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Dr. Paul Anastas
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U.S. Environmental Protection Agency

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Dear Dr. Anastas and Dr. Davis:

The following is a letter report from the Executive Committee of the Board of Scientific Counselors (BOSC) concerning the review of the Office of Research and Development (ORD) ***Nanomaterial Case Studies Workshop: Developing a Comprehensive Environmental Assessment Research Strategy for Nanoscale Titanium Dioxide***, which was held September 29-30, 2009, in Research Triangle Park (RTP), North Carolina. The BOSC chair participated as an observer of the workshop in RTP. The May 10, 2010 summary report of the Nanomaterial Case Studies Workshop (NCSW) was presented to the BOSC during its July 12-13, 2010 meeting at the ORD National Health and Environmental Effects Research Laboratory, Western Ecology Division in Corvallis, Oregon. Based on BOSC discussions of the NCSW report at that meeting, a draft BOSC response was prepared by Dr. Katherine von Stackelberg, Chair of the BOSC Decision Analysis Workgroup, with Executive Committee member input, and it was vetted, appropriately edited, and approved by the BOSC during a public teleconference on August 25, 2010.

At the NCSW, a valuable comprehensive environmental assessment (CEA) approach was taken as the framework for evaluating the broad implications of nanomaterials released to the environment and the workshop adequately reflected the breadth of stakeholders contributing to the assessment. The rationale for selection of titanium dioxide (TiO_2) was well laid out as the test case nanomaterial.

Introduction

In September 2009, the ***Nanomaterial Case Studies Workshop: Developing a Comprehensive Environmental Assessment Research Strategy for Nanoscale Titanium Dioxide*** was held. The goal of the

workshop was to identify and prioritize research needed to support a CEA of nanoscale-TiO_2 (nano-TiO_2) as a first step in refining a broader strategic approach for nanomaterials risk assessment research, consistent with objectives described in the EPA Nanomaterial Research Strategy (US EPA, 2010; which is readily available to the stakeholder community at http://www.epa.gov/nanoscience/files/nanotech_research_strategy_final.pdf), and the workshop organizers focused on use of the Nominal Group Technique (NGT) to achieve this goal. The BOSC Executive Committee was subsequently invited to review the report on the nanomaterial workshop, focusing specifically on the process followed to prioritize research needs and to comment on use of NGT as an overall strategy.

Overall Conclusions

NGT is a well-established technique particularly suited to "brainstorming" and reaching and identifying consensus opinion across a diverse set of stakeholders. First developed in the 1960s and 1970s, it is a technique that has been used for "group decision making." Following the process with clearly defined objectives can lead quite effectively to a list of prioritized issues, as it did in the case of this ORD workshop. It provides a relatively transparent process that can be explained more broadly, and is clearly better than ad hoc discussions or the free-form exchange of ideas from which it is difficult to track how a prioritized list was ultimately obtained.

If this process worked—it yielded the desired outcomes, it was effective and efficient in identifying research priorities, and the Agency considers it a success—then that is an important consideration. The prioritized list of focus areas for research developed through the workshop is valid and appropriate, and using NGT, as opposed to other less transparent, more *ad hoc* methods, is clearly a step in the right direction. From a decision analytic perspective, however, NGT as a process falls a bit short of the BOSC's expectations for a model or approach that will quantitatively and in a mathematically rigorous way evaluate the tradeoffs that need to be made. This explicit and quantifiable evaluation of alternatives and tradeoffs across alternatives is the hallmark of decision analytic techniques. NGT could be combined with a more formalized decision analysis process, but in and of itself is not formalized enough to be considered a robust method for evaluating and prioritizing alternatives. In addition, it would seem workshops like the NCSW need to be conducted on an ongoing basis, given that the question under consideration is so specific (e.g., particular uses of a specific nanomaterial). A more generalized approach might be preferable in the long run with respect to leveraging resources.

The process followed to identify the research needed to support a CEA of one specific nanomaterial is certainly a step in the right direction with respect to formalizing an approach that provides greater transparency in how the Agency has identified what research to pursue. It also represents a first step in refining a broader strategic approach for nanomaterials risk assessment research, but it is not a decision analytic method in and of itself and ultimately provides only a list of priorities in terms of research that reflects the consensus opinion of the group in the room as opposed to a formalized process for identifying priorities (research alternatives) with criteria against which the alternatives are compared (e.g., multi-criteria decision analysis [MCDA], value of information [VOI], or other similar techniques).

In addition, focusing on particular applications of individual nanomaterials, which may or may not represent the most common uses of the materials in practice and which by definition are context-specific, may not offer the most effective approach for identifying research priorities

more generally across all nanomaterials. Perhaps it makes sense to have a workshop (at which NGT could be used) that identifies a strategic decision making framework (e.g., decision tree or trees, or even a flow chart) that would be followed when evaluating a specific nanomaterial (e.g., Is it released to water? Yes; Is there information on…? Yes; and so on). That would result in a generalizable process to follow when evaluating any use of any nanomaterial as opposed to focusing on specific uses and constituents, which will lead necessarily to many more focused workshops that may not be as cost-effective or efficient in the long term.

