Preliminary Comments on the REA from Dr. H. Christopher Frey

Assigned as a lead discussant on REA, Chapter 4. Text in bold are the charge questions.

8. Does the Panel find the presentation of, and approaches used for, key aspects of the exposure modeling, including those listed below, to be technically sound and clearly communicated?

a. Representation of simulated at-risk populations (section 4.1).

The general underlying approach seems to be reasonable, but is not well explained here. The description needs extensive revisions. See detailed comments below for pages 4-2 through 4-15 for particulars.

b. Estimation of elevated ventilation rate (section 4.1.4.4).

This section does not do a very good job of explaining, justifying, and interpreting the approach used for elevated ventilation rate. This section, as all others in this chapter, needs extensive copy editing. The text would also benefit from being more formal, more specific, more precise, and more detailed, which would make it clear. This section needs more details on goodness of fit and other indicators of validity and model prediction error of of Equation 4-3. The material on elevated breathing rate is terse and there is no evaluation of the suitability or goodness-of-fit of this approach. I would characterize this section as in need of major revisions.

c. Representation of microenvironments (section 4.2).

See detailed comments below for pages 4-16 to 4-20. This section is missing an adequate justification for focusing on only five microenvironments. I agree that this is a suitable approach, but it is not sufficiently explained. In part, the lack of quantitative identification of the contribution of different microenvironments to peak exposures makes the text seem vague and subjective. If possible, the text should be quantitative regarding the fraction of peak exposures from previous analyses (or this analysis) that are from each microenvironment. Stronger quantitative support for claiming that the majority of peak exposures are related to outdoor microenvironments would be helpful. As noted in the detailed comments, the selected microenvironment for vehicles seem intuitively obvious but a rationale for including it has not been articulated. It would help to know if this represents personal vehicles or if it is somehow intended to represent all types of vehicles. Likewise, for indoor-other, more clarity on the purpose, key microenvironment, and choices made to quantify this microenvironment are needed. For example, given the focus on children as one key sensitive subpopulation, why is the school microenvironment not considered when developing input data for indoor-other? Or, by what reasoning and based on what data is a judgment supportable that office and school have similar ventilation characteristics?

Also missing here is consideration of the two different air quality scaling methods used to estimate air quality consistent with the current standard. This aspect of the analysis study design needs to be introduced and explained.

There appears to be misuse of the term "penetration factor" and lack of clarity and interpretation on some other points as detailed below.

d. Derivation of the exposure-response functions (section 4.5.2).

See also detailed comments on pages 4-25 to 4-27.

This section is a relatively minimalist treatment of the topic. In general, for any kind of curve fitting using regression, there should be a discussion of what functional forms and parameterizations were identified and compared, and which one(s) were selected, and why, for fitting and evaluation. There should be a systematic approach to model evaluation that takes into account statistical factors, such as goodness-of-fit metrics, and whether the model formulation is appropriate relative to the type of data and its characteristics, as well as regarding the biological plausibility of the inferred relationships. The precision and accuracy of the fitted model versus calibration data, and, if possible, evaluation of precision and accuracy for out-of-sample data (validation), would be important to include. The 95% interval for the mean is a confidence interval, not a prediction interval. The prediction interval would be the 95% frequency range of the model prediction.

The probit regressions given in Figure 4-1 may well be suitable but they are not adequately motivated or evaluated in the text. For example, why was probit regression selected?

Other General Comments

The writing style of this chapter needs to be substantially revised. It is written in a somewhat informal, breezy manner, with vague or ambiguous language and curious mixture of irrelevant specifics as well as omissions of needed details. The status of the writing is somewhat disappointing, since there have been similar chapters regarding exposure modeling in REAs from prior reviews not just for SO_2 but also CO, NO_x, and O_3. At this point, some of the key points can be fairly standardized and do not require *de novo* writing. However, since it is not the role of CASAC to correct poor writing, the comments here focus on technical issues.

The Policy Assessment does a better job than this REA in terms of clearly identifying the ways in which the current assessment is improved compared to the last review. Specifically, since the last review, the exposure assessment has been updated in the following important ways:

- Expanded CHAD
- Updated NHANES data
- Updates to the algorithms used to estimate resting metabolic rate

- Updates to the ventilation rate algorithm
- Updated population demographic data
- Analysis for a three year simulation period consistent with the form of the current standard
- Air quality data based on more recent emissions and circumstances since the 2010 revision of the standard.

