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Alliance Plans Panel To Address Key Scientific Issues In Risk Assessment

An alliance of risk assessors is planning to create a standing panel of experts that would address overarching scientific issues in risk assessment, providing an outlet for industry, academia and others to gain answers to those issues plaguing risk assessment that have not been resolved by EPA or other authorities.

The panel would be be modeled as a "[National Academy of Sciences (NAS)] 'lite' type standing panel" tasked with meeting twice a year to tackle issues that don't necessarily rise to the NAS' level of importance, according to a source familiar with the work being done.

"If industry or environmentalists have a problem, who do they go to?" the source says. While the federal government can go to NAS with questions, industry and other groups have no similar outlet. What's more, there are "a lot of issues out there, so NAS can't handle it all."

The panel would be created as an extension to the Alliance For Risk Assessment's soon to be completed project "Beyond Science And Decisions: From Issue Identification to Dose-Response Assessment," which looks at lingering issues with the implementation of the December 2008 National Academy of Sciences report, *Science and Decisions: Advancing Risk Assessment*, known as the "Silver Book."

The alliance has brought together a coalition of 45 industry, academic, non-profit and governmental groups, including EPA, lead by the non-profit group Toxicological Excellence In Risk Assessment (TERA), to reach consensus on guidance that highlights considerations risk assessors should take when using dose-response techniques. The coalition has held three workshops to discuss relevant issues, and is preparing to release final slides and case studies from the project.

In its final recommendations, the coalition concludes there is a lack of consistency in the problem formulation stage of risk assessment, better understanding is needed for mode of action and understanding what makes a substance toxic, linear modeling is not appropriate for non-cancer endpoints and more consideration in assessments needs to be given to background levels of contaminants, according to the source.

The conclusion that linear modeling is not a good method to use on non-cancer assessments directly contradicts the NAS' recommendations. Linear extrapolation, or modeling, is generally a conservative method of modeling dose-response, the basis of risk assessment, at the low doses of exposure found in the environment. The approach largely assumes no safe level of exposure and results in harms proportional to the dose. Non-linear modeling assumes there is a threshold dose level below which exposure is not reasonably anticipated to be harmful. Linear modeling, which generally produces conservative assessments of cancer risk, is often opposed by industry and other regulated entities, including other federal agencies.

Existing EPA guidelines apply conservative linear assessment to cancer risk assessments of chemicals that are mutagenic, or those whose biological mechanism for causing cancer is unknown, because it is considered health-protective in the face of uncertainty. The approach is not applied to non-cancer estimates of risk, where a threshold is assumed.

But *Science and Decisions* recommends performing cancer and non-cancer assessments similarly, by a "unified approach to dose-response assessment." The report recommends three different "conceptual models" of how to perform risk assessments, depending on whether the chemical or environmental contaminant exhibits non-linear or linear responses in individuals or the population at low doses or generally, and whether the response is dependent or independent of background exposure.

However, the coalition, which conducted a case study on the issue, found that linear extrapolation "was not helpful" since too many assumptions were needed, the source says. To begin with, linear modeling assumes there is no threshold, which the source notes is largely the basis for toxicology. In addition, a linear model with a 10X safety factor can result in risks as low as 1 percent, a level that toxicologists say is unmeasurable, the source argues. "Biology is not linear like that," the source says.

Risk assessment would further significantly benefit from better problem formulation, the source adds, as currently some of the most complex issues assessors are grappling with actually pose very little risk. For example, for years officials have been looking to regulate perchlorate — a naturally occurring substance that is used in rocket fuel, among other

things — that is present in some drinking water supplies. The concern is that perchlorate can interfere with iodine uptake into the thyroid gland, which governs metabolism in adults and affects development in infants and children.

However, the source says doctors have long said that there is not an iodine deficiency issue among pregnant women in the United States, and for those with lower levels, there are supplements available to solve the problem. EPA has been arguing for years over how to regulate perchlorate and what level would be appropriate, but since there doesn't seem to be a problem caused by the chemical, the source questions the wisdom of regulating it. If a proper problem formulation was done prior to undertaking the risk assessment, EPA could have saved a lot of time and money, the source says.

The workshop participants developed the proposed standing panel as a way to resolve lingering issues. "The workshop series was satisfying to folks . . . because they were able to collaborate and able to look at each others work in a way that was very collegial, but also very critical," the source says. The panel is designed to continue that work.

That is different from many other groups that are brought together "on X or Y," and disbands once the work is done, says an industry source. "This panel was brought forward to look at actualizing some of the challenges faced in *Science and Decisions*," the source adds. While there is "still additional areas in risk assessment that continue to move forward, might we not benefit from continuing that activity?"

"It seemed that the unique opportunity to engage with such panels of experts that have such deep experience with risk assessment, to address some of the most challenging aspects of dealing with risk assessment is appealing to many."

In particular, the source says, the panel should among other things address mode of action problems, and advancing a greater understanding of why a chemical poses a hazard. — *Jenny Hopkinson*