Melamine: Potential Endocrine, Reproductive, and Neurotoxic Activities

Ashley L. Bolden, MS

The Endocrine Disruption Exchange

mel · a · mine

A white crystalline compound used in the making of plastics.

TOXICOLOGY AND APPLIED PHARMACOLOGY 72, 292–303 (1984)

Urolithiasis and Bladder Carcinogenicity of Melamine in Rodents[1]

RONALD L. MELNICK,[2] GARY A. BOORMAN, JOSEPH K. HASEMAN, RICHARD J. MONTALI,* AND JAMES HUFF

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mini review

http://www.kidney-international.org

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Childhood urinary stones induced by melamine-tainted formula: how much we know, how much we don't know

Jie Ding[1]

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DOI: 10.1080/15287394.2010.511540

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COMPARATIVE NEPHROTOXICITIY INDUCED BY MELAMINE, CYANURIC ACID, OR A MIXTURE OF BOTH CHEMICALS IN EITHER SPRAGUE-DAWLEY RATS OR RENAL CELL LINES

Lan Choi[1], Min Young Kwak[1], Eun Hwa Kwak[1], Dong Hyun Kim[1], Eun Young Han[1], Taehyun Roh[1], Jung Yun Bae[1], Il Young Ahn[1], Jea Yeon Jung[1], Mi Jung Kwon[1], Dong Eun Jang[2], Seong Kwang Lim[2], Seung Jun Kwack[2], Soon Young Han[3], Tae Seok Kang[3], Seung Hee Kim[1], Hyung Sik Kim[3], Byung Mu Lee[1]

Use of urinary renal biomarkers to evaluate the nephrotoxic effects of melamine or cyanuric acid in non-pregnant and pregnant rats

O.J. Bandele [a,*], C.B. Stine [b], M. Ferguson [b], T. Black [a], N. Olejnik [a], Z. Keltner [a], E.R. Evans [b], T.C. Crosby [b], R. Reimschuessel [b], R.L. Sprando [a]

[a] Division of Toxicology, Office of Applied Research and Safety Assessment, CFSAN, U.S. FDA, Laurel, MD, United States
[b] Division of Applied Veterinary Research, Office of Research, CVM, U.S. FDA, Laurel, MD, United States

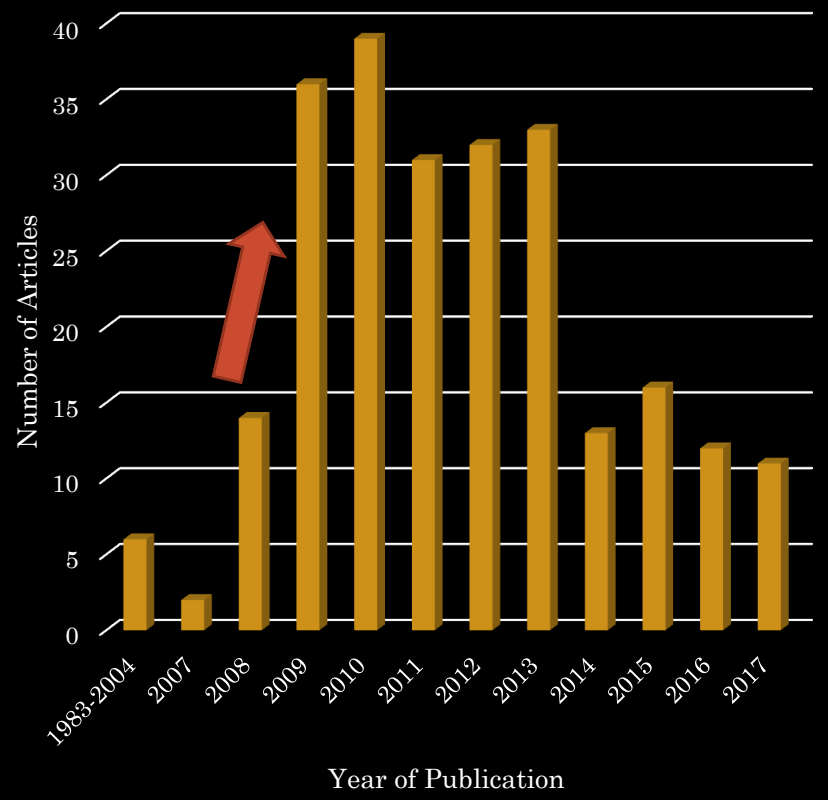
Pediatr Nephrol (2016) 31:2043–2054
DOI 10.1007/s00467-015-3222-3

