Comments to the Office of Management and Budget of the Council of Producers & Distributors of Agrotechnology, the Halogenated Solvents Industry Alliance, Inc., and People for the Ethical Treatment of Animals on the Tier 1 List 2 ICR ("ICR Addendum for the Second List of Chemicals; Tier 1 Screening of Certain Chemicals Under the Endocrine Disruptor Screening Program (EDSP); EPA ICR No. 2488.01, OMB Control No. 2070-[new]")

Summary

OMB should disapprove the Tier 1 List 2 ICR as it is prematurely and improperly submitted. The U.S. Environmental Protection Agency (EPA) has not yet fully complied with the Office of Management and Budget's (OMB) 2009 Terms of Clearance (TOC) for the approval of the Tier 1 List 1 ICR. About 18 months ago, we submitted a joint petition to EPA seeking its voluntary compliance with the 2009 TOC, however, EPA has never responded to our petition. Instead, EPA is proceeding with seeming disregard for our petition and acts as if OMB's TOC have no force of law or presidential authority.

Since we submitted this petition, it has become abundantly clear that the Tier 1 battery is overwhelmed by serious unresolved scientific, technical and information quality problems. These problems must be satisfactorily addressed before any additional test orders are issued. EPA has not yet demonstrated any practical utility for Tier 1 data in the 2009 ICR, and EPA's assessment of the Tier 1 data for a limited number of List 1 chemicals has underscored the need for adjustment, refinement, and possible exclusion of some of the assays from the battery. These data, generated at the expense of hundreds of millions of dollars and tens of thousands of animals, have not been proven to provide any additional informational value beyond the data already available for most of the List 1 chemicals in evaluating whether a substance may interact with the endocrine system. The Tier 1 data have no demonstrated utility for triggering Tier 2 testing due to the propensity of some assays to produce results that are inconclusive or positive, independent of an endocrine-related mechanism of action.

EPA's submission of the Tier 1 List 2 ICR is premature and signals that the Agency is marching forward without credibly responding to stakeholder input, without compliance with OMB's TOC, and without effective scientific peer review. Review of this ICR should be suspended until EPA has fully complied with these obligations and OMB should use its Notice of Disapproval to add four additional terms of clearance.

First, OMB should clarify which information collection requirements are currently approved and which are not. Tier 1 test order recipients are unable to distinguish between what they are required to do to comply and what demands EPA

makes that exceed the Agency's authority under a valid OMB control number. Are laboratories required to repeat assays if EPA's performance standards cannot be satisfied? Can EPA impose additional testing requirements as a condition for accepting Other Scientifically Relevant Information (OSRI)? Test order recipients comply with everything EPA demands, irrespective of whether the demands are legitimate, because the Agency threatens them with ruinous fines if they do not.

Second, OMB should direct EPA to modify the EDSP peer review process so that it complies with Section III of OMB's Final Bulletin on Peer Review and the president's Office of Science and Technology Policy's (OSTP) Scientific Integrity guidance. The current peer review process, operated through the Agency's FIFRA Scientific Advisory Panel (SAP), was designed and is being implemented in a way that ensures the Panel's work has no relevance for Agency decision-making. This is obvious from EPA's rushed timelines, short review periods, release of only limited data, and its submittal of this ICR before all of the SAP reviews had been held, much less completed. OMB should put a stop to this manner of managing the scientific peer review that is crucial to the EDSP.

Third, OMB should direct EPA to perform a rigorous, retrospective value-of-information (VOI) analysis showing whether the addition of Tier 1 data materially improves the Agency's ability to decide which substances have the ability to interact with the endocrine system and if (and which) further testing is warranted. If Tier 1 data do not have any material benefit compared to OSRI, they cannot have practical utility. If VOI analysis reveals some benefit, then OMB's statutory responsibility is to determine whether limited practical utility justifies the enormous testing burden.

Fourth, OMB should declare that no EDSP ICRs will be reviewed until EPA has complied with all TOC applicable to the Tier 1 List 1 ICR, the scientific issues and information quality problems with both the Tier 1 battery and Tier 2 tests are resolved, and the practical utility of the collected information is assured. It is no longer acceptable to ignore these deficiencies and proceed with a never-ending screening and testing program that will ultimately cost the public hundreds of millions of dollars and kill tens of thousands of animals.

