Appendix A

Summary of July 2000 Peer Review of the Draft Document "Planning and Scoping the Initial National-Scale Assessment: An Element of the EPA National Air Toxics Program"

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In July 2000, six non-U.S. EPA scientists completed a peer review of the draft planning and scoping document. The peer reviewers were:

Stephen Colome, University of California at Los Angeles, Southern California Particle Center and Supersite
Michael Dourson, Toxicology Excellence for Risk Assessment
Petros Koutrakis, Harvard University School of Public Health
Will Ollison, American Petroleum Institute
Richard Richter, Exponent
Lauren Zeise, California EPA

The reviewers were asked to focus their review on sections 3 and 4, which form the main body of the planning and scoping document and contain summary descriptions of the technical work that will be performed, and on appendices 4 and 5. Reviewers were asked to consider the appropriateness of approaches used to (1) process the State-derived National Toxics Inventory for dispersion modeling, (2) estimate ambient concentrations using the Assessment System for Population Exposure Nationwide (ASPEN) model, (3) estimate human inhalation exposures using the Hazardous Air Pollutant Exposure Model version 4 (HAPEM4), and (4) estimate, aggregate, and interpret associated cancer and non-cancer risks. A more detailed draft charge follows below.

Charge questions for independent external peer reviewers of the planning and scoping document, with reviewer comments and EPA responses

The NATA 1996 initial NSA is an application of a modeling approach that has been developed over the last several years. The EPA Office of Air and Radiation is applying this approach as part of its technical support for the Agency=s development of its program for hazardous air pollutants. While a number of the components of this assessment have been subjected to previous scientific peer review, their combined use in the full NSA approach has not. The Agency is seeking a peer review of this assessment approach for the following two main reasons: 1) to determine areas of deficiency in the initial NSA and recommend new analyses to improve them, and 2) to develop the necessary technical data on key limitations and uncertainties with the initial NSA and to formulate the best approaches to convey this information to its users.

Overall NSA Modeling Approach

1. *Is the overall design of the 1996 initial NSA scientifically sound for all pollutants in the assessment? Are the overall goals of the assessment clearly articulated? Does each component of the assessment provide the appropriate information to the subsequent components of the assessment?*

Comments:
Generally, reviewers considered the overall design of the initial NSA to be scientifically sound as

a screening exercise with proper caveats, and they found the overall goals to be well-articulated. Reviewers recognized that the assessment follows the "source, transport, ambient concentration, exposure, dose and health effect paradigm" and that it is consistent with the National Academy of Science paradigm and the EPA guidelines for risk assessment. Though reviewers noted that the appropriate components are included and build logically, several reviewers had concerns with specific aspects of the assessment. These concerns are presented in the relevant topic areas in the following pages.

EPA Response:
EPA agrees with the reviewers' comments and will try to address concerns in appropriate parts of the assessment, as well as in the NATA NSA Report.

2. *Is the approach of the initial NSA appropriate for the following purposes within the EPA national air toxics program: a) Informing efforts to determine priorities for regulatory programs and national, regional, and community-based initiatives? b) Assessing progress toward national risk-based goals? c) Informing efforts to allocate resources to further investigate (via monitoring, for example) problems on a broad or local scale? d) Supporting prospective assessments of estimated benefits of air toxics programs?*

Comments:
Reviewers generally agreed that the approach of the initial NSA is appropriate for the purposes stated (as listed above). Reviewers commented that, as a screening tool, the NSA may be very useful in priority setting and providing comparisons with different regions, as long as the NSA caveats are linked with the analysis. One reviewer commented that, because of the limitations in the design and analysis of the initial NSA, certain low priority concerns identified by the NSA would turn out to be high priority once given closer scrutiny. Reviewers think that the NSA has the potential for assessing progress toward national risk-based goals, but at least one reviewer believed that it may take several years of improving data and modifying the overall model before the model can be used for that objective. Reviewers generally considered the identification of areas for further investigation to be a good use of the initial NSA. Reviewers considered the approach of the initial NSA to be useful for supporting prospective assessments of estimated benefits of air toxics programs, but the initial NSA itself was not considered to be suitable.

One of the reviewers provided additional comments on the approach being taken for the initial NSA. The reviewer noted that EPA makes it clear that this is a screening process with coarse resolution. While the other components of the assessment are designed in keeping with this coarse level of estimation, the reviewer commented that the estimation of inhalation exposures using HAPEM4 is a very detailed procedure with a much finer level of resolution. The reviewer commented that it appears inappropriate to incorporate this level of detail into the assessment process given the goals of the NSA and the coarseness of the other parts of the assessment. The reviewer recommended that, since there are significant uncertainties in the input and modeling, the census tract results should be averaged within counties. The reviewer commented that this approach will cause several problems in interpreting the risk estimates. For example, for urban areas, it will likely decrease the risks in highly impacted areas, preventing identification of local areas with higher risks.

EPA Response:
The EPA agrees with the reviewers comments about the appropriateness of the approach being

taken in the initial NSA, and shares their common concerns about including appropriate caveats and limiting the assessment to its stated goals (which specifically exclude supporting regulatory actions).

Regarding the suggestion that some low-priority concerns identified by the NSA would turn out to be high-priority upon closer scrutiny, it is important to remember that EPA will use the NSA in combination with other elements of the air toxics program, especially the new national monitoring network. This should make it easier to identify previously unknown risks and to subject them to more rigorous analysis. While any national-scale analysis carries some risk of producing false negatives, the NSA represents a substantial improvement in EPA=s ability to find and focus on important air toxics risks.

EPA agrees that several iterations of the NSA may be needed before it will be fully able to fulfill its goals, and, for this reason, we have included a recursive improvement of data and methods as one of the goals of the NSA. In proposing to use the NSA to estimate future progress in reducing risks from air toxics, EPA understands that it may be necessary to recalculate some of the 1996 ambient concentrations and risks to reflect improved emission data, modeling methods, and dose-response information developed after the initial NSA has been completed. Because these improved tools and data will have been developed in part in response to the initial NSA, EPA considers this to be not only acceptable but desirable.

EPA also acknowledges that HAPEM4 may be more powerful and finely-resolved a tool than necessary to estimate exposures from ASPEN ambient estimates. EPA chose to use HAPEM4 for the assessment because: (1) running an exposure model is the best available response to criticisms regarding the use of ambient data as exposures; (2) use of HAPEM4 makes it possible to identify specific subpopulations (e.g., by age, gender, or race) that may have exceptional exposures; (3) use of HAPEM4 introduces elements of real variability into the assessment results in accordance with EPA=s risk characterization guidelines; and, (4) the effort is relatively small compared to the effort involved in compiling the NTI and modeling dispersion of HAPs. In addition, EPA cannot know the actual "value added" by this approach until we try it. When the initial NSA is complete, EPA intends to compare its results with simpler risk surrogates (i.e., toxicity-weighted emissions and ratios of ambient data to risk-based concentrations) to determine if a simpler analysis would produce essentially the same result.