Finally, ORD should recognize that the prioritized list is not static but rather dynamic and will change over time as new information is obtained. ORD also should ensure that EPA public affairs staff are included or briefed on subsequent workshops and issues so that they can lend communications advice to the workshop organizers.

Background Information

Following a September 2008 presentation by the Office of Science Policy (OSP) on the use of VOI techniques as a more formalized approach to identifying and prioritizing research needs in ORD, the BOSC Executive Committee formed a Decision Analysis Workgroup to pursue the topic. VOI can be challenging in the context of prioritizing basic research because in order to calculate the "value" of information, where value is typically defined in dollars, one needs to understand how the ultimate decision impacted by the research will change. The Workgroup determined that, in a broad sense, decision analytic approaches—of which VOI is one—seem to be conceptually very powerful for allocating resources and making tradeoffs, which is how these tools evolved in the first place.

The BOSC Workgroup convened a workshop in spring 2009 to discuss this issue. The invited participants included representatives from industry, other government agencies that have adopted more formalized evaluation techniques (e.g., U.S. Army Corps of Engineers), academics, and private consultants. The Workgroup developed three case studies to organize discussions around the topic and, following the workshop, prepared a report. The report concluded that decision analytic techniques span a broad range of methods that could clearly provide scientifically defensible frameworks for developing priorities. The logical rigor offered by decision tree analysis and scenario planning is useful, and at a minimum, specifying the underlying structure of the issue and identifying the forces that will determine how the chain of uncertainties could unfold, reduces the uncertainty that results simply from a lack of logical thinking (Collis D. The strategic management of uncertainty. *European Journal of Management* 1992;10(2):125-135). As with any other method or approach, however, one could not expect individuals to simply start using these techniques without a more concerted effort on the part of ORD to train decision makers, identify relevant analytic skills, and provide an environment in which decisions are made that differs significantly from the way decisions currently are made. The working culture of any organization relies on a system of shared attitudes, values, and beliefs; and the nature of this system will define appropriate behaviors and shape the decision-making processes of the senior managers (Bonn I, Christodoulou C. From strategic planning to strategic management. *Long Range Planning* 1996;29(4):543-551).

Approximately 5 months after the BOSC workshop, ORD's National Center for Environmental Assessment (NCEA) convened the Nanomaterial Case Studies Workshop. The motivation to move beyond traditional methods is clearly present within ORD, and the NCSW represents an

effort to follow a transparent, formal process for identifying research priorities. As stated in the NCSW summary report: "[it is] essential to use a more formal or structured decision-support process rather than a typical "free discussion" workshop discussion format. A second feature of fundamental importance was having a diverse, multi-disciplinary, and multi-stakeholder group of workshop participants to consider these issues." The report goes on to justify use of NGT as opposed to other approaches as being "appropriate given the nascent state of the science related to nanomaterial risk assessment and because it could be implemented more easily in the face of temporal and other constraints." For example, one constraint could be, as was identified in the May 2010 BOSC Decision Analysis Workshop Report (http://www.epa.gov/osp/bosc/pdf/deci1005proc.pdf), analytical skills with respect to use of decision analytic techniques. Use of NGT represents a step in the direction of a transparent, formalized process, and the list of priorities obtained from such a process stand on stronger footing than if more *ad hoc* methods had been used.

NGT as a Method for Prioritizing Research Investment Decisions

If this process worked—the Agency has determined it yielded the desired outcomes and was effective and efficient in identifying research priorities—then that is an important consideration, and clearly the list of priorities obtained from this process is more credible, transparent, and vetted as compared to closed-door discussions. From a decision analytic perspective, however, NGT as a process falls short with respect to expectations for a model or approach that will quantitatively, in a mathematically rigorous way, evaluate the tradeoffs that need to be made. That is, in part, because preferences are not constrained by cost or resource limitations.

NGT falls short of the goals of a decision analytic process in that NGT itself does not address how resources will be allocated, and does not explicitly identify the tradeoffs being made in the choice to fund this but not that. In other words, the most challenging issues are not actually addressed—although there are examples from the literature of explicitly linking NGT with multi-criteria decision analysis or some other actual decision analytic framework, which would achieve these goals (Thomas JB, McDaniel Jr. RR, Dooris MJ. Strategic issue analysis: NGT + decision analysis for resolving strategic issues. *Journal of Applied Behavioral Science* 1989;25(2):189-200; Frankel S. NGT + MDS: an adaptation of the nominal group technique for ill-structured problems. *Journal of Applied Behavioral Science* 1987;23(4):543-551).