Our December 2011 Petition to EPA Seeking Compliance with OMB's 2009 Terms of Clearance

On December 6, 2011, we submitted a petition to EPA asking the Agency to fully comply with the TOC set forth by the OMB on October 2, 2009, in its Paperwork Reduction Act (PRA) approval of ICR 2070-0176 titled "Tier 1 Screening of Certain Chemicals Under the Endocrine Disruptor Screening Program (EDSP)."[1] More than two years had passed since OMB issued this conditional approval, but in late 2011 EPA had made no publicly observable progress toward complying with the TOC.

In our petition, we summarized our request as follows:

[1] Office of Management and Budget (2009).

1. EPA must demonstrate that the information collected during Tier 1 screening of the EDSP is not duplicative of already existing information.

We noted that while OMB's TOC require EPA to accept what § 408(p)(1) of the Federal Food, Drug, and Cosmetic Act (FFDCA) refers to as Other Scientifically Relevant Information (OSRI) as sufficient to satisfy the test orders to the greatest extent possible, EPA had in fact rejected most OSRI that had been submitted for List 1 chemicals. We further noted that EPA must demonstrate non-duplication in order to justify the enormous burden of animal testing that the initial Tier 1 battery requires.

2. EPA must demonstrate the practical utility of the information collected in Tier 1 screening of the EDSP.

OMB's regulations implementing the PRA define *practical utility* as "the actual, not merely the theoretical or potential, usefulness of information to or for an agency, taking into account its accuracy, validity, adequacy, and reliability, and the agency's ability to process the information it collects..." (emphasis added).[2] The statutory purpose served by this information collection requirement is to enable EPA to distinguish substances that "may" have the potential to interact with one or more components of the endocrine system from substances that "may not" have this potential. As we wrote then, "[e]ach transparent and reproducible 'may' and 'may not' administrative decision made by EPA must be based on a solid scientific foundation to have practical utility" for the regulatory decisions the Agency intends to make.[3]

3. EPA has not demonstrated the scientific reliability and appropriateness of the current Tier 1 Battery assays.

We noted that EPA had launched a flawed Tier 1 screening regime by requiring assays to be performed that were not "validated test systems," as FFDCA 408(p)(1) requires. A validated test system is one that consistently produces data that meet *a priori* performance standards for the intended purpose, both within and across laboratories. During the May 2013 SAP meeting to review the performance of the Tier 1 battery in testing the List 1 chemicals,[4] it was apparent from both EPA staff and laboratory scientists conducting the tests that performance standards were not consistently met. Laboratories experienced difficulties in properly performing the assays, particularly the amphibian and fish assays. In addition, EPA has not described how it will use the Tier 1 data to make decisions about moving chemicals on to Tier 2 testing. Thus, any regulatory decisions based on such data will be arbitrary and capricious.

EPA also knew that its assays lacked the capacity to distinguish true from false positives. Even negative controls in EPA's so-called validation studies yielded

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[2] 5 C.F.R. § 1320.3(l).

[3] Chemical Producers & Distributors Association, Halogenated Solvents Industry Alliance and People for the Ethical Treatment of Animals (2011).

[4] FIFRA Scientific Advisory Panel (2013a).

false positives, a result that is fundamentally at odds with any coherent meaning of scientific validity and contrary to Congress' clear statutory requirements.

4. Practical utility of the data from Tier 1 screening cannot be demonstrated without the use of a scientifically sound weight-of-evidence approach that is applied to all information collected, including OSRI.

When OMB issued its conditional approval for Tier 1 screening of List 1 chemicals, EPA had published only a 2-page, content-free paper purporting to disclose how it intended to perform the novel task of weighing OSRI and Tier 1 screening data.[5] On September 28, 2011, EPA published a final guidance document that contractors and Agency reviewers are supposed to use for evaluating Tier 1 screening data.[6] This 47-page document was certainly an improvement over the barebones 8-page draft issued for public comment in November 2010.[7] However, the document remains too general to yield reproducible results across chemicals and across reviewers. Applications of this "guidance" that are not transparent and reproducible will be arbitrary and capricious. The document will require extensive revision based on the results of the July-August SAP meeting that reviewed EPA's application of scientifically sound weight-of-evidence methods to the results of five List 1 chemical case studies.[8] Until this document is revised for use by contractors and Agency reviewers, it makes little sense for a new ICR to be approved and issued at this time.

