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# Why Disclosure is Insufficient to Assure Research Integrity

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Conflict of Interest Disclosure is insufficient because:

- It is ineffective
- It is used to create rather than to avert bias
- It is unscientific

There is a better way . . .

## Conflict of Interest Disclosure Requirements for Peer-Reviewers and Their Spouses and Dependent Children:

- Compensated and non-compensated employment
- Consulting
- Grants
- Expert witness testimony
- Stocks
- Bonds
- Royalties
- Financial liabilities

U.S. Office of Government Ethics, 2007

1. Give credit to sources of funding.
2. Provide transparency of financial aspects of research.
3. Reduce bias by requiring providers of science to admit affiliations and sources of support.
4. Provide consumers of science the ability to counteract bias.
5. *Create Bias!*

Cain D, Loewenstein G, Moore DA. The dirt on coming clean: perverse effects of disclosing conflicts of interest. *Journal of Legal Studies*. 2005;34:1-24.

- Disclosure reveals the possibility of conflict and bias on the part of the provider of information.
- The consumer of information can then decide if the conflict has biased the information, to what degree, and to what overall effect.
  - handicap the credibility of information based on perceptions of affiliations and sources of support
- For disclosure to work, the consumer must be capable of properly evaluating the disclosure, the nature of the conflict, and its impact on the information. *This might be an unreasonable expectation.*
  - [CJB: What *OBJECTIVE* scale measures perception of bias ?  
... and what's the p-value ?]

- Providers of information appear to compensate for a perceived diminution of credibility by exaggerating interpretations and claims.
- Disclosure may unburden providers of information from a responsibility to properly limit interpretations and claims.
- Consumers of information may misinterpret disclosure as an assurance of honesty and lack of bias.

Cain D, Loewenstein G, Moore DA. The dirt on coming clean: perverse effects of disclosing conflicts of interest. *Journal of Legal Studies*. 2005;34:1-24.

## Industry influence on occupational and environmental public health.

Huff, J. 2007. Int J Occup Environ Health. 13(1):107-17.

- “Traditional covert influence of industry on occupational and environmental health (OEH) policies has turned brazenly overt in the last several years. More than ever before the OEH community is witnessing the perverse influence and increasing control by industry interests.”
- “Until public health is removed from politics and the influence of corporate money, real progress will be difficult to achieve and past achievements will be lost.” [emphasis added]
- “Scientists and clinicians must unite scientifically, politically, and practically for the betterment of public health and common good. Working together is the only way public health professionals can withstand the power and pressure of industry.” [emphasis added]

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- Egilman DS, Bohme SR. Over a barrel: corporate corruption of science and its effects on workers and the environment. *Int J Occup Environ Health*. 2005;11:331-337.3.
- Egilman D, Wallace W, Hom C. Corporate corruption of medical literature: asbestos studies concealed by W.R. Grace & Co. *Account Res*. 1998;6:127-147.
- Myers JP, vom Saal FS, ... Guillette LJ Jr., ... McLachlan JA.... 2009. Why public health agencies cannot depend on good laboratory practices as a criterion for selecting data: the case of bisphenol A. *Environ Health Perspect*. 2009;117:309-315.



## Beldon Fund “Grants”

**\$2.06 Million Spent On Conflict of Interest**

NRDC: \$860,000 (July 2000 - June, 2008)

CSPI: \$750,000 (Oct, 2000 - Nov, 2008)

PEC: \$450,000 (Oct, 2000 - Oct, 2005)

**\$30 Million Left to be Dispersed by 2010**

## Beldon Fund “Grants”

- “A grant to Center for Science in the Public Interest for its Integrity in Science Project to expose and prevent the destructive influence of corporate interests on scientific research, publications, and science-based policy.”
- “A grant to the Natural Resources Defense Council for its Environmental Health Program, with a specific emphasis on combating industry influence on the science and on the defense of precautionary toxic chemical policy through coalitions with state government officials.”

Sass J. Credibility of scientists: conflict of interest and bias. 2006. *Environ Health Perspect.* 114:A147-8; author reply A148.

- Akst, J., 2010. I hate your paper. *The Scientist* 24:36.
- Jefferson, T., P. Alderson, E. Wager, and F. Davidoff, 2002. Effects of editorial peer review: a systematic review. *J. Am. Med. Assoc.* 287:2784-2789.
- Henderson, M., 2010. End of the peer review show? *Brit. Med. J.* 340:738-740.
- Horrobin, D.F., 2001. Something rotten at the core of science? *Trends Pharm. Sci.* 22:51-52.
- Horrobin, D.F., 1990. The philosophical basis of peer review and the suppression of innovation. *J. Am. Med. Assoc.* 263:1438-1441.
- McCook, A., 2006. Is peer review broken? *The Scientist* 20:26.

McCarty LS, Borgert CJ, Mihaich EM. 2012. Information quality in regulatory decision-making: peer review versus good laboratory practice. *Environ Health Perspect.* 120(7): 927-934.

***Where Should We Focus:***

***On the Scientists ?***

***or***

***On the Scientific Evidence ?***

## 100 Authors Against Einstein (1931)

*“Why one hundred? If I were wrong, one would be enough.”*

## ***Gentlemen; This is a Football !***

Vince Lombardi

- *Science* seeks an understanding of the physical world through objective measurement of it's components and their relationships.
  - *Science* is about measurements, not about scientists.
  - *Science* assumes that the physical world is real can be perceived via the senses, aided by measuring devices.
  - *Science* asks for counterfactual proof of causal relationships.
  - *Objectivity* demands a mistrust of the scientist... “the *scientific method*.”

