SCIENCE ADVISORY BOARD
A Federal Advisory Committee to the U.S. Environmental Protection Agency

December 4, 2024

EPA-SAB-25-005

The Honorable Michael Regan
Administrator
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460

Subject: SAB Consultation on EPA's Draft Proposed Approach for Consideration of Chemical Co-exposure in TSCA Risk Evaluations

Dear Administrator Regan,

The Science Advisory Board (SAB) consultation process serves as a mechanism to provide individual expert comments for the Environmental Protection Agency's (EPA) consideration early in the implementation of a project or action. SAB consultations are conducted in public meetings and under the requirements of the Federal Advisory Committee Act (FACA), as amended (FACA; 5 U.S. Code 10, which include advance notice of the meeting in the Federal Register.

On October 15 and 16, 2024, the SAB held a public meeting and conducted a consultation with EPA staff on evaluating cumulative risks from multiple chemicals. Specifically, EPA asked the SAB to comment on a proposed approach to identify and evaluate chemical co-exposure or areas where multiple chemical exposures may occur in the same geographic space. The EPA provided charge questions (see Appendix A) and a draft evaluation approach proposal[1] for the SAB's consideration and response.

Individual written comments were requested from all members of the Science Advisory Board. All comments received are included and do not reflect SAB consensus advice or

Materials available on the SAB webpage and referenced within this document: https://sab.epa.gov/ords/sab/r/sab_apex/sab/advisoryactivitydetail?p18_id=2657&clear=18&session=13298933691211#charge

[1]Draft Proposed Approach for Consideration of Chemical Co-exposure in TSCA Risk Evaluations.

recommendations. We thank the EPA for the opportunity to provide these early comments on evaluating cumulative risks from multiple chemicals.

Sincerely,

/s/

Kimberly Jones, Ph.D.
Chair
EPA Science Advisory Board

NOTICE

This document has been written as part of the activities of the EPA Science Advisory Board, a public advisory committee providing extramural scientific information and advice to the Administrator and other officials of the Environmental Protection Agency. The Board is structured to provide balanced, expert assessment of scientific matters related to problems facing the Agency. This report has not been reviewed for approval by the Agency and, hence, the contents of this report do not represent the views and policies of the Environmental Protection Agency, nor of other agencies in the Executive Branch of the Federal government, nor does mention of trade names or commercial products constitute a recommendation for use. Reports of the EPA Science Advisory Board are posted on the EPA website at https://sab.epa.gov.

The SAB is a chartered federal advisory committee, operating under the Federal Advisory Committee Act (FACA; 5 U.S. Code 10). The committee provides advice to the Administrator of the U.S. Environmental Protection Agency on the scientific and technical underpinnings of the EPA's decisions. The findings and recommendations of the Committee do not represent the views of the Agency, and this document does not represent information approved or disseminated by EPA.

U.S. Environmental Protection Agency
Science Advisory Board

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Note: Consultation comments reflect individual member responses. These comments do not reflect SAB consensus advice or recommendations.

Individual Responses to Charge Questions on the *Draft Proposed Approach for Consideration of Chemical Co-exposure in TSCA Risk Evaluations*

Contents

Dr. C. Marjorie Aelion

General Comments about the Draft Report:

The draft report is well written, clear, and concise. It provides a detailed description of the AirToxScreen (ATS) model to estimate chemical exposure and risk and the databases used as inputs to the model. It provides a thorough assessment of strengths, limitations, and assumptions of ATS. It compares other models to ATS and identifies differences in the benefits and limitations of those other models and ATS. The report reiterates that the ATS model's use is as a screening tool, to identify areas that are good candidates for more detailed assessment. It emphasizes that computations are based on averages and the model is not intended to assess individual or local risk or exposure. The draft report then provides detailed examples and case studies of the use of the ATS model and includes maps/visual of the case studies. It also provides suggestions for some future modifications and enhancements to the AST tool that could extend the utility of the tool.

1. AirToxScreen is an EPA modeling tool that estimates ambient airborne chemical exposure and risk across the United States to the census tract level. Given the model's strengths, limitations, and assumptions, please comment on the appropriateness of using AirToxScreen for screening level chemical co-exposure in the context of TSCA chemical evaluation.

The report provides a thorough assessment of strengths, limitations, and assumptions of ATS. It states on p. 26 that ATS is just a screening tool and that the information can be used to identify "areas best served by additional analysis and higher tier evaluation". The screening tool seems appropriate, but it seems that it could go further by incorporating additional parameters in the model to more accurately identify risk and exposure, or more specifically, not to miss areas that may be of concern. An example is suggested in the response to question 2 below.

2. This draft document proposes multiple potential metrics to inform chemical co-exposure. These proposed metrics include:

--Number of chemical releasing facilities;
--Number of chemicals released from facilities;
--Number of chemicals meeting chemical risk benchmarks;
--Chemical risk combinations; and
--Bivariate distribution of individual chemical risk with potential chemical co-exposure
Please comment on the utility, strengths, and uncertainties of these metrics. Please include in your comments discussion of the methods used to develop these metrics.

The metrics are a good starting point to assess release and exposure. However, why not use release magnitude in your analyses, or even use a tier of large, medium and small releases? Page 30 of the draft report describes the Risk Screening Environmental Indicators (RSEI) model which uses TRI information and the opportunity it has to investigate co-exposure. Why not use data from the TRI in the ATS model? Maps based on number of small, medium and large releases could be generated similar to Figure 6.2. "Number of NEI

releases within a census tract" (p. 25). These maps could be compared to Figure 6.2, and identify if other areas are identified for additional analysis. By only using the National Emissions Inventory (NEI) number of chemicals released and number of NEI releases, and no metric associated with the quantity of release, some areas of concern could be missed.

In terms of uncertainty, the draft report references uncertainty several times and states that there is uncertainty in different databases and aspects of the model. But, the report does not quantify the uncertainty or indicate how the uncertainty is reported in the results. It would be helpful to report the quantified uncertainty associated with different aspects of the tool and have uncertainty illustrated in figures or tables in the draft report.

3. The two stated goals for this paper are: 1) support identification of potential PESS; and 2) consider chemical co-exposure as part of an individual chemical risk evaluation. Please comment on the extent to which the analyses and methodologies proposed within this document support these goals.

Yes, the analyses and methodologies support the goals to identify potentially exposed susceptible subpopulations (PESS) and consider co-exposure. However, there seem to be limitations on estimating exposure, particularly in rural areas. The report addresses limitations of using census tract data. Page 25 of the report states, "census tracts in rural locations tend to be larger in area, while those in urban locations tend to be smaller, and on page 18 that, "generated ambient air and exposure concentrations that are reported at the census tract level are based on the population weighted averages of the estimated census block centroid concentrations within a given tract. Census blocks with higher populations within a tract get weighted more than census blocks with lower populations within the same tract."

It is acknowledged that addressing differences in rural and urban areas in terms of spatial scale and data availability is difficult. Continuing to develop tools such as EJScreen and ATC without addressing issues such as these, themselves produce systemic environmental injustices for Tribal and rural populations, which ironically is what the tools are aiming to address. This will become even more of an issue as these tools are used by more and more agencies and researchers and become the gold standard for EJ analyses. It would be helpful if the ATC tool could continue to develop additional metrics and methodologies to address issues of systemic injustice in these EPA tools and increase the accuracy and application of the tools for all populations.

Dr. Maximilian Auffhammer

I commend the author team for a carefully crafted report. I am new to this process, so will focus on the areas within my area of expertise, which I think deserve further clarification.

It appears that the modeling excludes “background air toxics from other media”, which may be problematic if dose response functions for certain chemicals are nonlinear. The bias could go in either direction. If background concentrations are low, an additional e.g. ton of chemical released could have a large marginal impact on health we assume a dose response which resembles a “square root function”. In locations where the background concentration is high, the marginal contribution could be low. The bias hence crucially depends on the functional form of the dose response and the magnitude of the omitted background concentration. If these functional forms vary across chemicals, the bias would unknowable.

