May 29, 2019

Written Comments of Penelope A. Fenner-Crisp, PhD, DABT, for the June 5-6, 2019, Public Meeting of the EPA Chartered Science Advisory Board: Actions Related to Updating EPA Guidelines for Carcinogen and Noncancer Assessment

I appreciate the opportunity to provide written and oral comments to the EPA Chartered Science Advisory Board for consideration in its discussion of EPA's plans to revise its *Guidelines for Carcinogen Risk Assessment* and develop new guidelines for non-cancer risk assessment.

I am a Diplomate of the American Board of Toxicology and a member of the Society of Toxicology and the Society for Risk Analysis, having served in leadership positions in both organizations. I have been a risk practitioner for more than 40 years, about half of that time at EPA. Over those four decades, as a member of EPA's Risk Assessment Forum, and for a time, its Chair; as a Senior Manager in the Office of Chemical Safety and Pollution Prevention; and as an external contributor and peer reviewer, I have examined, conducted, published, contributed to, internally or externally peer-reviewed or overseen the development of hundreds of hazard and risk assessments. I also have been involved in the development of about a third of the more than 90 products listed on EPA's Human Health Risk Assessment Guidelines webpage as well as other relevant publications such as the Risk Characterization and Peer Review Handbooks.

Overview

EPA's risk assessment guidelines represent the agency's public expression of the scientific principles that inform and direct its deliberations as it works to describe the nature and impact of hazards and risks associated with exposure to environmental agents. To propose and expect that, before the end of 2020, the agency can succeed in articulating a set of principles that will find acceptance in the broader scientific community is hopelessly unrealistic, and naïve, at best. The proposed schedule does not provide the time needed for robust and credible science policy to be developed and for full engagement of the SAB, the NAS and other stakeholders in its review. In these comments, I outline specific activities, steps and associated timelines that would more likely lead to soundly-based and fully-vetted guidelines.

As detailed below,

- EPA should develop a realistic plan and request a formal review of that plan by the SAB before proceeding. This June meeting does not qualify as that consultation, given the short time dedicated to discussion.
- Based on my assessment, it would be realistic to plan for a four to six year process, under optimum circumstances. The time might be shortened somewhat by careful planning, but the idea of finishing everything by the end of 2020 is wholly unrealistic.
- Once a realistic plan is in place, EPA should begin implementation by addressing the unresolved issues from the 2009 NRC *Science and Decisions* report before writing any guidelines.
- Adequate agency resources and time need to be committed and sustained along with credible engagement of outside experts in both development and review roles.
- It would be wise to engage the NAS in the review of the *Science and Decisions*-related issue papers, the guidelines and the qualifications of the SAB review panel to confirm that the agency's outputs reflect an objective view of the state of the science.

Developing a realistic process

To illustrate the challenge that EPA faces, my first engagement in an agency effort to draft risk assessment guidance occurred over 35 years ago when a workgroup was convened to write systemic toxicity or non-cancer guidelines. Within two years, the attempt was abandoned, thwarted by the failure to agree upon the definition of "adverse," and the inability to design a severity scale and determine at what point along that scale an effect became "adverse." Currently there are no non-cancer guidelines as the agency never resolved this stalemate.

On June 5th, the SAB and the public will hear how the agency plans to update the 2005 cancer guidelines and develop first-ever non-cancer guidelines. This can only be an introductory presentation of process and timelines, and not a consultation on the substance of either guideline, given the minimal time committed for discussion. My comments will also focus on process and timing issues.

To begin with, EPA has unfinished business with regard to the agency's response to, and implementation (or not) of recommendations made by the National Research Council in its 2009 report *Science and Decisions: Advancing Risk Assessment (NRC, 2009)*. Affectionately known as the Silver Book, it presents recommendations on several intractable challenges that transcend any endpoint-specific guideline, among them:

uncertainty and variability, dose-response assessment, selection and use of default factors and cumulative risk assessment.

Although EPA has held internal staff-only events to begin discussion of these topics and crafting a plan to attack these difficult issues, no signs of progress have appeared in the public arena. No public workshops, no approaches presented for public review and comment. These issues need to be resolved before new or updated guidelines can be issued. They are important enough on their own to warrant a rigorous program of robust cross-Agency and external peer involvement in drafting the products, public discussions in many venues, peer review by a Science Advisory Board (sub)committee supplemented with representatives from the FIFRA Scientific Advisory Panel and the TSCA Science Advisory Committee on Chemicals, as well as additional outside experts to ensure both the necessary expertise and a balance of perspectives within the scientific community. It should include referral back to the National Academies of Sciences. After external peer review and public comment, revision would proceed, accompanied by a response-to-comments piece that provides the rationale and justification for acceptance or rejection of all comments received during external peer review and public comment. Once completed, relevant sections of the issue papers could be used as modules for the appropriate sections of the guidelines.

To get to this point and beyond, EPA must assure that the outputs reflect the contributions of staff from every corner of the agency, all Programs and Regions, in addition to ORD. If the results do not have scientific integrity or utility, the risk assessments that incorporate them will lack integrity and utility. In turn, risk management decisions dependent upon the risk assessments will be faulty. They will be subject to intense public scrutiny and legal challenge. They will fail and they will be overturned.

Assume that Step 1 for both the resolution of the *Science and Decisions* issues and the drafting of the guidelines is the development of Action Plans which present Steps and Timelines. They should be prepared in consultation with the SAB and other key players and then widely disseminated so that stakeholders will be aware of what is coming and when they might expect to see it.

