

**Comments to EPA IRIS on  
Diisononyl Phthalate (DINP) Review  
October 29, 2014**

From:

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## Conflict of Interest Statement

These comments represent my professional opinion on these issues. It was supported by funding from ExxonMobil Biomedical Sciences Inc.

This work was based information in the preliminary meeting materials and select scientific publications cited in my written comments.

## Comments on Question 2: Male Reproductive Effects

- Comprehensive search of literature
- Tables and figures help demonstrate consistent responses
- Clearly malformations and adverse effects that define phthalate syndrome are not observed with DINP
- Careful assessment of adverse effects will be needed to identify:
  - Potential hazard
  - Points of departure for risk assessment
- Cumulative assessment can only be based on:
  - Common mechanism of action
  - Common adverse effects

## Data review

- Exposure-response arrays are very useful:
  - Study consistency
  - Relative response
- Next Step:
  - Study evaluation and integration of evidence
  - Some studies may not be comparable or reliable (e.g., Lee)

## “Phthalate Syndrome” is a misnomer

- Defined by distinct adverse effects on reproduction including:
  - Reproductive tract malformations
  - Testis anomalies
  - Cryptorchidism
- “Anti-androgenic” mode of action is not a sufficiently specific definition
- Adverse effects in the syndrome have been shown to result from several unique molecular mechanisms of action
- May not be suitable for lumping

## Conclusions:

**DINP has not been shown to cause the “phthalate syndrome”**

- Effects from DINP are not the same as DEHP or certain other phthalates
- Other phthalates are also negative
  - For example, DEP, DMP, and DNOP
- Effects associated with DINP are reversible and not adverse