Although most of these points are addressed in the REA, they are not addressed in a sufficiently clear and organized manner. Furthermore, the implications of these changes and updates are not adequately discussed or interpreted.

Detailed Comments

- Page 4-1, line 5: "health effects information" is vague. This term is used in several places (e.g., again on page 4-2, line 1) but is not clearly defined. What specific "information"?
- Bottom of page 4-1 and top of page 4-2. It seems strange not to indicate that the simulation of population distributions is based on simulation of inter-individual variability in exposure (i.e. cross-section) and temporal variability in exposure for a given individual. The latter is sometimes referred to as intra-individual variability.
- 4-2/5-6: the idea that these individuals are simulated based on frequency distributions for model inputs is not conveyed clearly.
- 4-2, line 7: the word "though" is used repeatedly in this chapter. It is not the correct coordinating conjunction to use. Furthermore, consider breaking the compound sentences into two separate sentences rather than linking them with a coordinating conjunction.
- 4-2/15: 'distribution' not 'collection'
- 4-2/17: again, 'distribution' not 'collection'
- 4-2/26-29. Not parallel - needs to be copy edited and rewritten.
- Section 4.1.1: why is the analysis based on census blocks rather than, say, census tracts. It always helps to do more than just state what choice was made. The rationale for the choice should be given. For example, is there really adequate data to quantify variability in exposure concentrations among census blocks? What is the justification for this level of spatial resolution?
- 4-3/5-10: here and in other places, lists are given of APEX files. However, these files are not well-explained nor is the need for listing them clear to the reader. Thus, if they are listed, explain why they are listed (what is the purpose of this detail) and be more specific and clear as to what they contain and the significance. Otherwise, it seems sufficient to explain what are the inputs to APEX without getting into details of files. Such details can go in an appendix.

- 4-3/16: The word "calculate" is not really appropriate for a model that is making estimates based on data subject to uncertainty. 'Calculate" implies a high level of precision. A better word choice is "estimate". It is not clear HOW the ACS data are used to estimate the number of employed people. Explain more clearly, with more detail.
- 4-3/21: please explain why it is necessary to quantify both the block and tract level – this is not clearly explained and will not be self-evident to many readers.
- 4-3/23-24: not clear why this information is needed here. See earlier comment.
- 4-3/29: the text bounces between tracts and blocks, which is very confusing to the reader. Give a paragraph, perhaps before Section 4.1.1, that explains the spatial resolution selected and explains why both tracts and blocks are used in the same analysis.
- Page 4-4: in several places, the text refers to "population data." However, this term is vague and is not clearly defined. Defined, with specifics, after which this term should be used consistently.
- 4-4/3-6: at what geographic scale? Census tracts? This is another example of a compound sentence whose length, along with breezy vague text, leads to ambiguity. Break this into three sentences (asthma prevalence, 'population data', and income to poverty ratio). For each sentence, make clear the spatial resolution, and the temporal characteristics (e.g., from what time period, at what time resolution). In general, to be clear requires being more specific and not lumping too many topics into a single sentence.
- 4-4/6: Explain why family income to poverty ratio is needed and how it was/will be used.
- 4-4/8: prevalence of what? Insert "asthma". "Using this information, we…." This is vague. HOW was it used? Be more specific. i.e. what were the key steps? How was income to poverty ratio used, for example? What are the key equation(s) and their jusitification?
- 4-4/14: if the file is going to mentioned, state what it is for… i.e. insert 'for asthma prevalance'. But does this also include the income to poverty ratio data? Thus, is the file about more than just prevalence? Not very clear.
- 4-4/19-21: very hard to parse this sentence. "considering" is vague. Exactly how was this 'considered'?
- 4-4/22: what exactly was the "estimation approach" ? this has not been adequately explained.
- 4-4/24: The data in Table 4-1 contradict the statement that children have higher rates than adults. E.g., the is not true for females in Indianapolis.
- 4-4/26: "By our…" is awkward.
- 4-5/5: "These … values"… implies that the values were previously stated. However, this is not correct. The values given area aggregated summaries.