Another element critical to success is soliciting the involvement of external experts in Step 2, the drafting of products. The past two and a half years have seen the departure from EPA of so many talented and seasoned scientists, leaving significant gaps in the expertise required to do this work.

Only once the generic issues discussed in *Science and Decisions* are settled, can the focus shift to incorporating the findings into new or updated guidelines.

Any new or updated guidelines must be subjected to the same vigorous process employed in dealing with the unfinished business of *Science and Decisions.* But that's not all. On the assumption that tradition holds, the draft guidelines will have to go to the Office of Science and Technology Policy (OSTP) for interagency review, as other Federal agencies have a major interest and stake in what EPA says and does about science policy since EPA's risk assessment outputs have direct impact on their own decision-making. Draft guidelines also must go to OMB's Office of Information and Regulatory Affairs (OIRA) for additional scrutiny to determine their consistency with the Administration's point of view. This Executive Branch engagement would occur before the SAB has the opportunity to do its peer review and the public to provide comments. Each of the two Executive Branch offices can take at least 90 days to conduct its review. If done sequentially, it will consume at least six months of the development process.

So let's do the math and speculate on how long it might realistically be before we see finalized updated cancer and new non-cancer guidelines. As a frame of reference, the last significant risk assessment guidelines issued were the 2005 cancer guidelines. The kick-off workshop for revision of the previous (1986) version was held in Virginia Beach in 1989—16 years earlier.

The projected Steps and Timelines that I will describe are informed by my personal experience inside EPA and as an attentive observer since leaving the agency. I believe that they are solidly grounded in precedent.

<u>Steps for *Science and Decisions* Issue Papers and Guidelines</u>

1. Development of Action Plans in consultation with the SAB and other key players
2. Drafting, with engaged external peer involvement
3. Discussions in public forums
4. Internal review and sign-off
5. *Executive Branch review* (Guidelines only?)
6. *Revision in response to Executive Branch review*
7. NAS review of issue papers, guidelines, qualifications of SAB Panel
8. Revision in response to NAS review
9. SAB peer review and public comment
10. Revision and response-to-comments
11. Internal review and sign-off
12. Publication of final issue papers and guidelines

Timelines

Both of these tasks are labor-, process- and time-intensive. There will be intense pressure to speed up the process of production and of review. While there are likely to be a number of efficiencies that could be integrated into the process, they must be executed with great caution. This effort requires participation of the key players early and often, from planning to completion. We should learn from the recent abject failure of implementation of the CASAC streamlined process when we saw an unqualified panel that could only conduct a partial review, eroding the credibility of the agency and its supporting science.

Some efficiencies could occur if a) Action Plans for both initiatives are developed concurrently, b) the public discussions and drafting overlap, c) the Executive Branch reviews overlap, and d) EPA requests shorter time frames for NAS and SAB review and public comment.

In the end, separately or dovetailed, the two initiatives will take significantly longer than 18 months to complete. In my view, an optimistic timeline for both tasks, if blended intelligently, and no significant hurdles arise, is 4-5 years. However, a more realistic timeline would be 5-6 years because unanticipated hurdles always arise.

A closing thought I offer as speculation begins on the content and substance of the issue papers and guidelines: Be driven by what you know and understand about the biology underlying the information to be assessed and judged in accordance with these risk assessment guidelines and not by the magnetism of the manipulation of the data using some esoteric statistical techniques chosen to justify a pre-determined policy position.

Reference: NRC (National Research Council). 2009. Science and Decisions: Advancing Risk Assessment. National Academies Press, Washington, DC. Available at: http://www.nap.edu/catalog/12209/science-and-decisions-advancing-risk-assessment

PowerPoint Presentation

Oral Comments on Actions Related to Updating EPA Guidelines for Carcinogen and Noncancer Assessment

Presentation to the
EPA Science Advisory Board
June 5, 2019
by
Penelope A. Fenner-Crisp, PhD, DABT

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Conclusions

- **EPA should develop realistic plans and request a formal review of the plans by the SAB before proceeding (Step 1).**

- **It is realistic to plan for a 4-6 year process, at a minimum. Finishing by end of 2020 is wholly unrealistic.**

- **Begin implementation by addressing the unresolved issues from the 2009 NRC *Science and Decisions* report before writing any guidelines.**

Conclusions

- **Adequate agency resources and time need to be committed and sustained along with credible engagement of outside experts in both development and review roles.**

- **It would be wise to engage the NAS in the review of the *Science and Decisions*-related issue papers, the guidelines and the qualifications of the SAB review panel to confirm that the agency's outputs reflect an objective view of the state of the science.**

Steps

1. **Development of Action Plans in consultation with the SAB and other key players**
2. **Drafting, with engaged external peer involvement**
3. **Discussions in public forums**
4. **Internal review and sign-off**
5. ***Executive Branch (EB) reviews (guidelines only?)***
6. ***Revision in response to EB reviews***
7. **Referral to NAS**
8. **Revision in response to NAS review**
9. **SAB peer review and public comment**
10. **Revision and response-to-comments**
11. **Internal review and sign-off**
12. **Publication of final issue papers and guidelines**

Timelines

- ***Science and Decisions*** **issue papers: An optimistic timeline might be 2 ½-3 years, but a more realistic estimate would be 3-3½ years.**
- **Guidelines: An optimistic timeline might be 3-3½ years, but a more realistic estimate would be 4-5 years.**
- **Both tasks done in concert with no significant hurdles: 4-5 years. More realistic estimate, because unanticipated hurdles always arise: 5-6 years.**