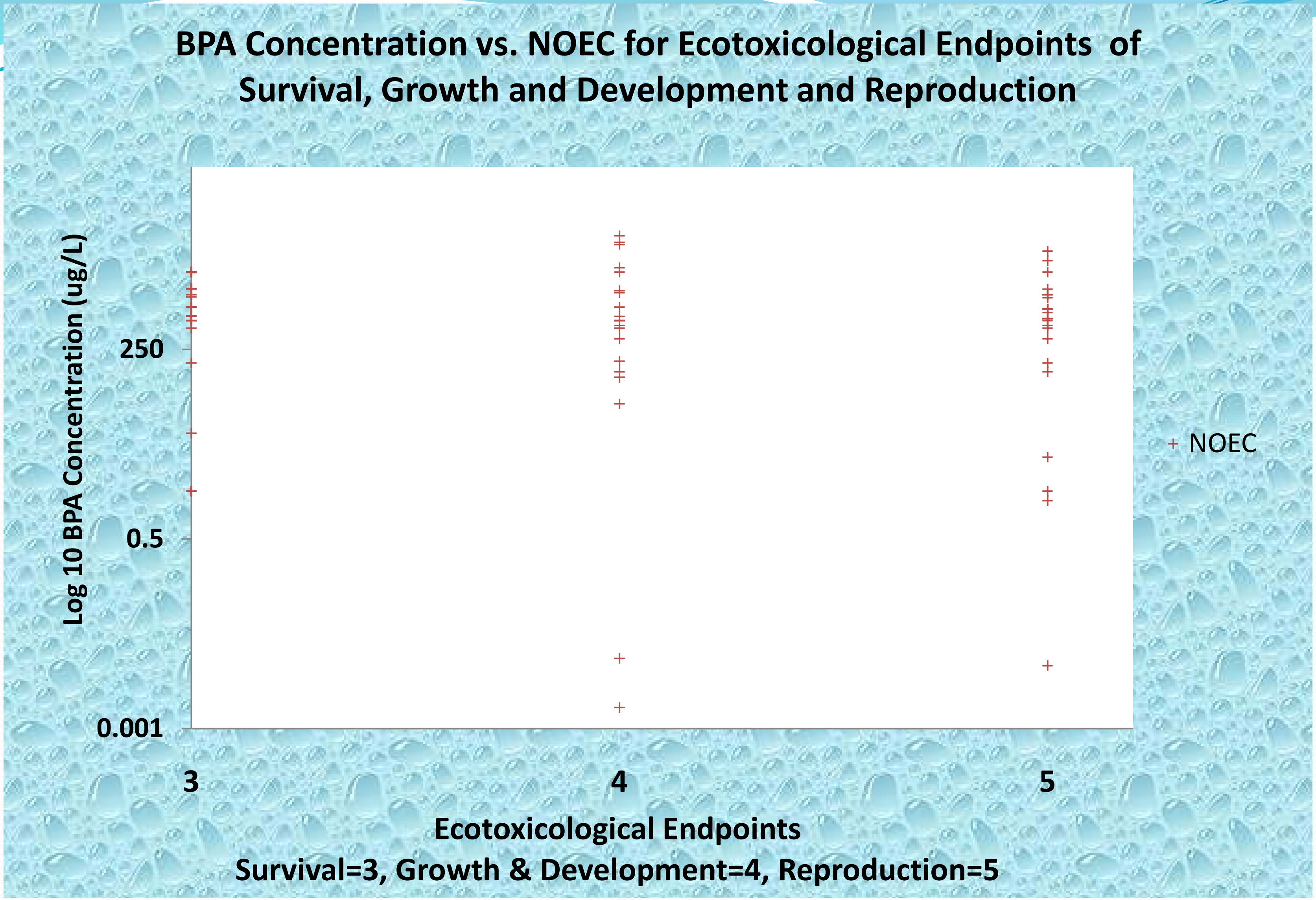

Figure 4. BPA Concentration vs. NOEC

The LOEC for BPA for all endpoints ranged from 0.0483μg/L to 12500μg/L, see Figure 5.