EPA Has Not Responded to Our Petition

In our petition we refrained from invoking the Administrative Procedure Act (APA) and EPA's administrative rules requiring the Agency to provide a timely response. We did that because we wanted to avoid unnecessary confrontation, and to work collaboratively and cooperatively with EPA toward a reasonable solution. However, in the 18 months since we filed the petition, EPA has not provided any response.

EPA also could have responded to us via the Response-to-Comments (RTC) document the Agency submitted to OMB along with this ICR.[9] The RTC is silent concerning our petition, however. Moreover, in the RTC EPA did not even credibly respond in a generic fashion to the issues we raised:

- With regard to duplication, the RTC turns the language of the PRA[10] on its head by attempting to shift the burden of proof to the public.[11]

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[5] U.S. Environmental Protection Agency (2009b).

[6] U.S. Environmental Protection Agency (2011).

[7] U.S. Environmental Protection Agency (2010).

[8] FIFRA Scientific Advisory Panel (2013c).

[9] U.S. Environmental Protection Agency (2013d).

[10] 5 C.F.R. § 1320.5(d)(1)(ii)-(iii) ("[A]n agency shall … demonstrate that it has taken every reasonable step to ensure that the proposed collection of information is not duplicative of information otherwise accessible to the agency"; the "agency shall seek to minimize the cost to itself

- With regard to the practical utility of Tier 1 screening data, EPA claims that the Supporting Statement "explains the utility of the data," when in fact the Supporting Statement does not ever mention practical utility.[12]
- With regard to the scientific reliability of Tier 1 assays for the purpose of screening for potential endocrine interactions, the RTC has nothing at all to say.
- With regard to the need for scientifically sound weight-of-evidence guidelines, the RTC merely references the document that we cited in our petition as lacking scientific rigor, transparency, and reproducibility.[13]

In short, the RTC is wholly unresponsive to the issues raised in our petition.

We think it is only reasonable that EPA should have responded in good faith, and that EPA's unresponsiveness has important implications for this ICR review. That is why we urge OMB to disapprove this ICR as improperly submitted and include in its Notice of Disapproval additional TOC to better motivate EPA to take account of constructive criticism instead of simply ignoring it.

The Limited Data from Tier 1 Screening Disclosed by EPA Show that Our Concerns Were Justified

Experience gained from conducting Tier 1 assays confirms that the concerns we raised in our petition were valid in 2011, and remain valid today. Tier 1 data lack practical utility; Tier 1 screening is even more burdensome than we had predicted; and Tier 1 screening is using even more animals than had been forecast.

Results from Tier 1 screening lack practical utility

We have already mentioned that in our petition we noted that assays EPA insisted on including in the Tier 1 battery were not "validated test systems," as FDCA § 408(p)(1) requires. The SAP peer review meeting held in May 2013[14] - a month after the ICR was prepared and ready for submission to OMB - confirms that

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of collecting, processing, and using the information, but shall not do so by means of shifting disproportionate costs or burdens onto the public") (emphasis added).

[11] U.S. Environmental Protection Agency (2013d): "If any EDSP Tier 1 order recipient believes data exists that is duplicative of data required by an EDSP Tier 1 Order, they are entitled to submit the data as OSRI along with a clear rationale why it would suffice for the required data. EPA will review all OSRI submitted. Implicit in the comment is the idea that EPA should bear the responsibility for making a determination of whether existing data are adequate for the EDSP prior to issuing an order. However, both FIFRA and FFDCA clearly indicate that it is the responsibility of the manufacturer and/or registrant to demonstrate that their chemical and/or product can be used safely."

[12] Ibid., citing U.S. Environmental Protection Agency (2013b).

[13] U.S. Environmental Protection Agency (2013d).

[14] U.S. Environmental Protection Agency (2013a) and FIFRA Scientific Advisory Panel (2013d).

we were correct. Even though the final SAP report on the meeting is not yet available, this conclusion is incontrovertible from reviewing the transcript.[15]

EPA provided the SAP with data from only 21 of the 52 substances that were subject to Tier 1 screening under the List 1 ICR.[16] The 21 substances were reportedly chosen by EPA to be representative of both the classes of chemicals included in List 1 and problems encountered in assessing them for potential endocrine action. However, EPA provided no criteria for their selection to the SAP or the public.[17] SAP panel members repeatedly stressed throughout the meeting that EPA must analyze the results of all 52 substances before reaching final conclusions about the adequacy of the assays.