EPA agrees that presenting the results on less than a county level would imply an inappropriate level precision. Accordingly, maps will show results averaged at the county level and graphs will provide distributions of results at the state or national levels. However, the distributions depicted by graphs will continue to be those of tract-level calculations, thereby avoiding the problem of averaging out local areas of high risk.

3. *Are the characterizations of model evaluation results and assessment uncertainties appropriate for the stated purposes of the model application? If not, what methodology and analysis would you propose to characterize uncertainties associated with the model predictions?*

Comments:
Three reviewers commented that the characterizations of model evaluation results and the qualitative descriptions of assessment uncertainties are appropriate for the stated purposes of a

screening assessment. One reviewer commented that the approach may be overly complex for screening purposes, and so, in presenting results, the EPA will need to guard against readers= over-interpretation of results. Caveats are critical. A qualitative analysis should be performed that would provide the public with a better understanding of the range of possible results and the EPA's best estimate of the likely risks. One reviewer would like to see EPA try to assess relative uncertainties among the 33 priority pollutants. Another commented that there is no sense of quantitative uncertainty in the report. One reviewer prefers a more direct exposure assessment approach that involves preliminary ambient monitoring and microenvironmental measurements, so that an effective monitoring program could be designed. Another reviewer stated that, where possible, EPA should provide a quantitative indication of the degree of impact for the different factors discussed, and an indication of whether the factors create a bias of under- or over-characterization.

EPA Response:
To the extent possible, EPA will prepare a more complete discussion of the uncertainties in individual components of the assessment. In addition, EPA will tabulate and discuss the uncertainties in the overall assessment as part of the risk characterization. EPA agrees that the planning and scoping document lacks a sense of quantitative uncertainties. EPA will provide quantitative analyses of uncertainty in the NATA NSA report, where possible, and qualitative assessments will be given where quantitative estimates cannot be developed. We anticipate that this more complete discussion of the overall uncertainties in the assessment will help readers understand the limitations of the information, avoid over-interpretation of the results, and identify research areas with the greatest potential for reducing uncertainties in future assessments.

EPA agrees with the comments regarding the desirability of analyzing relative uncertainties among the priority pollutants and of using personal monitoring data to develop microenvironmental factors. We intend to investigate these possibilities, but anticipate that incorporating these approaches will not be possible because of limitations in available data.

4. *Is there a subset of HAPs that should be treated differently than the others due to the potential for significant non-inhalation exposures? If so, how should they be addressed in this national screening assessment?*

Comments:
Reviewers were mixed on this issue. At least two reviewers expressed skepticism about, or otherwise did not support, the assessment of indirect exposures in the national screening assessment. Concerns with data availability and appropriate modeling tools were some of the reasons. Others thought that the model should not be further complicated by considering non-inhalation exposures but that HAPs with the potential for non-inhalation exposures should be separately listed and considered in future assessments, when data become available. Two others supported more generally considering these other HAPs, with one reviewer proposing that EPA perform further studies and design models specific to each HAP of interest.

EPA Response:
Overall, reviewers agreed with EPA=s determination that it is not practicable to quantitatively assess non-inhalation exposures and risks in the initial NSA. However, EPA remains concerned about the potential of some HAPs to pose important health risks through

bioaccumulation and oral exposure, and intends to discuss this issue qualitatively in the document. It is also important to remember that EPA considered multi-pathway exposure in its original selection of the 33 "high priority" HAPs, and substances such as mercury, PCBs, and dioxins and furans were included in this assessment largely on the basis of those concerns. Furthermore, EPA expects to use the NSA results as further demonstration of the need for research that will support quantitation of non-inhalation risks in future NSAs.

Emissions Inventory

The 1996 NTI has already benefited from extensive involvement of experts in inventory development during its compilation, review, and revision. Therefore, EPA is not requesting a review of the NTI itself, but rather a review of its use as part of the NATA NSA.

5. *Given the nature of the National Toxics Inventory, and the methods by which it was developed and reviewed, does its use for the initial NSA represent sound science?*

Comments:
Reviewers generally agreed that the NTI is the "weakest link" in the NSA, due to its impact on the risk assessment results, but they acknowledge that it is probably the best set of data available for this type of undertaking. One reviewer noted the importance of including appropriate caveats in all presentations of the data. Sources of uncertainty (e.g., varying levels of detail for individual states, regions, and pollutants) need to be conveyed in the graphical and tabular presentations.

EPA Response:
EPA will provide graphics and statistics regarding the sources of the data (e.g., percent from agencies or program offices) and describing how submitted data needed to be supplemented (e.g., percent of point source emissions with defaulted values for locations or other parameters, etc.).

6. *Have uncertainties in the NTI been characterized adequately in the conceptual plan?*

Comments:
There seemed to be a consensus that uncertainties could be better characterized in the report. Reviewers recognized that uncertainties were discussed qualitatively but that no quantitative evaluation was provided. One reviewer suggested developing and using a statistical sampling program to determine how well the NTI data represent actual emissions.

EPA Response:
The problem with a statistical sampling to assess how well the NTI matches "actual" emissions is that it presupposes that there are "actual" data available for comparison. The NTI is compiled of the best emissions data available, as provided by State and local agencies, EPA program offices and, in some cases, EPA estimation methods. In some cases, this may be "actual annual emissions" from measured data, but it is usually compiled by an estimation method via emission factors and or mass balance or similar methods. At this time, EPA does not have a set of "real" emission data for a geographic area for comparison with emission estimates. Therefore, it is not clear what statistical comparison is advised. EPA will provide more detailed information regarding the sources of the data (e.g., percent from agencies or

program offices) and describing how submitted data needed to be supplemented (e.g., percent of point source emissions with defaulted values for locations or other parameters, etc.).

ASPEN Dispersion Modeling

1. *The EPA Science Advisory Board previously reviewed the ASPEN dispersion model in its application for the Cumulative Exposure Project (CEP). Is ASPEN's application for the initial NSA consistent with the recommended uses of this model? Given the national goals of the initial NSA, is this model appropriate to use for the pollutants included in the assessment?*

   Comments:
   Reviewers generally agreed that use of ASPEN as a screening model for the initial national-scale air toxics screening assessment is consistent with the recommended use of the model. One reviewer recommended that an appendix be added describing the model, input data, assumptions, and output. One reviewer commented that the ASPEN model might be too complex for a screening level analysis, and that the framework should be kept simple and interpretable.

