

■ Experimental Biology 2017

The Caffeine Landscape

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Office of Food Additive Safety

U.S. Food and Drug Administration

■ Nawrot et al. 2003¹

Endpoints reviewed

- **General toxicity**
 - Acute lethality
 - Caffeinism
 - Unstable bladder
- **Cardiovascular toxicity**
 - Arrhythmia
 - Serum cholesterol
 - Heart rate
 - Blood pressure
- **Effects on bone and calcium balance**
- **Effects on human behavior**
 - Mood and performance in adults
 - Tolerance, physical dependence, and withdrawal
 - Effects in children
- **Mutagenicity/genotoxicity**
- **Carcinogenicity**
- **Reproductive and Developmental effects**
 - Effects on conception and female fertility
 - Effects on sperm and male fertility
 - Spontaneous abortion (miscarriage)
 - Fetal Growth
 - Preterm delivery
 - Congenital malformations
 - Postnatal development

¹Nawrot, P., Jordan, S., Eastwood, J., Rotstein, J., Hugenholtz, A., Feeley, M. Effects of caffeine on human health. Food Addit Contam. 2003; Jan;(1):1-30

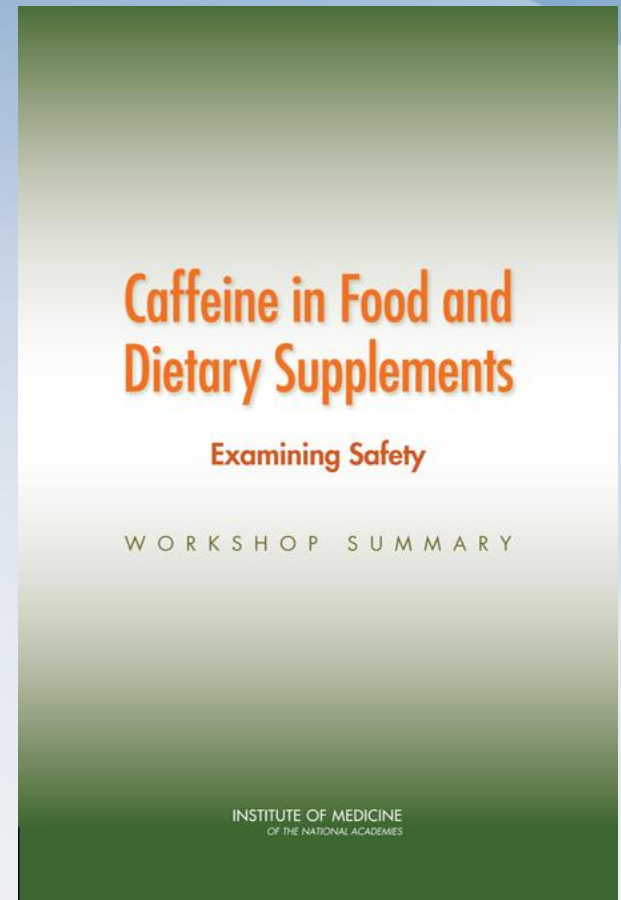
■ Changes in products containing added caffeine

- “Energy” drinks and “energy” shots became more popular and other caffeinated products have been introduced to the marketplace
- Concerns about changes in caffeine exposure (level & demographics) and marketing of these products especially to children or naïve consumers.

■ 2013 FDA sponsored IOM workshop

“Caffeine in Food and Dietary Supplements: Examining Safety”
(August 2013)

- Goal: Review the available science on safe levels of caffeine consumption in foods, beverages, and dietary supplements and to identify data gaps.



■ Summary of charge questions to IOM

- Exposure
- ADME
- Cardiovascular effects
- Neurological and behavioral effects
- Tolerance and withdrawal
- Populations that may be at risk
- Are the data supporting the safety of caffeine sufficient?

■ 2013 NIH workshop

- FDA participated in NIH Workshop, August 2013: “The Use And Biology Of Energy Drinks Meeting Summary: Current Knowledge And Critical Gaps”
 - Goal: Bring together subject matter experts to summarize the relevant research and highlight the most critical research gaps
 - Prevalence and patterns of energy drink and caffeine consumption,
 - Reasons for use of energy drinks by children and young adults, as well as in the military,
 - Potential for energy drink use to contribute to health disparities, and
 - Effects of energy drinks on nutrient and muscle metabolism, and on physical performance.

NUTRITION
REVIEWS

Supplement Article

Executive summary of NIH workshop on Energy Drinks: Current Knowledge and Critical Gaps

Barbara C Sorkin, Kathryn M Camp, Carol J Haggan, Padma Maruvada, Ellen Witt, and Paul M Coates

Sales of energy drinks in the United States have increased significantly since 2000, and while these numbers remain small relative to the total energy drink market, the FDA's recent department visits related to consumption of energy drinks have highlighted the need for further research and while these numbers remain small relative to the total energy drink market, the FDA's recent department visits related to consumption of energy drinks have highlighted the need for further research

NUTRITION
REVIEWS

Supplement Article

Regulatory status of caffeine in the United States

Leah S Rosenfeld, Jeremy J Mihalov, Susan J Carlson, and Antonia Mattia

This article summarizes the history of the regulation of caffeine, a key component of caffeine-containing energy drinks and other caffeine-containing energy products, in the United States. Caffeine as an ingredient in food has been regulated by the US Food and Drug Administration (FDA) since 1958, but the FDA has not

■ Summary of data gaps after IOM and NIH workshop

Rosenfeld et al. 2014¹

Data relating to caffeine's properties that influence exposure:

- Data demonstrating substitutive use or additive use?
- Data that accounts for variability in consumer sensitivity, habituation versus non-habituation, the timing of consumption in relation to the circadian rhythm, and the use of consumer recall surveys to estimate exposure
- Estimates of exposure need to include added caffeine and caffeine from all sources, including naturally occurring caffeine and stealth caffeine present as a component of other added ingredients (i.e., botanicals and extracts)

¹Rosenfeld LS, Mihalov JJ, Carlson SJ, Mattia A. Regulatory status of caffeine in the United States. Nutr Rev. 2014 Oct;72 Suppl 1:23-33

■ Summary of data gaps after IOM and NIH workshop

Rosenfeld et al. 2014¹

Safety Data on Subpopulations

- Data addressing caffeine's health risks to children and adolescents, largely related to incomplete development of the nervous system in youth
- More granular estimates of caffeine exposure for various age groups and vulnerable subpopulations, such as women of childbearing age, children, and adolescents

Monitoring of data sources that provide signals of possible adverse events relating to caffeine containing energy drinks

Identification of those studies from the vast literature on caffeine that most accurately characterize potential risks

¹Rosenfeld LS, Mihalov JJ, Carlson SJ, Mattia A. Regulatory status of caffeine in the United States. Nutr Rev. 2014 Oct;72 Suppl 1:23-33