The analysis estimates “cancer and non-cancer risk by applying health benchmark data to the exposure concentrations”. This assumes that people are stationary and do not move due to changes in environmental quality (or other e.g. economic effects). It is hence a static exposure analysis, which is of course a hard challenge to overcome. But compositions of local populations do change, sometimes quite quickly (see the American Southwest for example).

I struggle with the approach taken for spatial resolution. On the one hand, data re hyperlocal (e.g. census block), but decision are supposed to be made for broader geographic areas. Little guidance is given as to what the “broader” geographic decision relevant level of aggregation is. Some of the zoomed in figures are quite local. It would be helpful to take a stand and provide concrete guidance. Census tracts are still quite small in many areas of the US (see figure 7-1)

I struggle with what we are supposed to take away from the quite striking and beautiful bivariate maps. Why is the number of chemicals the relevant second dimension?
It is also important to state that the TRI is self-reported, so the usual reporting biases apply. These are not measured releases form what I understand. The same is true for the NEI?

Dr. Ronald Benke

These responses attempt to draw on the regulatory context for the Toxic Substances Control Act (TSCA) and relationships among environmental justice, potentially exposed susceptible subpopulations, and overburdened communities.

Charge Question 1:

AirToxScreen is an EPA modeling tool that estimates ambient airborne chemical exposure and risk across the United States to the census tract level. Given the model’s strengths, limitations, and assumptions, please comment on the appropriateness of using AirToxScreen for screening level chemical co-exposure in the context of TSCA chemical evaluation.

As stated on slide 5 of the Draft Proposed Approach for Consideration of Chemical Co-exposure in TSCA Risk Evaluations (EPA staff presentation at the public meeting on October 16, 2024), no group of people should bear a disproportionate share of the negative environmental consequences resulting from governmental and commercial operations or policies. The

AirToxScreen work and related screening approach developments have been nothing short of valiant. However, EPA staff is strongly encouraged to incorporate an appropriate amount of "environmental ground truth" from the sampling and analysis of air, water, soil, or vegetation into its evaluation. Because screening development work has concentrated on airborne chemicals, air sampling may be preferrable to other environmental media, especially if there is no analytical benefit from sampling and analyzing other media. Even at a minimal level, the measurement of selected environmental contaminants seems essential for comparing and confirming hot spots of chemical co-exposure. AirToxScreen appears to be a viable tool for both selecting sampling locations and identifying the chemical co-exposure contaminants for analysis.

Environmental measurements are intentionally suggested for the screening evaluation as a proxy for human health. Once the screening process demonstrates sufficiency from a measured environmental contaminant perspective, it should become more effective at addressing human health consequences in a phased development approach.

Charge Question 2:

This draft document proposes multiple potential metrics to inform chemical co-exposure. These proposed metrics include:

Number of chemical releasing facilities;
Number of chemicals released from facilities;
Number of chemicals meeting chemical risk benchmarks;
Chemical risk combinations; and
Bivariate distribution of individual chemical risk with potential chemical co-exposure

Please comment on the utility, strengths, and uncertainties of these metrics. Please include in your comments discussion of the methods used to develop these metrics.

Allow selected measurements of environmental media to directly inform work related to this charge question, so that the number of screening metrics can be reduced and preferred metrics can be optimized. Improved uncertainty determination for these modeling-based metrics is an intrinsic strength of incorporating environmental measurements into the screening development process.

Charge Question 3:

The two stated goals for this paper are:

1) *support identification of potential PESS; and*
2) *consider chemical co-exposure as part of an individual chemical risk evaluation.*

Please comment on the extent to which the analyses and methodologies proposed within this document support these goals.

Environmental sample analysis is needed to demonstrate that the proposed analyses and methodologies accomplish Goal 1 on identifying potentially exposed susceptible subpopulations (PESS). This could be accomplished in a case study.

For chemical co-exposure relating to Goal 2, one additional step is suggested beyond the risk levels already presented. Consider coupling exposed population estimates with the chemical risks to highlight areas with the largest number of implied adverse health effects. More discussion on compliance requirements for individual chemicals would be helpful. Past areas of noncompliance on an individual chemical basis should be mapped to encourage assessments of chemical co-exposure in adjacent or surrounding areas, with attention given to risk peaks and gradients.

Dr. Tami Bond

1. *AirToxScreen is an EPA modeling tool that estimates ambient airborne chemical exposure and risk across the United States to the census tract level. Given the model's strengths, limitations, and assumptions, please comment on the appropriateness of using AirToxScreen for screening level chemical co-exposure in the context of TSCA chemical evaluation.*

AirToxScreen follows accepted methods for simulating chemical exposure and risk, and I support its use. Further, use of AirToxScreen allows comparison of results in this report with other efforts, whereas discrepancies may arise if a different method is used.

I recommend a discussion of uncertainty of AirToxScreen output. This could be done with reference to prior work that uses the underlying tools; it doesn't have to be a separate investigation.

2. This draft document proposes multiple potential metrics to inform chemical co-exposure. These proposed metrics include:

--Number of chemical releasing facilities;

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--Bivariate distribution of individual chemical risk with potential chemical co-exposure

Please comment on the utility, strengths, and uncertainties of these metrics. Please include in your comments discussion of the methods used to develop these metrics.

The document proposes a set of metrics based *only* on an analysis of number of facilities and number of chemicals, and another set of metrics based on evaluating the output of AirToxScreen. The procedures for the two methods are not easily distinguished in the draft document. As a reader, I first encountered the emphasis on number and not release rate, and then carried that understanding forward to the entire body of methods. This meant that I thought AirToxScreen was being operated with no release rate, which I did not understand. I now see that one is expected to recognize that the use of AirToxScreen inherently incorporates release rate and therefore generates a different group of metrics, but this distinction isn't made clear in the document. Clarification should be provided with an explicit division of the number-based and the release-based calculations, their separate methods, and the outcomes that results from each pathway.

I can see how these two sets of metrics could be useful. The number-based metrics identify whether a location is burdened by several facilities, while the release-based metrics give a sense of whether the burden from any facility is high. As the entire scientific community is just beginning to explore how to combine multiple stressors, and how to represent the burden of cumulative impacts, I don't think that the exact uses of these different metrics can be foreseen.

3. *The two stated goals for this paper are: 1) support identification of potential PESS; and 2) consider chemical co-exposure as part of an individual chemical risk evaluation. Please comment on the extent to which the analyses and methodologies proposed within this document support these goals.*

   Please see my answer to #2. I think that the approach to understanding co-exposures will evolve over time as investigators use these tools. The utility of these tools will be brought forward in the number and strength of external analyses, not in my reflection upon them. Any alterations needed will probably arise through limitations encountered in those inquiries. This is a challenging area of inquiry, and I support going forward with the proposed metrics as long as occasional revisiting occurs with community input.

Dr. Aimin Chen

1. AirToxScreen is an EPA modeling tool that estimates ambient airborne chemical exposure and risk across the United States to the census tract level. Given the model's strengths, limitations, and assumptions, please comment on the appropriateness of using AirToxScreen for screening level chemical co-exposure in the context of TSCA chemical evaluation.

Response: AirToxScreen (ATS) is an effective tool to estimate total air pollution from chemical emission sources. The validity of the ATS can be elaborated with more data to support its use, particularly in various geographic regions and urban and rural areas. The validation may need to be at chemical level. Secondary chemical reaction after emission may not be captured, thus validation can be valuable to support its use nationally.

2. This draft document proposes multiple potential metrics to inform chemical co-exposure. These proposed metrics include:

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--Chemical risk combinations; and

--Bivariate distribution of individual chemical risk with potential chemical co-exposure

Please comment on the utility, strengths, and uncertainties of these metrics. Please include in your comments discussion of the methods used to develop these metrics.