Laboratory scientists reported to the SAP that they had substantial difficulty meeting assay performance standards as illustrated by the following comments from the transcript:

> [M]ainly what I will focus on is the cytotoxicity issue, issues with solubility of the test compounds at high concentrations and the suitability of the assays themselves.
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> So in terms of the steroidogenesis assay, I won't go into the details of the protocol, but one of the issues is the performance criteria, and that was discussed by EPA quite a bit.
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> In these cell lines, the H295R cells, there's actually quite a bit of variability in cell behavior, and that is the hormone production at basal level.
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> So in many of the cases, assays had to be repeated to get to or get close to the performance criteria, so there's quite a bit of variability. So in that respect, this decreases the usefulness of this assay. Not only does it have to be repeated many times to meet the criteria, so it's no longer rapid, nor is it actually cost-effective because it has to be repeated, but most importantly, this decreases the confidence of the data that's generated.[18]

Had the Tier 1 assays actually been fully validated before they were imposed on the public in violation of FFDCA § 408(p), these problems would not have occurred.

That these problems did occur means that scientists cannot have collective confidence that Tier 1 data have any predictive value for discerning whether the test

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[15] FIFRA Scientific Advisory Panel (2013a).

[16] Ten of the 63 substances targeted by EPA for screening in List 1 were abandoned from commerce to avoid the high cost of Tier 1 screening and potential advancement to the exorbitant cost of Tier 2 testing. These decisions were not based on public health risk.

[17] FIFRA Scientific Advisory Panel (2013a).

[18] Ibid. (comments of Dr. Sue Yi, Senior Toxicologist at Syngenta Crop Protection).

chemical may interact with hormonal systems. Data for which scientists lack confidence cannot have practical utility.

At the May 2013 SAP peer review meeting, EPA tried to extricate itself by denying that assay performance standards were actually requirements that laboratories had to meet:

> When we set performance criteria, these things are also more or less recommendations, they are targets in terms of what we're trying to achieve to ensure quality, you know, studies to be performed. So they're not established as bright lines in terms of, you know, kind of a pass/fail situation.[19]

However, laboratories properly treat performance criteria as binding rather than suggestive. There is good reason for this: EPA's test guidelines clearly state that laboratories must comply with the Agency's performance criteria.[20]

Of course, even this denial had its limits. Some assays simply had to be repeated, even if EPA had promised otherwise:

> But there would be situations where you fall short enough in enough of the criteria that you might deem the test unsatisfactory and would need to be repeating. So I think there would be some room for going back and revisiting these based upon this broader context to determine if we need to modify or at least loosen some of these criteria to allow better interpretation and at least more successes in terms of laboratory conduct of these assays.[21]

It was clear from the SAP meeting recommendations that EPA would have to go back and revise the assay performance criteria, create decision trees for laboratories to determine the conditions under which an assay should be repeated, better quantify performance criteria exceedances and their significance within the assay protocols, and in some cases, modify or completely eliminate certain assays. None of this has been done in advance of the release of the Tier 1 List 2 ICR.

The burden of Tier 1 screening is greater than EPA estimated

Comments submitted in 2009 on the Tier 1 List 1 ICR sought to correct EPA's gross underestimate of burden.[22] Underestimation took many forms, such as ignoring the burdens associated with preparing and submitting OSRI; ignoring the burdens of establishing, operating, and participating in test order consortia; and most amazingly, ignoring 65% of laboratory costs. We estimated at the time that the cost of the Tier 1 battery would average about $1 million per substance, not the

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[19] Ibid.; comments of Dr. Leslie Touart, Exposure Assessment Coordination and Policy Division, Office of Science Coordination and Policy, EPA.

[20] See, e.g., U.S. Environmental Protection Agency (2009a) (guidance is directive, using "must" 20 times).

[21] FIFRA Scientific Advisory Panel (2013a); Touart.

