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EPA Official Says 2013 'Critical Year' For EDSP As SAPs, Deadlines Loom

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A top EPA science official says 2013 is a "critical year" for the long-stalled Endocrine Disruptor Screening Program (EDSP), as officials prepare to convene several peer review panels on the program's data analysis and testing methods and seek to clear a major hurdle by finishing gathering data on the first batch of chemicals subjected to screening.

"I create a bit of a hype by saying this, but 2013 is a critical year for our program," Mary Manibusan, a top official in EPA's Office of Science Coordination and Policy (OSCP), told a recent meeting of EPA's pesticide advisors. "We've never been where we are today."

EDSP is intended to screen chemicals for potential endocrine-disrupting activity, the ability of chemicals to interfere with or mimic hormones in the body. It seeks specifically to screen for estrogen, androgen and thyroid effects. Tier 1 would employ a battery of five *in vitro* and six whole-animal *in vivo* assays to identify substances' potential to interact with the endocrine system. Following a weight-of-evidence analysis, any flagged chemicals could undergo more rigorous screening in a second round of animal-based tests that would seek to confirm endocrine-disrupting activity and obtain dose-response information that could help support risk assessments and regulatory decisions.

While the program was authorized in the 1996 Food Quality Protection Act and Safe Drinking Water Act (SDWA) Amendments, EPA has struggled to get the program off the ground.

EPA still has not validated the Tier 1 battery for regulatory use, let alone put any chemicals through the full program. EPA also has said that it faces a lengthy list of chemicals that it must screen -- roughly 10,000.

EPA in 2009 issued a first list of 67 chemicals (pesticide active and inert ingredients) to undergo Tier 1 screening, but the agency still has yet to finish collecting and analyzing the information. Moreover, the agency has yet to finalize a second list of chemicals to undergo Tier 1 testing, though it proposed a list of 134 substances -- most of which are SDWA chemicals -- in 2010 after congressional prodding. This second list is considered more challenging to implement than the initial list of pesticides, because it is more difficult to identify parties responsible for testing ubiquitous water contaminants.

Moreover, the Office of Management and Budget (OMB) has said it will not authorize EPA to collect EDSP test data for that second list of chemicals until it has analyzed data from the List 1 chemicals and subjected it, the Tier 1 assays and relevant weight-of-evidence guidance to peer review. OMB said the steps were needed to ensure the "practical utility" of the data and thus justify additional Information Collection Requests (ICRs). OMB also required EPA to consider already-available "other scientifically relevant information" and recalculate the burdens of supplying the needed test-order data later on (*Risk Policy Report*, Oct. 13, 2009).

Facing criticism from its Inspector General (IG), EPA in a 2012 Comprehensive Management Plan indicated that it plans to finalize this second test order list in fiscal year 2013, along with tackling several other pressing issues in the program, including determinations of which chemicals in the first list must undergo Tier 2 testing, finalizing the Tier 2 battery, and a series of peer reviews by the agency's Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) Scientific Advisory Panel (SAP). OCSP's Manibusan cited those SAPs as one reason why 2013 could be a watershed year for EDSP. *Relevant documents are available on InsideEPA.com.* (*Doc ID: 2413635*)

The SAP reviews will examine several aspects of EDSP. One SAP will review the performance of the Tier 1 screening assays both individually and as a battery on the List 1 chemicals, and the weight-of-evidence method EPA will use to determine which chemicals move on to Tier 2, while another SAP will review the inter-laboratory validation of the Tier 2 *in vivo* animal assays.

Manibusan also told the meeting that the agency is planning to seek science advisors' opinions on a plan to prioritize the universe of 10,000 chemicals that the agency says must go through EDSP. EPA has hinted that its plan will involve novel high-throughput screening technologies from the agency's ToxCast program to at least some degree. The peer review, as a result, could offer a key test of the agency's scientific readiness to use those technologies for decision-making purposes. The

agency in its EDSP21 work plan outlines prioritization as a near-term goal for use of high-throughput assays, with the ultimate long-term goal being to replace some or all tests in the current Tier 1 battery.