Response: These metrics are reasonable to use for the emission inventory. Seasonal variation of chemical release may not be captured by the current metrics and some higher concentration exposures in a short period of time may not be shown in the metrics.

3. The two stated goals for this paper are: 1) support identification of potential PESS; and 2) consider chemical co-exposure as part of an individual chemical risk evaluation. Please comment on the extent to which the analyses and methodologies proposed within this document support these goals.

Response: 1) Identification of potential PESS is highly possible when combining GIS data for NEI release and social determinants of health at Census Tract level. More details will be needed to identify pregnant women, lactating mothers, and young children who are more vulnerable to chemical mixture. Additionally, children with existing medical conditions may not be captured by census tract level analysis. 2) Co-exposure to chemicals in the ATS will be identified using the method described in the report. However, exposure to other not listed chemicals or chemicals from other exposure routes (ingestion and dermal) or indoor air pollution will not be captured for the co-exposure analysis. The proposed method is still a great step to understand co-exposure to

chemical in the ATS from inhalation exposures. Geographic or climate influences of exposure levels may not be considered in the current model, including mountains, valleys, temperature inversion, extreme heat, and other weather events.

Dr. Rebecca Fry

1. AirToxScreen is an EPA modeling tool that estimates ambient airborne chemical exposure and risk across the United States to the census tract level. Given the model's strengths, limitations, and assumptions, please comment on the appropriateness of using AirToxScreen for screening level chemical co-exposure in the context of TSCA chemical evaluation.

   The AirToxScreen is a valuable tool for screening co-exposures. Strengths of AirToxScreen is that it offers a dataset of most HAP chemicals for screening level evaluation across of number of co-exposure metrics and that we are able to identify areas of potential PESS at national to regional scales. Importantly, it can be used to identify areas of increased burden from co-occurring chemicals.

2. This draft document proposes multiple potential metrics to inform chemical co-exposure. These proposed metrics include:
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   --Chemical risk combinations; and
   --Bivariate distribution of individual chemical risk with potential chemical co-exposure
   Please comment on the utility, strengths, and uncertainties of these metrics. Please include in your comments discussion of the methods used to develop these metrics.

   These metrics are useful, however where possible of course we need to include chemical levels (not just number of chemicals). The methods used to develop these metrics appear appropriate.

3. The two stated goals for this paper are: 1) support identification of potential PESS; and 2) consider chemical co-exposure as part of an individual chemical risk evaluation. Please comment on the extent to which the analyses and methodologies proposed within this document support these goals.

   The analyses and methodologies support these goals.

Dr. Joshua Graff Zivin

I only have one comment on the Co-Exposure draft, and it should certainly be qualified by the fact that I am an economist with a highly imperfect understanding of the dose-response functions and risk estimation strategies that are central to this effort. All that said, I thought there was a missed opportunity to better characterize overburdened communities. I like the approach that counts the number of chemicals exceeding a risk threshold in a given location, but I would have also liked an approach that added up the risk from all chemicals in a location irrespective of whether each one exceeded some threshold (with appropriate caveats about what is means to add up across different exposure routes and types of cancer). This would allow us to see if there are any communities that are being burdened by lots of small insults that fly beneath the regulatory radar but add up to a considerable risk.

I hope this helps and makes sense. The study team should feel free to push back if my ignorance is nudging them in a direction that is not scientifically defensible.

Dr. John D. Groopman

The following comments on this outstanding presentation are framed by my perspective in cancer epidemiology and the application of technologies to measure dose from environmental exposures in individuals and populations. Thus, this framework would represent a complementary extension of the presentation at the SAB meeting.

Charge Question 1:

AirToxScreen is an EPA modeling tool that estimates ambient airborne chemical exposure and risk across the United States to the census tract level. Given the model's strengths, limitations, and assumptions, please comment on the appropriateness of using AirToxScreen for screening level chemical co-exposure in the context of TSCA chemical evaluation.

The first major point of clarification needed for a more in-depth evaluation of this proposal involves an understanding of the temporality of the exposure metrics being aggregated with this new tool. Clearly, its use as a cross-sectional view of air toxics provides a very narrow window of exposure similar to a daily weather forecast. Gaining an understanding of the power of these measurements to have a greater area under the curve over a longer term of time

would be essential. As part of this effort a series of layered data could prove to be quite informative. They include:

- Integrating the age distribution information at the census tract level would reveal the fraction of the population that are under the age of 20, 20 to 65 years of age and above. If a major focal point is on cancer that obviously requires many years of biological development concern for earlier life exposures can be quite important in the design of preventive measures.
- Similarly, since the elderly often have multiple chronic disease diagnoses these individuals might be at a greater level of susceptibility to exposures that might have less toxic impacts for individuals and by extension communities with an overall healthier status.
- Thus, integration of many available health data sets such as specific cancers, per capita income, age distribution, and projected changes over time could be layered into this tool to provide a more comprehensive view for defining the at-risk community.
- There was much discussion at the meeting with respect to exposures through the respiratory tract and I strongly feel that we cannot ignore the long-term pathology that COVID has impacted upon millions of people in the US. Prior data from other infectious diseases have shown that chronic inflammation by agents such as influenza can reduce the resiliency of the lung to environmental exposures and this in turn increases risk of more severe disease.

Charge Question 2:

This draft document proposes multiple potential metrics to inform chemical co-exposure. These proposed metrics include:

- *Number of chemical releasing facilities;*
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- *Number of chemicals meeting chemical risk benchmarks;*
- *Chemical risk combinations; and*
- *Bivariate distribution of individual chemical risk with potential chemical co-exposure.*

My comments for this question mirror the description above for question one. In addition, I feel that a greater discussion of the extrapolation of exposure to dose is required since an individual's dose estimate can have extraordinarily wide confidence intervals if the exposure monitor is distant. These exposure metrics can help inform the deployment of individualized or personalized dose technologies that can range from passive monitors, or active biomarker measurements using state-of-the-art adductomic technologies.

Charge Question 3:

The two stated goals for this paper are:

1)support identification of potential PESS; and

2)consider chemical co-exposure as part of an individual chemical risk evaluation.

My prior comments touched upon these issues already, but I would just reinforce those statements with the following:

- There are many data sets that have mapped health outcomes, SES, migration of subpopulations and projections for the future. These are available on a statewide, county wide and in many instances census tract data set levels. The layering of these data with the air toxics work would be a very valuable tool not only for the regulatory community but also for the health systems that need to provide care for community members. For example, a projection of the changing patterns of lung cancer or the earlier age of diagnosis of colon cancer in a community directly impacts the planning and deployment of cancer health services. The rapid advancement of new therapeutics based upon specific genetic changes in a tumor type has transformed treatments of diseases such as lung cancer.
- There are now a number of high-quality projections over the next 15 years to 2040 (JAMA, 2021) on the changing patterns of cancer incidence and mortality in the United States. In 2040 lung cancer will remain as the leading cause of cancer death but pancreatic cancer and liver cancer will be #2 and #3. Breast cancer mortality and colon cancer mortality is significantly declining, and it is evident that environmental exposures occurring today will become manifest in the cancers that are diagnosed 15 to 25 years from now this prospective component would be valuable to integrate into this overall effort.

Dr. Angela Leung

Overall the document is well-written and provides an initial proposed approach toward consideration of how to evaluate the topic of chemical co-exposures.

Although the use of the AirToxScreen (ATS) is intended to only serve as an initial characterization (that may used as a model across the risk evaluation process for other methods of capture) and Section 8 is appreciated as a future directions type of text, this can likely be even more strongly emphasized and made more clear. As it reads, it remains slightly unclear how other sources of exposure would be accounted for and potentially what other specific future applications might be possible. Even if proposed as plausible applications, they may be helpful. Thank you for addressing this important topic overall.