[22] Belzer (2009).

small fraction of that which EPA reported in its Supporting Statement. This estimate has proven accurate; numerous public commenters at the May SAP meeting confirmed that conducting the entire Tier 1 battery costs upwards of $1 million per chemical.[23] EPA continues to underestimate the burden in the Tier 1 List 2 ICR request available for public comment, calculating the Tier 1 battery burden at only about $639,000 per chemical.[24]

Furthermore, EPA has not included the burden of repeating assays even though the Agency knows it will be required.[25] This has always been a reasonable concern for novel test systems that have not been fully validated. In fact, the transcript of the May SAP review indicates that assays had to be repeated for some of the List 1 chemicals and this has driven actual costs even higher.

When assays have to be repeated, the quality of the resulting data become increasingly suspect and the ability of the laboratory to properly conduct the assay comes into question. But it also treats animals used in laboratory experiments as mere waste products having no greater moral content than reagents and solutions. This attitude is an abhorrent design element of the EDSP. EPA made the statement at the May SAP meeting that "[t]he EPA is committed to minimizing animal usage in the screening battery while maintaining the effectiveness of the battery to answer the question of whether a chemical has the potential to interact with the endocrine system."[26] Forcing laboratories to repeat assays violates this commitment.

The number of animals used is much greater than EPA estimated

Congress has directed federal agencies including EPA, through the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), to "eliminate unnecessary duplicative efforts" and "reduce, refine, or replace the use of animals in testing, where feasible."[27] This directive is aligned with OMB's orders under the PRA to ensure that agencies do not impose duplicative information collection requirements on the public. This massive use of animals for useless chemical testing is contrary to both laws.

Based on the testing protocols issued by EPA for the Tier 1 assays,[28] it was expected that conducting the entire Tier 1 battery would kill about 595 animals per chemical tested. In fact, considerably more animals are used for dose range-finding studies, optimization studies, and through culling of animals. As an example, the pubertal assays use 45 animals for the actual study, but nearly 200 excess animals are killed before the test even starts. In addition, two of the *in vitro* receptor binding assays necessitate the killing of 10-20 rats to get enough biological material

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[23] FIFRA Scientific Advisory Panel (2013a).

[24] U.S. Environmental Protection Agency (2013c).

[25] Borgert (2003) and Belzer (2009).

[26] FIFRA Scientific Advisory Panel (2013a).

[27] ICCVAM Authorization Act of 2000 (Pub. L. 106-545), §§3(b)(2) and (5); 114 Stat. 2722.

[28] U.S. Environmental Protection Agency (2013e).

required to run the tests. Other assays are available that measure receptor binding that do not use animals at all and are more human-relevant.

Review of the Tier 1 data from the 21 chemicals presented by EPA to the SAP in May also revealed that many of the animal test results were confounded by overt toxicity. This occurs when the maximum dose of the chemical administered causes lethal or sub-lethal responses in the animals that interfere with the interpretation of any possible endocrine-related findings. EPA is not able to use Tier 1 screening data in cases where overt toxicity occurred, wasting even more animals and increasing costs.

Adding the large number of animals killed in preparation of testing and the large number of animals killed in repeat testing, it is clear that EPA has grossly underestimated the actual number of animals killed to complete the battery to the Agency's satisfaction. It is essential that OMB consider the waste of animals as lacking practical utility under the PRA.

EPA has not maximized the use of OSRI

The OMB 2009 TOC states, "under the principles of the PRA, EPA should promote and encourage test order recipients to submit Other Scientifically Relevant Information (OSRI) in lieu of performing all or some of the Tier 1 assays, and EPA should accept OSRI as sufficient to satisfy the test orders to the greatest extent possible." However, EPA accepted OSRI submitted by test order recipients for the List 1 chemicals only 23% of the time.[29] Yet EPA also has failed to clearly show that it cannot make decisions about the potential of a chemical to interact with the endocrine system based on OSRI alone. During the recent SAP meeting on weight-of-evidence,[30] EPA itself demonstrated the satisfactory evaluation of a chemical's potential to interact by using only OSRI. Tier 1 data have practical utility if and only if they materially improve EPA's ability to scientifically discern whether a substance warrants Tier 2 testing. But the Agency has conducted no analysis that would credibly make such a showing.

Understanding the Tier 1 List 2 ICR in Context

It may be tempting for OMB to view this ICR as just another transaction among the more than 6,000 ICRs that OMB reviews each year. We hope that will not be the case. This ICR would expand both the scale and scope of a massive animal testing program that, as currently designed, cannot produce data that could be used to protect public health and the environment from adverse endocrine effects. There are a number of lessons that we have learned from devoting years of effort suggesting constructive reforms to the EDSP so that it stays within sensible policy boundaries and finally gains scientific merit.