Before EPA even proceeds with its new review efforts, the agency must also win approval from OMB for renewed ICR authority to finish collecting test data for the List 1 chemicals, since the current ICR expires Oct. 31.

But in recent comments on EPA's Aug. 9 proposal to renew the ICR, industry groups are pressuring the agency to analyze and submit for SAP review the Tier 1 data it obtains on all List 1 chemicals before proceeding with List 2. "[T]he time and resources spent in carefully analyzing the results of the List 1 Chemical screening data and refining the Agency's screening criteria and guidance documents *prior to the issuance of future test orders* will help to create a more informative, efficient Program moving forward," Bayer CropScience LP says in Oct. 8 comments on the ICR renewal.

Bayer, the Endocrine Policy Forum, an industry coalition group, and certain animal-advocacy groups also argue that EPA's proposed ICR renewal still underestimates the burdens industry will face in generating the needed data, despite EPA making upward cost revisions in the proposed ICR renewal. Those stakeholders in written comments suggest that EPA look to industry for actual data on Tier 1 screening costs from already-completed List 1 data generation.

The Center for Regulatory Effectiveness goes even further, citing the Information Quality Act (IQA) and Paperwork Reduction Act (PRA) in suggesting that OMB should not approve an ICR request of any kind until SAP review of all the aforementioned aspects of EDSP is done. Such rigor of review "is necessary to comply with EPA's IQA Guidelines, with OMB's IQA Guidelines, and with the PRA," the CRE comments say.

Manibusan insisted that EPA would ensure that the List 1 chemical data undergoes sufficient review, including public comment and SAP scrutiny, before the agency proceeds to List 2. She did not discuss the issue of data burdens. "We've never had the richness of the data from List 1 chemicals that we have today," Manibusan said. "So where we go is going to be critical . . . .We don't want to issue test orders unnecessarily."

But she did not say whether the agency would submit Tier 1 assay data on all 67 List 1 chemicals for SAP review and thus go beyond the management plan's stated intent that EPA will submit data on a subset of chemicals.

Putting data on all the chemicals through SAP review could complicate EPA's 2013 timeline, however; the agency will not receive remaining the Tier 1 data on List chemicals until early 2013 and likely will need another year to finish analyzing the data, according to Manibusan.

Moreover, the weight-of-evidence determinations of which chemicals should undergo further Tier 2 testing has long been a sticking point with EDSP, as industry and animal activists have argued that the agency has not explained how it will make these decisions. While EPA has released a draft weight-of-evidence document and a non-binding finalized document, these efforts have been panned by certain stakeholders (*Risk Policy Report*, Oct. 11, 2011).

Meanwhile, animal groups are pressing EPA to speed the incorporation of computational toxicology tools into EDSP assessments. In their comments on the ICR renewal, they ask EPA to reexamine the current two-tiered structure of EDSP to determine if it represents the most efficient procedure, also making the case that the agency should look to ToxCast assays' potential utility.

"The Renewal should describe how the data obtained will be evaluated for utility and compared with developing assessment tools," People for the Ethical Treatment of Animals and Physicians Committee for Responsible Medicine say in Oct. 9 written comments. "For example, EPA has recently favorably compared the results from a subset of ToxCast assays to certain EDSP Tier 1 assays."

Agency scientists in a recent study reported that ToxCast assays for certain endocrine endpoints yield results largely consistent with those from whole-animal and *in vitro* lower-throughput counterparts in Tier 1, boosting hopes that the higher-throughput assays can help prioritize chemicals for EDSP. The findings apply only to estrogen- and androgen-related activity, with the scientists saying that better thyroid assays are needed (*Risk Policy Report*, Oct. 9). -- *Puneet Kollipara*