   EPA Response:
   EPA is preparing a user's guide for the ASPEN model and for the emissions processing software. This documentation will be available to the SAB during their review.

2. *What significant scientific improvements should be incorporated in this model for future national-scale assessments? In particular, are there specific recommendations regarding issues such as the treatment of background and the level of geographic aggregation (census tract, county, state)?*

   Comments:
   One reviewer recommended that the ASPEN results be reported at the county and state level, rather than at the census tract level. Another reviewer commented that modeling air concentrations at the centers of census tracts seemed to be appropriate. Two reviewers commented that background values added to the ASPEN model output should not be neglected and should be used to assess exposure and risk.

   EPA Response:
   EPA is investigating the limitations imposed on the interpretation of the ASPEN results as a consequence of the uncertainties associated with the emissions data and modeling assumptions. It would appear that interpreting the results as being spatially accurate to the centers of census tracts is inappropriate, as the reviewer suggests. Background values added to ASPEN model output are used in exposure and risk calculations (please see HAPEM4 Exposure section).

3. *Can the uncertainties associated with the use of this model be characterized? If so, can a quantitative assessment of this uncertainty be implemented?*

   Comments:
   One reviewer commented that a quantitative assessment of model uncertainties should be

performed. Two approaches were proposed: (1) select several urban and rural areas with different types of terrain and meteorological conditions, perform a detailed modeling assessment, and compare the results to those from ASPEN, or (2) model the output at multiple receptors in some of the census tracts to determine the spatial variability of the estimated ambient concentrations within the tracts. One reviewer suggested that the uncertainty in the ASPEN simulations can be estimated through comparisons with observations. This reviewer recognized that exposure observations would have to be estimated by some other means. Another reviewer commented that too many things are going on at once in the model, and that a quantitative uncertainty analysis would not be believable.

EPA Response:
EPA agrees that useful information can be obtained by comparing ASPEN model results with more detailed analyses for selected areas, and we are currently performing such an analysis for one major urban area, with a view to compare these concentrations with those from ASPEN. Additional urban and rural areas could be included if resources permit. EPA has attempted to investigate the uncertainty associated with the ASPEN simulation results through a comparison with observations. All HAPs compare more favorably when the maximum estimated modeled concentration is examined within 30km of the monitoring site.

HAPEM4 Exposure Modeling

EPA's Office of Transportation and Air Quality (OTAQ) (formerly the Office of Mobile Sources) in conjunction with the Office of Research and Development=s (ORD) developed the Hazardous Air Pollutant Exposure Model (HAPEM). The initial versions of HAPEM were based largely on models developed and employed to predict carbon monoxide exposure for National Ambient Air Quality Standard (NAAQS) reviews and mobile source emission control assessments. Recently, the Office of Air Quality Planning and Standards (OAQPS) modified HAPEM for use as a modeling tool to predict inhalation exposure concentrations to HAPs. The most recent version, HAPEM4, has been modified to predict nationwide census-tract-level annual average human exposure levels.

1. *Is HAPEM4's application for the initial NSA consistent with the recommended uses of this model? Given the national goals of the initial NSA, is this model appropriate to use?*

Comments:
One reviewer did not think the use of HAPEM4 is appropriate and suggested that the use of HAPEM4 adds a level of complexity that is not necessary to the goals of the NSA. The reviewer believes that estimation on the census tract level will not generate meaningful contrasts that would be useful for planning and screening. Another reviewer commented that the model itself is conceptually sound, but he has reservations about the model relying on soft data rather than real measurements. Reviewers expressed concern that, due to uncertainties in inputs (e.g., emission inventories), the exposure estimates would have very large uncertainties. Reviewers had concerns that the use of HAPEM4 for estimating exposures provides too fine a resolution relative to the low resolution of other parts of the assessment. One reviewer commented that modeling at this level of detail is best applied locally, not nationally. Another reviewer commented that variability in risk across the population will not be sufficiently well characterized by the HAPEM4 approach with average ambient concentration as the input. One reviewer was concerned that the default assumptions used in modeling inputs would drive the results. At least

two reviewers suggested that alternative approaches to using HAPEM4 be considered, such as using ambient concentrations as the starting point for calculating risk. One of these reviewers thought it would be more scientifically defensible to use crude exposure estimates (based on emissions and monitoring data) and refrain from estimating risk. One reviewer believes that use of HAPEM4 is consistent with and appropriate to the goal of the initial NSA, and considers use of HAPEM4 preferrable to use of ambient air concentrations for estimating population risk.

EPA Response:
The EPA would prefer to use ambient data plus information on inhalation rates, body weights, etc., as an alternative approach to using HAPEM, but ambient data for HAPs are not available on the scale needed for this assessment. EPA acknowledges that HAPEM4 may be a more powerful and finely-resolved tool than necessary to estimate exposures from ASPEN ambient estimates. EPA chose to use HAPEM4 for the assessment because: (1) running an exposure model is the best available response to criticisms regarding the use of ambient data as exposures; (2) use of HAPEM4 makes it possible to identify specific subpopulations (e.g., by age, gender, or race) that may have exceptional exposures; (3) use of HAPEM4 introduces elements of real variability into the assessment results in accordance with EPA=s risk characterization guidelines; and, (4) the effort is relatively small compared to the effort involved in compiling the NTI and modeling dispersion of HAPs. In addition, EPA cannot know the actual "value added" by this approach until we try it. When the initial NSA is complete, EPA intends to compare its results with simpler risk surrogates (i.e., toxicity-weighted emissions and ratios of ambient data to risk-based concentrations) to determine if a simpler analysis would produce essentially the same result. Until these comparisons are made, EPA believes that it it important to clearly define the model's limitations when presenting the NATA outputs.

2. *Can the uncertainties associated with the use of this model be characterized? If so, can a quantitative assessment of this uncertainty be implemented?*

Comments:
One reviewer believes that it would be nearly impossible to quantitatively characterize uncertainty in the model for HAPs. Another reviewer commented that uncertainties could be determined in the future, but would require comprehensive field studies. Real human exposure measurements would be needed for a variety of geographic locations, seasons, and microenvironments, in order to evaluate models and quantitatively characterize their uncertainties. A third reviewer thought that the simplest method for quantitatively assessing uncertainty would be to compare modeled exposures to those reported from microenvironmental or personal exposure measurements. A fourth reviewer identified two major areas of uncertainty associated with the use of HAPEM: microenvironmental factors (MFs) and activity patterns. This reviewer thought that the impacts of the microenvironmental factors on the final results are negligible compared to the other uncertainties in the process, so characterization of the uncertainties in the MFs would do little to enhance the representativeness of the assessment. Since the activity pattern data include commuting (movement out of a census tract), characterization of uncertainty of the activity data may be important.