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[29] Bishop, PL. Willett, CE., and Sullivan, KM. 2013.

[30] FIFRA Scientific Advisory Panel (2013c) (transcript not yet available).

Submission of the Tier 1 List 2 ICR signals that EPA has no intention of responding to our petition, public comments, stakeholder input, or peer review

We have already noted the absence of any EPA response to our petition. More significantly, however, EPA has decided to march forward without addressing any of the issues we presented. These issues also have been raised - multiple times - by multiple public commenters. EPA continues to ignore them all.

OMB's novel idea of conditioning approval of the Tier 1 List 1 ICR with TOC was widely praised by everyone with an interest in ensuring that environmental health be protected in accordance with the best available scientific evidence. The TOC established reasonable minimum requirements for EPA to meet before expanding Tier 1 screening. None of the tasks OMB set forth was unreasonable or unusual, and each one was fully grounded in OMB's special authority in the PRA to regulate and control the generation of federal agency paperwork burdens. EPA's decision to ignore OMB's TOC sets up an unnecessary and entirely avoidable conflict.

Among the requirements in the TOC, one that is especially crucial is rigorous, independent, and external peer review. But EPA has decided to rush the Tier 1 List 2 ICR through before peer review could be completed. If this ICR is approved without incorporating any recommendations from the three SAP meetings held this year, it makes SAP review an utterly superfluous waste of highly regarded scientific talent, and seriously undermines public regard for the competence and good faith of the federal government. Many observers - and quite likely, many SAP members as well - would conclude that EPA has abandoned any pretense of caring about scientific quality. As a consequence, it will become increasingly difficult for EPA to attract high quality, experienced scientists to serve on advisory committees such as the SAP.

EPA publicly acknowledges that the terms of clearance are binding but the Agency refuses to abide by them

The public statements made by EPA officials have been consistently deferential to OMB's TOC and accepted them as binding. But in response to public commenters, who unanimously faulted EPA for failing to comply, EPA attempts to reinterpret the TOC in a way that makes them merely hortatory aspirations:

> EPA fully <u>intends to follow</u> the terms of clearance as additional information becomes available. (emphasis added)[31]

To fully <u>intend</u> to follow something is the same as committing to never satisfying anything.

Stakeholders recognize this as a direct challenge to OMB's authority under the PRA. Thus, if OMB approves the Tier 1 List 2 ICR, it is widely expected that EPA

[31] U.S. Environmental Protection Agency (2013d).

will interpret this as confirmation that the TOC are dead and that OMB has capitulated.

A serious substantive risk is that an OMB approval would allow EPA to preserve the Tier 1 battery as it exists today. No aspect of it would ever change unless and until EPA decided to change it, for whatever reasons it might choose. These reasons are unlikely to be science-based; we know this because EPA has decided to forego effective scientific peer review it received that would improve Tier 1 screening, and instead is moving forward into List 2 screening, and Tier 2 testing, without a scientific foundation.

On June 24, EPA published a 60-day Notice for a Tier 2 testing ICR, the breadth of which is astounding given how far away Tier 1 is from scientific resolution:

> This ICR addresses the information collection activities for those chemicals that were screened under Tier 1 of the EDSP and are now expected to proceed to testing under Tier 2 of the EDSP. The ICR covers the full range of information collection activities associated with Tier 2 of the EDSP, including the paperwork activities associated with the issuance of Tier 2 orders, initial responses from order recipients, paperwork activities associated with generating the data requested, and submitting the data to EPA pursuant to the order. Under the PRA, the ICR is intended to cover a 3-year period.[32]

Review of the Tier 2 ecotoxicity tests by the SAP in late June 2013 revealed numerous data quality and reproducibility issues associated with the attempts to validate these assays.[33] Even more costly and animal-intensive than the Tier 1 assays, Tier 2 ecotoxicity tests are not close to being validated and ready for use by contract laboratories, based on the many problems presented by EPA and the resulting recommendations from the SAP to modify and improve these assays.