Dr. Carla Ng

Overall, this report provides an interesting analysis of chemical co-exposures with number of releases, number of chemicals, and risk-based evaluation based on cancer thresholds. The use of tools such as Air Tox Screen, as illustrated here, can provide useful insight on the variability of releases and potential exposures across the nation. Some suggestions are provided that may help improve the clarity of the report and refine the messages and proposed approach.

Page 11, final sentence, are there any publications that point to this gap on non-chemical stressors that could be referred to here? This is an important limitation of the approach and thus documenting what currently is and is not possible would be particularly helpful here.

On page 12, second bullet point on limitations could be rephrased for clarity: "Exposure for each chemical is treated independently" and "OPPT is not calculating a total additive exposure or total additive risk across the chemicals included in the analysis." If that is the case, how is "co-exposure" defined? How is the combined nature of the exposure captured if not in an additive way? (by adding up number of co-exposures, if not concentrations)

Page 12, 3rd bullet point is first mention of cancer. Mention earlier in the document that cancer risk will be the basis of the analysis.

Page 12, Last sentence under "Proposed use of air tox screen": "In the future, EPA OPPT may consider the development of a tiered framework to incorporate a broader range of spatial scales." – this sentence is premature as scaling in ATS has not yet been discussed.

Page 13, in the second paragraph, the description of the different models used for estimating ambient concentrations within ATS is not entirely clear. For example, CMAQ is described as a "photochemical model" when in fact it is a suite of models that in general predicts the fate, transformation, and transport of air constituents. The explanation that comes later (on page 16) is more complete but still does not specify whether it's referred to as "photochemical" because it primarily models direct and indirect photolysis reactions for chemicals. While this may be clear to the atmospheric modeling community, users of this approach may be coming from other fields (i.e. those interested in identifying overburdened communities) so clearer descriptions would be helpful. It's also not clear what is meant by "but estimation of ….and fires is only modeled in this model." Does that mean to say that these secondary and non-point-source emissions are based on modeling only whereas in the AERMOD model it is based on emissions data (which as stated earlier in the paragraph are included in the NEI data)? If AERMOD has data-based estimates of

these latter categories, but CMAQ uses only model estimates, why are the two model outputs averaged rather than using the higher quality/more data-based values? Do users of this workflow have the opportunity to make these choices or is this simply a description of what comes pre-packaged in an ATS output?

Page 18, “generated ambient air and exposure concentrations… are based on population weighted averages of..” – in this section it would be helpful to provide (or reiterate) the units of these two model outputs, because the weighting by population does not make a lot of sense for an ambient air concentration. Why would having a denser population lead to a higher ambient air concentration? Or is it rather the associated risk, since there are more people being exposed?

Page 19, end of first paragraph: “OPPT focuses on the utility of the described methodologies for a screening level at broader spatial scales and not for predicting patterns at individual census tracts.” – Yet all of the results figures that follow in later sections provide results at the census tract scale (Figures 6.1-6.8). Needs to be clarified or restated.

Page 19, second paragraph: “Activity patterns are intended to capture a representative person…” – As these patterns are estimates and therefore introduce additional uncertainties into the model, might it not be better to further simplify and use the ambient air concentrations rather than the derived exposure concentrations? Could a sensitivity analysis be used to show the difference in the approaches? Given the uncertainties along the many steps proposed, the output should be considered in a relative sense in any event.

Page 20: A summary of the general workflow and types of analyses conducted would have been helpful as a first section in order to provide context for the description of the ATS approach that takes up the first part of this document. Some decisions and considerations only become clear within Section 6, which detracts from the clarity of the document.

Page 20-21 (and earlier) – referring to the analysis being done “at the regional to national spatial scale” is confusing because the data are aggregated (and shown) at the census tract level. Might be more helpful to say that “analyses at the census tract scale are shown for the entire US as well as for two regional case studies” so as not to confuse “spatial scale” with “model resolution.”

Page 24, second to last paragraph: “Higher number of releases are shown in Wyoming, Colorado, and California” – are these averaged across the total number of census tracts in each of those states or otherwise normalized for size of the state? Or is this due to the few tracts with >50 releases shown in Figure 6-3? It is interesting that in Figure 6-4, where the 5km buffer is employed, the picture appears much worse for California but generally the same for Colorado. Is this entirely due to population density? (That is, the census tracts being small in California lead to an underestimation of impact in Figure 6.3 that disappears once the 5km zone of influence is considered.)

Pages 31 – 32, discussion of number of tracts above cancer risk threshold: It is notable that the geographic distribution of "high risk" tracts does not mirror the number of release or number of chemicals results presented earlier (Figures 6.2-6.5). Does this indicate the risk-based ATS approach is more useful than the number of emission sites or number of emitted chemicals? Are the methods complementary in some way? How about the relative degrees of uncertainty associated with these three different analyses?

Page 34: Regarding the occurrence of a few common sets of co-occurring chemicals among many "one-offs", it seems appropriate here to note something about whether there are similar types of industrial activity that generate signature combinations of emissions.

Page 38, middle paragraph on analysis of co-occurring chemicals: Why not constrain the output to generate only integer number of chemicals? "On average 5.1 – 7.8 other chemicals"

Dr. Gloria Post

Charge Question 1:
AirToxScreen is an EPA modeling tool that estimates ambient airborne chemical exposure and risk across the United States to the census tract level. Given the model's strengths, limitations, and assumptions, please comment on the appropriateness of using AirToxScreen for screening level chemical co-exposure in the context of TSCA chemical evaluation.

Although I do not have specific expertise in air modeling, based on the information presented in the draft document, the AirToxScreen modeling tool appears to be appropriate for initial screening for locations with potential co-exposures to toxic air contaminants. The draft document makes it clear that the AirToxScreen does not provide definitive information and appropriately emphasizes the uncertainties and limitations of this modeling tool.

Charge Question 2:
This draft document proposes multiple potential metrics to inform chemical co-exposure. These proposed metrics include:

- *Number of chemical releasing facilities;*
- *Number of chemicals released from facilities;*
- *Number of chemicals meeting chemical risk benchmarks;*
- *Chemical risk combinations; and*
- *Bivariate distribution of individual chemical risk with potential chemical co-exposure*

Please comment on the utility, strengths, and uncertainties of these metrics. Please include in your comments discussion of the methods used to develop these metrics.

Number of chemical releasing facilities:
As discussed in the draft document, this metric is suitable only as a preliminary screen because it is associated with a number of important uncertainties. For example, multiple sources of release from a single facility may be counted separately in some jurisdictions and combined in other jurisdictions. Also, this metric does not consider the amount of the chemical released from each facility, such that facilities releasing very small amounts and very large amounts are considered equally. Additionally, the predicted number of facilities that release chemicals may be highly impacted by the widely variable sizes of different census tracts.

Additionally, it is my understanding that this metric includes only facilities/stationary point sources and does not consider other sources included in ATS, which are listed in Section 4.3 of the draft document, such as non-point sources and mobile sources, even though these other sources may be equally or more important sources of air toxics. As discussed below, it appears that some of the other metrics do include all sources, not just facilities/stationary sources. However, this is not clearly stated in the document. The sources that are included and not included, along with the rationale for inclusion and exclusion, should be clearly stated for each metric.

Number of chemicals released from facilities:
I generally agree with the information presented in the draft document regarding the strengths, limitations, and uncertainties of this metric.

Additionally, as for the "number of facilities" metric above, it is my understanding that this metric includes only facilities/stationary point sources and does not consider other sources included in ATS such as non-point sources and mobile sources, even though these other sources may be equally or more important sources of air toxics. As discussed below, it appears that some other metrics do include all sources, not just facilities/stationary sources. However, this is not clearly stated in the document. The sources that are included and not included, along with the rationale for inclusion and exclusion, should be clearly stated for each metric.

