Comment on *Risk versus Hazard – How to Regulate in the 21st Century*

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In this issue of the journal, Dr. Ragnar Lofstedt examines the current state of the EU regulatory framework with respect to chemicals and illustrates how the hazard-based approach sealed the fate of two important chemicals in the EU market-place. He also explores how the attitudes, technical knowledge and economic influences of the individual member states determine the outcome of environmental and chemical regulations. Lastly, Dr. Lofstedt provides some recommendations to improve consistency in the European regulatory process and ensure greater scientific, as well as, risk-based regulations.

Risk assessment has played a significant role in the development of environmental regulation in the United States since the early 1980's during which time the country needed to prioritize the clean-up of thousands of contaminated sites. The U.S. National Resource Council's Risk Assessment in the Federal Government: Managing the Process (aka, the Red Book)[1] set the foundation for risk based regulatory decision making which has been in use ever since. Since then, my colleagues and I have probably conducted more than 1,000 assessments of chemicals[2] or radionuclides in contaminated soil, sediments, air, water, and a host of consumer products. As we read Ragnar's paper, we are reminded of the road that the U.S. has taken on the journey to chemicals management and environmental clean-up. The early years (1975–1995) were not so different than that which is described in this paper; and even today, an outdated national approach to chemicals management has resulted in actions taken by individual states which will significantly affect business and commerce.

Dr. Lofstedt's paper is timely in many respects. The EU REACH regulation will have significant ramifications on global commerce. While it is touted as a risk-based regulation – for many chemicals, their registration actually hinges on a hazard-based approach, where those with inherent carcinogenic, mutagenic or reproductive toxic properties; those considered very persistent and very bioaccumulative, or those exhibiting characteristics of equivalent concern (currently understood to be endocrine disruptors or skin sensitizers) are automatically slated for eventual substitution irrespective of the risk posed to humans. Risk, after all is based on potency, toxicity and degree of exposure, not the perception that a chemical's detection warrants that it be feared or banned. Other EU regulations of chemicals including the Plant Protection Regulation and the Cosmetics Directive as discussed recently by Nordlander et al.[3], focus a great deal on the name of the hazard (e.g., mutagen, carcinogen, or endocrine disruptor) rather than the magnitude of the risk.

The two case studies presented by Dr. Lofstedt are good examples of regulation-by- hazard-assessment and clearly demonstrate how the regulatory process can be hijacked by those with personal or political agendas that are dependent upon public fear. In the case of BPA, the key issue was the non-repeatability of the vom Saal studies. The importance of repeatability is the underpinning of the scientific process and is critical to understanding how "real" a scientific discovery is[4]. As explained by Schooler[5], the "decline" effect, wherein new scientific discoveries are not repeated over time, could be due, in fact to statistical self correction. Equally important to the repeatability of a single study is the lack of repeatability in other animal models for understanding the relevance of any toxic effect to humans. There is the classic example of the rush to ban saccharin, because of bladder tumors discovered in the rat model. In

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1 National Research Council, "Risk Assessment in the Federal Government: Managing the Process" (the *Red Book*), (Washington, DC: National Academy Press 1983).

2 D.J. Paustenbach, *The Risk Assessment of Environmental Hazards: A Textbook of Case Studies* (New York: John Wiley & Sons, 1989), pp. 1157 (34 chapters by 51 contributors); Paustenbach, *Human and Ecological Risk Assessment: Theory and Practice* (New York: John Wiley and Sons 2002), pp. 1556 (33 chapters by 50 contributors).

3 K. Nordlander, C. Simon and H. Pearson, "Hazard v. Risk in EU Chemicals Regulation", 1(3) *European Journal of Risk Regulation* (2010), pp. 230–250.

4 J. Lehrer, "The Truth Wears Off – Is there something wrong with the Scientific Method?", *The New Yorker*, December 2010, pp. 52–57.

5 J. Schooler, "Unpublished Results Hide the Decline Effect", 470 *Nature* (2011), p. 437.

fact, this effect only occurred at exceptionally high doses and only in the rat – not mice or primates, and not in studies of humans. Despite these negative findings AND lack of an official ban in the U.S., the carcinogen stigma stuck and many other sugar substitutes eventually replaced it on the market.

The case study of DecaDBE is also quite useful in understanding the "guilty by association" problem that can result when hazard assessment is the basis for regulation. Further, this example illustrates the "fear factor" which arises when the public is made aware of the presence of the chemical in their bodies. While the detection of the chemicals is an indication of exposure, it is not necessarily an indication of adverse health effects or even that someone is at an increased risk. Nonetheless, using the tissue concentrations to understand chemical exposure for humans is a step toward reducing the uncertainty surrounding many exposure assessments and, ultimately, the potential for adverse effects. Unquestionably, the need to understand the significance of the chemicals which we measure at increasingly lower levels in the human body is the next frontier for risk assessment.