EDUCATIONAL REVIEW

Toxic environmental exposures and kidney health in children

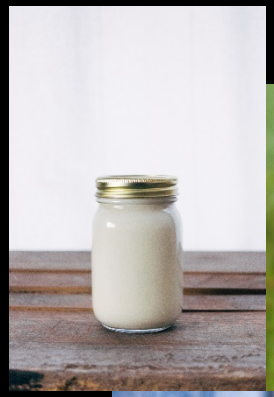
Darcy K. Weidemann[1] · Virginia M. Weaver[2,3] · Jeffrey J. Fadrowski[3,4]

Publication Trends for Melamine and Renal Effect

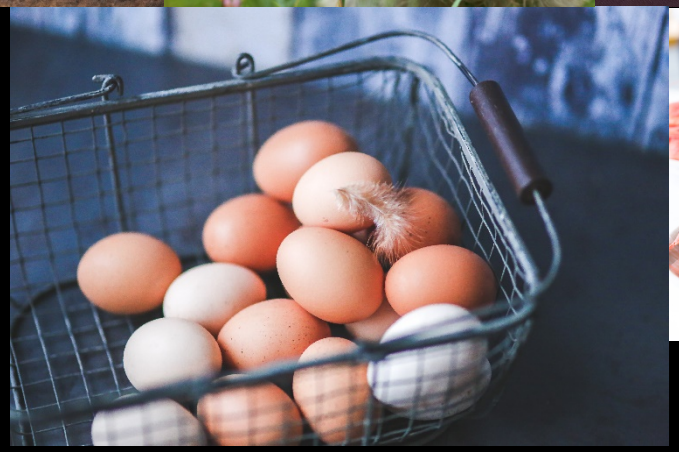


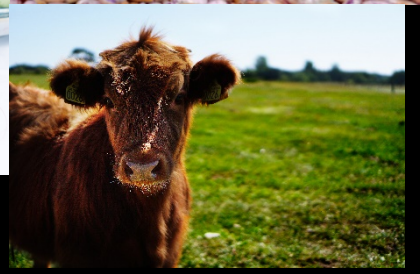
But…

More than baby formula

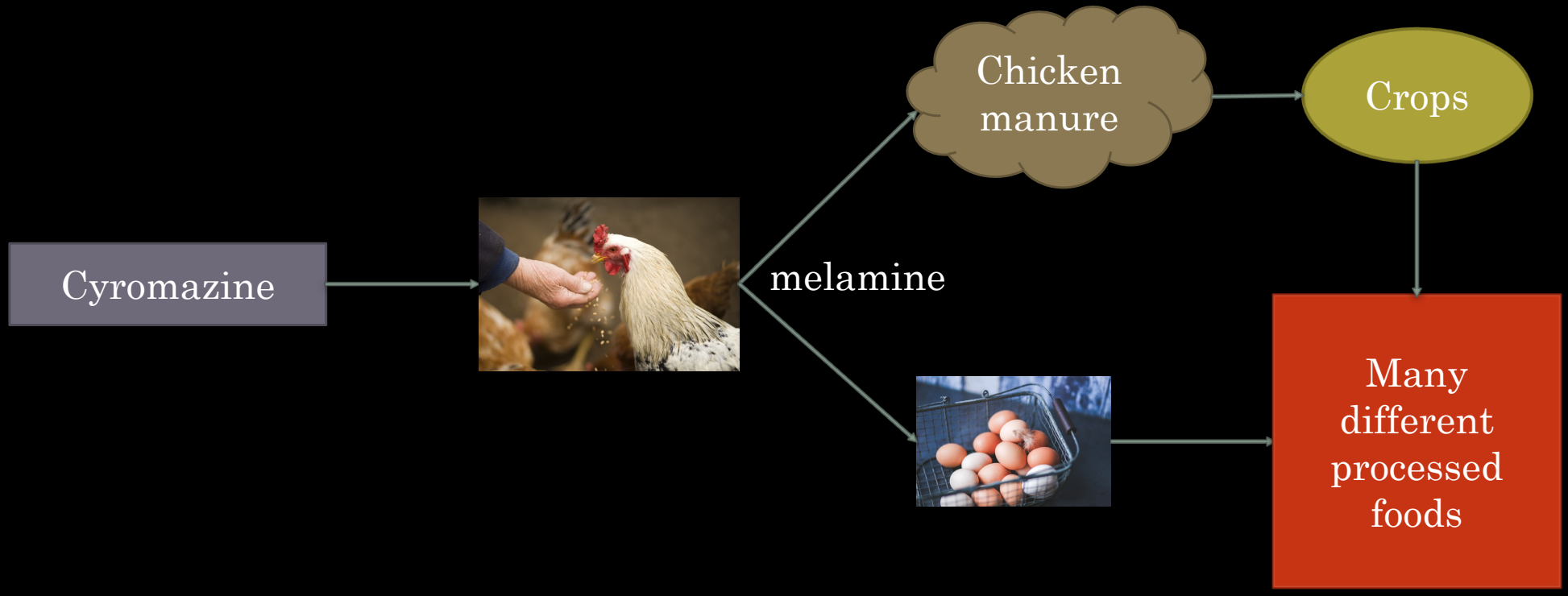






Cyromazine?


Cyromazine
Chicken manure
Crops
melamine
Many different processed foods

What other impacts might melamine have???

2011

The effect of exogenous melamine on rat hippocampal neurons

Yan Wang[1], Fei Liu[2], Yuejiao Wei[1] and Daicheng Liu[1]

Effect of melamine on potassium currents in rat hippocampal CA1 neurons

Jia-Jia Yang [a], Yu-Tao Tian [a], Zhuo Yang [b], Tao Zhang [a,*]

[a] *Key Laboratory of Bioactive Materials, Ministry of Education and College of Life Science, Nankai University, Tianjin 300071, PR China*
[b] *College of Medicine, Nankai University, Tianjin 300071, PR China*

2013

The reproductive toxicity of melamine in the absence and presence of cyanuric acid in male mice

Rong H. Yin [a], Xin Z. Wang [a], Wen L. Bai [a,*], Chang D. Wu [a], Rong L. Yin [b], Chang Li [c], Jiao Liu [a], Bao S. Liu [a], Jian B. He [a,*]

… fast forward 2016

Scoping Reviews

- New to environmental health research.
- Determination of body of evidence maturity.
- Identification of research gaps.
- Pinpoint bodies of evidence for systematic review.