Number of chemicals meeting chemical risk benchmarks
Regarding use of information on the number of chemicals meeting chemical risk benchmarks, the draft document (p. 11) states: "One of most important differences is that in this proposed approach, EPA OPPT is evaluating chemicals that may not share toxicological properties (e.g., different target tissues). As such, EPA OPPT is not performing dose additivity to calculate multi-chemical risk or cumulative risk," and on p. 19: "Additionally, OPPT chose not to use the total cancer risk calculated as an output for ATS since adding potential cancer risks across different tissue types and different modes of action introduces additional uncertainty and methodological considerations that are beyond the scope of this document," with similar statements also on p. 33 and 36.

Relevant to these points, it should be noted that estimation of total cancer risk by adding the cancer risks of all carcinogens present at a site, regardless of differences in the types of tumors caused by the various chemicals, is recommended in USEPA risk assessment guidance. For

example, see p. 8-12 and 8-22 of USEPA, 1989 (Risk Assessment Guidance for Superfund. Volume I. Human Health Evaluation Manual. Part A. https://www.epa.gov/sites/default/files/2015-09/documents/rags_a.pdf). As stated on p. 8-22 of USEPA (1989), "In the absence of adequate information, EPA guidelines indicate that carcinogenic risks should be treated as additive…" It should be noted that estimation of total cancer risk by adding the risk of the individual chemicals is is not based on the assumption dose additivity (in contrast to the statement on p. 11 of the draft document). It is rather based on a different assumption, response additivity, which is often used in risk assessment of mixture of carcinogens, including for air toxics (Zhou et al., 2015; https://pmc.ncbi.nlm.nih.gov/articles/PMC4596837/pdf/pone.0140013.pdf).

The draft document (p. 18) also discusses that the ambient air concentrations and resulting exposure concentrations are based on annual averages, and that variations in these concentrations may occur during the year. While this is true, the variations in concentration over time are not relevant to calculation of cancer risk, which is based on average exposure over time, although such variations are relevant to other types of risk metrics, such as metrics based on risk of non-cancer health effects. As such, it should be noted that the risk metric (cancer risk) used in the draft document is dependent on the average exposure over time, and use of the average concentration is therefore appropriate and relevant.

It is not clear whether this metric considers the cancer risks of releases from all sources included in ATS, including non-point and mobile sources, or only risks from chemicals released from facilities/stationary sources. As above, the sources that are included and not included for each metric, along with the rationale for inclusion and exclusion, should be clearly stated.

Chemical risk combinations:

I agree that information on the frequency at which specific chemical combinations occur is valuable in evaluating co-exposure to air toxics and for determining priorities for research on the effects of chemical mixtures. However, the information about this metric in the draft document (Section 6.3) needs clarification.

In the examples discussed in Section 6.3, specific combinations of chemicals make up a large percentage of all chemical combinations. However, it is not clear whether all of the chemicals in these frequent combinations usually arise from the same facility or from different facilities located near each other. For example, more than half of tracts with 12 chemicals above the 10^{-7} cancer risk level have the same combination of 12 chemicals. However, it is not stated whether the source of these 12 chemicals is always or usually the same facility or if they come from different facilities in these locations. Information about whether the co-occurring chemicals come from the same or different source is important for understanding and addressing co-exposure to air toxics, and it is recommended that it be provided as part of this metric.

Additionally, it is not clear why the evaluation is based on locations at which only a specific combination of chemicals (e.g., exactly 12 chemicals) occurs above the risk benchmark, but does not include other locations with that same combination along with other chemicals above the risk benchmark. Locations where the same 12 chemicals occur along with other chemicals also appear to be relevant to the frequency at which the specific combination of 12 chemicals occurs, although this type of analysis might be more difficult to conduct.

Like the "number of chemicals meeting chemical risk benchmarks" metric above, it is not clear whether this metric considers the cancer risks of releases from all sources included in ATS, including non-point and mobile sources or only the risks of chemicals released from facilities/stationary sources. As above, the sources that are included and not included for each metric, along with the rationale for inclusion and exclusion, should be clearly stated.

<u>Bivariate distribution of individual chemical risk with potential chemical co-exposure</u>:
In concept, this metric will provide valuable chemical-specific information on the frequency of co-exposure to other air toxics along with the specific chemical being evaluated. However, the information presented in the draft document on this approach needs clarification.

In contrast to the other metrics discussed above, it is stated that the risk of the specific chemical being evaluated is based on all sources of the chemical in air (e.g., non-point and mobile sources), not just facilities/stationary sources. The rationale for considering all sources for this metric, but not for the other metrics discussed above, is not clear and should be provided.

Additionally, it is not clear if the information on the number of chemicals that co-occur with the chemical being evaluated is based only on facility/stationary sources or on all sources, and this should be clarified. It does not appear to be supportable to evaluate the risk of the chemical of interest from all sources and the risks of co-occurring chemicals only on facilities/stationary sources, while noting that it is not clear whether this is what was actually done here.

Charge Question 3:
The two stated goals for this paper are:

1) support identification of potential PESS; and

2) consider chemical co-exposure as part of an individual chemical risk evaluation.

Please comment on the extent to which the analyses and methodologies proposed within this document support these goals.

The methodologies described in the draft document are potentially useful as screening approaches to identify potential PESS and evaluate co-exposures in individual chemical risk evaluation. However, as noted in the draft document, these approaches are not definitive and are intended to represent a first step in achieving these goals. Methodologies that provide more

definitive information will need to be developed if information on PESS and chemical co-exposures is to be included in TSCA risk evaluations.

Additionally, the draft document states (p. 49) that "… ATS also offers modeled information on chronic non-cancer health risks that could be incorporated in subsequent evaluations of chemical co-exposure as appropriate. Additionally, other pathways or routes of exposure may also be able to be considered and inform the full spectrum of co-exposures to which a population is exposed." I support the future development of approaches for considering non-cancer health risks and exposures from media other than air for use in TSCA evaluations of co-exposures to toxic chemicals.

Dr. Amanda D. Rodewald

1. AirToxScreen is an EPA modeling tool that estimates ambient airborne chemical exposure and risk across the United States to the census tract level. Given the model's strengths, limitations, and assumptions, please comment on the appropriateness of using AirToxScreen for screening level chemical co-exposure in the context of TSCA chemical evaluation.

I congratulate the EPA scientists who authored this draft report, which is well-written, thorough, and clear. Though admittedly this is not my specific area of expertise, the AirToxScreen tool seemed to be a rigorous and useful tool for estimating risk from multiple chemical co-exposures. The tool and process as described in the document convincingly make the case that this path forward represents a substantial improvement in our ability to understand and estimate risk from multiple chemical exposures, especially to PESS populations.

I was glad to see that "aggregate effects" from multiple exposures are considered, even if multiple exposures are to the same chemical. The ability to consider multiple chemicals that do not share toxicological properties, unlike cumulative effects analyses, is an important one. That said, the last sentence of section 2 on page 11 sounds as though there is not the ability to estimate dose additivity. Additional explanation of that would be helpful.

While I understand that several data and analytic constraints preclude consideration of non-chemical stressors, I am still concerned that they cannot be incorporated directly. Many non-chemical stressors disproportionately impact EJ and PESS communities, and a failure to consider them when estimating risk seems almost certain to underestimate negative outcomes for human health and well-being. Perhaps the draft report can still advocate for incorporating non-chemical stressors in the future.

ATS section 4.1 Page 12: The last sentence says that OPPT may consider developing a tiered framework to incorporate broader spatial scales. Why are estimates of risk across broader spatial scales not being pursued here in this document?

2. This draft document proposes multiple potential metrics to inform chemical co-exposure. These proposed metrics include:

--Number of chemical releasing facilities;
--Number of chemicals released from facilities;
--Number of chemicals meeting chemical risk benchmarks;
--Chemical risk combinations; and
--Bivariate distribution of individual chemical risk with potential chemical co-exposure

Please comment on the utility, strengths, and uncertainties of these metrics. Please include in your comments discussion of the methods used to develop these metrics.