One reviewer recommended that the report include a list of sensitivity tests and assumptions made throughout the exposure assessments, as well as describing any assumptions for individual pollutants, in cases where data may have been more limited.

EPA Response:
For the initial NSA, EPA will develop qualitative assessments of the uncertainities associated with the HAPEM4 modeling. For future NATA assessments, where feasible, EPA plans to quantitatively assess the uncertainties associated with the use of HAPEM4.

EPA will include a list of sensitivity tests and assumptions made throughout the exposure assessments, and describe any assumptions made for specific pollutants, in the NATA NSA Report.

3. *EPA is aware that nonambient, (e.g., indoor) sources make substantial contributions to exposure for some air toxics. How can we best incorporate this information into our communications with the public?*

Comments:
In their comments, reviewers recognized the importance of indoor and occupational exposures in individual exposures. Yet, there was general agreement that EPA should not include indoor or occupational exposures in the assessment, in part because it is too complicated and confusing, and also because it would not likely assist in meeting the goals of the NSA. It was recognized that indoor data are very limited for some of the HAPs and that little is known about the sources and national distribution of indoor levels for many of the HAPs. One reviewer considers the document to adequately address why indoor air sources are not included in this study. Another reviewer recommended communicating these exposures in qualitative terms (e.g., as primarily indoor or primarily outdoor), where sufficient data exist to make it possible to do this. Another reviewer commented that, since indoor sources often make important contributions to total human exposures, ignoring these sources may result in underestimation of risks and that this potential underestimation of risk should be explained. A need for actual human exposure measurements, which would allow determination of distributions of indoor concentrations and relative contributions of outdoor and indoor sources, was identified.

EPA Response:
EPA recognizes the need for additional data on actual human exposures to HAPs. For the initial NSA, we will communicate exposures and risks as only attributable to outdoor exposures to HAPs. Where possible, background concentrations of HAPs are included in the exposure assessment. We will clearly explain the treatment of background concentrations and indoor concentrations in the NATA NSA Report.

4. *What significant scientific improvements should be incorporated in this model for future national-scale assessments?*

Comments:
One reviewer recommended that, for application with HAPs, the model could be simplified and made computationally less intensive. Another reviewer commented that the use of HAPEM is unnecessary for meeting goals of the NSA, so it would not be useful to make additional improvements to HAPEM for use for the NSA. One reviewer commented that, conceptually, the model is fine, but the problem is with the input data. Another reviewer thought that added information would constitute an improvement and recommended that the EPA continue the improvement process. Another reviewer also saw a need to include child commuting and school exposures in HAPEM4, in part because of the importance of outdoor cohorts. This

reviewer also recommended that the model take behavior changes with age into account.

EPA Response:
EPA is working to improve many of the components of the HAPEM4 model. While we are working with other agency and non-agency groups to improve the key input data to the model, we are also attempting to improve the underlying principles behind the model. Improved exposure models (e.g., APEX, TRIM.Expo) are currently being designed and developed, and they are being designed to allow for easy updating as improvements are made in the scientific information needed for exposure modeling.

Health Assessment and Risk Characterization

1. *Is the conceptual risk characterization approach appropriate given the underlying science, EPA policy and guidance, and analytical needs? What are the strengths and the weaknesses of the approach?*

Comments:
Several reviewers consider the conceptual approach to be appropriate for use as planned, as a screening tool, and they consider it to be consistent with EPA guidance. One of these reviewers remarked that the first analysis of hazard identification is adequate and that the dose-response analysis may go beyond meaningful use of the data. Another reviewer suggests that the whole assessment process is more complex than is necessary to meet the major goal of the study, to assess the spatial variability of risks across the nation. Yet another reviewer considers the conceptual risk characterization approach to be problematic, mainly due to the likely large uncertainties in the exposure estimates that, coupled with the uncertainty in the unit risk estimates and reference concentrations, would result in a possible significant mischaracterization of risk.

One reviewer commented that "the strength of the scheme is also its weakness." It relies on consistent, standardized procedures for risk characterization which have undergone scrutiny in peer review and public comment processes. The initial assessment begins with chemicals having considerable evidence of carcinogenicity. Identifying other chemicals of concern may be problematic under the current approach. As an example, the reviewer noted that the bulk of genotoxic transformation by-products of mobile sources are likely to be overlooked. Also, the reviewer suggested that the bulk of chemicals impacting some important health effects, such as asthma, emphysema and cardiovascular morbidity, will not be addressed by this limited assessment.

One reviewer considered the major weakness to rest with the underlying toxicological data on many of the HAPs. Two reviewers were concerned that the likely large uncertainties in the exposure estimates, coupled with the uncertainty in the unit risk estmates and reference concentrations, would result in a possible significant mischaracterization of risk. One reviewer suggested that it may be preferrable to characterize risks of some representative urban areas in much greater detail.

EPA Response:
EPA disagrees with the suggestion that our proposed use of the dose-response analysis may go

beyond meaningful use of the data. We regard the use of unit risk estimates and reference concentrations as an important element of the NSA, allowing us to discriminate between HAPs on the basis of their relative toxicity. On the other hand, EPA intends to fully respect the uncertainty that surrounds these dose-response values, and avoid mixing risk estimates that have divergent levels of uncertainty.

EPA agrees that the assessment may be more complex than necessary to meet its goals. However, as already discussed above, the effort of running HAPEM4 is relatively small compared to compiling the NTI and modeling its dispersion. In addition, the use of HAPEM4 avoids the pitfall of using ambient data as exposures, makes it possible to identify subpopulations that may have exceptional exposures, and introduces real variability into the assessment results, in accordance with EPA=s risk characterization guidelines. Also, EPA cannot know the actual "value added" by this approach until we try it. When the initial NSA is complete, EPA intends to compare its results with simpler risk surrogates (i.e., toxicity-weighted emissions and ratios of ambient data to risk-based concentrations) to determine if a simpler analysis would produce essentially the same result.