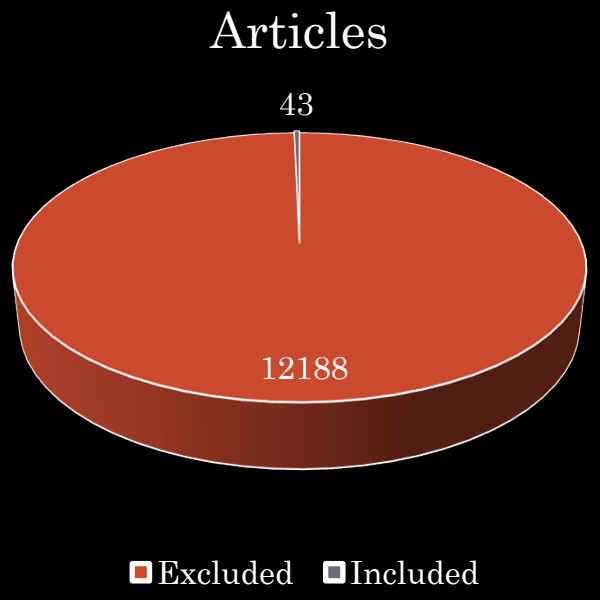
Objectives of study

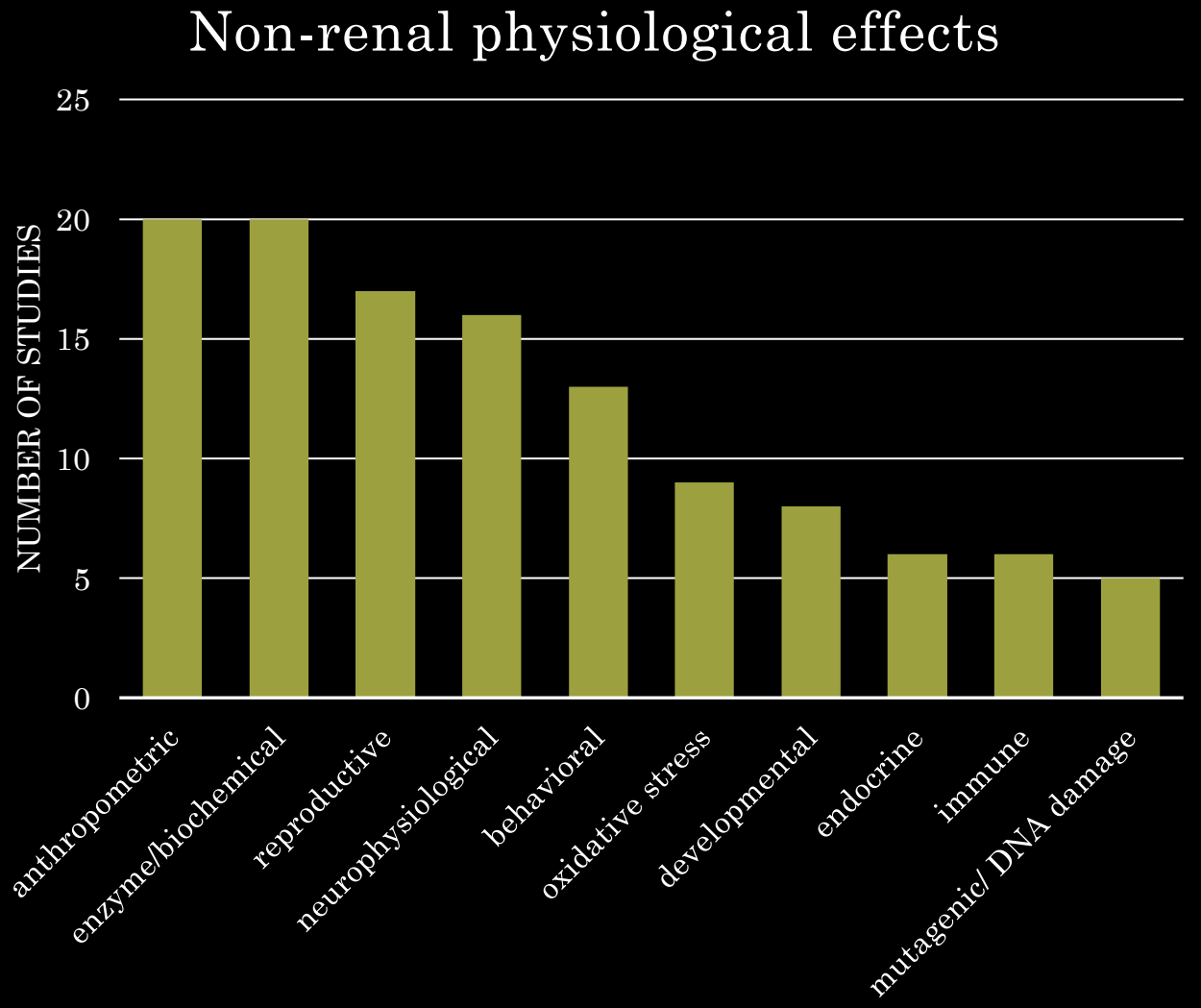
- Determine if a recommendation for systematic review of a specific endpoint is feasible.
- Identify research gaps.
- Prioritize future research.

Methods

- Developed search logic.
- Performed electronic searches using PubMed and Web of Science up to November 2016.
- Screened articles using DistillerSR®.
- Completed summary level data extraction.