Those metrics make good sense to me, but I was surprised by the absence of others that would seem to be critical to consider – such as magnitude of release and proximity of human population to release site/facility. The example described on page 23 was worrisome ("*For example, given two facilities with known releases within a census tract, a facility releasing a single kg per year was counted the same as a facility that may be releasing thousands of kg per year.*") Although the document did a good job with transparency when describing which metrics were included vs omitted, the authors might consider providing more justification for omissions that would seem obviously important to a lay person or non-chemical expert.

Regarding indoor air pollution, the following wording at the end of page 15 was unclear to me in terms of what "these emitted chemicals…" referenced and if those chemicals in the list were considered at all.

"*It is important to note that ATS does not consider possible exposures resulting from indoor air. These emitted chemicals come from a variety of source contributions including:*

- *point sources such as large waste incinerators and factories;*
- *nonpoint sources such as residential wood combustion, commercial cooking, and consumer and commercial solvents;*
- *mobile sources such as cars and trucks found on roadways and nonroad equipment including marine vessels, trains, aircraft, lawnmowers or construction equipment;*
- *biogenics such as those chemicals emitted from vegetation;*
- *secondary production such as those chemicals formed in the atmosphere; and*
- *fires which include wildfires, prescribed burning and agricultural-field burning"*

I was confused because the wording suggested that perhaps those listed sources were not being considered, despite at least the first describing point sources. Was the point simply that those sources contribute to indoor air pollution, but they're not being used to estimate risk from indoor air pollution (i.e., instead, those listed sources are considered as relevant within the AirToxicScreen tool)?

3. The two stated goals for this paper are: 1) support identification of potential PESS; and 2) consider chemical co-exposure as part of an individual chemical risk evaluation. Please comment on the extent to which the analyses and methodologies proposed within this document support these goals.

If the identification of potential PESS occurs at the census tract scale and does not explicitly consider distance to a release facility within census tracts, then I wonder if there will be bias in PESS identification among rural and urban census tracts given the size difference between them.

Dr. Jonathan Samet

1. AirToxScreen is an EPA modeling tool that estimates ambient airborne chemical exposure and risk across the United States to the census tract level. Given the model's strengths, limitations, and assumptions, please comment on the appropriateness of using AirToxScreen for screening level chemical co-exposure in the context of TSCA chemical evaluation.

AirToxScreen is an appropriate model to use as a basis for generating the starting point for the screening metrics.

2. This draft document proposes multiple potential metrics to inform chemical co-exposure. These proposed metrics include:

--Number of chemical releasing facilities;

--Number of chemicals released from facilities;

--Number of chemicals meeting chemical risk benchmarks;

--Chemical risk combinations; and

--Bivariate distribution of individual chemical risk with potential chemical co-exposure

Please comment on the utility, strengths, and uncertainties of these metrics. Please include in your comments discussion of the methods used to develop these metrics.

The various metrics fulfill the goal of offering screening approaches for identifying the exposure burden imposed on communities at the census track level and on those susceptible individuals within the census track. They are inherently overlapping and it would be useful to further explore

the specific contributions that each makes to characterizing chemical co-exposures. Does the choice of metric materially change the classification of a census track? For the count metrics, what are Spearman correlations among them, for example?

Figures 6-2 through 6-5 and Figure 6-7 document a limitation of the approaches for considering numbers of events or chemicals: dependence of counts on the geographic size of the census tracks. The prominence of Wyoming in Figures 6-2 through 6-5 is eye-catching, for example. These metrics need to be normalized in some way for the size of the census track, presumably with a measure of geographic density.

The document would be more useful, as might consideration of the various approaches and selection among them, if there were further exploration of the various combinations of chemicals in relation to sources.

1. The two stated goals for this paper are: 1) support identification of potential PESS; and 2) consider chemical co-exposure as part of an individual chemical risk evaluation. Please comment on the extent to which the analyses and methodologies proposed within this document support these goals.

In this document, EPA is attempting to address the "…requirement to identify and evaluate risks to potentially exposed or susceptible subpopulation(s) (PESS)." The updated definition of PESS includes "overburdened communities" along with groups considered as having increased susceptibility to pollutants, e.g., children and the elderly. Thus, PESS mixes vulnerability (increased risk of being exposed) with susceptibility (increased risk of an adverse event at a given exposure level). This conceptual mash-up is unfortunate, even though adopted. The present document addresses only one component of PESS, exposure burden or vulnerability. The analyses offer no insights into the exposures of susceptible populations and the risk considerations relate to "average" people within the census tracks. Activity patterns utilized to move from concentrations to exposures do not reflect the activity patterns of those who are susceptible. The document needs to more carefully describe what it does and what it does not do, distinguishing the two components of PESS. Absent such clarification, the document will mislead its users.

With regard to the second component of this charge question, the methods described do not advance assessment of individual chemical risks to reflect potential synergy or antagonism among multiple chemicals in determining the risk of a particular chemical. The various metrics document the need for such approaches but do not offer insights as to how to advance risk considerations. With the systematic review mandate followed under TSCA, would detailed review of all lines of evidence be needed to address risks of combined exposures?

Dr. Godfrey A. Uzochukwu:

Charge Question 1:

AirToxScreen is an EPA modeling tool that estimates ambient airborne chemical exposure and risk across the United States to the census tract level. Given the model's strengths, limitations, and assumptions, please comment on the appropriateness of using AirToxScreen for screening level chemical co-exposure in the context of TSCA chemical evaluation.

Response: AirToxScreen offers a readily available nationwide dataset of most HAP chemicals for screening level evaluation across of number of co-exposure metrics.

Charge Question 2:

This draft document proposes multiple potential metrics to inform chemical co-exposure. These proposed metrics include:

Number of chemical releasing facilities;

Number of chemicals released from facilities;

Number of chemicals meeting chemical risk benchmarks;

Chemical risk combinations; and

Bivariate distribution of individual chemical risk with potential chemical co-exposure

Please comment on the utility, strengths, and uncertainties of these metrics. Please include in your comments discussion of the methods used to develop these metrics.

Response: Analysis conducted - Identification of possible PESS at national and regional scales need clarification – kind of facilities, kind of chemicals and chemical risk combinations.

Charge Question 3:

The two stated goals for this paper are:

1)support identification of potential PESS; and

2)consider chemical co-exposure as part of an individual chemical risk evaluation.

Please comment on the extent to which the analyses and methodologies proposed within this document support these goals

Response: Method(s) of data collection, analyses and PESS at regional and national scales need more clarification. A standardized methodology is recommended.

Dr. Wei-Hsung Wang

1. AirToxScreen is an EPA modeling tool that estimates ambient airborne chemical exposure and risk across the United States to the census tract level. Given the model's strengths, limitations, and assumptions, please comment on the appropriateness of using AirToxScreen for screening level chemical co-exposure in the context of TSCA chemical evaluation.

   Response

   AirToxScreen (ATS) is a peer-reviewed, screening level modeling tool which evaluates air toxics across country, informs the collection of air toxics information, and characterizes areas of greatest potential concern to the general population in order to estimate the airborne chemical exposure and the corresponding pollution risk at the geographic scale of census tracts nationwide. The assumptions, strengths, limitations (cautions), and uncertainties of ATS were carefully considered and comprehensively described in Section 4 of the draft document and thus it is appropriate to use ATS to identify geographic patterns of risk and ranges of risks posed by a suite of air pollutants. Further, it is explicitly stated in Section 4 that the results from this analysis tool are intended to communicate the degree to which air concentrations, exposures, and risk vary across the United States at wider spatial scales based on geography and should not be used to interpret individual chemical exposures and risk.