EPA agrees that the risk characterization will include large uncertainties in both the exposure and dose-response elements, which could create significant mischaracterizations of risk when combined. However, all risk assessments that rely on modeled exposures in combination with modeled dose-response assessments are subject to the same combination of uncertainties, and EPA does not believe that this assessment creates exceptional difficulties in this area. We intend to use EPA=s risk characterization guidelines as the basis for describing and discussing these uncertainties individually and in combination, with appropriate cautions against over-interpretation of the results.

EPA agrees that the reliance on consistent, standardized, and well-reviewed procedures for risk characterization creates some limitations in the assessment. We have limited the number of HAPs to those we currently believe are the major contributors to health risk, but were not able to include either mixture effects, transformations products, or chemicals lacking peer-reviewed dose-response assessments in the initial NSA. EPA hopes that future NSAs will be more complete in this regard as data improve.

EPA agrees about the desirability of characterizing risks within representative urban areas in much greater detail. Although this type of assessment is beyond the scope of the initial NSA, urban-scale assessments are a separate, essential element of the EPA Urban Air Toxics Strategy.

2. *Does section 3, which describes the conceptual model for the assessment, adequately explain the elements that will (and will not) be quantified by the assessment, within the context of the assessment=s stated purpose?*

Comments:
Three reviewers commented that the conceptual model is adequately described in the context of the assessment's stated purpose and as an introduction. One of these reviewers commented that it was not clearly explained, though, why the approach took particular directions. Where justification is given, the reviewer recommends that more technical details and supporting

references be provided. The section where risks to subpopulations is described was identified as needing greater explanation.

EPA Response:
For the NATA NSA Report, EPA will provide more technical detail in support of the selection of the directions taken in the conceptual model.

3. *Have population cohorts (section 3.3.5) been selected appropriately? Considering availability of tract-specific census data, are there other cohorts that might be useful to assess separately?*

Comments:
Generally, reviewers thought that the population cohorts had been selected properly. Nonetheless, many provided recommendations for other possible cohorts.

One reviewer suggested that the population cohorts selected be compared with those used by EPA=s Office of Pesticide Programs. Another reviewer recommended considering addition and assessment of cohorts that spend substantial amounts of time outdoors (e.g., outdoor children, summer camp children, outdoor workers). One reviewer commented that socioeconomic status would be another important way to divide and study the population. The same reviewer noted the importance of taking into account life stages in assessing exposure and in developing risk estimates. The reviewer recommends that the NSA work toward a goal of characterizing risks resulting form early in life exposures. One of the reviewers recommends that no further level of detail on cohorts be added, as that would go beyond available data.

EPA Response:
EPA designed the population cohorts not to overlap, and to cover the complete population. This was done so that the sum of all individual cohorts within a tract would be equal to the total population in the tract. The reasoning behind this decision was to create a total population exposure estimate that accurately reflected the true population within each tract. In this way, concerns about exposures to children and differences in exposure associated with race would be built into the results. In selecting population cohorts, we used the CHAD behavioral database to ensure that each group had enough individuals to be valid. We believe it would be possible to expand beyond our choice of 40 cohorts (4 races by 5 ages by 2 genders) until a larger behavioral database becomes available. EPA agrees with the recommendation regarding socioeconomic status, but decided to use race instead as a more tightly-linked indicator of environmental justice.

EPA agrees about the importance of taking into account life stages in assessing exposure and in developing risk estimates, and we have done exactly that. Cancer risk estimates will be based on the time-weighted some of exposures to each life stage; hazard quotients for risks other than cancer will be calculated separately for children and adults.

4. *Is the plan's use of dose-response information (section 4.3) consistent with EPA policy and guidance, and with sound science? Should different sources of information, or a different prioritization scheme, be considered?*

Comments:

The reviewers agreed that the use of dose response information is consistent with EPA policy and guidance and with sound science.

One reviewer considered the prioritization scheme to be reasonable; however, he noted that much information in EPA's IRIS is out of date and strongly suggests that EPA upgrade the IRIS information. Another reviewer thought a different prioritization scheme should be considered due to the differences in uncertainty of available does-response information across the 33 HAPs. This reviewer suggested that relative exposure estimates could be used for the NSA instead of risk estimates. A third reviewer thought that, where IRIS values are outdated, EPA NCEA should be consulted and provisions should be made to rely on alternative estimates, in some cases those used by the California EPA.

One reviewer suggested several specific changes to dose-response information, and those comments follow. The data are sufficient to estimate cancer potency for methyl mercury, which was observed to cause kidney cancer in repeated studies in rodents. It is an IARC Group 2B carcinogen, and should be noted as such in Table 3 of the report. The estimate for vinyl chloride should consider the recent analysis and comments on it in the last revision of the EPA Carcinogen Guidelines. The estimate for 1,3-butadiene, released as a draft, was based on human occupational data and does not take into account several issues and is viewed by some as an underestimate, as outlined in a report from the Science Advisory Board and other comments received by the Agency. It was unclear from the write-up whether the value reviewed in draft would be used or a more recent value. Hexavalent chromium is a potent carcinogen when inhaled and significantly less potent when ingested. The logic of using the RfC for particulates for characterizing its risk is unclear. Potency estimates for hexavalent chromium derived from occupational epidemiologic studies are available. The approach taken to estimate dioxins and dibenzo furans is misguided. It would be preferable to develop values for characteristic mixtures, than to make the extreme assumptions that when identities of the congeners are unknown they either have potency identical to TCDD or are equivalent to the least potency congener. Use of the California upper confidence limit for lead is a reasonable approach to take, with the caveat being that human data suggest the estimate should be higher. EPA should consider using its most recently released assessment for TCDD, or collaborating with NCEA if an Agency value is to be used. If this is not possible, there is a California value that can be used which has gone through an extensive process albeit some time ago. If risks are to be estimated risks, they should be estimated for the nitro-PAHs as well. The compounds listed in Table 3 are identified by IARC as 2B carcinogens, are genotoxic, and are reasonably presumed to be carcinogenic. The table does not contain all the IARC classifications and one is incorrect. Nickel compounds are incorrectly identified as IARC 2B, when they are IARC Group 1 (nickel, metallic and alloys are Group 2B). TCDD is a also an IARC Group 1 and should be identified as such. The IARC Group 2A chemical to be identified in the table is hexachlorodibenzo-p-dioxin mixture (since polychlorinated dioxins are 2A). IARC 2B chemicals to be identified are mercury (methyl) (since methylmercury compounds are 2B), the two dibenzacridines, 7H-dibenzo[c,g]carbazole, the 3 dibenzopyrenes, the 2 dinitropyrenes, 5-methylchrysene, 5-nitroacenaphthene, 6-nitrochrysene, 2-nitrofluorene, the 2 nitropyrenes. Since mercury and inorganic mercury compounds are an IARC group 3, mercuric chloride should be listed as such; also, chrysene and 1,2-dichloropropane are IARC Group 3 chemicals.