As with the Tier 1 List 2 screening ICR, the ICR for Tier 2 testing is premature. Due to the inability of the laboratories conducting validation studies to produce consistent and concordant results, Tier 2 ecotoxicity tests have not been properly validated to show that they yield data that can scientifically and objectively estimate dose-response relationships for bona fide adverse endocrine effects. This is a prerequisite for compliance with FFDCA § 408(p), so it is impossible for Tier 2 testing to have practical utility at this time. It is difficult to see how OMB exercises its statutory authority to ensure that Tier 2 testing accomplishes its statutory purpose while minimizing burden when the Agency has made it obvious that it is unconcerned about burden or the practical utility of the information collected.

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[32] U.S. Environmental Protection Agency (2013f).

[33] FIFRA Scientific Advisory Panel (2013b).

Our Recommendations

We represent very different constituencies that do not often agree on regulatory policy. However, we are wholly in agreement that Tier 1 screening is completely misguided. Though it began as perhaps a reasonable approach for scaling the chemical screening burden to minimize costs while ensuring data quality, it has been transformed into a program that has neither scientific nor logical boundaries and a fast-receding connection to its 1996 statutory foundation. It is time for a serious mid-course correction.

OMB should disapprove the Tier 1 List 2 ICR as prematurely and improperly submitted

EPA has rebuffed every attempt made by knowledgeable stakeholders to help guide Tier 1 screening toward a successful result. EPA has ignored our petition, and more than once the Agency has replied to public commenters in a superficial and disingenuous manner. More to the point, EPA has decided to utterly disregard OMB's responsible efforts to ensure that the EDSP proceeds in a scientifically grounded and lawful way. For these reasons, OMB should disapprove this ICR as prematurely and improperly submitted.

Submission was premature because it preceded completion of SAP reviews that are essential for ensuring that the EDSP attains even a minimal standard of scientific credibility.

Submission was improper because EPA did not fulfill any of the obligations set forth in OMB's TOC. EPA did not actively promote and encourage test order recipients to submit OSRI; the Agency impeded these efforts by refusing to establish *a priori* objective and reproducible standards for acceptance. EPA did not accept OSRI to the maximum extent possible; the Agency rejected most of the data derived from rigorous tests conducted for pesticide registration, and it has not demonstrated how the information gained from Tier 1 screening (or Tier 2 testing for that matter) is any better than what these tests produce. EPA has not published a report describing instances in which it had rejected OSRI, nor has the Agency provided any coherent explanation for its decisions. EPA has not provided a report that, for the first time, would accurately estimate the burden of Tier 1 screening; the Agency corrected a few minor errors but ignored the most glaring mistakes commenters had identified. And EPA, thus far, has not supported its own scientific peer review program whose purpose is to resolve legitimate concerns about the scientific merits of the Tier 1 battery, standard evaluation procedures for Tier 1 data, and weight-of-evidence evaluation of OSRI and Tier 1 data. Instead, it has rushed this ICR to OMB before the SAP final reports have been received, before the information in the reports has been digested, before the Agency has responded in writing to the SAP's recommendations, and before recommendations have been implemented.

OMB should use its disapproval to impose additional terms of clearance

It is clear that despite issuing the TOC, OMB has been unsuccessful in constructively guiding the Tier 1 program on a path that would comply with both FFDCA § 408(p) and the PRA. Additional efforts appear to be necessary to remedy this situation. We offer four suggestions for additional TOC that OMB could include with its Notice of Disapproval.

Clarify which information collection requirements are approved and which are not

OMB should reiterate what EPA must do to comply with the 2009 TOC. Although the public comments of EPA officials have properly acknowledged that the TOC are binding, the Agency's written statements on the subject say they are not. For this reason, it may be necessary for OMB to clarify some of the language to ensure that it is not misconstrued, and to clarify when EPA's failure to abide by the TOC renders OMB's approval moot.

Perhaps a more important reason for OMB to add clarity is to empower knowledgeable stakeholders to protect their statutory rights against being penalized for failing to comply with unapproved information collections. Are laboratories required to repeat assays if EPA's performance standards cannot be satisfied? Can EPA impose additional testing requirements as a condition for accepting OSRI? If TOC are binding, at what point does EPA noncompliance render OMB's approval moot? EPA has threatened test order recipients with ruinous penalties for failure to comply, then taken the position that once OMB has approved the ICR there are essentially no limits on what it can require test order recipients to do.