2. *This draft document proposes multiple potential metrics to inform chemical co-exposure. These proposed metrics include:*

--Number of chemical releasing facilities;
--Number of chemicals released from facilities;
--Number of chemicals meeting chemical risk benchmarks;
--Chemical risk combinations; and
--Bivariate distribution of individual chemical risk with potential chemical co-exposure.

Please comment on the utility, strengths, and uncertainties of these metrics. Please include in your comments discussion of the methods used to develop these metrics.

Response

I found that the proposed metrics for evaluation of chemical co-exposure were reasonably defined and logical. Assumptions and uncertainties associated with these metrics were well thought. The rationale for developing the analysis steps was clearly explained and justified. In addition, the tables and figures of the supporting examples were very informative.

I also have a couple of general comments:

(a) Although the scope of the draft document is limited to under the statutory language of TSCA and thus nuclear materials are excluded from TSCA, radon is listed on the chemical substance inventory. Since radon is a progeny of radium which is concentrated (or technologically enhanced) from various phases/processes of oil and gas extractions, for future studies it may be prudent to include radiation exposure into risk evaluation.
(b) The draft document does not consider non-chemical stressors. Because EJ framework consists of a spectrum of environmental stressors, I am curious about how EJ principles are effectively incorporated into this risk assessment using only chemical stressors.

3. *The two stated goals for this paper are: 1) support identification of potential PESS; and 2) consider chemical co-exposure as part of an individual chemical risk evaluation. Please comment on the extent to which the analyses and methodologies proposed within this document support these goals*.

Response

The proposed analyses and methodologies were based on sound science and thus support the two stated goals. For risk assessment, it is prudent to understand the synergistic health effects from exposure to multiple air toxics for potentially overburdened communities.

Dr. Douglas Wolf

1. AirToxScreen is an EPA modeling tool that estimates ambient airborne chemical exposure and risk across the United States to the census tract level. Given the model's strengths, limitations, and assumptions, please comment on the appropriateness of using AirToxScreen for screening level chemical co-exposure in the context of TSCA chemical evaluation.

This effort would benefit from a re-examination of the problem formulation effort that was originally conducted. It appears that this presentation focused on an assumed solution by using the AirToxScreen tool. Although other tools are listed, since it is not clear what is the problem that is trying to be solved and there is no conceptual model around which to examine the available information, it is difficult to know if this is the correct tool.

The problem formulation for this effort is not clear nor is there a clear problem statement. Sections 1 and 2 include a lot of areas which seem to be excluded in the scope. The scope has narrowed the effort considerably so it is unclear how this effort will address EJ and PESS without considering aggregate exposure and modifying factors.

This work should go back and revisit the problem formulation discussion. It would benefit from considering these publications.
https://www.tandfonline.com/doi/full/10.1080/10408444.2016.1211618

http://dx.doi.org/10.1080/10408444.2016.1211617

https://www.sciencedirect.com/science/article/abs/pii/S0273230018303076?via%3Dihub

https://nap.nationalacademies.org/catalog/12209/science-and-decisions-advancing-risk-assessment

2. This draft document proposes multiple potential metrics to inform chemical co-exposure. These proposed metrics include:

--Number of chemical releasing facilities;

--Number of chemicals released from facilities;

--Number of chemicals meeting chemical risk benchmarks; --Chemical risk combinations; and

--Bivariate distribution of individual chemical risk with potential chemical co-exposure
Please comment on the utility, strengths, and uncertainties of these metrics. Please include in your comments discussion of the methods used to develop these metrics.

I have provided numerous comments below that address specific sections of the document. Some summarized comments regarding the effects piece.

Cancer risk estimates are calculated values or policy-based values or a combination. The assumption here is that a 10 to the minus whatever is a real number. It is not, it is a protection goal or action level and has no relationship to a response. It would be better that this effort first focuses on the Common Exposure Grouping, figuring out the Common Effects Grouping is a different exercise altogether.

The suggested approach ignores important aspects of carcinogenicity risk and response. Repeated exposure, dose, temporal relationship of exposure and response, and cancer is a long-term process. Risk evaluation is a mitigation strategy. You cannot attribute exposure directly to the cancer response. If that were the case, then what you are saying is that the regulatory agency has been a complete failure in protecting the public and I do not believe

that is the case.

Effects is not a way to group chemicals for exposure. One identifies all the potential chemicals that are available to group then a relevant effect to determine which chemicals in the potential group should be aggregated for cumulative risk. Effects are a way to group chemicals as part of the weight of evidence evaluation to further compare across data sets. For examples see

https://doi.org/10.1071/EN23105; https://doi.org/10.3389/ftox.2024.1394361; https://www.oecd.org/en/publications/case-study-on-the-use-of-integrated-approaches-for-testing-and-assessment-iata-for-chronic-toxicity-and-carcinogenicity-of-agrichemicals-with-exemplar-case-studies-ninth-review-cycle-2023_c3b9ac37-en.html

3. The two stated goals for this paper are: 1) support identification of potential PESS; and 2) consider chemical co-exposure as part of an individual chemical risk evaluation. Please comment on the extent to which the analyses and methodologies proposed within this document support these goals.

"developing prospective methodologies to better identify PESS and characterize the potential exposure" "characterizing potentially overburdened communities"

Stop here, heavy enough lift for this first effort.

"development of a more formalized tiered framework"

This should be the focus of this work.

Specific comments

Executive Summary

"identification of potential PESS" "consider chemical co-exposure as part of individual chemical risk evaluation"

It should be made clear that exposure does not equal risk and the number of chemicals does not equal risk but rather the potential for there to be a risk. Also exposure does not equate to identifying potential susceptible subpopulations but could point to where populations of concern could be. Identifying a susceptible subpopulation is an active process based on a series of factors which are not related to strait exposure.

“communities”

Is the focus on communities or susceptible subpopulations?

Section 1

“The consideration and evaluation of PESS under TSCA can include, but is not limited to, a wide variety of different individuals or groups, such as children, the elderly, pregnant women, overburdened communities, and Tribal communities”

These various definitions would imply an excessive burden on the risk assessor to come up with a variety of assessments within a single site and various levels of remediation. Will one PESS take precedence within a single site or decision context?

“there are communities that may experience disproportionate risks from chemicals due to greater exposure or susceptibility to environmental and health harms”

Will there be an effort to differentiate these various influencers on risk? Greater exposure is very different than greater susceptibility. It will be important to define the driver for particular populations as it will have a great impact on mitigation strategies at the local level.

“To support identification of potential PESS”

I am not clear how exposure defines a susceptible subpopulation. It is my understanding that susceptibility is a biological or sociological set of characteristics that define the population that result in individual or population level increased susceptibility, not the fact that they are exposed.

“To consider chemical co-exposure as part of an individual chemical risk evaluation by”

Since this this the main goal of this common exposure group effort, this should be the focus of this specific proposal and not PESS nor what common effect is being evaluated. If PESS is being specifically addressed based on EJ issues then how will it be used from an EJ perspective to describe the co-exposure grouping for that EJ community?

“evaluate aggregate and cumulative exposure”

This should be the focus of this effort, which will be massive enough.

Section 2

“PESS are subpopulations “who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women workers, or the elderly.”

These are the traditional susceptible subpopulations. How will these be used to further define common exposure groups? When performing the final assessment, is there evidence that the current 10X UF for intraspecies differential susceptibility is not sufficient to achieve protection goals for RfD based risk assessments? For low dose linear no threshold models following the cancer guidelines and using the default approach when there is no mode of action data or for mutagenic chemicals, are there data to suggest the current risk assessments are not protective?

“multiple chemicals released concurrently to air water, and land are likely in many locations.”

How will aggregate exposure be incorporated with cumulative exposure estimates?