As stated in the NCSW report: "the ultimate goal is to develop a broad, long-range strategy for determining where research should be directed to best support efforts to conduct comprehensive environmental assessments of nanomaterials. This new research strategy will likely evolve as different case studies are considered and as new information on existing case studies becomes available. Thus, it will not be a static document, but one that reflects an evolving understanding of nanomaterials and their (broadly defined) environmental implications."

The workshop organizers acknowledge that there is no one-size fits all strategy; research is always context specific—the research to pursue with respect to the use of nano-TiO_2 as a sunscreen agent is different from the research to pursue with respect to use of nano-TiO_2 as a water disinfection agent—and yet the goal is that by developing a number of these case studies, it may be possible to identify a common set of issues across all case studies that represent the important questions to be asked and addressed by research.

Given that the ultimate goal is to develop a broad, long-range strategy for determining where research should be directed to best support efforts to conduct CEAs of nanomaterials generally, it may make sense to hold some workshops that are more directed to comprehensive evaluation frameworks in which one would develop a decision tree or series of decision trees that address questions organized by the modules shown in Figure 1 of the workshop report. It would seem that having workshops that focus on specific applications of particular nanomaterials will not be efficient or cost effective in the long term.

Ideally, a CEA would provide a generalized and generalizable framework for identifying context-specific research needs. The yes and no answers to a set of questions—Is the material released to water? Is the material released to air?—send the analyst to another set of questions. This approach makes the process for evaluating research needs more generalizable. As it stands right now, there are (or will be) a series of case studies that are quite specific with respect to particular scenarios of use of nanomaterials (that may not even reflect the most common uses of these materials in practice), and the workshop results appear to reinforce the qualitative ideas that already existed about what is known and unknown about a particular application of a specific nanomaterial. Therefore, the question becomes: What are the real outputs of this workshop? In essence, the research still has not been prioritized—the important questions to be asked with respect to a particular use of a nanomaterial have been identified, but there is no sense for how to best evaluate those questions.

The NGT process from the workshop resulted in a series of prioritized questions. Question 4-10 was the highest "ranked" question from the workshop report: "Are available methods adequate to characterize nano-TiO_2 exposure via air, water, and food? What properties of nano-TiO_2 should be included in such exposure characterizations?" There is still a challenge in translating the ranked questions to actually prioritizing research. Are available methods adequate? How does one know? What are the criteria by which that question is being judged, i.e. what is the definition of "adequate"?

Several of the prioritized questions from the workshop are excerpted here:

- ✧ Are current EPA standard testing protocols adequate to determine nano-TiO2 ecotoxicity? If not, what modifications or special considerations, if any, should be made in current ecological tests? For example, what are the differences in characterization of testing material (as raw material, in media, and in organisms), dispersion methods, and realistic exposure routes between testing conventional materials and nanomaterials (commercial use)? (5.2-1)

- ✧ Are the current EPA harmonized health test guidelines for assessing toxicity adequate to determine the health effects/toxicity of nano-TiO_2? (5.3-1)

- ✧ What criteria, especially associated with an inert colloid particle, should the EPA use when evaluating harmonized test protocols?

- ✧ What set of widely shared reference samples of nano- and conventional TiO_2 would be most useful for integrating the results of different investigators regarding particle characterization and particle toxicology?

Based on the output of the NGT approach, these priority questions are a valid outcome of the NCSW process. This list of prioritized **questions** differs from prioritized **research**, however, and one wonders how many workshops are required before one could identify a broad, long-range strategy. One approach might be to conduct a workshop that endeavors to develop a decision tree or trees that could be followed in evaluating research priorities rather than focuses on a specific case study (where the case study itself may not even represent the most common uses in practice of a particular nanomaterial). For example, following the modules given in Figure 2-1 of the workshop report, starting with "feedstocks," answering a set of questions—Does the manufacturing process lead to releases in air? (yes, no, unknown), Does the manufacturing process lead to releases in water? (yes, no, unknown)—then leads to a further series of questions. By identifying all the "unknowns" in answering these questions, one would ultimately have a list of issues that need to be addressed before a CEA could be conducted. Prioritizing that list then would be the function of a more formalized decision analysis model that would more explicitly identify priorities (e.g., fundamental unknowns related to predicting outcomes are likely of higher priority than adding to a sparse database in some other area, etc.).

Nonetheless, that said, use of NGT in the NCSW led to a context-specific list of priorities that are valid and appropriate, and use of this approach is clearly a step in the right direction even if it falls short of a decision-analytic approach. This (or any) list of priorities, however, must necessarily be dynamic in that the list reflects the best scientific understanding available at the time of the workshop. As research is conducted and knowledge grows, the list will change over time and should not be regarded as static options.

The BOSC is pleased to submit this report and we hope it aids in this and future CEAs, as well as the broader quantitative application of decision analysis tools and VOI approaches in environmental assessment and risk analysis. In particular, we are hopeful the report contributes to the further strategy of research identification and prioritization for nanomaterial CEA. The BOSC is prepared to comment further on this topic or provide additional details as needed.

Sincerely,

Gary S. Sayler
Chair, BOSC