Dr. Lofstedt writes that some in the EU believe that a risk based approach to regulations is inappropriate because risks cannot be adequately anticipated and controlled, and others believe that there is so much uncertainty with the risk assessment process that the true risk cannot be identified or confirmed. With respect to the first notion we believe that it is possible to anticipate and control most risks. Although previous chemical management programs did not require industry to prove that their chemicals were safe before placing them on the market (i.e., government had to prove that they were unsafe in order to remove them and the data to make a reliable assessment were often lacking), the new framework in the EU and revisions to those planned elsewhere have changed this paradigm. The ability to anticipate risks has never been greater and, in fact, and our capacity to characterize risks is much improved. We believe the next challenge is how to get the various stakeholders to reach agreement on the magnitude of the various types of which risk which they considerable acceptable. With respect to uncertainty, there will always be some; but our techniques for characterizing the uncertainty have increased considerably over the past 15 years. Equally important as a quantitative description of the uncertainty is the transparency; a key part of the risk communication process. Only when the risk assessment methodology is transparent, can a regulator be confident that their risk management decision will achieve what they desire with respect to protecting public health or the environment.

In the U.S., a risk based approach to environmental regulations continues to be the recommended method to develop scientifically defensible legislation that is protective of human health and the environment; although short-comings of the approach have been identified and recommendations for improvement have recently been made[6]. Recommendations made by the Committee on Improving Risk Analysis Approaches Used by the USEPA (Committee) are worthy of consideration as the EU moves forward in developing consistent environmental regulations. Specifically, the Committee's recommendation on revamping the risk assessment framework to first identify the potential problem associated with existing conditions and determining what options are available for altering those conditions and then follow with the traditional risk assessment may maximize the utility of the risk assessment.

In the last section of the paper, Dr. Lofstedt makes 8 recommendations for improving the usefulness and consistency of regulatory decision making in the EU. We are particularly fond of three of them.

First, the peer review of regulations is a good idea. How that peer review board is established has become a Gordian knot and we in the United States have done only an average job in recent years in setting up our advisory panels. Often, the best scientists are "screened out" due to perceived, real or imagined conflicts of interest. Although there is a clear need for those with "real conflicts" to be heavily scrutinized, care should be taken to ensure that true experts in the field are not wrongly excluded from participating.

Second, the proposal for an SAB for the European Parliament makes sense. At various times in the United States, Congress or the President has convened special groups to evaluate topics which require immediate attention. And, in the past, the Office of Science and Technology Policy (OSTP) and the National Academy of Science, as well as the National Academy of Medicine, have served as on-going advisors to the administration. As mentioned by Ragnar, at times, the Office of Information and Regulatory Affairs

6 National Research Council, "Science and Decisions: Advancing Risk Assessment. Committee on Improving Risk Analysis Approaches Used by the U.S. EPA" (Washington, DC: National Academy Press 2009), pp. 403.

(OIRA) has helped the administration develop more reasonable and cost-effective approaches to the regulation of chemicals in various media.

Third, perhaps the most novel of Dr. Lofstedt's suggestions is to attempt to improve the knowledge of journalists. He correctly notes that they have a phenomenal impact on public perception and, accordingly, public outrage. However, there is currently no mechanism for insuring that what they communicate represents the weight of scientific evidence. A suggestion that journalists be accountable to a "science advisory board" which would give advice, rather than censor various pieces, could go a long way in preventing genuinely inaccurate information from being published by typically reputable papers, magazines or journals. And, when really "incorrect" or slanderous pieces are printed that seriously (and erroneously) impact an industry or a person, the journalist should be held accountable (financially or otherwise).

We have made many advances in both the practice of risk assessment and risk communication over the past 30 years[7]. Dozens of guidance documents have been developed and we better understand our limitations as scientists. It appears that the next step for optimizing our use of chemicals and to insure proper oversight is to improve the level of communication. Indeed, not just the level of communication but also the method since the traditional scientific journal or newspaper is no longer the key way persons obtain information. To date, scientists and regulators have failed to give adequate consideration to the impact of emails, social networking blogs, on-line publishing, and other instant media with respect to how society might respond; nor the swiftness and severity of that response. For sake of society, all of us in the risk assessment community should do what we can to insure that risk science doesn't erroneously or inadvertently lessen the quality of daily life, drug development or use, or new scientific discoveries.

7 Paustenbach, "Retrospective on U.S. Health Risk Assessment: How Others Can Benefit", 6 *RISK: Health, Safety & Environment* (1995), pp. 283–332; John Graham and Jonathan Wiener (eds), *Risk Versus Risk: Tradeoffs in Protecting Health and the Environment* (Harvard Univ. Press 1995); NRC (1996); NRC (2009), *supra* note 6.