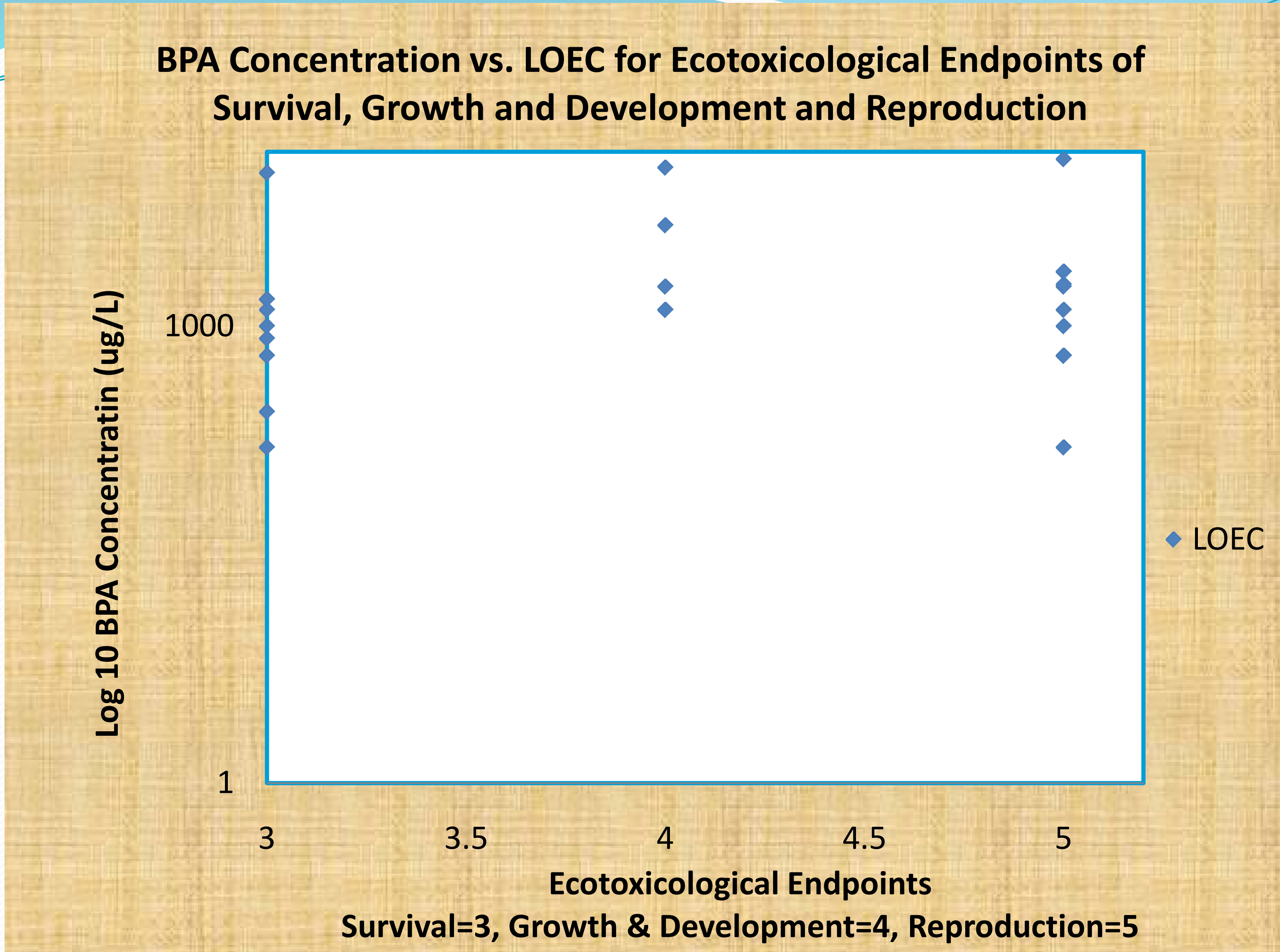

Figure 5. BPA Concentrations vs. LOEC

Using the weight of evidence approach, the toxicity dataset for BPA suggests that adverse effects of mortality, growth and development and reproduction are most likely to occur between the concentrations of 0.0483µg/L and 2280 µg/L based on repeated measurements of these endpoints.