- Table 4-1: add a more useful indication of variability, such as the coefficient of variation or standard deviation, or a 2.5 to 97.5 frequency range. Min and max range is less useful because it can be subject to random fluctuation.
- Footnote to table 4-1 – how was this "derived" from the mentioned data?
- Table 4-1 and 4-2 are redundant. Cut one of them.
- 4-6, section 4.1.3: it would help the reader to add a sentence or two on whether/why commuting is an important activity to include in the analysis. It is implied that the need for this is self-evident, but instead the need or purpose for this should be explained. Also, the reader wonders about whether or how commuting between blocks within a tract is handled.
- 4-7/8-9: For clarity, does this refer to inter-tract commuting? Presumably, inter-block commuting within a tract is not simulated, but this point is not clear.
- 4-7/11-12: if file names are given,then be more specific as to their content. E.g., how are "commuting times" given? Are they stratified in any way? Not clear.
- 4-7/21: the concept of a "conditional variable" needs to be explained clearly. Otherwise, this term is undefined.
- 4-7/17-28: This is very hard to follow. This reads like a laundry list of input files but the basic purpose and concepts related to these data have not been clearly defined. Thus, this is probably not the right place for this list.
- 4-7/30: A reference is given to Appendix F. Appendix F seems to do a better job of describing the APEX model than does this chapter. Although Appendix F dives into some details that aren't needed in the main paper, consideration should be given to elevating some of the information from the Appendix to the main paper, to provide the reader with a better explanation of APEX. For example, "METS distributions" is unclear at this point.
- 4.1.4.1 – before getting into status variables, it may help to first explain the choice of microenvironments. This would avoid some confusion. For example, on p 4-8, line 4, when "car" is mentioned, the reader wonders also about transit buses, and other transport modes. If a decision has been made to bound some MEs out of the analysis, this would be helpful to know before reading about status variables, so that the reader isn't wondering about things that are intentionally excluded.
- 4-8/7: need to break this into two sentences. These two clauses do not fit together.
- 4-8/1st paragraph. Not clear if air conditioning use prevalence is a status variable.
- 4-8/16: determined how? With regard to this paragraph, which are inputs? Which are inferred and, if inferred, how?
- 4-8/27-28: seems like reverse causality – ventilation rate is related to energy expenditure, not the other way around.
- 4-8/31: awkward wording.

- 4-9/2: what is "diverse" about this? Not clear.
- 4-9/19 or after – the effect of the "new algorithm" (what really is new about it – is it the same functional form with recalibrated parameter values?) should be mentioned… e.g., based on Table 10 in Appendix H, it seems that there isn't much difference in predictions of RMR for the "New" versus "Old" algorithm. This should be mentioned.
- 4-11/4-5: what is PROC TRANSREG?
- 4-11/19: give equation
- 4-11/24-25: is this meant to be a mean value? Is there variability or uncertainty in this value?
- 4-12/16: "somewhat"? unclear
- 4-12/21: WHY does APEX use only 55,000 of 180,000 person-days of diaries?
- 4-12/26: Not clear how these files "develop" activity patterns. Explain.
- 4/12/31: summary statistics such as what?
- 4-13/11: "this issue"? not clear. Individuals who have never had asthma is the immediate antecedent. This paragraph ends with a run-on sentence, and in general is not well written.
- Section 4.1.5.1 I didn't review this section because I am a co-author on the cited Che et al. (2014) paper mentioned in this section.
- 4-16/28: location codes – are these microenvironments? Not very clear.
- 4-16/general… "work" is not given in Table 4-4. The general idea of limiting the analysis to a few microenvironments is reasonable, but not enough is done here to explain this. The inclusion of outdoor and near-road makes sense. Some rationale should be provided for why vehicle is included. I don't disagree that it be included, but there should be a reason for it – e.g., because vehicle occupants typically receive higher exposure concentrations compared to other microenvironments (based on some quantification). Residential makes sense since people spend a lot of time in their residence. Indoor-other seems to be equated with work in the text but this is not very clear. How much do these 5 microenvironments contribute to daily exposure? While it may be that the "majority" of peak exposures occurred while outdoors, more quantitative support should be given for this point.
- 4-17/1-6. What is a "relative location"? Ambient air "is drawn to calculate" ? doesn't make sense. It is not clear as to how tract-level ambient concentrations are quantified. This should be explained. Later, in the REA, it is mentioned that APEX was apparently run for two different air quality scenarios based on different methods for scaling air quality to just meeting the current standard, but this aspect of the exposure modeling study design seems to be omitted in this chapter.
- 4-17/24: this implies that the presence of AC and outdoor temperature are among variables for which sufficient data are not available. Is this really the intended meaning?