With respect to the non-cancer endpoints, exclusion of mercury emissions and associated

exposure to methymercury is problematic. It is of interest that methylmercury is included in Table 3 but not in Table 4, given the public health concern for developmental effects potentially associated with high fish consumption.

EPA Response:
EPA agrees that the IRIS database contains some information that may be out of date, and is working to upgrade the IRIS information. Given the 3-year time-frames for IRIS updates that are now typical of new assessments, this effort has only recently begun to show results. Many new IRIS assessments are expected in the next few years, and these will be incorporated into future NSAs. EPA disagrees with the suggestion that relative exposure estimates could be used for the NSA instead of risk estimates. The use of unit risk estimates and reference concentrations is a critical element in our ability to distinguish the most important HAPs, and to aggregate risks of multiple HAPs.

EPA agrees that some IRIS values are sufficiently outdated that they should not be used. We have substituted draft assessment values for vinyl chloride and 1,3-butadiene for the current IRIS information for those substances. The value for 1,3-butadiene is from an unpublished update of the draft assessment (described by the commenter) that addresses the concerns with the draft. Mercury emissions have been returned to the assessment, but we are evaluating them as inorganic, rather than methyl, mercury. We will conservatively assume that 34% of chromium emissions (which the NTI does not speciate) are the hexavalent form. The choice of the RfC for particulate hexavalent chromium over the RfC for chromic acid mist is based on our assumption that the vast preponderance of chromium exposure will be to the particulate form. EPA will encourage the Science Advisory Board to address this issue in reviewing the draft NSA.

EPA agrees with the comment on the limitations of the approach to dioxins and furans, but is constrained by the nature of the NTI emission data. We are actively encouraging State and local authorities to use our emission factors for individual CDD/F sources, which do contain values for characteristic mixtures, for the 1999 NTI. Within EPA, the OAQPS has collaborated with NCEA in choosing dose-response values for the NSA, and OAQPS has followed their suggestion to use the current assessment for TCDD. Given the relatively low level of expected inhalation risks for CDD/Fs (ingestion risks being the major concern for these compounds), EPA expects this decision to have little impact on the results. EPA would certainly include risk estimates for nitro-PAHs if possible, but we lack emission data to do so. We believe our overall approach to the POM category respects the potential importance of these compounds in contributing to total risk, however, and we are working with State and local authorities to improve POM speciation in the next inventory. Table 3 will be corrected as suggested.

5. *Considering current dose-response information for the initial NSA=s 33 HAPs and EPA policy and guidance, is the methodology for aggregating cancer risks appropriate? Of particular interest for this topic is the aggregation of carcinogenic risk by summing within categories based on weight-of-evidence classifications.*

Comments:
Three reviewers supported the methodology for aggregating cancer risks as appropriate, and

one of these noted that this approach is based on EPA methods for mixtures risk assessment. One reviewer especially likes the idea of using weight-of-evidence classification but cautioned that the weight-of-evidence classifications will likely change when the EPA puts forward its new cancer guidelines. Another reviewer noted that this approach would be wrong in certain cases but recognized that the data are not available to specify anything other than a linear additive model. It was also noted that aggregation is needed to present an overall screening analysis.

One of the reviewers noted that aggregating on the basis of weight of evidence, TCDD would be separated from other similar acting compounds and risks from it would be summed with quite dissimilar compounds like benzene and vinyl chloride. If one wanted to distinguish, for the chemicals on the list, it would be preferable to do so on the basis of mechanism of action (e.g., those interacting with the Ah receptor) or magnitude of uncertainty in the estimate rather than by weight of the evidence category. However, the reviewer stated, this would introduce more confusion and complication than it would be worth.

Another concern was the implicit assumption, for the analysis, that exposure to the young, as well as *in utero* exposure, produces the same risk as the same exposure late in life. This appears to be an incorrect assumption for some chemicals being assessed (e.g., for 7,12-dimethylbenzanthracene, vinyl chloride, and at least nitro-PAHs) based on studies in rodents. The reviewer commented that, if life-stage dependent potencies/unit risks could be assigned for some chemicals, then it would be best to first aggregate for a given age at exposure to provide an idea of differential risk due to age.

Another reviewer expressed concern with the EPA=s plan to show total risk at the county level, since this information could be misused or misunderstood. The reviewer thought that it was important to put appropriate caveats on any maps illustrating county level total risk. Another reviewer expressed concern about presenting county-level estimates of total risk and stated a preference that EPA leave information presented in groups rather than presenting summaries.

EPA Response:
EPA believes it is justifiable to sum risks of cancers caused by different modes of action under the additivity-of-effects recommendations in the recent draft guidelines for risk assessments of mixtures. As long as these modes of action are either additive or totally independent this process should not produce a biased result. Within groups of similar compounds (e.g., CDD/Fs or POM), EPA does intend to combine risks associated with similar modes of action. Because TCDD is a probable carcinogen rather than a known carcinogen, its risks will be not be combined with those of benzene and vinyl chloride. EPA agrees that combining cancer risks on the basis of mode of action would be a superior method, but this information is lacking for most HAPs. EPA does propose to combine noncancer hazard quotients according to the magnitude of uncertainty in the estimate, as suggested by the reviewer.

The comment concerning the implicit assumption that exposure to the young, as well as in utero exposure, produces the same risk as the same exposure late in life is partly correct. The unit risk estimates EPA uses to estimate lifetime cancer risks in all its programs are generally intended to be applied across a lifetime of exposure that includes exposure during childhood. Where unit risks are based on animal data, they implicitly incorporate exposure during the entire life cycle. Some recent IRIS assessments have included separate unit risks for adults and whole life exposure, and the NSA will use the higher whole-life values. Nevertheless, EPA has

recognized Agency-wide shortcomings in the way its risk assessment guidelines consider children, and is working to improve these methods. Future NSAs will incorporate these improvements as they appear. The exposure assessment portion of the NSA will, as already described, use a time-weighted whole life exposure estimate for cancer risk.

EPA shares the reviewers' concerns with presenting risk estimates at the county level. This will be done only on maps (i.e., not in graphs or tables), accompanied by appropriate caveats. Graphs and tables of risk will separate risk by source sectors and uncertainty in the health effects data, but not by geographic area.

