Comments on Scientific Question #2 (DiNP) and USEPA IRIS Preliminary Materials

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Epidemiology Studies: DiNP and Male Reproductive Outcomes (Question 2)

- <u>Joensen et al. (2012)</u>: urinary phthalate excretion and testicular function.
- <u>Jurewicz et al. (2013)</u>: urinary phthalate excretion and sperm parameters.
- Main et al. (2006): phthalates in breast milk and levels of reproductive hormones in infant boys.
- Mieritz et al. (2012): urinary phthalate excretion and pubertal gynecomastia in healthy boys including an assessment of serum testosterone.

Results of Epidemiology Studies: DiNP and Male Reproductive Outcomes (Question 2)

Author, Year	Testosterone	LH	FSH	Estradiol	Sperm	Sperm	Sperm
					Concentration	Motility	Morphology
Joensen, 2012							
%MiNP	_	1	+	-	_	1	_
ΣDiNP	_	_	-	-	_	_	_
Jurewicz, 2013							
MiNP	_	nr	nr	_	_	+/-	_
Main, 2006							
MiNP	_	_	-	nr	nr	nr	nr
Mieritz, 2012							
MiNP	_	nr	nr	nr	nr	nr	nr
ΣDiNP	_	nr	nr	nr	nr	nr	nr

nr = not reported

Conclusions and Recommendations

- Epidemiological evidence: measured levels of the phthalate DiNP (typically as MiNP or as ΣDiNP) are not associated with decreases in male reproductive outcomes, including reproductive hormones and sperm parameters.
- Authors ignore the negative (i.e. null) results in favor of emphasizing the occasional positive result (typically involving other phthalates than DiNP and its metabolites).
- Additional observational studies of DiNP and its metabolites on (human) male reproductive outcomes could prove useful but only if the study designs correct limitations. More crosssectional studies that fail to adjust for confounders are unlikely to provide additional insights. Controlling for the possible confounding effects of other phthalates seems especially appropriate.
- Given the overwhelmingly null epidemiological results, the extent to which results reported in rats exposed to DiNP can be applied to benefit the public's health (e.g. through regulation or recommendations) is an issue that requires serious methodological consideration.