Also, what are the "other variables" e.g, would this include characteristics of housing type, characteristics of the building envelop, age of the building, etc? Even if not available, it would help to be clear regarding what variables are known to be associated with variability in AER, and whether the quantifiable variables are sufficient to adequately explain variability. Also, it is not clear why "city" is an influential factor. It seems more logical that climate zone is an influential factor and that city might be used as a surrogate for climate zone. Is there some other intended role of "city" as a factor?

- 4-18/8: geographic region isn't really the key factor here – it is climate zone.
- Tables 4-5 and 4-6. The tables are mentioned in the text but not interpreted or discussed. Some justification/explanation is need for imposing minimum and maximum values on a lognormal distribution – this can change the effective parameters of the distribution (e.g., the simulated GSD will not be as large as the input GSD). Variability in AER among study areas, with respect to temperature and between residences with and without AC should be interpreted, particularly to the extent (if any) that this may be influential in simulation results.
- 4-19/5: use "dependent" rather than "conditioned"
- 4-19/7-11: this text is generally unclear. How exactly is prevalence different from usage? How does AER represent AC usage? The last two sentences are very hard to understand.
- Section 4.2.3: seems to imply that office is used to represent "all other" – as such, a rationale/justification should be given. Since children with asthma are a key sensitive group, why is more attention not given to schools as an "other" microenvironment? Are offices and schools similar with regard to AER and indoor exposure to ambient SO2?
- 4-20/18: the use of the term "penetration factor" seems incorrect here and in several places. Commonly, penetration factor is part of the infiltration factor. Here, the intended meaning seems to be the ratio of indoor to outdoor concentration (I/O ratio). Penetration factor is not the same as the I/O ratio. See also line 30.
- 4-20/20-21: SO2 is far more soluble than NO2. Does this have implications for deposition or loss processes in the indoor environment that are different than for NO2?
- 4-20/25: "broadly defined uniform distributions" is (a) vague and (b) implying multiple distributions. For the latter, what do these distributions depend upon?
- 4-20/26-32: I/O ratio not penetration factor. Limited data – in what way? Indicate the sample size or other characteristic that conveys the "limited data". What is meant by "location" – is this "study area" or census block? Be more specific.
- 4-21/6: "geographic area" not "size"
- 4-21/9: linear interpolation? (say so).
- 4-21/22: "estimated" not "derived"
- 4-22/1: above "specified," not "varying"

- 4-22/4-13: Given how APEX is used in the PA, the choice of bins seems difficult to understand. For example, why is there so much resolution for low concentration bins below 100 ppb? The total number of bins would be helpful. e.g. 15 bins up to 150 ppb, 5 bins between 150 ppb and 250 ppb, and how many bins above 250 ppb? Is there some rationale for the varying choices of bin widths and why there is much higher resolution (narrower ranges) for lower concentrations?
- 4-22/31: "information" is vague. Summaries of what quantities, more specifically?
- 4-23/12: "this information" refers to what? The antecedent is controlled studies. Doesn't seem to be correct or clear. The binning approach described previously does not appear to be harmonious with the choice of benchmark concentrations given in this paragraph.
- Table 4-9 and more broadly in the text, the issue of oral versus nasal breathing needs some more discussion. Although the point that many of the controlled experiment with low SO2 concentrations were based on oral breathing, whereas others were based on free-breathing is an important consideration, it is also the case that at high ventilation rates there can be a transition from nasal to oral breathing. Such a transition is typical of real-world behaviors and thus perhaps should be discounted as readily as seems to be the case in this chapter.
- 4-25/1-2: replace "described" with "that correspond to". Insert "as described" before "in the second draft"
- 4-28/23: it doesn't make sense to say that algorithms account for variability in input data. Input data are inputs to an algorithm. Perhaps the intended mean is that variability is accounted for in input data, and is also quantified based on algorithms – but will need to say a bit more (at least give an example).
- 4-29/7: "In any event," ? delete this.