Calculation of a PNEC

- The PNEC, which is the conservative estimate for HC5, is the observed value with rank *k* and was determined as follows;

$$y = 0.05(n + 1) = 3.35,$$

$$then\ HC_5 = X_k = X_3 = 0.01ug/L$$

Equation 1 (van der Hoeven 2001)

Where ;

- n is the total number of observations

$$\text{Largest integer below } y = k, y = 3$$

To determine an estimate for HC_5 by interpolation;

$$Z_k + (Z_{k+1} - Z_k)(y - k)$$
$$= 0.061\mu g / L = estimate\ of\ HC_5$$

Equation 2 (van der Hoeven 2001)

Next, determine the sensitivity of underestimating is 0.05 by interpolation.

$$z_k + (z_{k+1} - z_k)(0.05 - q_{k,n}(\alpha)) / q_{k+1.n}(\alpha) - q_{k,n}(\alpha)$$

$$With\ n = 67,\ k = 1,\quad (Using\ lower\ bound\ est.\ for\ Z_1 = -2.69897,\ rank\ Z_2 = -2.1023)$$

$$q_k = 0.0437,\quad q_{k+1} = 0.0688\ \{inverse\ beta\ distribution\ with\ parameters$$

$$[k_{1,}(n + 1 - k_1)]\quad and\quad (k_1 + 1, n - k_1)\}$$

$$= 0.00282\,\mu g/L$$

This also represents the lower bound estimate for the one sided 95% CI.

Equation 3 (van der Hoeven, 2001)

To find the lower bound CI

$$z_k + (z_{k+1} - z_k)(0.05 - q_{k,n}(\alpha)) / q_{k+1.n}(\alpha) - q_{k,n}(\alpha)$$

$$= 0.02\,\mu g/L$$

To find the upper bound of 95% *CI*

$$z_{k_2} - (z_{k_2} - z_{k_2-1})(q_{k_2,n}(\alpha) - 0.05)/(q_{k_2,n}(\alpha) - q_{k_2-1.n}(\alpha))$$

Where $k_2 = 8$ *and from ranks* $Z_{k_2} = 0.623249, \quad Z_{k_{2-1}} = 0.380211$

$q_{k_2} = 0.05381, \quad q_{k-1} = 0.04372$ {*inverse beta distributions with parameters*

$[k_2, (n+1-k_2)]$ *and* $k_{2-1}, n+2-k_2,$ (*indicates as* $q_{k_{2,n}}(\alpha)$ *and* $q_{k_{2-1,n}}(\alpha)$}

$$= 3.40\,\mu g / L$$

Equation 4 (van der Hoeven 2001)

Results

- The NOEC for BPA for all endpoints ranged from 0.002 to 10400µg/L, see Figure 4.

- The LOEC for BPA for all endpoints ranged from 0.0483µg/L to 12500µg/L, see Figure 5.

- WOE, the toxicity dataset for BPA suggests that adverse effects of mortality, growth and development and reproduction are most likely to occur between the concentration of 0.0483 µg/L and 2280 µg/L based on repeated measurements of these endpoints.

Results (contd.)

- The HC_5 estimate (PNEC) is 0.06 µg/L.
- The sensitivity for which the probability of underestimating is 5% is 0.003 µg/L.
- The 95% confidence interval is (0.02, 3.4) µg/L.
- The reported concentration of BPA found in the aquatic environment is between 0.0005 µg/L to 8 µg/L (Belfroid, 2002; Kuch, 2001).

Research Conclusion

- The results of this research suggest that the aquatic environment is not sufficiently protected from adverse effects of BPA at the established concentration of 8μg/L or less.

Uncertainties/Problems

- Variability/Representativeness Assumption may be violated
- Toxicity in the lab invariably greater (overestimated for field) and thus correspondently HC5 may be too low (underestimation)
- Experimental limitation
- The use of the NOEC and LOEC
- Sampling replacement assumption
- Randomness
- Statistical uncertainty

Public Health Implications

- Species in the wild are sentinels for human exposure
  (Canary in the mine).
- Some species are a part of the food chain thus, another viable route of exposure for humans to these chemicals.
- Similarity between mammalian systems and some of the species in the wild
- Having an updated BPA aquatic hazard assessment will help to determine risks for both humans and wildlife populations from environmentally relevant concentrations of BPA.

Overall Conclusion

Having an updated hazard assessment for BPA will foster the protection and proper management of BPA and the aquatic environment.

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