6. *Considering current dose-response information for the initial NSA's 33 HAPs and EPA policy and guidance, is the methodology for aggregating non-cancer risks appropriate? Of particular interest for this topic are: (1) the summation of hazard quotients within target organs, (2) the categorization of sums by ranges of uncertainty factor, and (3) the inclusion of all target organs (as opposed to only the organs associated with the critical effect).*

Comments:
Two reviewers believe that the summing of HQs within target organs is appropriate, particularly given that it is a screening assessment. Another reviewer commented that exposure estimates across the population would not likely be provided in sufficient detail to enable confident application of the hazard quotient approach and, then, aggregation of noncancer risks. One reviewer stated that, given an exposure assessment that is sufficiently detailed for confident evaluation of non-cancer risks, an important consideration in aggregation will be the extent to which background processes are contributing to the effect of concern. Since, in some cases, background processes may be operating by similar mechanisms to the chemical in question, consideration should be given to the possibility for linear dose response contributions. If the assumption of linearity is unsupportable, then a means of aggregation across chemicals appearing to operate via the same mechanism is reasonable. If mechanism of action is unknown, summation of hazard quotients within target organs is a reasonable approach.

One reviewer commented that categorizing sums by ranges of uncertainty factors is somewhat awkward, and suggested that EPA consider the confidence statements from EPA's IRIS. Another reviewer was supportive of the categorization of sums by ranges of uncertainty factors because it could aid in the interpretation of results. Another reviewer cautioned about categorizing and aggregating on the basis of ranges of uncertainty factors, noting that sometimes uncertainty factors are metabolic adjustments for different-sized animals or adjustments for variability within the population. Other times, they are indicative of uncertainty in scaling, within species heterogeneity and study design. Thus, the reviewer commented that aggregation on the basis of uncertainty factor, without regard to mechanism of action or target site, is not a reasonable approach.

One reviewer commented that the inclusion of all target organs was at first confusing and that it does lead to conservative statements of risk. He noted that several publications and new EPA mixtures guidelines statements suggest developing target organ-specific RfDs. He recommended exploring or at least citing this possibility (since few target organ RfDs are currently available).

One reviewer stressed the importance of clearly communicating this information. The reviewer

recommended, as an example, providing a few simple equations in the report to show how risk is calculated. In addition, the reviewer recommended that the best approach to take, in presenting results, is to present the final results in a number of ways, such as most likely risk, upper-bound risk, and range of risks. This would improve understanding of the risk information.

EPA Response:
EPA does not see any reason why aggregating noncancer risk should be more problematic that aggregating cancer risk. EPA agrees about the potential importance of background concentrations to total noncancer risk. However, none of the background concentrations used in this assessment exceeds a tiny fraction of the reference dose, so this concern is moot for the initial NSA. EPA agrees that summation of hazard quotients within target organs is a reasonable approach where modes of action are unknown.

EPA agrees that categorizing sums by ranges of uncertainty factors is somewhat awkward, and that it might be better to consider confidence statements from IRIS. Unfortunately, the other sources of dose-response assessment (CalEPA and ATSDR) do not provide such statements. EPA agrees that different uncertainty factors connote different sources of uncertainty, but believes this 2-category separation is still better than combining all hazard quotients. In setting the breakpoint at 100, the practical effect of this decision will be to separate HAPs whose RfC is based on human data from those based on animal data, which we think is fair.

EPA agrees that it would be preferable to have organ-specific RfCs, and (while few now exist) it seems possible that such a recommendation may emerge from the initial NSA. EPA also agrees that applying the RfC for the critical effect to all effects is conservative, and we will ensure that the report clearly explains this. EPA believes that the current description of the risk calculations is very clear to risk assessment scientists (as one reviewer explicitly said) and we are not sure if adding equations to the report would make it clearer or more obtuse to the lay reader.

Uncertainty

1. *Does the conceptual plan appropriately characterize aggregate uncertainty in an adequate and transparent way? Does the conceptual plan adequately integrate the uncertainty, qualitative or quantitative, into the presentation of the analyses such that the eventual consumer of the NATA will understand the nature and magnitude of uncertainties associated with the concentration, exposure, and risk estimates? If not, how can we improve the treatment of uncertainty in the assessment?*

Comments:
The reviewers generally agreed that the conceptual plan does not appropriately characterize ~~aggregate~~ uncertainty in an adequate and transparent way. One reviewer commented that the conceptual plan does describe, in a transparent and straightforward fashion, the uncertainties associated with individual segments fo the assessment, while another reviewer notes that many of the uncertainties associated with the assessment are discussed qualitatively, but that there is no attempt at quantifying them. A third reviewer commented that the document deals with uncertainty only superficially. Another comment was that caveats need to be given with all

model results. Aggregate uncertainty should only be presented qualitatively, one reviewer commented, especially since this is a screening tool and not yet a quantitative tool for making certain contrasts between pollutants or even geographic regions.

One reviewer recognized that it is difficult to make the nature and magnitude of the risk transparent, and recommended contracting with an expert in risk communication and a journalist who specializes in scientific reporting, in order to present the analyses so that the eventual consumer of the NATA will understand the nature and magnitude of uncertainties associated with the results. Another reviewer commented that the conceptual plan should explain how the qualitative and quantitative factors will be integrated for the uncertainty analysis, in order to give the consumer an appreciation of the uncertainty in the various estimates presented in the NSA. A third reviewer noted the importance of providing a quantitative evaluation and discussion of the uncertainties associated with the input, modeling, and output, in order to put the risk estimates in proper perspective. Because the general public and the press will tend to focus on point estimates of risk, one reviewer recommended that EPA prevent a misrepresentation of the risk assessment information by presenting the estimated range of risks, as well as the best estimate, rather than simply presenting the upper-bound values. Two other reviewers recommended characterizing uncertainty of individual steps/components. One noted that it is necessary to provide a list of the different types of uncertainty anticipated within the source, transport, exposure, dose, and effect paradigm. He recommended that qualitative boundaries of these uncertainties be set, and that these boundaries then be investigated by conducting field studies. Including the results of these studies and currently existing information will make it possible, the reviewer thought, to focus on components of the program which may contribute most of the uncertainty.

One reviewer suggested that EPA present information on risk uncertainty in terms of a data needs endpoint [rather than a "dead bodies" [replace "dead bodies" with the term morbidity?] endpoint]. He added that, perhaps, the assessment should stop with exposure estimates. Another reviewer commented that EPA should be able to state results in terms of a level of confidence about risk within a range (e.g., "we are 95% sure that risk is in the range of x to y"). A third reviewer stressed the importance of identifying where uncertainty is and how much there is. Another recommendation was to select one area/city to focus on for the assessment. A somewhat similar recommendation was to base the NSA on indicator regions, with the goals of characterizing, as well as possible, exposures in representative geographical regions, performing validation personal monitoring studies, and then using the results and insights to develop a more comprehensive assessment.