“Because an individual may be simultaneously exposed to multiple releases of the same chemical via combined routes (e.g. oral, dermal, and inhalation) and/or pathways (e.g. air, land, and water), EPA’s OPPT has begun to perform aggregate assessment”

Has OPPT consulted with OPP as aggregate exposure is standard practice in pesticide human health and environmental risk assessment.

“and/or stressors”

Why were modifying factors not included?

Section 3

The problem formulation for this effort is not clear nor is there a clear problem statement. Sections 1 and 2 include a lot of areas which seem to be excluded in the scope. The scope has narrowed the effort considerably so it is unclear how this effort will address EJ and PESS without considering aggregate exposure and modifying factors.

This work should go back and revisit the problem formulation discussion. It would benefit from considering these publications.
https://www.tandfonline.com/doi/full/10.1080/10408444.2016.1211618

http://dx.doi.org/10.1080/10408444.2016.1211617

https://www.sciencedirect.com/science/article/abs/pii/S0273230018303076?via%3Dihub

https://nap.nationalacademies.org/catalog/12209/science-and-decisions-advancing-risk-assessment

"more health protective"

What is the comparator, what evidence is there that the current methods are not adequately health protective?

"same geographic space"

What about the temporal aspect of co-exposure, particularly for air toxics and volatile compounds.

"The consideration of non-chemical stressors including the full consideration of factors that impact susceptibility or vulnerability and may cover an array of biological, social, and behavioral factors more in line with a cumulative impacts analysis is not considered here due to limited availability of quantitative data and vetted methodologies."

Then how will EJ and PESS be addressed as these features are related to modifying factors not just exposure, or rarely exposure, in reality.

"Although EPA may expand the scope of this effort in the future, at this time, there are some additional key limits to the scope of this proposed approach"

All of these limiting parameters will significantly diminish the probability of success.

"Finally, OPPT is focused on evaluation of chemicals that have existing cancer risk values as described in the datasets used"

I believe this is the wrong focus, especially if only considering inhalation exposure. Cancer risk values are not a common effect group but conclusions based on mathematical analysis and used to determine protection goals.

Section 4.1

"ATS then estimates census-tract level cancer and non-cancer risk by applying health benchmark data to the exposure concentrations. For the purposes of this evaluation and to support development of the proposed approach, OPPT has chosen to focus on cancer risk which is characterized as the calculation of an upper-bound lifetime individual cancer risk estimate that incorporates both the estimated exposure concentration and inhalation unit

risk (IUR) estimate”

First of all, since the goal of this effort is to create common exposure groups, there is no need to focus on any effects. Second since modifying factors are being ignored, most of which impact the effects side, it again does not make sense to focus on effects, finally cancer risk is not a relevant effect. Cancer risk is a calculated value and not an effect, thus it makes no sense as a common effect grouping measure. Also, it is off target for the goal of this effort which is about improving the exposure metrics. Finally, using a noncancer effect would make more sense and be more measureable. If there is an insistence of using only inhalation exposure and not aggregate exposure, it would be suggested to focus on an effect most relevant for inhalation exposure.

“risk estimates”

Risk estimates are an outcome of the total evaluation not a way to create a common effects grouping.

Section 4.4

As a screening level tool, it is a potential overinterpretation of the data to use it for a more quantitative measure of exposure. Is it not best used as a way to identify the potential collection of chemicals that might be in the common exposure group as the first step toward creating a common exposure group for further evaluation?

Section 6

“OPPT then investigates the number of chemicals per census tract reaching defined risk thresholds to identify screening level patterning of chemical co-exposure at these risk levels ranging from the regional to national scale (Section 6.2). Finally, OPPT analyzes the specific chemical combinations of tracts with the same number of co-occurring chemicals to determine whether some chemical combinations are more prevalent than others (Section 6.3)”

These seem like very different goals.

number of releases

number of chemicals

number of chemicals per census tract

risk levels regional

risk levels national

prevalence of combinations

“Summary of Analysis Steps”

It would be useful to turn this into a structured framework with a visual representation and a series of questions that need to be answered that lead you to the desired outcome.

Section 6.1.5

This is the most important part of the document. These illustrated examples should show how to work through the framework step by step to achieve the goal and answer the problem statement. However to do that one would have to have a well-constructed problem statement, a conceptual model that illustrates the components that need to be addressed to solve the problem, and a workable framework that leads the scientist through the data acquisition and interpretation.

Section 6.2

This part makes no logical sense to me.

Section 6.2.2

I believe this would all be meaningless data. Cancer risk estimates are calculated values or policy-based values or a combination. The assumption here is that a 10 to the minus whatever is a real number. It is not, it is a protection goal or action level and has no relationship to a response. It would be better that this effort first focuses on the Common Exposure Grouping, figuring out the Common Effects Grouping is a different exercise altogether.

Section 6.2.3

Without looking at aggregate exposure, which is what any cancer risk estimate would be based upon, this evaluation will not provide anything useful on a chemical by chemical basis. Then compounding the evaluation across a large number of chemicals will not be interpretable.

This ignores important aspects of carcinogenicity risk and response. Repeated exposure, dose, temporal relationship of exposure and response, cancer is a long-term process. Risk evaluation is a mitigation strategy. You cannot attribute exposure directly to the cancer response. If that were the case, then what you are saying is that the regulatory agency has been a complete failure in protecting the public and I do not believe that is the case.

“Additionally, this methodology allows for the evaluation of chemical co-exposure across various potential estimated cancer risk benchmarks and the calculation of the change in number of co-occurring chemicals across those evaluated benchmarks.”

This is an assumption not a reality.

Section 6.3

I would delete this entire piece and focus only on looking at developing a Co Exposure Grouping Strategy for air toxics.

Section 6.3.2

Effects is not a way to group chemicals for exposure. One identifies all the potential chemicals that are available to group then a relevant effect to determine which chemicals in the potential group should be aggregated for cumulative risk. Effects are a way to group chemicals as part of the weight of evidence evaluation to further compare across data sets. For examples see

https://doi.org/10.1071/EN23105; https://doi.org/10.3389/ftox.2024.1394361; https://www.oecd.org/en/publications/case-study-on-the-use-of-integrated-approaches-for-testing-and-assessment-iata-for-chronic-toxicity-and-carcinogenicity-of-agrichemicals-with-exemplar-case-studies-ninth-review-cycle-2023_c3b9ac37-en.html

Section 7.1

As expressed above, delete the effects piece and focus on determining the potential exposure and the populations as potential risk exposed to those chemicals.

Section 8

“developing prospective methodologies to better identify PESS and characterize the potential exposure” “characterizing potentially overburdened communities”

Stop here, heavy enough lift for this first effort.

“screening level information” “number of facilities” “potential chemicals”

Beyond these two pieces of information it is all conjecture.

“development of a more formalized tiered framework”

This should be the focus of this work.

Appendix A. Charge Questions for the Draft Proposed Approach for Consideration of Chemical Co-exposure in TSCA Risk Evaluations

1. AirToxScreen is an EPA modeling tool that estimates ambient airborne chemical exposure and risk across the United States to the census tract level. Given the model's strengths, limitations, and assumptions, please comment on the appropriateness of using AirToxScreen for screening level chemical co-exposure in the context of TSCA chemical evaluation.

2. This draft document proposes multiple potential metrics to inform chemical co-exposure. These proposed metrics include:
   --Number of chemical releasing facilities;
   --Number of chemicals released from facilities;
   --Number of chemicals meeting chemical risk benchmarks;
   --Chemical risk combinations; and
   --Bivariate distribution of individual chemical risk with potential chemical co-exposure

   Please comment on the utility, strengths, and uncertainties of these metrics. Please include in your comments discussion of the methods used to develop these metrics.

3. The two stated goals for this paper are: 1) support identification of potential PESS; and 2) consider chemical co-exposure as part of an individual chemical risk evaluation. Please comment on the extent to which the analyses and methodologies proposed within this document support these goals.