This is an indefensible abuse of statutory authority that OMB is uniquely positioned to correct. OMB can do so by clearly stating in its TOC exactly what test order recipients must do to comply with Tier 1 test orders and listing examples of the kinds of demands EPA might make that would exceed its authority under a valid OMB control number. Armed with this knowledge, test order recipients would be much better equipped to resist improper and illegal demands for information beyond the scope of the OMB control number, exercising their rights as Congress intended when it wrote the public protection provisions in 44 U.S.C. § 3512.

Direct EPA to modify the EDSP peer review process so that it complies with Section III of OMB's Final Bulletin on Peer Review and OSTP's Scientific Integrity guidance

There should be no question by now that the scientific content of the EDSP meets the definition of "highly influential scientific information" found in the OMB Final Bulletin on Peer Review.[34] To date, however, EPA has not subjected the EDSP

[34] Office of Management and Budget (2005); Section III: *Highly Influential Scientific Assessments* are defined as those that could have a potential impact of more than $500 million in any year, or be novel, controversial, or precedent-setting or have significant interagency interest.

to anywhere near this level of scrutiny. It is not even listed in EPA's Peer Review Agenda.[35]

Several provisions of Section III are especially appropriate for EDSP peer review. First, Section III mandates a much higher level of public participation in the process than EPA has thus far permitted. Knowledgeable stakeholders have been justly critical of how EPA has provided very little time for SAP members to review public comments along with agency-provided materials. Peer review meetings are dialogues between EPA staff and the more than two dozen independent, scientific experts who assist the SAP in the reviews, some of whom are more knowledgeable than EPA staff. Second, peer reviews compliant with Section III must include a final report prepared by the reviewers themselves and a publicly-disseminated written response by EPA explaining the Agency's agreement or disagreement with the views expressed in the report, the actions the Agency has undertaken or will undertake in response to the report, and the reasons the Agency believes those actions satisfy the key concerns stated in the report.

OMB also should include along with this directive a reminder that EPA must comply with the Scientific Integrity guidelines published by OSTP.[36] Instead of keeping crucial scientific and technical information secret, EPA must "[f]acilitate the free flow of scientific and technological information, consistent with privacy and classification standards." As the guidelines say:

> Open communication among scientists and engineers, and between these experts and the public, accelerates scientific and technological advancement, strengthens the economy, educates the Nation, and enhances democracy. Consistent with the Administration's Open Government Initiative, agencies should expand and promote access to scientific and technological information by making it available online in open formats. Where appropriate, this should include data and models underlying regulatory proposals and policy decisions.[37]

To further protect the integrity of the SAP, EPA must be reminded that it is forbidden from interfering with its deliberations and the preparation of its reports.[38]

Require EPA to conduct a retrospective value-of-information analysis of Tier 1 screening results to determine how much Tier 1 data have improved the Agency's capacity to make science-based decisions when compared to relying on OSRI alone

Much of the OSRI submitted prior to Tier 1 testing was rejected by EPA as not fully informing the determination of whether or not a chemical had the potential to

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[35] U.S. Environmental Protection Agency (2013g).

[36] Holdren (2010).

[37] Ibid.; Section I.3.

[38] Ibid.; Section III.5.

interact with the endocrine system. But EPA has not shown that Tier 1 assays provide systematically better data than OSRI.

There is no justification for holding OSRI to quality standards that Tier 1 assays do not meet. To ensure that Tier 1 testing is not duplicative of information already available and that testing was warranted, EPA should conduct a retrospective value-of-information analysis to determine whether or not Tier 1 data provided substantial additional insight. This analysis should be conducted as part of the TOC requirement that EPA report on OSRI it rejected and the reasons for rejecting it.[39]

Declare that no EDSP ICRs will be reviewed until EPA has complied with all TOC applicable to the Tier 1 List 1 ICR, and the scientific issues and information quality problems with both Tier 1 screening and Tier 2 testing are resolved and practical utility is assured

It appears to be EPA's intent to avoid complying with OMB's 2009 TOC. In writing, the Agency expresses only an aspirational intent to follow them, someday. An effective remedy for this intransigence is to publicly state that OMB will not even review any further EDSP ICRs unless and until EPA complies with these TOC. Instead of wasting scarce staff hours, OMB should commit to return, as improperly submitted and without review, any such ICR immediately.

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