- **The scientific method is unique among modes of human inquiry; outside of science, the pedigree of the performer is paramount.**
- **The scientific method mistrusts the scientist, eschewing his pedigree in favor of a data pedigree:**
  - Randomized
  - Double-blinded
  - Placebo-controlled
  - Statistically tested
  - Replicated
  - Failed falsification

Borgert CJ. 2007. Conflict of Interest or Contravention of Science? *Regulatory Toxicology and Pharmacology* 48:4-5.

Borgert CJ. 2007. Conflict of interest: kill the messenger or follow the data? *Environmental Science & Technology*, 41(3): 665-666.

- The scientific method, properly administered, removes the scientist as far as possible from the process of observation and data acquisition.
- Scientific “consensus” is provisional and achieved only as the range of tenable interpretations narrows, consistent with an increasingly broad and probative data set.
- Perhaps the only argument of legitimate scientific discussion is how well-controlled the measurements and experimental conditions and how unequivocally the interpretations are supported by the data.
- Compromise and vote are anathema.

Borgert CJ. 2007. Conflict of Interest or Contravention of Science? *Regulatory Toxicology and Pharmacology* 48:4-5.

Borgert CJ. 2007. Conflict of interest: kill the messenger or follow the data? *Environmental Science & Technology*, 41(3): 665-666.



## *1° Validity: Minimal epistemic status*

### **Minimum Requirements of Scientific Evidence Are Few *but* Firm**

1. measurements have been authentically identified within an explicit margin of error that is testable and reproducibly small enough to avoid ambiguity;
2. extraneous factors that could affect the measurements and conclusions have been measured and adequately controlled;
3. measurements and conclusions have been consistently replicated by independent investigators.

Gori GB. 2002. Considerations on guidelines of epidemiologic practice. *Ann Epidemiol.* 12(2): 73-8.

Gori GB. 2001. The costly illusion of regulating unknowable risks. *Regul Toxicol Pharmacol.* 34(3): 205-12.

McCarty LS, Borgert CJ, Mihaich EM. 2012. Information quality in regulatory decision-making: peer review versus good laboratory practice. *Environ Health Perspect.* 120(7): 927-934.

Borgert CJ, Mihaich EM, Ortego LS, et al. 2011. Hypothesis-driven weight of evidence framework for evaluating data within the US EPA's Endocrine Disruptor Screening Program. *Regul Toxicol Pharmacol.* 61:185-191.

## 2° Validity: Reliability & Transparency

### Klimisch Codes: Klimisch et al., 1997

- “test species, test substances (purity, origin), number of animals evaluated, scope of investigations per animal (e.g., clinical chemistry, organ weights, hematology, histopathology), description of changes or lesions observed, control and historical control groups, test conditions, route of administration, dose schedule and dose concentration (including analytical verification)”
- diets, composition of water bottles and cage materials, bedding, stressors such as handling and manipulation, and any other factors that could affect hormonal systems, as well as details on the mathematical and statistical algorithms used to analyze the data
- GLP; Guideline Studies;
- Published studies

Klimisch HJ, Andreae M, Tillmann U. *Regul Toxicol Pharmacol.* 1997;25:1-5.

McCarty LS, Borgert CJ, Mihaich EM. 2012. *Environ Health Perspect.* 120(7): 927-934.

Borgert CJ, Mihaich EM, Ortego LS, et al. 2011. *Regul Toxicol Pharmacol.* 61:185-191.

## *2° Validity: Reliability & Transparency*

***The pedigree of the data should be made perfectly transparent, online, as a requisite for publication.***

### **Post Online:**

- Experiments
  - Experimental design details
  - Analytical characterization of materials
  - Raw laboratory notebooks
  - Instrument outputs
  - Statistical algorithms used to analyze data
- Reviews
  - Literature search parameters (databases)
  - Search terms and search results
  - Criteria for selecting and prioritizing literature
  - Criteria for evaluating literature

Borgert CJ. 2007. *Regulatory Toxicology and Pharmacology* 48:4-5.

Borgert CJ. 2007. *Environmental Science & Technology*, 41(3): 665-666.

Schrierder et al., 2010. Enhancing the credibility of decisions based on scientific conclusions: Transparency is imperative. *Toxicological Sciences*. 116 (1), 5-7.

### *3° Validity: Relevance and Probative Design*

- Counterfactual Study Design:

Counterfactual experiments test whether the effect of interest still occurs when a putative causal step is prevented under conditions that would otherwise produce the effect of interest.

- Predictive Value

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Borgert CJ, Mihaich EM, Ortego LS, et al. 2011. *Regul Toxicol Pharmacol.* 61:185-191.

### *3° Validity: Relevance and Probative Design*

- Counterfactual Study Design
- Predictive Value:
  1. Positive: Fraction of positive tests that correctly indicate the condition.
  2. Negative: fraction of negative tests that correctly indicate absence of the condition.
  3. Actual incidence of the condition

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Borgert CJ, Mihaich EM, Ortego LS, et al. 2011. *Regul Toxicol Pharmacol.* 61:185-191.

- Would Arnold et al., 1996 (Science paper on estrogenic synergy of pesticides - retracted in 1997 for alleged fraud) have been published had 1° and 2° validity been explicit components of peer-review ?
- Would Aril Potti's work on genomics of small cell lung cancer have been published (4 papers recently retracted from prestigious journals) had 1° and 2° validity been explicit components of peer-review ?
- Would even half the public health scares published in peer reviewed journals be in print today if 3° validity been an explicit component of peer-review ?

*Development of Western science is based on two great achievements: the invention of the formal logical system (in Euclidean geometry) by the Greek philosophers, and the discovery of the possibility to find out causal relationships by systematic experiment (during the Renaissance).*

Albert Einstein (1953)