One reviewer commented that, in some cases, the treatment of uncertainty in the overall exposure estimate can be improved by reducing the uncertainty. For example, uncertainty of risks for chemicals involved in long range transport or multiple pathways of exposure may be reduced by collecting data from the literature or analyzing for content in biological samples in those who appear to be highly exposed and representatives of the general population. An exploration of data currently available that may be useful for the initial NSA should be undertaken.

Without a better handle on the accuracy of average exposure estimates and how average and high end exposures vary, one reviewer commented, one should be very cautious in making risk estimates and even more cautious in performing evaluations of non-cancer endpoints.

EPA Response:
EPA agrees that the uncertainty analysis can be improved. First, the results will receive appropriate caveats. Second, EPA will attempt to place quantitative ranges on uncertainties where it is possible to do so. Third, uncertainties associated with each portion of the assessment will be described within the "methods" section for that portion. Fourth, the risk characterization will present a much more methodical treatment of all uncertainties combined, including a table with both qualitative and quantitative information (where possible) and a discussion of the effects of combined uncertainties. EPA anticipates that quantitative uncertainty estimates may not be possible in some cases, however. The information on relative uncertainties associated with different assessment components will help to inform the research agenda. We are hopeful that this process will eventually produce meaningful reductions in the uncertainty of these national-scale assessments.

As suggested by one reviewer, EPA intends to perform several detailed local assessments, in part to correlate their results with the NSA. These assessments will be done separately, as described in the EPA Urban Air Toxics Program. EPA also intends to expand its personal monitoring program, and these data will be incorporated into future NSAs.

EPA agrees with comments regarding the difficulty in rendering the risk characterization, including its uncertainties, transparent and will pay special attention to this issue in the draft report. One strength of presenting the risk estimates in the form of distributions of census tracts nation-wide will be to discourage readers from focusing on point estimates of risk. This presentation will provide multiple descriptors of risk, rather than single values. And, as suggested, EPA intends to be cautious in its characterization of risks.

2. *Can a quantitative estimate of uncertainty be undertaken? If so, can you make specific suggestions about quantifying uncertainties associated with the (1) inventory, (2) dispersion modeling, (3) exposure modeling, (4) dose-response assessment, (5) quantitative risk estimates, and (6) accumulation of risk across HAPs?*

Comments:
One reviewer believes that, at best, a quantitative estimate of uncertainty could be undertaken for individual steps in the overall mode, with the greatest likelihood for quantitative characterization being for the emissions inventory and the dispersion modeling. Even there, the reviewer noted, so many assumptions need to be made that the estimates will depend more on the assumed factors and not on the quantifiable elements. For the last three individual steps (#4, #5, and #6), the reviewer commented that a quantitative estimate of uncertainty would not provide meaningful uncertainty estimates. The reviewer considered it essential that the qualitative sources of uncertainty be identified and clearly communicated with the overall caveats of the model.

Another reviewer stated that a quantitative evalutation of the uncertainties can and should be conducted for the study. The reviewer believes that the uncertainties for the inventory, air dispersion modeling, and exposure modeling could be estimated through some form of statistical sampling. He recommended that several different types of areas could be randomly selected and evaluated as to how well the input data and modeling results predict actual ambient concentrations. The results could then be used to better estimate the risks. For the quantitative

calculations, the reviewer commented that a Monte Carlo simulation could be used to calculate the range and distribution of risks based on variations in inhalation rates, exposure duration, and body weights. Final results should be presented in a number of ways, such as most likely risk, upper bound risk, and range of risks.

With regard to EPA undertaking quantitative estimates of uncertainty for the exposure modeling, one reviewer commented that, to the extent that reliable data could be found to test different exposure modeling components, that should be done. In addition, if the NSA will be used to make important decisions, validation studies should be conducted. The reviewer recommended that the exercise would best be conducted within a value-of-information framework.

Another reviewer commented that, with regard to quantitatively addressing uncertainty in the dose-response assessment, addressing the uncertainty in the RfC would be difficult (and that is why only qualitative statements of confidence are given in IRIS). Given enough resources, the commenter stated that it would be possible to quantitatively assign the appropriate level of precision to the RfC and also to estimate the risk above the RfC (by using newer EPA methods). The reviewer commented that quantitative risk estimates (i.e., #5) and accumulation of risk across HAPs (i.e., #6) are not contemplatable unless the RfC is further quantified.

As for quantifying uncertainty in the risk estimates, one reviewer commented that, after decades of argument, the degree to which cancer risk is over- or under-estimated by the use of standard procedures is still unclear. While the document presents, in multiple places, the dogma that cancer risk procedures produce upper bound estimates, there are a variety of reasons, including a bit of quantitative information, to believe that this characterization is speculative and may be in error for various chemicals. It is beyond the scope of the NSA to perform analyses to try to get a quantitative handle on the degree of uncertainty in cancer dose response assessment.

EPA Response:
EPA agrees with the comment on the difficulty in estimating uncertainty quantitatively for parts of the assessment. We intend, however, to develop these estimates where possible. EPA will use Monte Carlo simulation to describe variability in exposure to different receptors, but does not posses sufficient distribution data for the inventory data or for dispersion model inputs to use this method elsewhere. Results will be presented as frequency distributions of cental tendency risks in different census tracts. The dispersion model and exposure model have already undergone peer review, and should not need further validation for this assessment.

EPA agrees with the comment regarding the difficulty in quantitatively addressing uncertainty in the dose-response assessment, since such assessments generally lack this information. However, EPA disagrees that a quantitative expression of uncertainty in the dose-response assessment is necessary for aggregation of risks across HAPs.

EPA acknowledges the recurring issues concerning the degree to which cancer risk is over- or under-estimated by the use of standard procedures. We intend to characterize our risk estimates as the high end of the spectrum, but not the worst case.

Additional Comment

Comment:
One reviewer noted the need to improve the explanation of the HAPEM4 outputs (e.g., average exposure concentrations for each of the 40 subgroups or just one average exposure concentration?). The reviewer recommended re-writing parts of the exposure modeling section to make it easier to understand the steps involved and adding simple equations to clarify how ambient concentrations are being converted to exposure concentrations.

EPA Response:
EPA will substantially clarify both the methods and results sections that describe the HAPEM outputs.