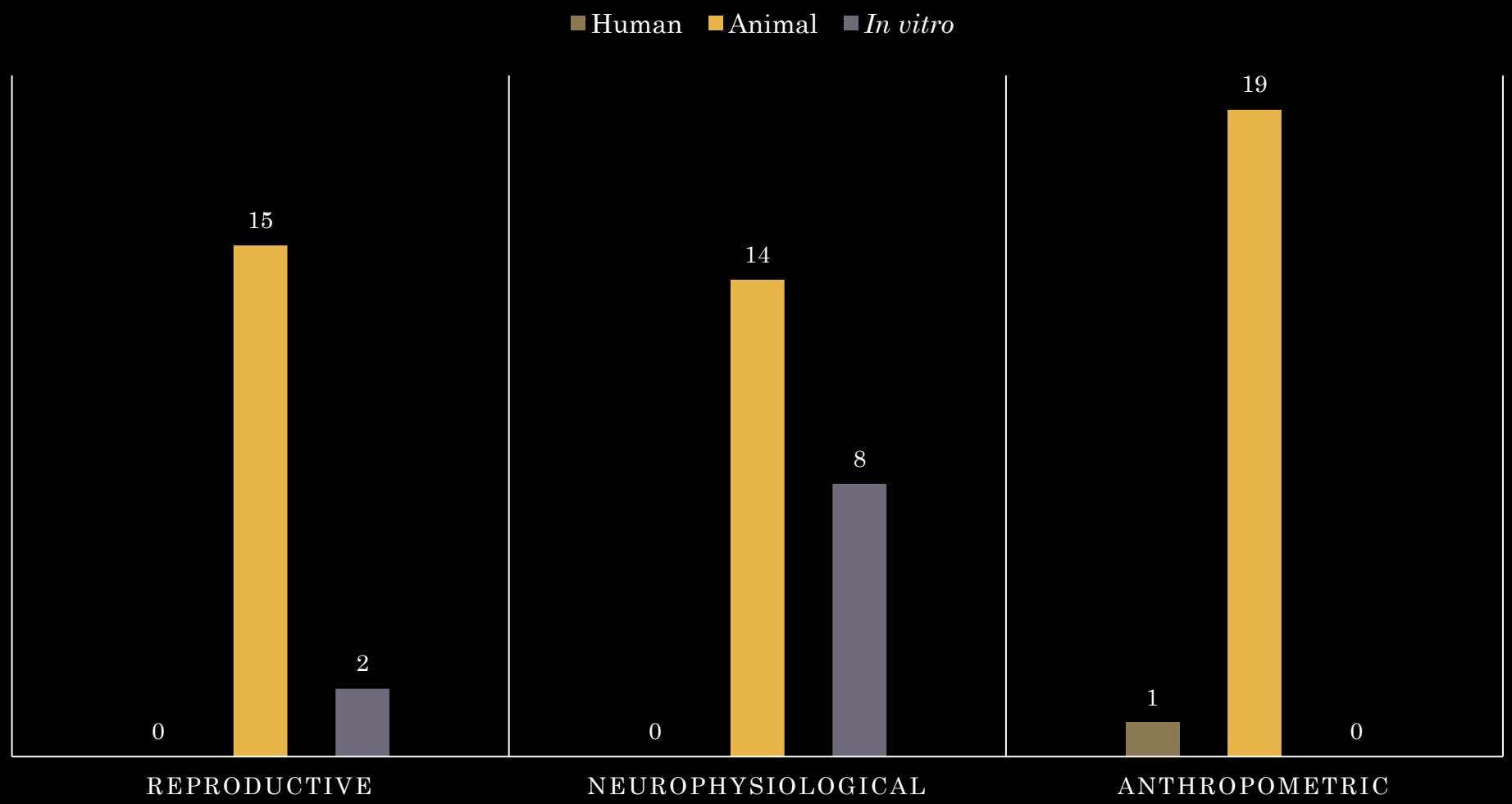
Results





- 100% published between 2010-2016
- 74% assessed *in vivo* models
- 35% assessed *in vitro* models

Endpoint Distribution



Anthropometric

- Endpoints for analysis included body weight, body length, and fetal growth.
- Studies had measures from several different life stages.
- Models included fish, rodent, human, and chicken.
- No relevant mechanistic data seems to be available.

Reproductive

- Studies of both male and female reproduction were found. Endpoints included sperm count, follicular atresia, and oocyte competence.
- There were studies that might provide mechanistic support.
- Replication of endpoints maybe lacking.
- While different models included rodents and chicken there are no human studies available.

Neurophysiological

- There were several studies that replicated similar endpoints primarily evaluations related to hippocampal function.
- *In vitro* assessments were completed that might provide mechanistic support.
- Relevant studies were completed in rodents and fish but none in humans.
- There were also behavioral studies that could be incorporated that assessed learning and memory.

Future Directions

- Lack of human studies.
- Lack of mechanistic studies.
- Little to no research on immune, cardiovascular, respiratory, metabolic endpoints.

Recommendations

- Identified three areas that could be assessed using systematic review.
- For reproduction and anthropometric endpoints more studies in humans and more mechanistic support might strengthen these bodies of evidence.
- Neurophysiological area had the most robust literature base and is likely the best to move forward to systematic review.

Thanks

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Publication: Melamine, beyond the kidney: A ubiquitous endocrine disruptor and neurotoxicant? Bolden AL, Rochester JR, Kwiatkowski CF. Melamine, beyond the kidney: A ubiquitous endocrine disruptor and neurotoxicant?. Toxicology Letters. 2017 Oct 5;280:181-9. http://www.sciencedirect.com/science/article/pii/S0378427417311396